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August 7, 2006

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During the current funding period, the GCRC has continued to provide resources and support to over 250 subprojects, over 600 investigators, and over 60 academic departments and divisions within the School of Medicine. Together, these GCRC-supported investigators received over \$191 million in PHS funding, demonstrating our Center's continued commitment to furthering NIH-supported clinical research.

Our latest Annual Report details the Scientific Achievements and productivity of our previous funding year, including a bibliography of 111 publications arising out of research conducted on the GCRC.

Scientific highlights of Grant Year 44 included significant publications in the areas of drug addiction, cardiovascular risk assessment, transverse myelitis, community nursing, HIV/AIDS, Neurofibromatosis, and ADHD.



From the Program Director

Christopher D. Saudek, M.D., is on vacation. Look for his comments in a future issue of *On the Research Subject*.



From the Vice Dean for Clinical Investigation

Organization Policy on Pharmacy and Therapeutics Committee and JHM IRB (Policy No. 103.19) Version 2 and WIRB Review
by Daniel E. Ford, M.D., M.P.H.

The Organization requires review and approval by a representative of the Pharmacy and Therapeutics (P&T) Committee for any use of drugs, biologics, or complimentary and alternative medicines (CAMs) in a research protocol prior to final JHM IRB action on a protocol. This objective will be accomplished by ensuring that every JHM IRB that reviews drug research has as a member an individual who is also a member of the P&T Committee. When a JHM IRB assigned P&T



Current Issues in the GCRC

A GCRC Progress Report
by Gerald Stacy, Administrative Manager

member must be absent from a meeting, either a P&T member from another JHM IRB can be designated as an alternate to serve this function or the P & T member may provide his/her comments to the chair prior to the meeting. The P&T IRB members will provide information to the P&T Committees of the three Organization hospitals (JHH, JHBMC, and HCGH) to assure proper communication regarding drug research approved for conduct at the Hospitals.

WIRB Review of Protocols

As of July 1, 2006, SOM faculty have the option of submitting all new applications to the JHM IRBs for review, regardless of the source of support for the project. Effective January 1, 2007, all new applications for human subjects' research must be submitted to the JHM IRBs for review. We will no longer have WIRB review new protocols. JHM IRB initial review fees of \$2000 and continuing review fees of \$1000 will be charged against the applicable study budget. We will not charge for amendments. We will continue our contractual relationship with WIRB as they will continue to review amendments, change in investigators, continuing reviews, etc. for studies originally approved by them. During the transition we will carefully monitor review times of the IRB Committees and make changes to the process if necessary. To read more about the rationale for this decision go to our website, <http://irb.jhmi.edu/ChangesinWIRBReview.html>



Ask the RSA

*The Office of Human Subjects Research
Compliance Monitoring Program*

by Susan Bonura, RSA

The compliance monitoring program conducted by the Office of Human Subjects Research began in June 2004. Approximately 90 IRB approved protocols have been reviewed by the compliance

monitors since that time. But what is compliance monitoring?

Compliance is adherence to all trial-related requirements, Good Clinical Practice (GCP) requirements and applicable regulatory requirements. Monitoring is the act of overseeing the progress of a clinical trial and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, GCPs, Standard Operating Procedures (SOPs), and applicable regulatory requirements.

The goals of the monitoring program are:

- (1) to assure that human subject rights and safety are protected according to GCP,
- (2) to verify conformity with regulatory and institutional requirements for JHM-IRB and WIRB approved protocols,
- (3) to gauge study progress in between a study's initial approval and the continuing review cycles, and
- (4) to serve investigators by providing education on regulatory requirements and GCP.

The monitoring program is intended to provide a "snap-shot" of the daily operation of selected studies and an evaluative summary about the selected study's progress. The information gathered through the program is provided to the IRB and the Vice Dean for Clinical Investigation. Suggestions based upon the findings are provided to the Principal Investigator and the study team.

A study's conformity with applicable regulatory requirements is evaluated by the monitoring team and includes the requirements of the Institution (JHM-IRB), the WIRB (if applicable), the government (FDA, DHHS), and the Sponsor (NIH or commercial). The monitoring team verifies that all IRB, Federal and Sponsor required documentation is present and includes approved informed consent forms, IND annual reports and drug accountability information and prompt reporting of adverse events to NIH.

The compliance monitoring program assess attention to human subject safety requirements by observing and evaluating the principal investigator's and the study team's adherence to: the approved consent process; proper screening and enrollment of eligible subjects; use of a data and safety monitoring plan, if required; appropriate and prompt reporting of unanticipated problems and protocol changes; and documentation of protocol procedures in the subject record and data collection forms.

In addition, the program evaluates studies for regulatory and procedural compliance by observing the enrollment rate, consent process and signed/dated consent forms, assessment of inclusion and exclusion criteria, protocol consistency, data collection, event reporting and presence of source documentation.

The program provides education and assistance to the PI and study personnel in the areas of document organization, corrective action plans, quality improvement mechanisms, SOP development, and general regulatory guidance and GCP.

The following general steps are followed in the monitoring process:

1. a study is chosen from the IRB active studies database,
2. the regulatory and subject information are inspected,
3. observations are written in a summary report,
4. the PI is offered recommendations for corrective action plans or quality improvement,
5. the report is reviewed by the Vice Dean of Clinical Investigation, the Assistant Dean of Human Subjects Research Compliance, and the IRB that approved the study.

You may contact the compliance monitoring team at the office of the JHM-IRB at 410-955-3008. The monitors' offices are located in Reed Hall, Suite B-130. The monitors, Jenna Schulcz, Lea

Olverson and Fred Luthardt may also be contacted via email at jschulc1@jhmi.edu, lolvers1@jhmi.edu and fluthard@jhmi.edu.



Creating a DSMB Charter

Creating a DSMB Charter

by Jeannette Cooke, RSA Assistant

Data and Safety Monitoring Board (DSMB) charters pre-specify the standard operating procedures for the DSMB members. The charter and membership of any DSMB must be included in the Data and Safety Monitoring Plan (DSMP) of any protocol conducted on the GCRC that includes a DSMB⁽¹⁾.

Current regulations impose no requirements on the specific content of DSMB charters. The following sections are commonly seen in DSMB charters received in the GCRC and published charter templates (see the resource list below for information on accessing published charter templates). [Please note this list is not exhaustive and is only meant as an example of the possible sections that could be in a DSMB charter. These sections are not required; the author of the study-specific DSMB charter should use their judgment in determining whether the design and risk of the study warrants the inclusion of these sections.]

- **Title page** – study title, study number, principal investigator, sponsor, date of charter
- **Table of contents**
- **Introduction** – brief description of the study and reason for establishing the DSMB
- **Primary responsibilities/objectives of the DSMB**
- **DSMB membership** – description of the composition of the DSMB, contact information for the members and chair of the DSMB, voting status of each member,

conflicts of interest, confidentiality, and DSMB chair responsibilities

- **DSMB meetings** – description of the frequency, venue (such as in person and/or conference call), and character (such as open and/or closed) of the meetings
- **Reports to the DSMB** – description of the format and content of the reports, who will prepare the reports, and method of distribution
- **DSMB minutes** – description of the format and expected content of the minutes, who will prepare the minutes, and method of distribution
- **Statistical methods** – description of the monitoring procedures that will be used by the DSMB to guide their recommendations regarding terminating and continuing the study
- **Document retention** – description of the types of documents to be kept, where these documents will be kept, who will keep the documents, and what will be done with the documents after the study has ended

Reference:

- 1) National Center for Research Resources, National Institutes of Health, Department of Health and Human Services, Division for Clinical Research Resources, Program Guidelines, October 2005, http://www.ncrr.nih.gov/clinical/DCRRguidelines2005/GCRC_Guidelines_October2005.pdf

The following resources provide information, examples of guidance, and templates on the establishment and operation of clinical trial data monitoring committees:

DAMOCLES Study Group. (2005). A proposed charter for clinical trial data monitoring committees: helping them to do their job well. [Electronic version]. *The Lancet*, 365, 711-722.

<http://www.abdn.ac.uk/hsru/documents/damocles2.doc>

<http://www.abdn.ac.uk/hsru/documents/damocles-charter.doc>

Grant A.M., Altman, D.G., Babiker, A.B., Campbell, M.K., Clemens, F.J., Darbyshire, J.H., et al. (2005). Issues in data monitoring and interim analysis of trials. [Electronic version]. *Health Technology Assessment*, 9(7).

Ellenberg, S.S., Fleming, T.R., & DeMets, D.L. (2002). *Data Monitoring Committees in Clinical Trials: A Practical Perspective*. West Sussex, England: John Wiley & Sons Ltd.

<http://www.niams.nih.gov/rtac/clinical/DSMBCharter.htm>

<http://www.fda.gov/OHRMS/DOCKETS/98fr/01d-0489-gdl0002.pdf>



Helpful Hints for Successful Protocol Approval

Current Hints

by Shernice Madison, Administrative Assistant

- Be sure to download the latest GCRC application which is available on the web at <http://www.hopkinsmedicine.org/gcrc/>.
- Submission deadlines are available on the GCRC website.
- Submit the application along with the required supporting documents and forms. Details are listed in the *Application Process* section of the website.
- Call the GCRC office with any questions about the application form or process prior to submission. The GCRC number is 410-614-2717.
- Indicate that you will be using the GCRC when you complete the eIRB application.



Criteria for CHR Review and Approval of New and Continuing Human Subjects Research

Federal regulations lay out specific criteria for IRB review and approval of new and continuing human subjects' research. To assist researchers, and to facilitate the review process, Committee on Human Research (CHR) has developed guidance on the preparation and submission of research applications, including forms, instructions and checklists, that help to ensure that applications provide all of the information and documentation required for review.

For complete information, see the CHR website at <http://www.jhsph.edu/CHR/PolicyGuidelines>.



The Office for Human Research Protections (OHRP) and Duke University School of Medicine will sponsor a National Human Subject Protections Conference entitled, "*Crossing the Line: What is Acceptable Risk?*" on Monday, September 25 and Tuesday, September 26, 2006, at the Sheraton Imperial Hotel and Convention Center in Durham, North Carolina. Co-sponsors of the conference are the University of North Carolina at Chapel Hill, North Carolina State University, Family Health International, RTI International, National Institute of Environmental Health Sciences, Copernicus Group IRB, U.S. Environmental Protection Agency, and Department of Veterans Affairs.

This conference will focus on the concept of "acceptable risk" in the conduct of biomedical and behavioral research. Topics during this two-day conference will include the risks associated with

research on environmental hazards in emergency research and in psychiatric studies, including the use of placebos in study design and continuing assessment of subject competency and the effects of recent information concerning anti-depressants on the design of psychiatric studies. Breakout sessions will focus on risks particular to vulnerable populations. The faculty will include academic experts who will address key topics and issues in biomedical and behavioral research. In addition, representatives from the OHRP, U.S. Food and Drug Administration, National Institutes of Health, National Institute of Environmental Health Sciences, U.S. Environmental Protection Agency, and Department of Veterans Affairs will provide federal regulatory updates.

Topics during the conference will include a variety of learning opportunities for all those interested in the protection of human research participants and include:

- Additional risks posed in research involving vulnerable populations such as children, prisoners, and students
- The best means of communicating risk within the informed consent process
- Special considerations in genetic testing, web-based research, psychiatric studies and international research
- HRPP accreditation, use of central IRBs, and the impact of media coverage of research and clinical trials.

This conference should be of special of interest to those persons currently serving or about to begin serving as members of IRBs as well as investigators, legal counsel, patient advocates, public health officials, privacy officials, compliance officers, laypersons, sponsors and contract research professionals.

For further information, contact Faten Habib, Duke University School of Medicine, Durham, NC. Phone: 919-668-5104, Fax: 919-668-5125, Email: habib003@mc.duke.edu



FDA News

For the latest in FDA news, visit their homepage at <http://www.fda.gov/>.



WIRB Protocol Deviations & Violations/Unanticipated Problems Reporting System

Federal Regulation 21CFR 56.108(b)(1) requires the IRB to "follow written procedures for ensuring prompt reporting to the IRB...of...Any unanticipated problems involving risks to human subjects or others..." Therefore, the WIRB provides two reporting forms: the Protocol Deviations and Violations/Unanticipated Problems Reporting Form and the Protocol Deviations/Violations Log. A full explanation of these forms can be found on the WIRB website: http://www.wirb.com/shell.php?content=content/qquick_protocol_variances.



Good Clinical Practices

The Association of Clinical Research Professionals (ACRP) is hosting a seminar on *Good Clinical Practices*. The seminar will be held November 3 and 4 in Arlington, Virginia and offers 16.5 contact hours.

You can register on the web at: <http://www.acrpnet.org/education/gcp/index.html>.



News from the NIH Office of Biotechnology Activities

New Informational Brochure Available for Potential Participants in Gene Transfer Research -- Potential research participants, as well as those who enroll participants in trials - such as investigators and trial coordinators - may be interested in a new brochure that OBA has developed to assist in decisions regarding participation in human gene transfer research. The brochure titled "Deciding whether to participate in human gene transfer research?" helps potential participants understand fundamental concepts in gene transfer research and suggests questions they should pose to their physicians and to research staff in order to make a fully informed decision about participation.

Up to 50 brochures are available free of charge from OBA. Requests can be sent to OBA by email at: oba@od.nih.gov. Please provide a full mailing address and specify the number of brochures desired. Alternatively, the brochure is available in PDF format from the Informed Consent resource page on the OBA website, <http://www4.od.nih.gov/oba/rac/ic/index.html>.





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