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implement what we thought best. As a result, the 80 or so GCRCs around the country are experimenting with a wide variety of configurations, among them, full-time or part-time RSAs who are IRB chairs or former chairs, physicians, nurses, or investigators.

We decided to build an RSA program around a full-time, non-faculty staff member with experience in overseeing clinical trials and in dealing with human subjects' issues. We wanted an RSA who would work closely with the IRB, but not be on it. We also wanted someone who would work closely with the GCRC administration, but report directly to the principal investigator to maintain independence.

Susan Bonura turned out to be our person. To facilitate communications with faculty investigators and provide oversight, we decided to have two experienced faculty investigators (Drs. James Casella and Wendy Post) act as RSA Advisors.

From my perspective at least, the RSA program here has been a great success. Susan has more than met expectations, being thoroughly committed to seeing that every proposed protocol meets human subjects standards in substance and in documentation. She labors over each protocol before our Advisory Committee review, discusses human subjects' issues at the review, and oversees the subsequent resolution of issues raised. She also keeps track of amendments, IRB approval status, and myriad details as studies progress. Jeannette Cooke, Susan's assistant, has provided another level of competence and productivity.

Kudos also to Drs. Casella and Post who continue to meet on a regular basis as an RSA team. They have played their roles beautifully,



From the Program Director

The Research Subject Advocate Program

by Christopher D. Saudek, M.D.

The Research Subject Advocate (RSA) program has been up and running for 3 years now, so it is worth taking stock.

The NIH's NCCR, our funding institute, provided little definition to the RSA position. We were left from the onset to define and

helping Susan with the sometimes confusing intricacies of academics and clinical research, and interfacing with faculty as necessary.

Finally, a “thank you” to our soon-departing Principal Investigator, Michael Klag. He has been supportive and involved in the RSA program as well as other aspects of GCRC activity. We will miss him as he moves across the street and up a few levels!



Current Issues in the GCRC

A Brief Update

by Gerald Stacy
Administrative Manager

During the current funding period, the GCRC has provided resources and support to approximately 270 subprojects. Our latest Annual Report details the Scientific Achievements and productivity of our previous funding year, including a bibliography of 146 publications arising out of research conducted on the GCRC.

Scientific highlights of Grant Year 43 included significant publications in the areas of AIDS/HIV, ophthalmology, neuroscience, pharmacology, geriatrics, diabetes mellitus, alcoholism, endocrinology, genetics and pulmonology.



Accountability in Research Studies

by Jared Christopher, RN
Program Manager, GCRC-OPD

Accountability in research at JHU is analogous to accountability at JHH. Ultimately, all responsibility lies with the Principal Investigator (PI), just as it does with the Attending in the hospital setting.

Whenever there is a patient occurrence, no matter how small, the PI or his/her designee must address it. For example, when patients or subjects have adverse drug reactions, the PI will be immediately notified by the primary nurse. At that point, the subject must be physically evaluated by the investigator or designee.

In another example, if a subject falls or has another physical mishap, the PI must attend to it. Perhaps the incident is reported to you as one in which the subject seems fine, and you may wish to take the nurse's word for it. As we are all busy, that is a very tempting reaction. However, no Registered Nurse or research assistant in this institution is as qualified to evaluate the patient during a physical incident or a drug interaction as is the PI. This is reasonable. You are the person who knows the most about the study, perhaps even with singular insight as to side effects and pharmaceutical issues of which a support person could not possibly have knowledge. We have excellent nurses and support persons in this Institution, but their training is no substitute for the training of a physician.

It is also important, in your absence, that the designee understands that the ultimate responsibility for the study is yours. Likewise, it is also important that that person has a genuine

interest in the preservation of the integrity of your study, as well as your license. So, it behooves all of us to select our designees with care. Patient safety, study integrity and our licenses are at stake.

We hope this reminder will help you to protect yourself at all times. The integrity of your studies and the safety of your subjects, along with protection of your practice are paramount. We thank you for continuing to work with us in ways which benefit us all.



From the Vice Dean for Clinical Investigation

**Accreditation Granted by the Association
for the Accreditation of Human Research
Protection Programs (AAHRPP)**

by Michael J. Klag, M.D., M.P.H.

Johns Hopkins Medicine has received full accreditation by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). The site visitors could not have been more laudatory about the outstanding commitment of the institution, IRB chairs and members, staff and researchers to the protection of research participants. They recognized the extraordinary strides that we have made and the dedication to excellence that pervades all of our efforts. In awarding accreditation, the AAHRPP council agreed and indicated that we have a "stellar" program. This is a wonderful achievement!

A review of the AAHRPP web site (<http://www.aahrpp.org/www.aspx>) indicates that few organizations have passed this very high bar. This achievement is possible because the organization provided the necessary resources, we had the right people--Barbara Starklauf and Judith Carrithers, especially--and faculty and

staff were willing to go to any length to do the right thing. It is a fitting tribute to everyone's hard work and we should all feel pleased.

Thank you for your commitment to research participant protection.

Paul Lietman Steps Down as IRB 3 Chair

Dr. Paul Lietman stepped down as chair of IRB 3 effective June 30, 2005, the end of his term. Paul has contributed to our IRBs for many years, first as a member of JCCI and, since summer 2001, as chair of IRB 3. He has brought to this work an impressive commitment to research oversight, advocacy for research, and expertise in drug development. We are deeply grateful to Paul for his many contributions and hope faculty will join us in thanking Paul for all he has done.



Ask the RSA

Good Clinical Practice: Informed Consent of Trial Subjects

by Susan Bonura, RSA

As the Research Subject Advocate, I have observed the consenting of numerous research subjects. The consent processes for these volunteers were conducted by any one of several persons authorized by the IRB to do so, including principal investigators, co-investigators, research nurses or research coordinators. In some instances the entire consent form was read verbatim to the subject while in other situations, each section of the consent form was discussed, but not read. Others conducting the consent process gave little explanation as to the research being conducted, the procedures being done, the risks of participation, nor other important aspects of the

research. These consents were conducted in private rooms and busy corridors and lasted anywhere from 5 minutes to 3 hours.

According to Guidelines for Good Clinical Practice (GCP), "The investigator, or a person designated by the investigator, should fully inform the subject or, if the subject is unable to provide informed consent, the subject's legally acceptable representative, of all pertinent aspects of the trial including the written information given approval/favorable opinion by the IRB/IEC."

The GCP also state, "If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial, and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative."

"Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:

- (a) That the trial involves research.
- (b) The purpose of the trial.
- (c) The trial treatment(s) and the probability for random assignment to each treatment.
- (d) The trial procedures to be followed, including all invasive procedures.
- (e) The subject's responsibilities.

(f) Those aspects of the trial that are experimental.

(g) The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.

(h) The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.

(i) The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks.

(j) The compensation and/or treatment available to the subject in the event of trial-related injury.

(k) The anticipated prorated payment, if any, to the subject for participating in the trial.

(l) The anticipated expenses, if any, to the subject for participating in the trial.

(m) That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.

(n) That the monitor(s), the auditor(s), the IRB/IEC, and the regulatory authority(ies) will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.

(o) That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.

(p) That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.

(q) The person(s) to contact for further information regarding the trial and the rights of

trial subjects, and whom to contact in the event of trial-related injury.

(r) The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.

(s) The expected duration of the subject's participation in the trial.

(t) The approximate number of subjects involved in the trial.”

The following tips can be applied in order to conduct a good consent procedure: (1) use the IRB-approved consent form as a template to guide the discussion and to ensure that all elements of the consent form are discussed, (2) the complete details of the project should be provided in both written and verbal formats with ample opportunity for questions and answers, (3) participants should be given the opportunity to read the entire consent form and to ask any questions before they sign the document, and (4) during the course of the study, provide ample opportunities for participants to ask additional questions and to have any aspect of the project re-explained to their satisfaction.

The complete GCP can be found on the Food and Drug Administration web site: <http://www.fda.gov/cder/guidance/959fnl.pdf>.



Helpful Hints for Successful Protocol Approval

What happens after Review of your Protocol by the Subcommittee?

by Shernice Madison, Administrative Assistant

Each month the GCRC receives an average of 12 new studies for review. This includes adult, pediatric, NBRU, oncology and ACTG protocols. Each of these protocols is

accompanied by a GCRC application and human subjects section. These documents are included on the agenda for the next scheduled protocol review committee meeting and are assigned primary, secondary and statistical reviewers. All of these studies are reviewed by the Research Subject Advocate (RSA).

The reviewers present their comments, both written and oral, at the appropriate protocol review subcommittee meeting. There are several possible conclusions of the discussion held on each protocol: (1) scientific approval of the study as submitted; (2) scientific approval with an administrative deferral; (3) scientific deferral; or (4) disapproval.

If a study is not approved, the Principal Investigator is sent a letter which details the concerns of the committee. The PI is given an opportunity to respond and to submit revised documents, as applicable. There is no deadline for this response. However, some investigators do not respond in a timely manner and this creates an incomplete file in the GCRC.

If you have submitted a protocol which was not approved at its first review, please do us a favor and let us know whether or not you wish to have your protocol withdrawn from consideration. Thanks!



Children Involved as Subjects in Research: Guidance on the HHS 45 CFR 46.407 ("407") Review Process

The Office for Human Research Protections (OHRP) has issued guidance on the HHS 45 CFR 46.407 review process required under subpart D of the HHS Protection of Human

Subjects Regulations at 45 CFR part 46. In particular, OHRP offers guidance on the following topics: (1) IRB findings necessary to submit a protocol to OHRP for 407 consideration and/or review; (2) steps in the submission process; (3) OHRP's response to submissions; (4) the schedule and details for 407 panel review; and (5) potential outcomes of the 407 review process. This guidance, which applies to HHS-conducted or -supported research, can be found at:

http://www.hhs.gov/ohrp/children/guidance_407_process.html (HTML format) or http://www.hhs.gov/ohrp/children/Guidance_407_Process.pdf (PDF format)

Guidance on Reporting Incidents to OHRP

The Office for Human Research Protections (OHRP) has issued guidance on procedures institutions may use to file incident reports with OHRP. Incident reports include reports of unanticipated problems involving risks to subjects or others; serious or continuing noncompliance with Department of Health and Human Services (HHS) regulations at 45 CFR part 46 or the requirements or determinations of the institutional review board (IRB); and suspension or termination of IRB approval. In particular, OHRP offers guidance on the following topics: (1) Applicability of incident reporting requirements; (2) information to be included in incident reports; (3) time frame for reporting incidents; (4) OHRP focus on corrective actions when reviewing incident reports; and (5) OHRP's response to incident reports. This guidance can be found at: http://www.hhs.gov/ohrp/policy/incidreport_ohrp.html (HTML format) or http://www.hhs.gov/ohrp/policy/procedures_for_reporting_052505.pdf (PDF format).



OHRP Launches Public Outreach Campaign

The Office for Human Research Protections (OHRP) has launched a new public education campaign, *Taking Part in Research: It's Your Decision*. The goal of the campaign is to provide information about participating in clinical trials and other research studies.

The centerpiece of the campaign is a six-panel pamphlet that guides readers through a series of questions to consider as they discuss the option of participating in research with their health-care provider, family members, and others.

OHRP has distributed copies of the pamphlet to 6,000 research institutions throughout the country in order to gain broader access to local communities.

Bulk copies (up to 300 per requestor) are available free by calling **(800) 444-6472**.

A copy of the pamphlet, along with related information, is available at www.hhs.gov/ohrp/outreach. The pamphlet can be downloaded and reproduced locally.

"The advancement of healthcare and the development of new and better treatments depend on the participation of individuals in clinical trials," emphasized ACRP President and CEO Thomas L. Adams. "I commend OHRP Director Bernard Schwetz and his team in taking this vital message to the public, and encourage all ACRP members to order the pamphlets and put them into circulation."



Updated WIRB Forms

Several WIRB forms have been updated recently. Copies of the new forms are available on the *Download Forms* page at www.wirb.com. These forms may also be requested by contacting a WIRB Client Service Representative at 1-800-562-4789 or e-mailing clientservices@wirb.com.

The WIRB Initial Review Submission Form has been revised. Effective April 1, 2005, only the Initial Review Submission Form with the revision date of 01-2005 will be accepted (revision date of 01-2005 is located in the lower left hand corner of the form). This new version supersedes all previous Initial Review Submission Form versions and includes significant changes and updates.

The forms for reporting Adverse Events have been updated. Current versions are labeled 011305 in the lower left corner.

New forms and instructions for reporting Unanticipated Problems / Protocol Deviations & Violations are now available. Current versions are labeled 011305 in the lower left corner.

A new single submission form for requesting review of Changes in Research / Subject Recruitment Materials has also been posted.

Please be sure to use the current versions when submitting to WIRB.



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