PEER REVIEW NOTES
January 2002

From the CSR Director's Desk……..……..……....……...1

New Personnel at CSR..……..……..……..…...……3

Working Group Reviews of CSR Integrated Review Groups……...4

Delivery of Grant Applications and Other Materials to NIH……6

New Instructions For Evaluating Grant Applications Involving Human Subjects……6

Human Embryonic Stem Cells……8

From the CSR Director's Desk

Special Thanks to Reviewers

As the first order of business, I want to express special thanks to all the reviewers who participated in review meetings following the terrorist attacks on the World Trade Center and Pentagon. Concerns about additional attacks and delays resulting from both increased security and a reduction of flights across the country made travel extremely stressful and inconvenient during last year's October-November round of study section meetings. Despite these problems, not one meeting had to be canceled. Most reviewers attended their meetings by one or another means of travel.

Because of the extraordinary resolve demonstrated by reviewers, the course of peer-reviewed science at the National Institutes of Health (NIH) was preserved. In a small way, this diminished the terrorists and their acts. I am extremely proud to be part of such a dedicated community. Again, my thanks to the reviewers and to everyone involved in the NIH peer review process.

Reorganization Activities

I also want to express special gratitude to members of Study Section Boundaries (SSB) Teams that have met since September 11. The Oncological Sciences SSB Team was originally scheduled to meet September 11-13, 2001, but was delayed until December 11-13, 2001. Three other SSB Teams met during this trying period: (1) Cardiovascular Sciences; (2) Bioengineering Sciences and Technologies; and (3) Surgery, Applied Imaging and Applied Bioengineering.

The SSB Team meetings are part of the Center for Scientific Review's (CSR's) Phase 2 reorganization, as recommended by the Panel on Scientific Boundaries for Review (PSBR). The Phase 1 PSBR report (http://www.csr.nih.gov/EVENTS/summary012000.htm) suggested that CSR redesign study sections within 24 Integrated Review Groups (IRGs). In this Phase 2 process, CSR recruits experts to participate on IRG-specific SSB Teams. These teams meet and

propose guidelines for each IRG and its study sections. The proposals are then posted on the CSR Web site for public comment and may be modified before going to the CSR Advisory Committee for discussion and final approval. All SSB Team recommendations are posted at http://www.csr.nih.gov/PSBR/IRGComments.htm.

To date, CSR has convened a total of seven SSB Team meetings. The first three SSB Teams met and drafted guidelines for their IRGs in 2001: (1) Hematology, (2) Biology of Development and Aging, and (3) Musculoskeletal, Oral and Skin Sciences. Public comments on their proposed guidelines have already been received. Proposed guidelines from the Cardiovascular Sciences and Bio-engineering Sciences and Technologies SSB Teams are available for comment through February 28 and March 1, 2002 respectively. Beginning in March 2002, proposed guidelines from the Oncological Sciences SSB Team will be available for comment.

At its meeting, the Surgery, Applied Imaging and Applied Bioengineering SSB Team raised fundamental questions about following the PSBR recommendation to distribute applications to be reviewed in its IRG according to their organ system or disease focus. These questions require additional thought and deliberation, and will be discussed by the CSR Advisory Committee at its meeting on January 28-29, 2002. Following that meeting, we will inform the scientific community of progress in designing new study sections in the Surgery, Applied Imaging and Applied Bioengineering IRG via our Web site.

Redesign of the CSR Web Site

Redesign of CSR's Web site is nearly complete. I was recently given a preview tour of the site that left me impressed with how much the user experience has been improved. We have reorganized the content, redesigned the look and navigation, and added a helpful new search tool. I encourage you to look for the launch of the new site in a couple of months at http://www.csr.nih.gov.

Applications on CD

In a pilot program that has been very well received by test study sections, CSR has been scanning applications and distributing copies to reviewers on CD. The lightweight and extremely mobile CDs replace the cumbersome paper copies of unassigned applications usually sent to reviewers. Scanned applications on the CD are in "smart" pdf format, have the quality equivalent to black and white photocopies, and are bookmarked for easy navigation and reference. Assigned applications are still sent as high-resolution paper copies. Reviewers who bring their laptops to meetings can refer to the scanned applications on the CD, while members who do not bring a laptop are supplied paper copies at the meeting. In the June/July 2002 review cycle, three more IRGs will be added to the program. CSR hopes to make CDs available to all study sections by the end of 2002.

Internet Assisted Peer Review

CSR is dedicated to making the review process efficient. To this end, we have implemented a Web-based system for retrieving reviewer critiques prior to the study section meeting. Reviewers post their critiques and initial scores by a deadline set by the Scientific Review Administrator (SRA). Sometime after the deadline, the curtain is raised and all study section

members who have posted critiques can read the comments and scores of other members online. Members are blocked from reading critiques and scores of applications with which they are in conflict and also are blocked from reading critiques for their assigned applications if they have not posted their own reviews.

About 77 study sections used the system during the October/November 2001 review round. This number will increase during the February/March 2002 round to include approximately 136 out of 155 large study sections. If your study section has not yet been given access to the new Internet Assisted Peer Review System, it will very soon.

Ellie Ehrenfeld, Director, CSR

New Personnel at CSR

CSR continues to actively recruit SRAs to fill new and vacant positions.

Dr. Randolph Addison is the new SRA for the SSS-U Study Section that reviews small business, shared instrumentation, and other grant applications focused on innovative microscopic instrumentation and techniques. Dr. Addison received his Ph.D. in biochemistry from Cornell University. He recently was an associate professor of biochemistry and molecular biology at Georgetown University.

Dr. William Benzing has become the SRA of the Brain Disorders and Clinical Neuroscience 2 Study Section. He comes to CSR from Gliatech, Inc., in Cleveland, where he was a senior project leader. Dr. Benzing received his Ph.D. in neurosciences from the University of California in San Diego.

Dr. Joyce Gibson is the new Chief of the Cardiovascular Integrated Review Group. She will also serve as the SRA of the Pharmacology Study Section. Dr. Gibson recently was the Executive Director of Metabolic and Cardiovascular Diseases Research at Novartis Pharmaceuticals Corp. in Summit, New Jersey. She received a M.Sc. and D.Sc. in nutrition from Harvard University.

Dr. Mary Ann Guadagno is now the SRA for the Epidemiology and Disease Control 3 Study Section. She comes to CSR from the National Institute on Aging, where she coordinated grant reviews for its Behavior and Social Science of Aging Review Committee. Dr. Guadagno received a Ph.D. in economics from The Ohio State University.

Dr. Peter Perrin has become the SRA for the new fellowship study section (F-10) that evaluates fellowship applications related to basic and clinical aspects of respiratory, cardiovascular, digestive, and renal systems. Dr. Perrin was an assistant professor of medicine in the Department of Medicine at the University of Pennsylvania in Philadelphia. He also earned his Ph.D. there in parasitology.

Dr. Luci Roberts is the new SRA for the Behavioral and Biobehavioral Processes 1 Study Section. She recently conducted research in the Laboratory of Comparative Ethology at the National Institute of Child Health and Human Development. She earned her Ph.D. in zoology from the University of Maryland in College Park.

Dr. Sherry Steusse was hired to become the new SRA of the Brain Disorders and Clinical Neuroscience 5 Study Section. She currently is managing the Brain Disorders and Clinical Neuroscience Fellowship Study

Section. Dr. Steusse was a professor in the Neurobiology and Pharmacology Department at Northeastern Ohio Universities College of Medicine.

Dr. Denise Wiesch has moved to CSR to be the SRA of the Epidemiology and Disease Control 2 Study Section. She comes from the National Institute of Allergy and Infectious Diseases, where she was a program officer in its Division of Allergy, Immunology, and Transplantation.

Working Group Reviews of CSR Integrated Review Groups

In September 1998, the CSR Advisory Committee recommended that CSR form Working Groups to evaluate the organization, management, and leadership of its Initial Review Groups (IRGs) and their study sections. In developing these Working Groups, CSR sought active, widely respected researchers in disciplines related to those reviewed by the IRGs. Over the course of the past 2 years, Working Groups have evaluated all 19 IRGs and submitted their reports to the CSR Advisory Committee. These reports and CSR's responses are summarized below.

Scope and Breadth of the Science Reviewed

The Working Groups acknowledged the impact workload has on a study section's effectiveness. Study sections that reviewed 60 to 80 applications per review cycle tended to have the optimal levels of responsibility and scope. Review quality and reviewer morale suffered when study sections reviewed more than 90 or less than 50 applications. The Working Groups, however, noted that some study sections with the preferred workload suffered because they were fragmented and operated like two or three small study sections or covered too wide or narrow an area of science.

Working Groups suggested that at least five IRGs be examined for overlap, workload balance, or cohesiveness of the areas covered, i.e., the three neuroscience IRGs, the Endocrinology and Reproductive Sciences IRG, and the Nutritional and Metabolic Sciences IRG. The Working Groups also focused on scientific areas that were emerging, declining, or in need of clustering. They noted a need to cluster clinical research, muscle biology research, and lipid/lipoprotein research. Informatics, proteomics, and genomics research were also recognized as emerging fields that CSR needs to address.

Many Working Group recommendations and concerns are being addressed by the CSR Study Section Boundary Teams as they reorganize the IRGs. CSR, however, has already responded to some recommendations by creating new study sections and adjusting the scientific boundaries of existing sections. The Pathology C Study Section was added to the Oncological Sciences IRG, and a new muscle biology study section was created. The boundaries of the Molecular, Cellular and Developmental Neuroscience study sections also were adjusted, and additional adjustments have been made in a number of other IRGs.

Appropriateness, Qualifications, and Stature of the Reviewers

With few exceptions, the Working Groups found reviewer expertise, qualifications, and fairness to be outstanding. Nevertheless, they noted that many study sections could benefit from the participation of more senior reviewers, clinicians, women, and

minorities. CSR also was encouraged to offer reviewers greater incentives, such as extensions to their current funding or more flexible terms of service.

Modifying funding periods requires Institute approval, and the NIH Directors have been reluctant to embrace this proposal because of the cost and the principle of only funding peer reviewed research. CSR, however, is working with the Acting NIH Director and her Committee Management Office to modify the current appointment structure. Proposals include establishing more flexible service terms; developing a new, limited service category for senior reviewers; and establishing new recruitment strategies to help CSR address its diversity needs.

Policies, Procedures, and Management of the Meeting

The Working Groups acknowledged the usefulness of CSR's orientation materials and pre-meeting presentations. They suggested, however, that the Chairs and SRAs provide new and temporary reviewers additional training on (1) preparing a critique, (2) de-emphasizing their focus on methodological details, (3) scoring applications, and (4) critiquing applications effectively during the meeting. They also suggested that CSR explore ways to provide Chairs additional training in the art of group dynamics and consensus building as well as in the practice and policies of peer review.

The Working Groups found it excessive to assign a reviewer more than 10 written reviews or more than a total of 14 written and reading assignments. Study section meetings with more than 30 reviewers were also seen as problematic.

Opinions varied on the policy and process of "not scoring" applications, and some Working Groups encouraged CSR to revise this practice. The Working Groups, however, were unanimous in their dislike of modular budgets. The lack of a budget justification was particularly problematic. CSR has discussed modular budgets with the NIH Office of Extramural Research and has been advised that this policy will be evaluated soon.

CSR has developed a Best Practices document for SRAs that includes a wide range of meeting management advice, including guidance on making reviewer assignments. In December 2001, CSR began work on developing an SRA guide for training new and temporary reviewers. CSR also is exploring training options for study section Chairs.

To address concerns about "not scoring" applications, CSR is considering (1) relying more on the electronic review module, (2) having a brief study section discussion on the weakness of these applications, or (3) allowing reviewers to informally share their thoughts on these applications at the beginning of the meeting.

Accommodation of New Directions and Emerging Areas

The Working Groups described many applications as innovative, but few were considered novel or high impact/risk. While Working Group members generally felt these applications were reviewed appropriately, they noted that newer or less experienced reviewers tended to dwell unnecessarily on methodological concerns. As noted above, CSR is developing procedures for training new reviewers that cover the elements of an effective critique.

Fairness of Reviews for all the Grant Mechanisms

The Working Groups examined the review of regular R01, AREA (R15), Fellowship and Exploratory (R21) applications, and applications from new investigators. There was a strong consensus that these applications receive appropriate review, but it was suggested that clustering them within the study section or moving some of them to a separate review group could enhance their peer review.

Beginning in October 2001, all Fellowship applications will be reviewed in dedicated Fellowship study sections. SRAs have been advised to cluster the review of other applications (i.e., new investigator applications, R15s, and R21s). Clustering, however, may not always be possible, due to the schedules of reviewers and program staff who may not be able to attend the entire meeting.

In summary, the 19 Working Groups have made a number of valuable observations and suggestions. CSR has already acted on many of these and is working to address the others. A more detailed summary of the comments of the Working Groups is available on the CSR Web site: http://www.csr.nih.gov/NewsFlash/newsflash.htm.

Delivery of Grant Applications and Other Materials to NIH

The events of last fall have led to increased security concerns at NIH and the implementation of a number of new practices. The receipt of 47,000 grant applications, thousands of progress reports, and other related materials each year pose particular challenges.

Effective November 13, 2001, all grant applications and other deliveries addressed to the CSR must come via the United States Postal Service (USPS) or a recognized courier, such as FEDEX, UPS, DHL, etc. Individuals may no longer personally deliver grant applications to the Rockledge II Building. Several Institutes and Centers have published notices in the *NIH Guide to Grants and Contracts* indicating that they also will no longer accept personal deliveries for copies of responses to Requests for Applications, contract proposals, and other materials.

All USPS mail addressed to NIH must use the unique NIH zip code: 20892. Courier deliveries to the Rockledge II Building need to use the zip code 20817. All USPS mail addressed to the National Library of Medicine must use its unique zip code: 20894. Mail addressed to the National Institute of Environmental Health Sciences in North Carolina should use the zip code 27709. For type 5 progress reports, the USPS mailing label included with the face page of the report should be used. If a type 5 progress report is to be delivered by courier, the geographic zip code provided by the Institute/Center should be used.

The cooperation of applicant and grantee institutions is greatly appreciated as NIH implements additional screening procedures. These are important security measures to provide for the safety of all individuals who handle mail. Further details can be found in the *NIH Guide to Grants and Contracts* announcement of November 12, 2001: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-012.html.

New Instructions For Evaluating Grant Applications Involving Human Subjects

In June 2001, NIH adopted a definition of clinical research that includes the following: (1) Patient-oriented research, that is, research conducted with human subjects (or on material of human origin, such as tissues, specimens, and cognitive phenomena) in which an investigator (or colleague) directly interacts with human subjects. (Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual.) (2) Epidemiologic and behavioral studies. (3) Outcomes research and health services research.

To address concerns noted in a recent study by the General Accounting Office, NIH has revised applicant requirements and reviewer responsibilities for proposals involving clinical research. Beginning in February 2002, each project within an application involving human subjects must be evaluated, and an evaluation must be included in each reviewer's critique under the following five headings: (1) Protection of Human Subjects From Research Risks, (2) Data Safety and Monitoring Plan, (3) Inclusion of Women Plan, (4) Inclusion of Minorities Plan, and (5) Inclusion of Children Plan.

Protection of Human Subjects From Research Risks

Applications involving human subjects should be evaluated for how well they address (1) risks to subjects, (2) adequacy of protection against risks, (3) potential benefits of the proposed research to the subjects and others, and (4) importance of the knowledge to be gained. This evaluation is independent of any other evaluation, and it is important to note that NIH no longer requires Institutional Review Board approval at the time of peer review. If an application indicates that the proposed research is exempt from human subjects regulations, reviewers should determine whether the information provided justifies an exemption. This section may also be used to communicate issues related to the inclusion of human subjects, which are not serious enough to cause a concern.

Data Safety and Monitoring Plan (required only for clinical trials)

Applications to conduct clinical trials should be evaluated for how well they follow the principles of data and safety monitoring. All biomedical and behavioral clinical trials must be monitored to ensure that they are conducted safely and effectively and to recommend conclusion of a trial if significant benefits or risks are identified or if it is unlikely that the trial will be concluded successfully. Risks associated with participation in research must be minimized to the extent practical, and the method and degree of monitoring should be commensurate with risk.

Inclusion of Women and Minorities Plans (required for all clinical research)

Applications to conduct clinical research also should be evaluated for how well they address requirements for the inclusion of women and minorities. All NIH-supported biomedical and behavioral clinical research projects involving human subjects must include women and minorities unless a clear and compelling justification is provided showing that inclusion would be inappropriate or detrimental to the health of the subjects or the purpose of the research. Applications proposing an NIH-defined phase-III clinical trial must also include plans to conduct valid analyses to detect significant differences in the effect of the intervention in different subpopulations.

Reviewers are therefore asked to evaluate separately the inclusion plans for women and minorities by addressing the following questions.

Inclusion Plan: Does the applicant propose a plan for appropriate representation? How does the applicant address the inclusion of women and minorities and their subpopulations in presenting a research design appropriate to the scientific objectives of the study? Does the research plan describe the composition of the proposed study population in terms of sex/gender and racial/ethnic groups? and does it provide a rationale for selection of such subjects?

Exclusion: Does the applicant propose an exclusion of minorities or women when representation is limited or absent? Does the applicant propose an exclusion by showing that inclusion would be inappropriate or detrimental to the health of the subjects or the purpose of the research?

Analysis Plans: (NIH-defined phase-III clinical trials) Does the research plan include either (1) an adequate description of plans to conduct analyses to detect significant differences of clinical or public health importance in intervention effect by sex/gender and/or racial/ethnic subgroups when the intervention effect(s) is(are) expected in the primary analyses, or (2) an adequate description of plans to conduct valid analyses of the intervention effect in subgroups when the intervention effect(s) is(are) not expected in the primary analyses?

Inclusion of Children Plan

Finally, children (individuals of *all* ages under 21) must be included in all research involving human subjects, including research that is "exempt," unless there are scientific or ethical reasons not to do so. Reviewers are asked to evaluate the acceptability of the proposed plan for including children or the justification for not including them. Attention should be paid to the appropriateness of the population studied in terms of the aims of the research, ethical standards, all applicable Federal laws and regulations, the expertise of the investigative team in dealing with children at the age(s) included, and the appropriateness of the facilities.

Additional information on the review of grant applications having a human subject component is available at the following NIH Internet address: http://grants.nih.gov/grants/peer/hs_review_inst.pdf.

Human Embryonic Stem Cells

Over the past year, there have been a number of changes in NIH policy regarding grant applications proposing the use of human embryonic stem cells (HESCs). The most recent policy announcement was published in the *NIH Guide to Grants and Contracts* on November 7, 2001: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html.

HESC research applications may only be considered for Federal funding if the cell line proposed for use is listed on the NIH Human Embryonic Stem Cell Registry: http://escr.nih.gov. Cell lines on this registry are in compliance with the criteria established by the President on August 9, 2001. HESC research applications must specify the particular cell line to be used and include the NIH identification number in their description section (often called the abstract).

Requests for administrative supplements to expand a research project to study HESCs

should be discussed with project officers and will be handled according to the usual procedures for each Institute and Center. These applications also need to identify the cell lines on the HESC Registry that are to be used. Grantees who wish to rebudget existing funds may do so but are also limited to the cell lines that are in the HESC Registry.

For the most current information about policies involving HESCs, investigators should consult the Stem Cell Information Page: http://www.nih.gov/news/stemcell/index.htm.