

A National Cancer Clinical Trials System for the 21st Century:

Reinvigorating the NCI Cooperative Group Program



INSTITUTE OF MEDICINE

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IOM Committee Members:

John Mendelsohn (*Chair*)
M.D. Anderson Cancer Center

Harold L. Moses (*Vice-Chair*)
Vanderbilt-Ingram
Comprehensive Cancer Center

Susan G. Arbuck
Consultant,
Susan G. Arbuck MD LLC

Donald Berry
M.D. Anderson Cancer Center

Michael A. Carducci
Johns Hopkins University
School of Medicine

David M. Dilts
Oregon Health and Science
University

Susan S. Ellenberg
University of Pennsylvania School
of Medicine

Gwen Fyfe
Independent Consultant

Stephen S. Grubbs
Helen F. Graham Cancer Center

Hedvig Hricak
Memorial Sloan-Kettering Cancer
Center

Richard Kaplan
United Kingdom National Cancer
Research Network

Minetta C. Liu
Lombardi Comprehensive Cancer
Center, Georgetown University

Lee N. Newcomer
United HealthCare

Edith A. Perez
Mayo Clinic

Charles L. Sawyers
Memorial Sloan-Kettering Cancer
Center

Richard Schilsky
The University of Chicago

Ellen V. Sigal
Friends of Cancer Research

Consultant
Michaele Chamblee Christian
National Cancer Institute (retired)

Study Director
Sharyl Nass
Research Associate
Erin Balogh

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C-Change

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Oncology Drug Development

- One of the most active areas in drug development.
 - Over 800 cancer therapeutics in development.
 - More new drugs for cancer than any other disease recently.
 - 53 new indications approved in oncology (7/05 to 12/07)
(18 new molecular entities, 35 supplemental applications).
- With many cancer therapies already in use, and more in development, it can be difficult for physicians to assess which treatment is best for an individual patient.
- The Cooperative Groups conduct trials that impact clinical practice decisions and provide important information to patients.

Cooperative Group Trials Complement Industry Trials

- Industry trials primarily develop novel therapeutic agents and gain FDA approval for clinical use.
 - R&D efforts entail enormous costs and are critical to progress in cancer treatment.
- Cooperative Group trials play a complementary role in advancing science and patient care by addressing questions important to patients but less likely to be top priorities of industry, including:
 - Comparative effectiveness of approved therapies
 - Combining novel agents from different sponsors
 - Therapies for rare diseases
 - Optimal duration, dose of treatment with drugs in clinical use
 - Multimodality therapies
 - Screening and prevention strategies
 - Rehabilitation and quality of life following therapy

Examples of Cooperative Group Program Accomplishments

- Improvement treatments of childhood cancer, solid tumors and hematologic malignancies in adults, adjuvant therapy, and combined-modality treatment.
 - High rate of participation in pediatric Cooperative Group trials.
 - Showed equivalent survival rates for radical vs. total mastectomy + radiation and for mastectomy vs. lumpectomy + radiation.
 - Defined therapy of adult AML patients; refined leukemia classification using cytogenetics and molecular genetics.
 - Showed benefit of adjuvant therapy for breast, lung, colon, and gastric cancer and melanoma.
 - Defined the value of chemotherapy & radiation for cervical cancer.

Cooperative Group Accomplishments (continued)

- Advances in cancer prevention and detection.
 - Tamoxifen reduced the incidence of breast cancer by nearly 50% for women at increased risk of breast cancer.
 - Aspirin reduced the risk of colorectal adenoma in patients with a history of colon cancer.
 - Finasteride reduced prevalence of prostate cancer by 24% at 7 years compared with placebo.
 - Refined imaging methods for screening, diagnosis, and treatment.

- Publication of negative findings & previously unknown treatment risks.
 - Negative findings more likely to be published if NCI sponsored. (Ramsey and Scoggins, 2008).
 - Important secondary effects of cancer therapy reported.

Challenges for the Cooperative Group Program

The Cooperative Group Program is at a critical juncture:

- The clinical trials infrastructure has not evolved to adequately incorporate the rapid pace of biomedical discovery.
- Processes are inefficient, with excessive delays; many trials are never completed.
- Government oversight has become extensive and complex.
- Funding is stagnant and inadequate.
- Industry trials are moving overseas.
- Biomarker-driven selection of appropriate treatment (personalized medicine) will enhance outcomes of trials, but also raise trial costs.

Committee Charge

Review the organization and operation of the NCI Clinical Trials Cooperative Group Program and recommend ways to:

- Improve the design, review, and operation of clinical trials.
- Reduce time from initial concept to final approval.
- Prioritize trials and sites on scientific merit and performance.
- Increase clinician and patient participation.
- Make greater use of technologies (e.g., imaging, biomarkers) to:
 - Select therapies for development and testing,
 - Match patients and therapies, and
 - Monitor patient responses.
- Define standards for minimal data requirements to establish safety and efficacy of experimental therapies.
- Reduce costs and adequately fund high-quality trials.
- Promote greater collaboration among various stakeholders.

Committee Conclusions

In an ideal cancer clinical trials system,

- A dynamic system would:
 - efficiently respond to emerging scientific knowledge
 - involve the broad cooperation of stakeholders
 - leverage evolving technologies to provide high-quality, practice-changing research
- Clinical trial participation would be the preferred option for patients and physicians (access to innovative therapies, reimbursement for patient care).

A 21st Century Clinical Trials System

The committee concluded that the academic, governmental, and commercial sectors must join with the public to develop a 21st century clinical trials system to more effectively leverage scientific advancements and translate them into public health benefits by improving the science, technology, efficiency, and timely completion of the very best cancer clinical trials.

Goal I: Improve the speed and efficiency of the design, launch, and conduct of clinical trials

1. Consolidate some front office operations of the Cooperative Groups (reduce the number of disease-site Committees through consolidation, or elimination by peer review).
2. Consolidate “back office” functions (such as patient registration, storage of standardized data and images, credentialing of sites). Streamline the protocol development process and facilitate trial conduct.
3. Transagency effort to streamline and harmonize government oversight and regulation. Clarify the authority and accountability of central IRBs.
4. Facilitate public-private collaborations.

Goal II: Incorporate innovative science and trial design into cancer clinical trials

5. Maintain accessible central biorepositories of tumor specimens collected in the course of trials. Provide access and funding through peer review.
6. Develop and assess innovative designs for clinical trials that evaluate cancer therapeutics, biomarkers and combinations of therapies.
7. Develop national unified standards for imaging procedures and biomarker tests, to ensure quality and comparability.

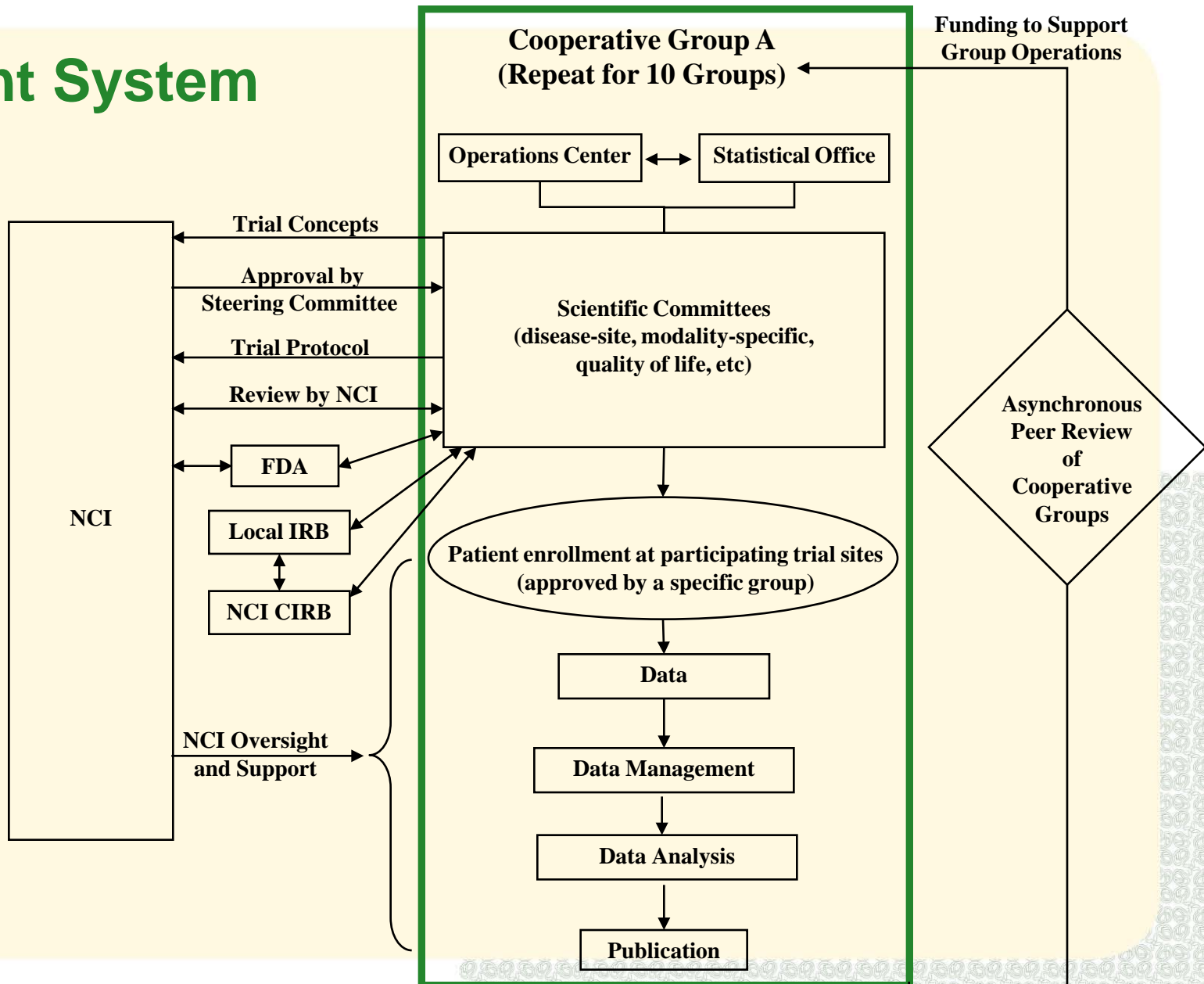
Goal III: Improve prioritization, selection, support, and completion of cancer clinical trials

8. NCI role in trials not involving an NCI-held IND should focus on facilitation, rather than oversight. Prioritization via peer review should be strengthened.
9. Increase the speed, volume and diversity of patient accrual in high-priority trials, regardless of origin. Eliminate sites with poor quality of performance, or low accrual rates.
10. NCI should allocate a larger portion of its research portfolio to Cooperative Group trials and increase the case reimbursement rate to cover costs.

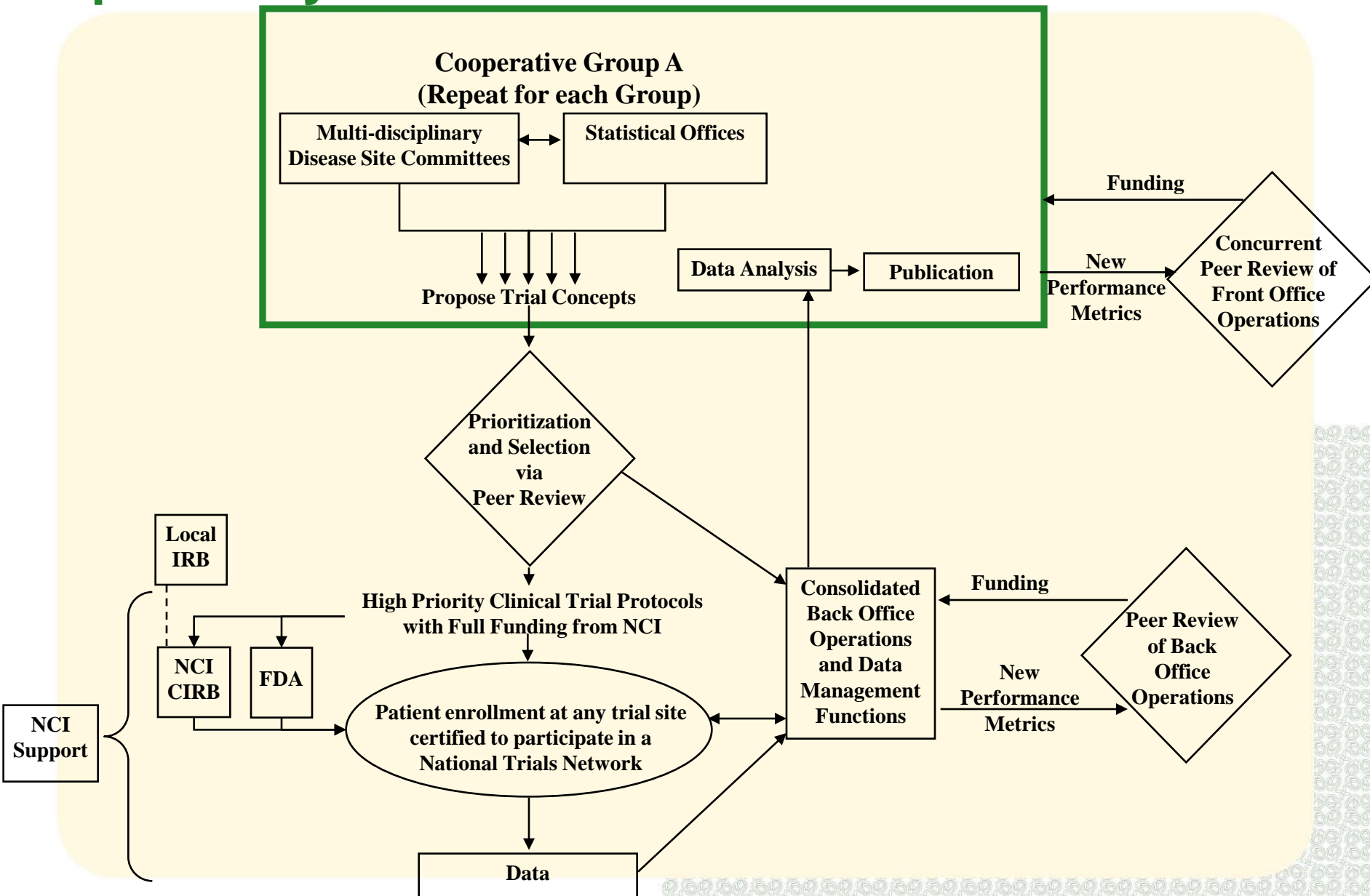
Goal IV: Incentivize the participation of patients and physicians in clinical trials

11. All stakeholders should ensure that clinical investigators have adequate training and mentoring, paid protected research time, the necessary resources, and academic recognition.
12. Health care payment policies should value the care provided to patients in clinical trials and cover non-experimental costs.

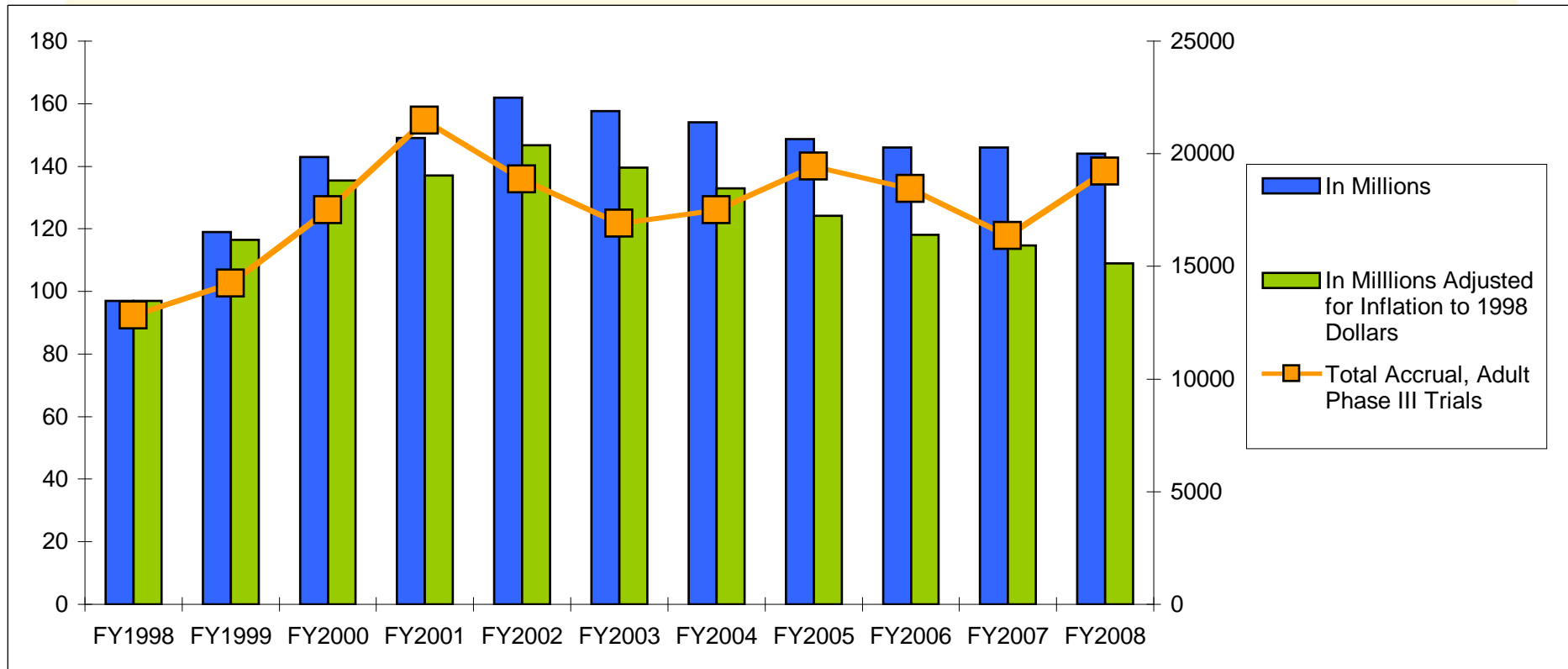
Current System



Proposed System



Funding for the Cooperative Group Program, FY 1998 – FY 2008 and Total Accrual



Source: NCI, 2009

Some Key Messages

1. Clinical trials make tremendous contributions to improving cancer care. It is imperative that the processes for designing, opening and completing clinical trials become more efficient and streamlined, with more rigorous prioritization.
2. All stakeholders share the goal of improving patient care. They include clinical investigators, pharma/biotech, government funding and regulatory agencies, patients and their advocates, and health care payors, and each looks at the shared goal through different lenses. They all need to participate and collaborate in implementing these recommendations.

Some Key Messages

3. Clinical trials should place increasing emphasis on innovative design and the use of biomarkers (lab tests and imaging) to target therapy for individual patients (personalized treatment).
4. The value of designing and carrying out clinical trials must be recognized by adequate reimbursement of costs. And the non-experimental costs of care for patients on clinical trials should be paid for by insurance.

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