

Meeting Minutes
Department of Health and Human Services
National Institutes of Health
National Institute of Diabetes and Digestive and Kidney Diseases Advisory Council
September 24, 2008

I. CALL TO ORDER

Dr. Griffin P. Rodgers, Director, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), called to order the 178th meeting of the National Diabetes and Digestive and Kidney Diseases Advisory Council at 8:30 a.m. on Wednesday, September 24, 2008, in Conference Rooms E1/E2, Natcher Building (45), NIH, Bethesda, Maryland.

A. ATTENDANCE – COUNCIL MEMBERS PRESENT

Dr. David Altshuler	Dr. Juanita Merchant
Dr. Nancy Andrews	Dr. William Mitch
Dr. Janice Arnold	Dr. Brian Monahan
Ms. Janet Brown	Dr. Jerry Palmer
Dr. Charles Elson	Dr. David Perlmutter
Dr. James Freston	Ms. Margery Perry
Dr. William Henrich	Ms. Lisa Richardson
Dr. David Klurfeld	Dr. Anthony Schaeffer
Dr. Mitch Lazar	Mr. James Schlicht
Dr. Mark Magnuson	Dr. Patrick Tso

B. NIDDK STAFF AND GUESTS

Abankwah, Dora - NIDDK	Donohue, Patrick – NIDDK
Akolkar, Beena – NIDDK	Doo, Edward – NIDDK
Amir, Syed – CSR	Edwards, Michael – NIDDK
Appel, Michael – NIDDK	Eggerman, Thomas – NIDDK
Arreaza-Rubin, Guillermo – NIDDK	Eggers, Paul – NIDDK
Barnard, Michele – NIDDK	Evans, Mary – NIDDK
Barri, Michael – Pharmaceutical Product Development Inc.	Farishian, Richard – NIDDK
Blondel, Olivier – NIDDK	Fonville, Olaf – NIDDK
Bloom-Davila, Maria – NIDDK	Fradkin, Judith – NIDDK
Carrington, Jill – NIDDK	Fuchs, Bruce – OSP/OSE
Castle, Arthur – NIDDK	Gallivan, Joanne – NIDDK
Chamberlain, Joan – NIDDK	Gansheroff, Lisa – NIDDK
Chang, Debuene – NIDDK	Garfield, Sanford – NIDDK
Chianchiano, Dolph – National Kidney Foundation	Giambarresi, Leu – AUA Foundation
Connaughton, John – NIDDK	Greene, Lucy – NIDDK
Costello, Frank – OB	Groves, Reed – CSR
Cowie, Catherine – NIDDK	Haft Renfrew, Carol – NIDDK
Curtis, Leslie – NIDDK	Hanlon, Mary – NIDDK
Densmore, Christine – NIDDK	Harris, Kimberly – NIDDK
DeSanti, Andrea – SSS	Haupt, Allison – American Society of Nephrology
Doherty, Dee – NIDDK	Hays, Dustin – NIDDK
	Hilliard, Trude – NIDDK

Hogan, Michelle – Nephrology Times
Horlick, Mary – NIDDK
Hoshizaki, Deborah – NIDDK
Hyde, James – NIDDK
James, Stephen – NIDDK
Jerkins, Ann – CSR
Jones, Teresa – NIDDK
Ketchum, Christian – NIDDK
Kim, Sooja – NIDDK
Kranzfelder, Kathy – NIDDK
Krensky, Alan – OPASI
Kuczmarski, Robert – NIDDK
Kusek, John – NIDDK
Leschek, Ellen – NIDDK
Linder, Barbara – NIDDK
Malik, Karl – NIDDK
Malozowski, Saul – NIDDK
Manouelian, Denise – NIDDK
Margolis, Ronald – NIDDK
Matsumoto, Dan – NIDDK
May, Michael (Ken) – NIDDK
McGowan, Melissa – NIDDK
McKeon, Catherine – NIDDK
Miles, Carolyn – NIDDK
Miller, Megan – NIDDK
Miller, David – NIDDK
Moxey-Mims, Marva – NIDDK
Mullins, Christopher – NIDDK
Newman, Eileen – NIDDK
Nyberg, Leroy – NIDDK
Papier, Wendy – NIDDK
Perry Jones, Aretina – NIDDK
Pike, Robert – NIDDK
Podskalny, Judith – NIDDK

Pope, Sharon – NIDDK
Ramm, Louise – NCR
Goter-Robinson, Carol – NIDDK
Robinson, Terra – NIDDK
Robuck, Patricia – NIDDK
Rosenberg, Mary Kay – NIDDK
Rosenblum, Dan – National Center for Research Resources
Sahai, Atul – NIDDK
Salomon, Karen – NIDDK
Sankaran, Lakshmanan – NIDDK
Sato, Sheryl – NIDDK
Scanley, Anne – NIDDK
Sechi, Salvatore – NIDDK
Seeff, Leonard – NIDDK
Serrano, Jose – NIDDK
Sheard, Nancy – CSR
Sherwin, Robert – Yale University
Singer, Betsy – NIDDK
Smedberg, Paul – American Society of Nephrology
Spain, Lisa – NIDDK
Star, Robert – NIDDK
Stone, Arthur – NIDDK
Tatham, Thomas – NIDDK
Torrance, Robert – NIDDK
Wallace, Julie – NIDDK
Wellner, Bob – NIDDK
Williams, Garman – NIDDK
Woynarowska, Barbara – NIDDK
Wright, Daniel – NIDDK
Wright, Elizabeth – NIDDK
Xie, Yining – NIDDK
Zellers, Charles – NIDDK

C. ANNOUNCEMENTS

Dr. Griffin P. Rodgers, Director, NIDDK

Dr. Rodgers made the following announcements during the meeting:

NIH Director

Dr. Elias Zerhouni, the NIH Director, has announced his intention to step down from that position on October 31, 2008. He extends his appreciation to all in the NIDDK and NIH family, both intramurally and extramurally. He and the Secretary of HHS are working together to make certain that the transition to a new administration is smooth. There is no report yet on the appointment of an Acting Director.

Retiring Council Members

Four Council members are completing their terms:

- Ms. Janet Brown and Dr. Jeffery Flier have served on the Subcouncil for the Division of Diabetes, Endocrinology and Metabolic Diseases.
- Drs. Janice Arnold and William Heinrich have served on the Subcouncil for the Division of Kidney, Urologic and Hematologic Diseases.

Dr. Rodgers thanked the retiring Council members for their service. The time and effort they have committed to NIDDK's Council demonstrate their commitment to research and to the improvement of human health.

NIDDK Grantees

- Dr. Bert O'Malley of the Baylor College of Medicine will receive the National Medal of Science from President Bush in a ceremony at the White House on September 29, 2008. Dr. O'Malley is Chair of Molecular and Cellular Biology at Baylor College of Medicine. He is one of eight leaders in science to be honored by the President as recipients of the 2007 National Medal of Science. The award is the highest honor in the Nation for scientists. It recognizes pioneering scientific research in a range of fields, including biological, physical, mathematical, behavioral and engineering sciences. Dr. O'Malley is recognized as a founder in the field of molecular endocrinology. He is being presented with the award: "For his pioneering work on the molecular mechanisms of steroid hormone action and hormone receptors and coactivators, which has had a profound impact on our knowledge of steroid hormones in normal development and in diseases, including cancer." Dr. O'Malley has been an NIDDK grantee since 1997.

NIDDK Staff

- Ms. Betsy Singer, Director, NIDDK Office of Communications and Public Liaison, will retire in January 2009 after 40 years of public service. During her 28 years at NIDDK, Ms. Singer has demonstrated a strong commitment to improving public health by directing the establishment of new educational programs for diabetes and kidney disease, and new awareness campaigns and information clearinghouses. She also planned NIDDK's 30th, 40th and 50th Anniversary celebrations. Before she retires, she will start planning the Institute's 60th Anniversary, which will be celebrated in 2010. After leaving NIDDK, Ms. Singer plans to continue her community service and advocacy as a member of the Environmental Sustainability Board of Howard County, Maryland, and as co-founder of the Howard County Climate Change Initiative.
- Dr. Laura Moen, a Program Officer in the Division of Kidney, Urologic and Hematologic Diseases, has accepted a position at the National Center for Complementary and Alternative Medicine (NCCAM). During her 3-year tenure in the Division, Dr. Moen was the Director for multiple programs, including the Renal and

Urology Training Program, and several areas of kidney disease research. Dr. Moen also served as an active member of several trans-NIH working groups and committees, including the STEP program committee, the Program Leadership Committee, and subcommittees of the Molecular Libraries Roadmap Working Group.

NDDK Recipients of the NIH Director's Award

This year, a total of 30 NIDDK staff members received the NIH Director's Award. Among the group that received the Scientific and Medical Awards, the NIDDK Mouse Models Group was recognized, including: Drs. Christian Ketchum, Kristin Abraham, Guillermo Arreaza Rubin, Maren Laughlin, and Lisa Spain. Many of the nominations for awards to NIDDK staff came from either the NIH Office of the Director (OD) or other Institutes and Centers (ICs). A few examples include:

- Dr. Phil Smith: Nominated by the NIH OD for his exceptional work in helping implement the second cohort of Roadmap programs.
- Dr. Brent Stanfield: Nominated by the NIH OD for his work on the revitalization of peer review team.
- Dr. Catherine McKeon: Nominated by NHLBI for her work on the genome-wide association studies policy development team.
- Drs. Dan Matsumoto and Laura Moen: Nominated by the NIH OD for the extraordinary contributions they made in support of the NIH extramural science program of the Division of Extramural Activities Support (DEAS) re-engineering team.
- Ms. Melissa McGowan and Ms. Betsy Singer: Nominated by NHLBI for their exceptional team performance in the planning and implementation of the NIH "*We Can! Program*," a childhood obesity prevention program.

II. CONSIDERATION OF SUMMARY MINUTES OF THE 177th COUNCIL MEETING

A motion was made, and unanimously passed by voice vote, to approve the summary minutes of the 177th NIDDK Advisory Council meeting (May 23, 2008), as submitted.

III. FUTURE COUNCIL DATES

The Council's attention was directed to future meeting dates:

2009

February 18 (Wednesday)

May 13-14 (Wednesday and Thursday)

September 9 (Wednesday and Thursday)

2010

February 24-25 (Wednesday and Thursday)

May 12-13 (Wednesday and Thursday)

September 22-23 (Wednesday and Thursday)

Most of these meetings are planned for a single day—Wednesday. However, the NIDDK requests that Council members also reserve the following day, Thursday, to ensure flexibility should a situation arise for which a longer meeting is required.

IV. ANNOUNCEMENTS

Dr. Brent Stanfield, Director, Division of Extramural Activities, NIDDK

Confidentiality

Council members are reminded that material furnished for review purposes and discussion during the closed portion of the meeting is considered privileged information. The outcome of such discussions during the closed session may be disclosed only by the staff and only under appropriate circumstances. All communications from investigators to Council members regarding actions on applications must be referred to the Institute. Any attempts by Council members to handle questions from applicants could create difficult or embarrassing situations for the members, the Institute, and/or the investigators.

Conflict of Interest

Advisors and consultants serving as members of public advisory committees may not participate in situations in which any violation of conflict of interest laws and regulations may occur. Responsible NIDDK staff shall ensure that a committee member does not participate in and is not present during review of applications or projects in which, to the member's knowledge, any of the following has a financial interest: the member, or his or her spouse, minor child, partner (including close professional associates), or organization with which the member is connected.

To ensure that a member does not participate in the discussion of, nor vote on, an application in which he/she is in conflict, a written certification is required. A statement is provided for the signature of the member, and this statement becomes a part of the meeting file. Dr. Stanfield asked each Council member to read carefully the statement about conflict of interest in his or her folder, sign it, and return it to him before leaving.

At Council meetings at which applications are reviewed in groups without discussion, i.e., "en bloc" action, all Council members may be present and may participate. The vote of an individual member in such instances does not apply to applications for which the member might be in conflict.

The following special instructions apply to Council members from multi-campus institutions of higher education: An employee may participate in any particular matter affecting one campus of a State multi-campus institution of higher education, if the employee's disqualifying financial interest is employment in a position with no multi-campus responsibilities at a separate campus of the same multi-campus institution.

V. REPORT FROM THE NIDDK DIRECTOR
Dr. Griffin P. Rodgers

Appropriation and Budget Update

FY 2008: In June 2008, there was a supplemental appropriation of \$150 million for the NIH, which translated into an increase of about half of a percentage point for each Institute and Center. With its \$9.1 million share of these funds, the NIDDK used a little more than half to increase support for research project grants. It used the remainder to resolve some shortfalls in research centers, other research categories, the intramural program, and the administrative budget. Recently, the Congress has been discussing a second economic stimulus package that would cover a wide range of programs throughout the Federal Government. For science and education, a potential \$1.2 billion dollar increase has been mentioned, which would tentatively include a \$500 million dollar request for the NIH. The fate of this proposal is highly uncertain given a very difficult budgetary landscape.

FY 2009: The President's FY 2009 budget request for the NIDDK is \$1.708 billion—an increase of about 0.1 percent over the original 2008 appropriation, unadjusted for the supplemental. However, if one factors in the \$9.1 million the NIDDK received in FY 2008 supplemental funds, the President's FY 2009 proposal is a lower amount than the NIDDK's FY 2008 current budgetary base.

The Congress is continuing to work on FY 2009 appropriations bills, but there has been no final action. A Continuing Resolution for six months or longer is considered likely. The original House and Senate proposed increases for NIDDK for FY 2009 were about 3.5 percent and 2.9 percent, respectively, over the original FY 2008 level. However, if the \$9.1 million in FY 2008 supplemental funding is considered, the House and Senate recommended levels would represent 3.0 percent and 2.4 percent increases, respectively, above the FY 2008 base adjusted for the supplement.

Until the FY 2009 appropriation is resolved, the NIDDK plans to fund its non-competing grants at 80 percent. For competing research project grants, the Institute is cautiously optimistic about its payline, but continues to be concerned about the decline in R01 applications, which has been discussed with the Council previously. For the current Council round, the gradual erosion of applicant demand for R01s has continued—with a four percent drop from one year ago. This is a continuation of the declines seen in almost every Council round for the last two years. However, the prospects for the February Council appear better—with a two percent rise in applications from the previous year. It remains to be seen whether this upswing signals a change in the trend.

With respect to paylines, the NIDDK should be able to maintain the FY 2008 payline of 19 percent for new investigators and 17 percent for all other applicants, even if there is no funding increase in FY 2009. If there is congressional action close to the House and Senate recommended levels, the NIDDK would be able to mitigate its percentage reduction in each application, or consider raising its R01 payline somewhat further.

FY 2010: Proposals for the FY 2010 budget are under development by the Administration, but will not be made public until the President's budget request is released early in calendar year 2009. Subsequent changes in the budget request will be likely under a new Administration.

Special Statutory Funding Program for Type 1 Diabetes Research

On behalf of the Secretary, HHS, the NIDDK administers this Special Statutory Funding Program, which involves multiple NIH ICs and the CDC. At a previous Council meeting, the NIDDK reported on a congressional funding extension for this program for a single year, FY 2009. Now, the Congress has extended the program's funding to encompass two additional years: 2010 and 2011. This total funding extension of three years will have a beneficial effect on the ability to continue large research consortia. For example, it will be possible to sustain basic research in such areas as the Beta Cell Biology Consortium and the Animal Models of Diabetes Complications Consortium. Clinical research will also continue in consortia such as the Type 1 Diabetes TrialNet and the study of The Environmental Determinants of Diabetes of the Youth or TEDDY. The latter program will not only help to define environmental triggers of type 1 diabetes, but will also illuminate the connection between type 1 diabetes and another autoimmune disease, celiac disease. Importantly, the new funds provided will enable the NIH to capitalize on its investment in the Type 1 Diabetes Genetics Consortium and to initiate new work in the fine mapping and functions of the genes for type 1 diabetes. As mentioned at a previous Council meeting, the NIDDK has requested and received authority to make multiyear awards, for up to five years, for some projects in this program. That means that that the NIH can continue to fund some five-year investigator-initiated projects when there is only one year remaining in the Special Statutory Program. The NIH has initiated this multi-year funding approach with the new Type 1 Diabetes Pathfinders' Award, which will support up to ten new investigators who have creative approaches to addressing the major obstacles in type 1 diabetes research.

Peer Review Enhancement Update

In response to requests from a number of Council members, the NIDDK prepared Institute-specific information in follow-up to a presentation at the last Council meeting regarding an NIH self-study for the purpose of enhancing peer review. That presentation was made by Dr. Lawrence Tabak, Director of the National Dental Institute, and a co-chair of one of the *ad hoc* committees leading the self-study effort along with Dr. Jeremy Berg, Director of the National Institute of General Medical Sciences.

Across the NIH, the self-study process revealed a decline from 1998 to 2007 in the percentage of awards made to initial (not amended) R01 applications (A-0 applications) relative to total awards. At the same time, an increase occurred in the percentage of awards for amended R01 applications (A-1 or A-2 applications) relative to total awards. It should be recognized that the 1998-2007 time period included the five-year period of the NIH budget doubling, which commenced in FY 1999 and continued through the end of FY 2003.

In considering these data, some individuals have felt that some NIH study sections may be exhibiting a “queuing” behavior in reaction to the budgetary landscape. An expectation has now developed that applications will probably undergo one or two amendments before being funded.

Because the NIDDK has a broad research mandate and an investigative community that uses many Study Sections, a logical question to ask is whether the NIDDK experience parallels that of the NIH proper. The answer is that the NIDDK’s trends are similar to the NIH trends, but not identical.

- In 1998, the NIH-wide data show that A-0 R01 awards represented slightly more than 60 percent of total awards, while comparable percentages for A-1 and A-2 awards were about 30 percent and 10 percent, respectively. For NIDDK, the comparable percentages in 1998 were about 65 percent for A-0s, 30 percent for A-1s, and 5 percent for A-2s. The percentage of A-0 awards subsequently began to fall off both at the NIH and NIDDK levels, while the percentages for A-1 and A-2 applications began to rise.
- By 2006, the A-0 and A-1 proportional trend lines intersected for both NIH and NIDDK applications. That year, A-0 awards dropped below 40 percent of total awards for both the NIH and the NIDDK. The A-1s began approaching 40 percent of NIH-wide awards and exceeded 40 percent of NIDDK awards.
- By 2007, both NIH and NIDDK data revealed that an applicant was more likely to be funded on an A-1 application than on an A-0 application. The NIH data for 2007 show A-0s at approximately 30 percent of total awards, A-1s at 40 percent, and A-2s at 30 percent. The comparable 2007 data for NIDDK show A-0s approaching 20 percent of total awards, A-1s at about 45 percent, and A-2s approaching 35 percent.

The decline in the percentage of awards for A-0 applications is one of the issues addressed in the recently announced implementation of recommended actions from the NIH Peer Review Enhancement Initiative:

<http://enhancing-peer-review.nih.gov/index.html>

As discussed at previous Council meetings, the self-study of the NIH peer review process has included several stages. An initial diagnostic or data-gathering stage occurred from June 2007 through February 2008. It featured an in-depth evaluation of the existing peer review system. The NIH established an internal working group under the NIH Steering Committee and an external working group under the Advisory Committee to the Director, NIH. It garnered input from a variety of sources including a Request for Information, NIH staff surveys, and a range of *ad hoc* meetings both internal and external to the NIH. The information and suggestions gained were synthesized in a second phase, from March 2008 to June 2008, which focused on the design of an implementation plan with key recommendations.

The overriding goal established by the NIH Director was to fund the best science, by the best scientists, with the least amount of administrative burden. On June 6, 2008, the NIH Director announced the Peer Review Enhancements and Implementation Plan. A Peer Review Oversight Committee (PROC) was created to consider the phased-in implementation of selected actions. Major priorities in the Plan are to engage the best reviewers; ensure quality and transparency of review; provide balanced and fair reviews across scientific fields and career stages; and provide for continuous review of peer review.

Over the past two years, the NIDDK has kept the Council apprised of this process. Council members and others are encouraged to visit <http://enhancing-peer-review.nih.gov/index.html> for updates.

Assigned Discussants:

Dr. Mitch commented that the NIH should be commended for undertaking the self-study of the peer review system and for recognizing the existence of problems that need to be addressed. One difficulty is that members of study sections tend to think about how scores translate into funding. This thinking can affect the funding rates for initial and amended applications, as discussed earlier in the Council meeting. Are there plans to determine the overall percentage of applications that will be funded, and also, will an effort be made to compare the new and previous methods of review?

Dr. Stanfield replied that the implementation steps are still under development. One concept is that each reviewer would score each of the review criteria on the seven-point scale separately, using whole numbers. Those scores could range from one to seven, with one being the best possible score on a given criterion. There may also be a global score that is not derived directly or arithmetically from the scores on the seven criteria. The global score for an application would be reported out as the study section's final score to a single decimal point, starting with 1.0 as the best possible score. The global scores from a given study section meeting would then be percentiled with scores from the two previous meetings—in the same way that percentiling has been done for quite some time. Thus, the global scores under such a new system would look very similar to current scores, but would be a little coarser. The major benefit is that the applicants, the NIH staff and the Council would have a huge amount of insightful information about each application because of the scoring on each individual criterion. Moreover, information would be provided on unscored applications, for which the NIH currently gives no detailed feedback, only the written Summary Statement. It is unclear at this time whether changes along these lines would be pursued as a pilot or how they might be evaluated.

Dr. Elson remarked that the principles and goals of the NIH self-study of peer review are commendable. It will be essential to see how new approaches impact the applicant pool, not just those who perform peer review. It is likely that budget constraints may make it difficult to retain talented individuals in research careers—especially physician-scientists. A key factor in retention will be the degree to which the peer review system continues to expect preliminary data as a requisite for obtaining R01 grant support. If the peer review system is changed in a way to place limitations on an investigator's opportunity to submit amended

applications, it will become increasingly difficult for investigators to obtain preliminary data. Where will a young investigator turn if he or she does not compete favorably on an A-1 amended application, and has no opportunity to revise and submit that application any further? Where will the funds come from to obtain the preliminary data that the study sections demand? At a time when the numbers of applications are declining and the process for amending applications may become more constrained, a sea change among reviewers may be needed in order to retain scientists in the biomedical research enterprise. Dr. Rodgers commented that retention is a serious concern, and that several variables of peer review will be changing in order to enhance the percentage of applicants who receive awards at the initial A-0 stage in the application process. The supply-demand equation will also likely change for budgetary reasons.

Dr. Lazar noted that there seems to be an assumption that the proportional fall off in the percentage of funded A-0 applications is necessarily detrimental. If this fall off has led to A-1 and A-2 that were improved via the amendment process, then science may have been better served than it otherwise would have been if less robust A-0 applications were funded. It is probably important to look beyond the trends regarding the percentages of funded A-0, A-1 and A-2 applications to see what has been happening with the actual numbers of applications at each stage, and their quality.

Something that needs to be considered is that the drop in percentage of funded A-0 applications was due to the reduced payline owing to budgetary changes. That drop put pressure on the A-1 and A-2 process—creating the appearance of queue, as has been discussed. The critical issue is the quality of applications. If the new goal is to increase A-0 applications, the assumption is that they are of higher quality than amended applications, or stated another way, that the amendment process does little to improve an application. Is this assumption really correct?

A closer look at numbers of applications may be helpful to the discussion. Despite the trend of reduced percentages of funded A-0 applications, the actual numbers of A-0s have increased from 782 to about 1,300 over the last ten years. It is important to underscore that this increase covers the five years during which the NIH budget doubled (starting in FY 1998 and ending in FY 2003). With the doubling of the NIH budget came a doubling of new applications. Indeed the incoming tide of new applications continued through 2006 when they peaked at 1530 in FY 2006. Any changes that have occurred in the flat-budgetary period following the five-year NIH budget doubling need to be considered in that context. Indeed, while the numbers of applications have fallen slightly over the past few Council rounds, this is only relative to the post-doubling peak. Considering things in a longer-term horizon, the numbers of applications remain very high.

Perhaps a good way to look at the situation is to consider success rates. Based on data provided by NIDDK, it appears that the types of A-0s that were funded between the tenth to the thirtieth percentile rank in 1998, are now getting funded as amendments. Thus, the types of A-0s that were not funded initially, but were worthy of some further consideration, are now being funded after revision--after they have been improved by the amendment process. This situation is probably reasonable because A-0s funded in 1998 probably included some

inferior science. Now these A0s are being amended before they get funded and may be better for it.

General Council Discussion:

Costs of Rewriting and Re-reviewing Applications: In considering the value of the application amendment process, one needs to think about the costs of rewriting the application and re-reviewing it. One may believe that the A-2 process results in better science, but that may not be the case, or there may be only marginal improvements. Could NIH adapt a model used by scientific journals and find some way for reviewers to identify major vs. minor problems in an application, and to enable funding for an application with only minor problems? Dr. Rodgers commented that there is indeed a cost to the queuing process, but there may also be an implicit contract with investigators that, if they revise their applications to respond to a study section's critique, their amended applications are likely to be funded.

Rapid Movement of Science Can Affect Usefulness of Amendment Process: Science moves more quickly than the process for amending applications, so the feedback provided by study sections may be moot. If the science has already moved in a different direction, the amendment process is not useful and will be reduced to an academic exercise. Moreover, study section comments may encourage scientists to be less creative in order to gain broader support in the peer review system for an amended application.

Impacts on Investigators at Different Career Stages: There has been great concern about nurturing young and new investigators to keep them in the research pipeline. What about more senior, highly productive, established investigators who may be giving up research careers because of problems in the NIH system?

Final Success Rates of New Applicants vs. Experienced Investigators: As the percentage of funded A-0 applications has fallen, an inevitable queue has developed. In 1998 vs. 2008, what has been the ultimate funding success of new applicants vs. experienced ones? Can we tell an investigator at any career stage that, if he or she is responsive to study section critiques and amends and resubmits an application, funding will be likely?

Dr. Stanfield remarked that if applications are divided into three subsets--R01s from new investigators, new R01s from established investigators, and competitive renewal R01s from established investigators--the competitive renewals from the established investigators compete more favorably for funding than do applications in the other two categories. Moreover, the new R01 from an experienced investigator fares better in funding competition than does an R01 application from a new investigator. This trend has been in place for many years; however, it may have changed in the last year or so because the NIH has provided special emphasis funding for many more new investigators.

Dr. Rodgers underscored that it is not known whether overall the science or the grantsmanship is getting better in amended applications, or whether it would be advantageous scientifically to fund an investigator at the A-0 stage if he or she is very likely

to be funded later via the amendment process. The NIH will welcome the advice of National Advisory Council members as the peer-review recommendations for change unfold, budget parameters are better known, and it is possible to gauge the implications of changing paylines.

Possibility of Funding More Grants at Lower Budget Levels To Retain Scientists in Research: Tension exists between the funding size of each individual grant and the numbers of investigators who receive grants. Have there been previous discussions about reducing the amount of funding for individual grants so that the budget can be dispersed among more investigators to keep them in the system? Does the Institute have the flexibility to do this?

Dr. Rodgers replied that the Institute has some limited flexibility to make adjustments; however, the NIDDK and other NIH components have to follow NIH-wide policy. Often that policy is dependent on imperatives put in place as a result of the budgeting process and assumptions about the dynamics of the NIH grant system. On a practical level, another issue is whether investigators can actually do the research they propose if their funding level is dramatically reduced in order to spread funding to other scientists. The result could be sub-optimal productivity across the NIH research community.

Discouraging Amendment of Applications That Are Unlikely To Be Improved: The Council discussed whether the NIH should send a clearer signal to investigators that some applications are unlikely to be improved via amendment and should probably not be resubmitted. These applications may be technically satisfactory, but they lack the impetus of a creative and innovative scientific idea, so the amendment process will not really improve their competitiveness for funding. It is not feasible to coach investigators on idea generation. In contrast, other applications may be scientifically robust at the outset, but may need some minor technical refinements that would be very easy to make. Some way should be found to support these applications on initial peer review so that the amendment process can be avoided.

Dr. Star noted that, because there is now an NIH target for funding specific numbers of new investigators, the NIH is expending more funds on A-0 applications for this group, and the A-1s and A-2s are dropping off. However, expanding this approach would need more discussion, because it is imperative to avoid a point at which inferior research is funded.

Dr. Rodgers noted that NIH efforts to reduce the burden on reviewers may focus more attention on the relative scientific strengths and weaknesses of applications; encourage greater coherence of thought among reviewers; minimize variability in scores; and shorten the time between initial peer review of applications and ultimate funding decisions. The priority of continuously reviewing the review process can help to address this issue. It may be possible to develop specific metrics that will enable the NIH to determine whether subsets of the applicant pool are being advantaged or disadvantaged and to then take corrective action.

Council Member Survey Results and Discussion

Dr. Stanfield reported that 17 of 21 satisfaction surveys had been returned by the Council members. Most members are generally satisfied with Council operations; however, several would prefer to see more opportunities for Council members to discuss presentations and express their views on important program topics, budgetary matters, and policy considerations. To that end, Dr. Stanfield presented some discussion points and suggestions. Options include creating more time for Council deliberations by:

- Eliminating or shortening the scientific presentations or having them only once or twice a year;
- Having only brief scientific presentations from Council members themselves;
- Holding two-day Council meetings once or twice a year and using the two-day format for a scientific presentation and consideration of a report on the Division of Intramural Research; and/or
- Limiting the number of topics covered at a Council meeting.

Council Questions and Discussion

Council members had differing opinions about whether one-day meetings are conducive to the optimal use of a Council member's preparation and travel time. Some members also questioned whether dedicating an hour or more of a one-day meeting to a scientific presentation is the most productive use of limited meeting time. While there was a general recognition that the scientific presentations have been excellent, several scientific members noted that they have access to these types of presentations at conferences and at their local research institutions. The public members or those involved in community practice were more inclined to favor continuing the scientific presentations, but perhaps in a shortened format or on a less frequent schedule. One member suggested offering the scientific presentations over the lunch hour so that interested members could attend, without taking time from the formal Council agenda. Another member suggested that the topics of the presentations be focused on NIDDK programs, so as to complement and inform the Council's advisory functions. One member suggested a format of "scientific pearls." These would be very brief presentations by Council members regarding a recent scientific development they consider particularly interesting and important—usually described in a single journal article.

There was a general consensus that the NIDDK should develop a format that would have fewer and possibly shorter scientific presentations, so that Council members have more time to discuss important topics such as attracting and retaining research investigators; the dynamics of the research enterprise in terms of trends in applications, paylines, and other indicators of the state and direction of the NIDDK portfolio; and the implications of new developments/initiatives/policies at the NIH level. It was agreed that any changes in format would apply to the full Council meeting, not the Subcouncil meetings.

When asked about the costs of one-day vs. two-day meetings, Dr. Stanfield replied that the NIDDK's primary consideration is the high value to the Institute of the Council's advice for

strategic policy-setting. One or more two-day meetings can be scheduled and budgeted, if that is the Council's preference.

VI. SCIENTIFIC PRESENTATION

***How Does Apolipoprotein AIV Regulate Food Intake and Body Weight?
Dr. Patrick Tso, Professor of Pathology, Department of Pathology and
Laboratory Medicine, University of Cincinnati***

Dr. Tso presented his laboratory's work investigating the role of apolipoprotein IV as a satiety factor, its interactions with other factors, and its locus of action.

VII. ADVISORY COUNCIL FORUM

***How Can Clinical and Translational Science Awards (CTSAs) Help Meet NIDDK's
Needs?
Dr. Robert S. Sherwin, C.N.H. Long Professor of Medicine, Section of
Endocrinology, Yale University School of Medicine***

Dr. Rodgers introduced Dr. Sherwin, who serves as the Principal Investigator for the Clinical and Translational Science Award (CTSA) site at Yale, and also as the Director of the NIDDK Diabetes Endocrinology Research Center and the JDRF Center for the Study of Hypoglycemia at Yale. Dr. Sherwin thus has a well-formed perspective on the national Consortium of medical research institutions funded through the CTSA program, which is administered by the National Center for Research Resources (NCRR).

As Dr. Barbara Alving, Director, NCRR, has reported to the Council in the past, CTSA institutions are working together to improve the way that biomedical research is conducted across the country; to reduce the time it takes for laboratory discoveries to become treatments for patients; to engage the communities in clinical research efforts; and to train the next generation of clinical and translational scientists. Investigators within the CTSA Consortium are focusing on ways that they can use their resources to address the research needs of individual NIH Institutes and Centers.

http://www.ncrr.nih.gov/clinical_research_resources/clinical_and_translational_science_awards/

Dr. Sherwin began by noting that he and Dr. Ken Polonsky are the two liaisons between the NIDDK and the CTSA program. As an NIDDK grantee for 32 years, he is committed to helping to make this new program successful. Dr. Sherwin then commented on a number of questions that the NIDDK asked him to address in his presentation.

As General Clinical Centers (GCRCs) Go Away, How Can/Will the CTSAs Provide Infrastructure Support for Ongoing NIDDK-Funded Projects? The transition from GCRCs to CTSAs is a major concern of clinical investigators currently working in diabetes research. In answering this question, Dr. Sherwin suggested that it is important to realize that the CTSA mission is much broader than that of the previous GCRCs, and therefore, the CTSAs have needed to partially reallocate funds from GCRC activities to support other functions.

The CTSA's are therefore requesting Principal Investigators and the NIH Institutes and Centers to share a larger percentage of the cost of studies, through charge-backs. This may be more of an issue for NIDDK than for other NIH components because of the historically large and valuable role that the GCRCs have played in metabolic research. However, the NIDDK can benefit from CTSA's because they are designed to support a much broader variety of clinical research disciplines, which are receiving NIDDK support and are important to the Institute's mission. The CTSA's will offer a more comprehensive research infrastructure that will benefit more NIDDK investigators. They will also promote translational research for which there is a large potential payoff for NIDDK.

CTSA's will also support NIDDK investigators more effectively than GCRCs. In CTSA's, scientific goals can be achieved safer, faster, cheaper and better because of the range of research resources available to investigators. These include expertise in clinical trial design, biostatistics, bioinformatics, clinical research ethics, regulatory procedures, protocol development and IRB processes. Other areas of CTSA support are in the areas of budgeting and contract services for studies, patient recruitment, and research nursing beyond the traditional setting. CTSA's essentially provide "one-stop shopping" where young or experienced investigators can obtain all the assistance they need to launch a clinical protocol. This broad capability was not available in the GCRCs. Another way in which CTSA's can provide more effective support is through pilot studies, and through university-wide, novel core technologies. Moreover, seed grants with very short review cycles can enable junior researchers and basic scientists to pursue rapid development of translational programs and pilot data, and to form interdisciplinary collaborations. The CTSA's also set standards to enhance the training of personnel, including nurses, research coordinators, and community researchers. By defining standards, competencies, and metrics, CTSA's can improve the quality and efficiency of conducting clinical research. Further support is provided by the IT networks developed through CTSA's, which can facilitate collaboration and communication, and speed the dissemination of best practices. Perhaps most importantly, CTSA's are leading academic institutions, faculty, and students to make investments in these transformational programs that give clinical research a more prominent place on the academic agenda.

What Is Being Done by CTSA's To Enhance Coordination of Multi-center Trials? Dr. Sherwin responded to some specific questions posed by NIDDK about CTSA activities.

- Will CTSA's respond to solicitations for multi-center applications or clinical trial sites? This will happen, but there are some qualifications. Because CTSA's are in a start-up phase, this type of activity will probably occur with small groups of CTSA's that have existing expertise, such as genomics or phenotyping, within their organizations. The program encourages networking among CTSA sites, and that can lead to multi-center research over the next year or two.
- Will the response differ from that of a site without a CTSA? Multi-center research efforts involving institutions with a CTSA program will be different from those at other institutions. CTSA programs will be more cost-effective because of partnerships with the ICs to share resources. CTSA's will provide ready access to

efficient, centralized clinical research resources that an IC might otherwise have to generate itself.

- Can CTSA's facilitate multi-center pilot studies or provide access to additional resources? As noted previously, such studies can be pursued via small collaborations among CTSA's that already have specific resources in place.
- How will CTSA's enhance coordination of multi-center protocols? At present, clinical research management is probably the highest priority for the CTSA Consortium. A Task Force is dealing with many of the issues surrounding clinical trial design and implementation. There is an annual workshop for process improvement. Pilot studies test different approaches to enhance the review process and to help investigators develop protocols. The CTSA Consortium has several committees in place to improve clinical research processes by addressing issues such as regulatory support and alternative approaches to meeting Institutional Review Board requirements. Each CTSA site in the Consortium has to develop its own programs and then try to intersect with other CTSA's that may have a longer history and some important research resources already in place.

What steps are being taken to improve the recruitment of patients and of underserved populations? CTSA's are striving to facilitate recruitment of patients for clinical studies. To this end, most CTSA's have launched campaigns and other initiatives; have developed specialized offices for recruiting study participants; and are working toward improved relationships within local communities and with academic leaders through the use of telephone contacts, websites, and mobile units and vans. One example is the convening of events, such as a strategic planning meeting, between community leaders and the scientific leaders at a local academic research institution. Underserved populations are being reached in a variety of ways. Special programs have been developed in Iowa, Indiana, California, New York, and Pittsburg. Links with community health care centers is another avenue for reaching underserved populations. In addition, pilot studies can be an important means of focusing on disease areas of special concern to underserved populations. For example, the National Heart, Lung and Blood Institute is planning to pilot a sickle cell disease research consortium that would enable all CTSA sites to participate.

How are the CTSA's reducing resource duplication and the need for resource duplication? Because CTSA's are university-wide infrastructure, administered under one roof, they can achieve their primary goal of enhancing the safety, speed, and rigor of patient-oriented research. Efficiency and cost savings derive from the centralized provision of technologies and core laboratory operations. Collaborations with categorical centers and departments in the joint support of centralized resources can help to maximize support for clinical research. Improved accessibility and availability of resources will flow from CTSA efforts to identify, catalogue and organize existing scientific, educational, regulatory, and community resources. All these factors reduce the possibility of resource duplication and the need for redundancy in resource support, thereby improving efficiency and cost-effectiveness. However, the CTSA funding levels

alone are not sufficient to meet all resource needs for clinical research. Therefore, it is essential for the CTSA sites to work together with Department leaders and Center Directors at universities to reduce costs through sharing and collaborating.

To what extent are resources available to help Principal Investigators to design grant applications with appropriate power calculations and to support their education in biostatistics? Support for biostatistics and study design is a key CTSA function, and, as a result, resources in those areas now exceed those offered by GCRCs in several ways. First, by funding a much larger cadre of Ph.D.s and Masters level biostatisticians, the CTSA program is providing investigators with much greater support for their grant application process. Second, CTSA provide investigators with specialized consultative services in areas such as genomics, proteomics, human genetics, clinical epidemiology, cost-benefit analysis, and medical decision-making. Third, an intensive education program is offered in biostatistics, epidemiology, and health economics for students, fellows, faculty members, and research staff throughout the academic institution housing a CTSA. These features are major strengths of the CTSA program and are expected to improve the quality of clinical research applications to the NIH.

What are opportunities for interactions with trainees and training programs (CTSA K12 and T32)? A primary mission of the CTSA is to develop the next generation of clinical scientists. In pursuing this mission, CTSA will focus on attracting talented individuals; training them to use cutting-edge research tools and gain skills to work within complex research teams; and supporting their professional education and development. These objectives are best accomplished at the university level by fostering a community of well-trained clinical scholars. The importance of pursuing a research career and of focusing on translational research should be emphasized in degree-oriented programs at all levels—the M.D., Ph.D., and Master’s levels. If we don’t nurture clinician scientists, we are going to have a major gap in terms of translating basic science into technologies and interventions that will benefit patients directly. Yale University is an example of the type of support that can be provided. Over the last two years, Yale supported 20 junior faculty through K awards, or directly, through the CTSA program. Yale also has 14 clinically trained physicians who are seeking a Ph.D. and seven more on the list to start. All the junior faculty and Ph.D. students have three mentors from diverse backgrounds, who meet with them twice a year. Yale has supported four graduate school candidates from the school of nursing, public health and biomedical engineering, as well as 17 M.D./Ph.D. students and medical students. A new six-month course for M.D./Ph.D. students will concentrate on translational research. Yale has expended about \$2.5 million in support of these efforts.

What is being done to reduce barriers and burdens associated with pediatric research? CTSA have a specific mandate to help develop pediatric scientists. Some CTSA sites have set aside specific funding for pediatric research. The CTSA Consortium has a pediatric oversight committee with representatives from all the CTSA sites. There are pediatric liaisons to all the key function committees of the CTSA Consortium, so the pediatric research community is actively involved in the CTSA initiative. Considerable

effort has been directed to improving the pediatric protocol review process, and workshops are planned to reduce barriers and burdens associated with pediatric research.

Does the CTSA Consortium plan to develop a national bioinformatics infrastructure for clinical and translational science? Currently, there are no plans to develop a specific national biomedical research infrastructure. Instead, the focus is on information exchange and agreement across the CTSA sites on best practices and standards to facilitate data sharing. There is flexibility for individual CTSA sites to develop the infrastructure that best serves their needs, but that also incorporates national standards that facilitate information exchange with other sites. Collaborative efforts under way include IT-supported social networks; cataloguing of translational resources across the CTSA sites; and development of systems for clinical research and electronic data management. The informatics area is improving across the CTSA sites, but this process will take time. Are there opportunities for interactions between CTSA sites and disease-focused research centers? Yes, centers can take advantage of the CTSA education and training program, which is a major innovation. Also helpful to the centers is the opportunity for cost-sharing with the CTSA sites for pilot studies, translational cores, biostatistical support, bioinformatics, and the potential for access to biorepositories. CTSA pilot funding and IT support can also be useful for different centers programs. At Yale, the Diabetes Endocrinology Research Center (DERC) has developed a translational core with trained personnel who are developing the capabilities to do complex metabolic studies. This effort is co-supported by the DERC, the Yale CTSA, and the Juvenile Diabetes Research Foundation. Another CTSA partnership is with the Yale Cancer Center. This partnership features joint funding of pilot grants and a state-wide network for cancer clinical trials. There is also joint support for cores for biostatistics, study design, biomedical informatics, immune monitoring, and genomics/proteomics. A single administrative group provides joint financial administration of the trials, and follows protocol development and quality assurance issues in a centralized, efficient way.

What steps can NIDDK take to ensure that its research communities can best leverage CTSA resources? The CTSA Consortium and the individual CTSA sites are academic homes for clinical research, but they are not the engines that make it move forward. The CTSA Consortium provides the structural components needed to make disease-specific research projects work. The opportunities offered by the CTSA Consortium to NIDDK include large infrastructure to support clinical trials; extensive educational and training resources; opportunities for collaboration with NIDDK disease-focused centers in diabetes, obesity, and other areas; resources for studies of rare diseases, genetics, and phenotyping; information and core technologies; and infrastructure that permits more meaningful community engagement. The NIDDK can take steps to take advantage of these opportunities. The NIDDK can work with the CTSA liaisons to determine clinical management needs and team with the Consortium to improve and make use of clinical research operations. For example, the NIDDK's participation in the CTSA clinical management workshop would be welcome. Through this process, the NIDDK can also evaluate CTSA progress and provide input into shaping CTSA priorities. At some point, it would probably be useful for the NIDDK to develop a prototype for a multicenter pilot trial with the CTSA Consortium. Right now, however, the NIDDK can use its process for

soliciting research applications to encourage its investigative community to leverage CTSA resources. Also, the NIDDK can focus on K12 and T32 mechanisms—perhaps even targeting those programs to be incorporated into the CTSA educational structure. For example, at Yale, all T32 grantees take the courses that the CTSA provides and thus receive training that is similar to that of the Ph.D. students. It might be more feasible for the NIDDK to invest in that type of approach with its disease-specific grantees, rather than to set up its own separate infrastructure.

Are the CTSA Consortium Priorities and NIDDK's Needs and Priorities Aligned? Dr. Sherwin shared with the Council the following current priorities of the CTSA Consortium and asked members to think about how well they align with the NIDDK's needs and priorities.

- Develop a system of continuous quality improvement in clinical research management (IRB, contracts, grants management, Medicare and insurance payments, clinical site organization).
- Develop a coordinated/federated approach to research career development, training and education across the spectrum of translation and clinical disciplines.
- Create a national, searchable, and interactive inventory of resources for translational and clinical research, including people (e.g., genomics, proteomics, etc.) and services (data coordination, bioinformatics, etc.).
- Develop a proof-of-principle approach through several clear examples of networks for the enrollment of study participants and the conduct of clinical trials that eventually could make the CTSA Consortium a network of networks—each focused on particular diseases/conditions, but also linked by common data systems and informatics.
- Develop a national system of electronic data management and data sharing, complemented by information technology tools.
- Develop a national biobank, a national phenotyping system, and an effective national model for community engagement.

It is imperative to keep in mind that CTSA's are a work in progress. The National CTSA Consortium is still in the building phase, as new institutions are joining each year. The CTSA Consortium needs to be permitted the time to build strength and prove its worth to the NIDDK, other ICs, and the broad research community. The Consortium is developing an Implementation Plan, which will provide a framework for addressing a wide range of issues, such as those raised by NIDDK. Concomitantly, the NIDDK and other ICs should probably be determining what they would like to derive from the CTSA effort, including the establishment of metrics for evaluating CTSA programs and holding them accountable for their performance. If enthusiasm for moving the CTSA Consortium forward is sufficiently strong, it is likely to be a very important effort to strengthen the national clinical research enterprise.

Assigned Discussants

Dr. Perlmutter questioned if it will be possible to achieve all the goals of the CTSA Consortium and of the individual CTSA sites or are they too all-encompassing relative to the size of the program? Perhaps CTSAs should focus on actions that are achievable and implement them well. Compared to the previous individual GCRCs and K12s, the CTSA Consortium offers a much larger scale of support for clinical research that could be parlayed into greater institutional investment. That would be a strength of the CTSA structure. However, the scope of the CTSA Consortium might also present a problem with regard to enrollment of patients. Research institutions are currently struggling with ways to establish patient registries across campus that are broadly workable, and that can be linked to all the clinical information that is needed. If the CTSAs can enhance patient enrollment that would help not only NIDDK investigators, but all investigators. Is this a responsibility of the CTSA Consortium or of the individual CTSA sites?

Dr. Sherwin responded that this issue is within the purview of the individual CTSA sites, but that all the CTSA sites share best practices and there is an overarching IT key function committee. As the CTSAs learn from each other, they can speed the process. Clearly, the IT issues are imposing, and their resolution will require budgetary investments, which the universities are making. The CTSAs have made translation research much more attractive within the university communities and that has spurred active support of the CTSA efforts by the research institutions.

Dr Palmer commented that with the advent of the CTSA Consortium, clinical and translation research now has a home within academic institutions, rather than being left to different divisions or departments. However, given that the CTSA Consortium's agenda is very broad and expansive, one wonders whether funding is adequate to accomplish it. If not, how will the Consortium respond? Are the CTSAs supposed to recover more funds in subsequent years from essentially a charge-back mechanism and how would that enable the CTSAs to support what they need to do? The GCRCs have really been the backbone of major clinical trials in the United States, and care must be taken to sustain those types of efforts in the CTSA Consortium.

Dr. Sherwin replied that CTSA budgets are constrained, as they are for other segments of the research enterprise. Partnerships with the universities can help, but there will surely be increased costs to investigators. The CTSAs will use a charge-back mechanism, but will try to do so as gradually as possible and to recover partial costs rather than full costs of services provided. Junior investigators who have core grants will be able to use resources without charge, but other, more established investigators will be asked to help offset CTSA costs. Thus, the CTSA Consortium will be run more like a business than the GCRCs were. However, because the infrastructure provided by the CTSAs is superior, the overall quality of the product will be greater. The NIH and its ICs may need to fund the CTSA programs more than they have to date, but they will have an increase in the benefits they derive.

Dr. Palmer then asked if the CTSAs can inspire the next generation of clinical researchers. The CTSAs largely provide resources and infrastructure. However, the excitement and drive to undertake a clinical research career will still need to come from mentors who are scattered throughout the research community. How will CTSAs inspire junior investigators to take advantage of the Consortium's infrastructure and to pursue the types of clinical research that are on the Consortium's agenda?

Dr. Sherwin noted that excitement about research is a key ingredient to the success of the CTSA enterprise and the broader national research enterprise. He pointed out that the CTSA Consortium has mentored scholars, who also benefit from the CTSA committee structure and

frequent scientific presentations. At Yale, there is also a partnership with the Rockefeller Foundation, which brought its scholars in for presentations, poster sessions, and discussions about the issues surrounding academic research careers. Ultimately, the goal is to create a community of junior scholars that are the brightest and most talented and to engage them in an organizational structure. The concept is to make individuals feel that they are part of a research community, and mentoring is absolutely critical for achieving this. Yale is forming a society of local mentors, whose efforts will go beyond merely talking with people to actually providing helpful comments on the preparation of grant applications. At Yale, the recruitment of minority investigators and women investigators has been very encouraging. The new approaches fostered by the CTSA Consortium create a very structured nurturing environment, which is generally superior to *ad hoc* processes for establishing mentoring relationships.

Dr. Andrews pointed out that not all CTSA sites are starting from the same level of development and this needs to be considered. For example, some sites, such as Duke University, may have a different structure because they had a strong clinical research foundation in place prior to becoming a CTSA site. Duke has a clinical research institute, and less than five percent of its clinical research was done in a GCRC prior to the start of its CTSA program. Moreover, its clinical data base has been in existence for decades. It has also had a culture in which basic and clinical investigators have interacted for quite some time, and that interaction helps to promote translational research. Other CTSA sites may need more time to develop. As the CTSA Consortium moves forward, it will undoubtedly face challenges. For example, there may be cultural issues as this program confers greater prominence on clinical investigation in many academic medical centers. There may also be a need to integrate engineering within CTSA translational research efforts at those sites that do not already have such integration. Another consideration is that the national need for biostatisticians is great, and many of them are already professionally committed. Yet, despite these and other challenges, the CTSA offer many opportunities for new directions. The CTSA Consortium may even want to consider international studies in different populations to shed light on the onset and progression of disease.

Dr. Andrews then asked if M.D.-Ph.D. programs for clinical investigators would be beneficial. What would be the advantages of this approach?

Dr. Sherwin said that such a program would be a very good thing. Most fellows who are doing clinical research with only two years of research experience are not ready to compete in the real world against investigators who are better trained. If they had more experience, they would be more competitive. If we want to attract clinically trained individuals to research careers, they are going to need a level of research training that is close to that of a Ph.D. in order to be competitive in the current world of research.

General Council Discussion:

Importance of Translational Research: The CTSA Consortium's emphasis on translational research is extremely important to the NIDDK. The lack of translational research is one of the primary barriers to developing more effective treatments to combat the epidemic of diabetes.

Prioritization: If funds become increasingly limited, will there be areas of conflict between the CTSA Consortium and other NIH-funded Centers such as the Diabetes Endocrinology Research Center (DERC) at Yale? Will there be an ultimate problem of prioritization?

Dr. Sherwin responded that the Yale CTSA provides benefits to the university's DERC through such activities as the planning for jointly funded pilot studies. More pilots will be possible because of cost-sharing. The only potential problem for investigators who use the CTSA is that they will probably be charged more than they were previously charged, particularly if they used a GCRC. However, the CTSA's will attract more clinical investigators in all areas and that is very positive.

CTSA's as a Roadmap Initiative: Dr. Alan Krensky, the first Director of OPASI, noted that the CTSA Consortium grew out of the Roadmap process. It reflects the vision of the NIH Director to create a space to enable programs that had not been previously undertaken. However, once the new effort is under way, it needs an organizational home. In this case, the organizational home for the CTSA Consortium is the NCRR. However, there remains a need to leverage funding for this new, innovative program from a variety of sources—including the ICs and philanthropic sources. Keeping the idea alive and exciting will be up to the various CTSA sites. With thoughtful development, the Consortium offers an important opportunity to strengthen the clinical research enterprise without increasing bureaucracy.

VIII. CONSIDERATION OF REVIEW OF GRANT APPLICATIONS

A total of 1,166 grant applications, requesting support of \$287,827,627 were reviewed for consideration at the September 24, 2008 meeting. Funding for these 1,166 applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, an additional 1,210 applications requesting \$374,653,228 received second-level review through expedited concurrence. All of the expedited concurrence applications were recommended for funding at the Scientific Review Group recommended level. The expedited concurrence actions were reported to the full Advisory Council at the September 24, 2008 meeting.

VIII. ADJOURNMENT

Dr. Rodgers thanked the Council members for their attendance and valuable discussion. There being no other business, the 178th meeting of the NIDDK Advisory Council was adjourned at 4:00 p.m., September 24th, 2008.

I hereby certify that to the best of my knowledge, the foregoing summary minutes are accurate and complete.



Griffin P. Rodgers, M.D., M.A.C.P.
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