

## National Research Advisory Council – December 3, 2007

### Members present:

Marie Bernard, Chair  
Dudley Childress  
Jeffrey Drazen  
Robert Kelch  
David Korn  
E. Albert Reece  
Richard Wenzel

### Guest:

Allison Haupt, Alliance for Academic Internal Medicine (AAIM)

### VA staff:

Lynn Cates, Gena Clemons, John Concato, Brenda Cuccherini, Seth Eisen, Joe Francis, Jay Freedman, Sandra Issacson, Joel Kupersmith, Tim O'Leary, Alex Ommaya, Ronald Przgodzki, Peter Peduzzi, Michael Selzer, William Yancy

### **Meeting Minutes:**

The meeting of the National Research Advisory Council (NRAC) was called to order at 8:35 a.m. by Dr. Bernard. NRAC members were asked to review the minutes from the last meeting and approved them unanimously.

### Biomedical and Clinical Research - Dr O'Leary:

Dr. O'Leary reviewed the statistics for biomedical and clinical research program. In general, about 25 percent of proposals are approved for funding; however there has been a slight decrease in the number of proposals received. With respect to Career Development, applicants for Advanced Career Development are doing slightly better than first round applicants. Dr. O'Leary attributes this to the fact that second round applicants have established a strong relationship with a mentor.

With respect to Ph.D. Research Career Scientist (RCS), a review of the program suggests that RCS awardees are more productive with respect to merit funding and publications than their peer group. Under new review criteria greater emphasis will be placed on research scholarship. Dr. Eisen will be undertaking a more formal evaluation of the Career Development Program.

The Cooperative Studies Program has 20 active studies, of which: 5 are in mental health, 4 cancer, and 4 in general or cardiac surgery. Four studies are presently in planning.

Major new initiatives in 2008 will focus on Information Technology Standardization and Matrix Management of the Cooperative Studies Coordinating Centers. The goal for IT Standardization is to make Cooperative Studies IT state-of-the-art in terms of data collection, data management, and communication of clinical/research data. Emphasis

will be placed on standardization across coordinating centers, the use of web-based communications and the protection of sensitive data.

Report from CRADO – Dr. Kupersmith:

James B. Peake, MD, has been nominated to be the VA Secretary. His Senate hearing is scheduled for December 5, 2008. ORD is presently recruiting for a Director to manage our VA non-profit research foundations. We are still under a Continuing Resolution, which will continue at least through the middle of December and may continue into next year. Both the House and Senate propose a VA research budget of \$480 million. If we receive this increase ORD will increase funding to all four research services. VA is also interested in targeting a modest amount of funds for breakthrough projects that are not likely to be funded through the usual merit review process. The key to this new initiative is to balance rigorous science with the flexibility to be innovative. NRAC members encouraged ORD to partner with non-VA collaborators on this initiative. Dr. Kupersmith and Gena Clemons spoke briefly about strategies to more effectively communicate the impact and value of VA research.

Vietnam Veterans of America (VVA) Letter to NRAC – Dr. Bernard:

Dr. Bernard open the discussion concerning a draft letter emailed to the Committee in response to the letter sent by VVA to NRAC and presented at the September NRAC meeting. Committee members had no substantive concerns or changes. Editorial changes were shared with Dr. Freedman who will incorporate the changes into a revised draft to be shared with Committee for final approval.

Health Services Research Update – Dr. Eisen:

Dr. Eisen spoke concerning 3 topics: medical informatics, career development evaluation, and DoD/VA collaboration. With respect to informatics, VHA added almost a billion progress notes to its medical record in 2006. While VA has been recognized for its wonderful electronic health record (EHR), a lot of data is in text format and not readily available for analysis. This includes: radiology reports, pathology reports, pulmonary reports, laboratory reports, progress notes, and discharge summaries. These reports are easily accessible through the computer but they are difficult to analyze systematically. The goal of this HSR&D initiative is to figure out a way to access text-based data for research. To date HSR&D has had two meetings with VA informatics experts to start thinking about how to do this with VA text data. We have identified numerous informatics researchers in VA. The focus of ORD's efforts is on collaboration and to communicate to the field that ORD has a strong commitment to fund informatics research. To facilitate research in this area, ORD will create a data base of text information as well as a system for analysis. Data security will be very important. Processes for extracting, cleaning, reformatting and de-identifying text will be developed and data bases for text data mining developed. VA investigators will be encouraged to collaborate with non-VA investigators.

Career Development Award (CDA) Program Evaluation: with HSR&D about 20 percent of budget devoted to Career Development. HSR&D funds between 20-30 applicants each year. Since 1998 HSR&D has received about 300 applications and funded around 46 percent. Most are physicians, and most are internists. About 31 percent of Investigator Initiated Research (IIR) is conducted by Career Development awardees. Goal of evaluation is assess the impact of CDA program; its utility in recruitment and retention of clinical investigators and its impact on the quality of health services research. Potential methodological issues concern how we define health services

research, which in turn will impact the selection of a comparison group, and how we will assess program costs. We expect to employ a mix of quantitative and qualitative methods.

Update of VA Geriatrics Research – Dr. Francis:

Recent Heightened attention to OIF/OEF research has raised concerns of a perceived reduction in geriatric research. In addition, fewer proposals are being assigned to the Aging and Clinical Geriatrics (ACGC) Merit Review Subcommittee (last 3 review cycles there have been too few proposals to justify holding an ACGC meeting). Finally, there has been concern that new eligibility requirements for non-clinician PhDs may impact some VA geriatric investigators.

A review of the numbers show however that aging and clinical geriatric topics continue to represent a significant portion of the ORD effort. However, proposals to ACGC have fallen from 20-30 per round in 1994-1999, to 10 or fewer per round since 2000. Geriatric proposals are competitive when assigned to other merit review committees, and there is no evidence that PhD eligibility requirements have been prejudicial to GRECC researchers.

It is critically important for ORD to maintain the distinctness of VA research from the National Institute on Aging and other funding sources. VA must focus its research efforts on unique opportunities where it can make the greatest difference for veterans. This includes translation research, genomic medicine, and emerging methods for rapid discovery and learning. To further enhance veteran-centric aging research, ORD has hired a scientific program manager dedicated to aging and geriatrics research. ORD leadership has met with the GCAC and the GRECC research leadership and is committed to developing and releasing a cross-service Aging Solicitation in FY08. The solicitation will focus on the interaction of aging with combat injuries and deployment exposure, complex geriatric syndromes prevalent among veterans, chronic care and care giving, behavioral and social problems including suicide in older veterans, and understanding genomic and other determinants of successful aging in veterans.

*Discussion:* The NRAC appreciated the update and agreed that the numbers show ORD has an active commitment to aging research, and endorsed the steps outlined to further expand veteran-centric aging and geriatrics research.

Rehabilitation Research Update – Dr. Selzer:

Dr. Selzer noted that the Scope of Rehabilitation research is expanding to include Repair, Replace and Restore. RR&D is seeing a significant increase in proposals; however, the service presently has only one program manager. RR&D is in the middle of a tremendous recruitment effort. In addition the service will be adding a special projects manager to focus on increasing collaboration with HSR&D, clinical and basic science research. There has been a very strong response to ORD's OEF/OIF solicitation. OEF/OIF related research represents about 80 percent of RR&D's portfolio. A state of the art conference on TBI is planned for the spring. RR&D investigators have received major awards in the past few months. Rory Cooper, PhD received the 2007 National MS Society da Vinci Lifetime achievement award. John Donoghue, PhD was awarded the Zulch Prize, Hugh Herr, PhD the Heinz award for Technology, and Bruce Sangeorzan, MD the 2007 Magnuson Award.

### What Can Diets Do for Obesity and Related Diseases? – Dr. Yancy:

Dr. Yancy from the Durham VAMC was introduced by Dr. Seth Eisen. The prevalence of obesity in the population has increased significantly over a relatively short period of time. Obesity as a public health problem is taking over for smoking as a concern. Our diets have change and physical activity has declined. Low carbohydrate diets have been around for a long time. Further, Dr. Yancy reviews a number of popular diets with respect total calories per day and number of carbohydrates per day. Most studies are of healthy individuals, making generalizability to the veteran patient population difficult. A comparison of low-carb and low-fat diet randomized control trials show significant improvement serum lipid levels for the low-carb diet. Recent study looking at low-carb diet for Type 2 diabetes show significant weight loss, improved hemoglobin A1c, and a reduction in the number of diabetic medicines taken by patients receiving the intervention.

### Genomics Medicine – Dr. Przygodzki:

*Veteran consultation project:* Nine focus groups of veterans from different regions, sex, age ethnicity and income strata were solicited about their opinions, beliefs and values regarding genomic medicine. The study was conducted by the National Human Genome Research Institute through a cooperative agreement with the Genetics and Public Policy Center. Preliminary results note (1) a greater altruism and sense of community, (2) a lesser expectation of compensation for study and (3) an acknowledgement for community leaders to voice the veteran's opinion and concerns among the veterans as compared to the general population. Similarly to the general population though are concerns pertaining to trust, data privacy and loss of benefits. Final analysis will determine areas requiring further inquiry, which will be incorporated into a survey of 850 veterans receiving VA healthcare.

*HNPCC working group:* The group identified microsatellite instability (MSI) testing and mismatch repair gene sequencing as feasible, reliable, and a standard of care which should be easily translatable into VA clinical practice of patients with Hereditary Nonpolyposis Colorectal Cancer (HNPCC). The group also identified the need for genetic counseling before and after testing.

*Genomic activity among VAMCs survey:* A survey was distributed to all 154 VAMCs requesting information about what genetic tests (excluding infectious disease testing) are provided and where; whether there is access to educational materials for patients and healthcare providers; and if and where genetic counseling was provided. One hundred fourteen VAMCs responded, with 99 identifying themselves as performing such tests. The most prevalent type of test provided was of the heritable type, and included testing for hemochromatosis, factor II and V Leiden. Most testing was off site (university affiliate or commercial laboratory). Few sites provided educational tools for either patients or healthcare providers, with nearly three-quarters lacking both. Genetic counseling was provided at both VAMC and university affiliates.

*Planned studies:* A concept letter was accepted by CSP for the "Serious Mental Illness Cohort Study." The longitudinal study will investigate patients with schizophrenia and bipolar disorder as well as normal controls utilizing genome wide association studies (GWAS). Similarly, a PTSD genetics working/planning group was convened to assess the feasibility of a GWAS study on patients with this disorder.

*Endocrine tumor working group:* The group identified feasibility, predictive and diagnostic clinical utility for assessing the germline and/or tumor mutation testing for VHL, RET (MEN2), SDHB and SDHD genes. Germline testing for MEN1 is useful as a screening tool, however is questionable from a clinical utility perspective. The group also expressed the need for genetic counseling before and after testing. Also expressed was the need to identify mechanisms of obtaining and recording family history into the electronic health records.

*Resources Development:* Current developments include (1) establishing a VA central IRB; (2) reorganization of review for CSP DNA banking to be managed centrally; (3) establishing of a genomic epidemiology panel of the CSP Merit Review Board in FY08; (4) development of educational programs and tools for physicians and other health professionals through a collaborative effort between the VA Employee Education Services and the National Coalition for Health Professional Education in Genetics to be introduced in FY08; (5) Interaction of the Health Services Genomics Workgroup to identify the framework for planning and delivery of genomic services to the VA population.

#### Research Methodology in VA's Cooperative Studies Program – Drs. Peduzzi and Concato:

Dr. Peduzzi provided an overview of VA's Cooperative Studies Program (CSP) and its capabilities. The two major challenges in conducting multi-site clinical trials are recruitment and retention of study subjects. Dr. Peduzzi described the special requirements necessary for the recruitment and active following of 38,000 subjects for the shingles vaccine study, the largest adult vaccine trials ever undertaken. The objective of the study was to test the safety and efficacy of Oka/Merck vaccine to prevent herpes zoster (shingles). Most participants (95.3 percent) were actively followed to the end of the study. The Vaccine was proven to be safe and effective, and licensed by FDA.

A second Cooperative Study focused on testing a robotic training device for improving arm movement in persons recovering from a stroke. This study involved collaboration between RR&D and MIT (which developed the training device). The study randomized 158 subjects to one of 3 treatment arms. Subjects were drawn from 4 VA sites and followed over a 2 year period.

Dr. Cancato next spoke concerning observational research, describing two studies: one concerning acetylcholinesterase (AChE) activity in veterans of the first Gulf War, and a second one concerning neuropsychological and mental health outcomes of OIF.

The first study addresses whether serum AChE activity is associated with symptoms of Gulf War Veterans Illness (GWVI), by examining relationships of deployment and post-military symptoms with serum activity of AChE and related enzymes. The study utilized a population of 488 veterans from Iowa at enlistment, who served in the first Gulf War. Measurements included demographics, military, clinical characteristics from the original Iowa study (1995-96), and follow-up based on mental health symptoms using nested case-control methods. Study findings do not "rule out" a role of AChE and related enzymes in the etiology and pathogenesis of symptoms among veterans suggesting that neither deployment to the Gulf nor symptoms compatible with GWVI are associated with long-term serum AChE activity.

A second study builds on the work of Vasterling (JAMA 2006) which reported neuropsychological changes associated with serving in Iraq. Baseline data was collected prior to deployment. The new study will link to this prior study. The aims of the current effort are to determine the long-term prevalence and trajectory of PTSD, determine if neuropsychological findings persist, and ascertain whether there is an association of neuropsychological changes/TBI with PTSD. The challenge is to locate a “closed group” of soldiers as they become veterans and scatter across the country. There is no clean control group since in the current conflict every one is deployed and many times.

It is important for the CSP planning committee to define cogent objectives for the follow-up study that can be addressed by the integration of prior work and the proposed research protocol. The analytic plan must produce valid yet understandable results.

At 2:55 p.m. the meeting was adjourned.

I hereby certify that, to the best of my knowledge, the foregoing minutes are an accurate and complete record of the substance of the meeting.

Jay A. Freedman, PhD  
Designated Federal Officer  
National Research Advisory Council

Marie A. Bernard, MD  
Chair  
National Research Advisory Council

These minutes will be formally considered by the Council at its next meeting, and any corrections or notations will be incorporated in the minutes of that meeting.