

APOR NEWSLETTER

News from the Association for Patient Oriented Research

PRESIDENT'S COLUMN

DECEMBER 2005



by Emil J Freireich, M.D.

Plans for Clinical Research 2006 are moving rapidly ahead. We have received 81 abstracts for the annual meeting, and the program committee is hard at work putting together what should be an outstanding scientific meeting. It will take place in Washington, DC March 16-18, 2006. We expect to have an outstanding program, which will be capped by Dr. Barbara Alving's presentation on Saturday morning. This meeting should be of interest to all APOR members and guests.

In addition to attending the science at the meeting, I would encourage members to attend our annual business meeting. This year we are going to elect officers and board members and review our bylaws, our finances, and focus on the future direction of the Association. We will have reports from our standing committees: advocacy, education, membership, academic affairs and finance.

A major advance for patient oriented research is the announcement of the new institutional Clinical and Translational Science Awards (CTSA). www.ncrr.nih.gov/clinicaldiscipline.asp

These were first announced at a meeting in Washington, DC on October 17, 2005. The APOR position paper prepared by Dr. Barry Collier of our Board, with assistance of the board of directors, was submitted to NIH and placed on their web page. We feel it had an impact on the development of this RFA. I believe that APOR members should be strongly supportive of this initiative, which is clearly designed to strengthen patient oriented research by creating an academic home for patient oriented physician-scientists in academic institutions. I hope many institutions will submit proposals. As a reminder, the receipt date for letter of intent is February 27, 2006, which precedes our annual meeting. The application receipt date is March 27, 2006, shortly after our annual meeting in Washington, DC. Institutions with NCRS supported

programs, such as the GCRC's, K30 training grants, T32 Roadmap grants, and NCRS K12 programs are all important components of this new initiative, and therefore investigators in institutions that have these awards are particularly well-placed to compete for this competition.

APOR has formed "The APOR Foundation", which provides for tax-free contributions to APOR in support of all of its programs (Tax ID 31-1627330). For APOR members, for patients, or for anyone who feels that patient oriented research is an important activity, which needs to be strengthened, charitable contributions made before the end of the fiscal year will be tax-deductible. Currently



Gold Lifetime Membership \$3,000
Platinum Lifetime Membership \$5,000

released restrictions on charitable gifts before December 31, 2005 make it especially beneficial to donate this year. These will provide an important resource for our organization.

I would like to remind members of the opportunity to become Lifetime members. Lifetime members will have their names listed permanently on our web site and this can be obtained for as little as \$3,000 for gold lifetime membership and \$5,000 for a platinum lifetime membership. Lifetime membership is an expression of support for patient-oriented research by those for whom our discipline is an elemental priority. It will insure members a historical presence and honor their dedication to the success of APOR in strengthening patient oriented research.

Looking forward to seeing you in Washington, DC the evening of March 16th!



AMERICAN CLINICAL RESEARCH: THE FUTURE ARRIVES

The Clinical and Translational Science Awards (CTSAs) announced October 12, 2005 by Elias Zerhouni open up enormous opportunities to alter the landscape of clinical research. In a parallel article in the New England Journal of Medicine (Zerhouni EA. N Eng J Med 2005; 353: 1621-1623), Zerhouni explained that the CTSAs will permit clinical investigators to propose transformative efforts appropriate to their institutions. "The CTSAs aim to advance the assembly of institutional academic "homes" that can provide integrated intellectual and physical resources for the conduct of original clinical and translational science. We anticipate that the creative installation and development of these environments will, over time, enhance the theoretical underpinnings of the discipline, provide much-needed educational programs, contribute to the growth of well-structured and well-recognized career pathways, and provide a research environment that is more nimble, conducive to, and responsive to the demands of modern translational and clinical research"



Elias Zerhouni

The aim is to provide flexibility and support to institutions choosing to "re-engineer" their clinical and translational research programs in order to combine existing NIH-funded programs creatively. The NIH asks applicants to consolidate General Clinical Research Centers (GCRCs), T32 and K12 programs, and other resources, as appropriate. Importantly this coalescence of resources may be augmented by up to \$6 million in new money.

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We hope you will become a member of APOR and bring us suggestions of how APOR can more effectively enhance clinical research nationally and internationally, and, equally important, how the organization might help you and your institutional colleagues in furthering recognition and support for clinical research.

AMERICAN CLINICAL RESEARCH: THE FUTURE ARRIVES

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An important additional goal is not only to foster patient-oriented research and bench-to-bedside research, the traditional foci of the GCRCs, but also the heretofore neglected bedside-to-trench focus. "As disease burden has shifted from acute conditions to chronic conditions primarily seen in community rather than tertiary centers, new approaches for forging relationships with local and regional community partners will become increasingly critical, according to Zerhouni, "therefore, opportunities for appropriate partnerships with other institutions and industry will also be encouraged."

"In addition to the much-needed improvements in the policies and practices of health care delivery as we know it today, medical and public health practices in this nation will have to undergo a profound transformation in the coming decades if we are to succeed in providing access to care for all Americans at reasonable costs," according to Zerhouni, "Given that knowledge of many fundamental aspects of biology in health and disease is still insufficient to translate current findings reliably into new and more effective prevention and treatment, this goal can be attained only through continuous investment and advances in basic biomedical and behavioral discovery coupled with efficient translational science. It is our intention and hope that this focused and significant commitment to the creation of a new, vital, and reinforced academic discipline and home for translational and clinical science — along with an explicit effort to maximize the effectiveness of NIH resources directed to this area of research — will ensure that extraordinary scientific advances of the past decade will be rapidly captured, translated, and disseminated for the benefit of all Americans."



Barbara Alving



Anthony Hayward

Barbara Alving and Anthony Hayward are leading the transition from the GCRCs to the new entities emerging from the CTSA initiative. To their credit they and their colleagues rolled out the complex new initiative October 17th in front of perhaps 250 clinical investigators and answered intricate and detailed questions with remarkable absence of confusion and contradiction. All were clearly on the same page. An unusual sidebar to the roll-out has been a studious omission of reference to the "G word" (GCRC), obviously the elephant in the room. In developing the guidelines for submitting the CTSA proposals, NIH seemed determined to focus the minds of the clinical investigators on genuinely new approaches, unencumbered by reference to the structure and methodology of the traditional GCRCs. The goal seemed to push all institutions to deconstruct their clinical research enterprise into its most elemental components, so those components can be reconstructed in an innovative, efficient, optimized, and creative way.

This strategy is evident in the structure proposed for the CTSA application (see below), which illustrates the comprehensive deconstruction and reconstruction that is the goal of the CTSA:

CTSA Program Functional Components

- Development of Novel Clinical & Translational Methodologies
- Pilot and Collaborative Translational & Clinical Studies
- Biomedical Informatics
- Design, Biostatistics, & Clinical Research Ethics
- Regulatory Knowledge & Support
- Participant & Clinical Interaction Resources
- Community Engagement
- Translational Technologies & Resources
- Research Education, Training & Career Development

Overall Integrated Approach/Governance

- Approach to the Intent of this Initiative
- Participating Institution(s)
- Innovation
- Institutional Commitment
- Governance
- National Collaboration, Sharing, & Dissemination Plan

Finally, in the absence of specifically scientific presentations in the proposals, an enormous economy of size is mandated. GCRC renewals not uncommonly entailed some 2000 pages of text describing 50-250 individual research projects. The CTSA proposals will be limited to about 250 pages without appendices.

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What does Multidisciplinary Mean?

One of the strangest interludes in the roll-out of the CTSA was a clarifying videocast in early November 2005 to emphasize the breadth expected of a CTSA. It included representatives of the Dental (Bruce Pihlstrom), Nursing (Lauren Aronson), and Complementary Medicine (Richard Nahin) disciplines. The purpose was to be clear that potential CTSA applicants understood that multidisciplinary was serious business, which might be being underestimated based on the October 12 CTSA RFA and the October 17 CTSA meeting. They believed institutions might be interpreting multidisciplinary to mean "many disciplines in the medical school". That is unacceptably narrow and is not the intent of the CTSA initiative. The CTSA is meant to be maximally inclusive, and will be judged on this criterion. How far should multidisciplinary go? Well, here is the list of disciplines specifically mentioned in that videocast as optimally included in a CTSA, depending on local circumstances:

- Alternative Medicine
- Biomedical Informatics
- Biomedical Engineering
- Biostatistics
- Complementary Medicine
- Dentistry
- Nursing
- Nutrition (Dieticians)
- Osteopathic Medicine
- Pharmacy
- Public Health

A complete listing of what constitutes Clinical and Alternative Medicine is available at the NIH website:

<http://nccam.nih.gov/health/whatisam/> where mention is made of homeopathy, naturopathy, chiropractic,

aromatherapy, as well as Ayurvedic, Native American, and Chinese traditional medicines. The CTSA initiative is open not only to traditional medicine schools but also to osteopathic medicine schools which have clinical research programs.

Clinical Research: The Popularity Contest

Elias Zerhouni has sometimes lamented the difficulty of introducing change across the powerful NIH Institutes. He has likened it to being in a rowboat with a megaphone calling orders to ocean liners in a harbor. However if Google is any guide, Zerhouni has the rapt attention of the extramural community. Google started life as a search engine, but it is now a benchmark of language use and a serious metric of what is eliciting the excitement and enthusiasm of the public.

With the roll-out of the CTSA Initiative in October 2005, the phrase "Clinical and Translational Science" became for the first time a major element of the discourse of biomedical research infrastructure. There were only 2 hits for this phrase prior to September 2005, but that rapidly jumped to 651 hits by December 15. And proving the agility of clinical investigators and deans, "Clinical and Translational Science Institutes" are already creeping out of the woodwork and onto Google. No doubt there will be an exponential growth of those in the next 4 months.

Zerhouni's partiality to the term "translational" throughout his tenure has also had its impact. As recently as 2001, "translational research" sites primarily dealt with linguistics. Now they usually relate to clinical research. The number of hits for "translational research" increased more than 15-fold just in the past 12 months, an astonishing growth.

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THE CTSA PROGRAM: ARE THERE WINNERS AND LOSERS?

The CTSA is the biggest change in organization of clinical research since the introduction of the General Clinical Research Centers Program in 1961. It aims to be transforming. Yet not everyone benefits equally from the CTSA Initiative as written. The application guidelines require that degree-granting academic institutions may apply for one and only one CTSA. For institutions like Harvard, with multiple GCRCs, but one degree-granting entity, this means that they can submit only one CTSA application (i.e., MGH and Brigham & Women's must work together) and that means that the up-to-\$6 million new money in the CTSA has to be shared among them. In a sense such institutions are penalized for something that has nothing to do with the quality of their scientific and educational enterprise.

In addition there is no room for the discussion of science and scientific programs in the proposal, a fact which has raised "where's the beef" questions among institutions whose science is very strong. The specific omission of science from the CTSA application caught GCRC directors completely by surprise, since emphasis on the quality of science was so central to evaluation of the GCRCs at the times of their renewals in the past.

How many institutions will be ready to step up to the plate and compete for the new entities? It is only guesswork at this stage but certainly 20 are seriously considering a full application for the March 27, 2006 competition. However most of those 20 are quite capable of producing a strong application, and given the circum-

scribed nature of the application, any one of them could be among the institutions winning a CTSA award.

Based on the above considerations, the following might be considered some of the winners and losers in terms of the structure and rules of the CTSA initiative.

Winners:

- Institutions with only one GCRC.
- Institutions with strong Clinical Research education programs.
- Institutions with Roadmap T32, NCRR K30 and NCRR K12 Programs.
- Institutions with excellent but not necessarily outstanding Clinical Research.
- Institutions which have highly organized Clinical Research infrastructures
- The disciplines of Health Services Research and Epidemiology
- Community outreach and bedside-to-trench research

Losers:

- Strong institutions with multiple associated GCRCs
- Institutions that are not Top 40 research universities.
- Institutions which do not award degrees in clinical research
- Institutions with tepid or ambiguous dedication to clinical research
- Institutions with limited multidisciplinary: lack of a critical mass of Pharmacy, Nursing, Dental, or Public Health Schools

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OPASI: ZERHOUNI'S OTHER NEW INITIATIVE

NIH has established a new Office of Portfolio Analysis and Strategic Initiatives (OPASI), in order to identify new biomedical research opportunities, to facilitate research portfolio management, and to enhance the evaluative efficiency of the research process. Although it might at first seem to be only a bureaucratic rearrangement in Building 1, closer inspection reveals that OPASI has the potential to radically alter the way NIH does business, possibly even long after current leadership have departed.

The NIH Director has multiple constituencies, including the biomedical research community, the American public (including the disease-specific advocacy groups) and the American government. New initiatives must, at some level, be understood by all. If the NIH budget appropriation is to prosper, the Administration and Congress must be convinced that generous NIH support is needed, that the money is being spent on things that appeal widely to the American people, and that the NIH research portfolio is optimally managed to get to best possible bang for the buck. That is where OPASI comes in.



*Raynard S.
Kington*

Just as the Roadmap Initiative promised better responsiveness to the needs of the American people, and played well with the Congress, so OPASI has equally impressed the cognoscenti among Congress and congressional staffers. Developed over the past 18 months by a working group under NIH Deputy Director Raynard S. Kington, OPASI promises a business-like approach that will include strong emphasis on metrics, a promise to provide better information about the reach and nature of the current NIH research, identify areas of research that are falling between the cracks or are ripe for broad initiatives, and a budget (ultimately perhaps 5% of the NIH budget) that will fund them.

Initiatives begun with input from OPASI will be completed within 5 years, and then terminated, or if they show exceptional promise, be taken on by one of the categorical Institutes for continued support. In the aggregate, OPASI is meant to make NIH more nimble, dynamic and responsive to emerging scientific demands and opportunities.

PATIENT ORIENTED RESEARCH

“The present era in biomedical science is historic. The opportunities to translate exciting basic science to patient-oriented research have never been better. Also patient-orientated research leads to important and novel basic science investigations. The need for physicians-scientists who undertake patient-oriented research should be a major priority for the future of health care in this country.”



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SPECIAL THANKS TO CONTRIBUTORS TO THIS ISSUE:

- › KARL ANDERSON
- › THOMAS COMMON
- › ROBERT ECKEL
- › EMIL J. FREIREICH
- › ROXANNE HALL
- › DAVID ROBERTSON
- › ROBERT W. SCHRIER
- › BRIAN SCROGGINS