



# Office of Human Research

**T**he OHR, located in Suite 1100, 1015 Chestnut St., provides administrative infrastructure and support for the following research programs and Committees:

- Division of Human Subjects Protection (Institutional Review Boards)
- Division of Clinical Trials Support
- Research Biosafety Program including the select agents program
- Institutional Biosafety Committee
- Volunteer Program

## **Division of Human Subjects Protection (DHSP)**

Thomas Jefferson University has four IRBs approved under its Federalwide Assurance (FWA) from the Office of Human Research Protections of DHHS. Three of the IRBs are on campus and the fourth is at the Methodist Hospital Division of Thomas Jefferson University Hospital. The IRBs and their administrative support staffs are organized under the Division of Human Subjects Protection (DHSP) within the Office of Human Research (OHR). The primary responsibility of the IRBs is the protection of human subjects involved in biomedical and behavioral research. The major work of the IRB consists of the assessment of research related benefit-risk ratios, and assuring that informed consent is properly obtained and documented for research subjects. IRBs have a responsibility to society and to the Jefferson community in particular, to review and approve worthwhile studies in a timely fashion.

The IRBs review research protocols, consent forms, adverse events, amendments to protocols, advertisements for recruiting research subjects, and any other matters pertaining to the conduct of research on human subjects. Protocols extending beyond one year require a continuing review. A central purpose of the IRBs is to sustain a collaborative and supportive balance among the interests of participant safety, researchers at Thomas Jefferson University, Thomas Jefferson University Hospital and Methodist Hospital and the requirements of federal regulations. Maintaining this balance demands significant effort and time from the faculty, Hospital and University employees and outside members who constitute the IRBs, the Chairs of the Boards, the Director, and the administrative staff in the DHSP.

The Director and Associate Director of the DHSP and the IRB Chairs wish to express sincere thanks for the tremendous effort of the many conscientious IRB members, and the administrative staff of the DHSP. The contributions of these highly motivated and dedicated individuals help make our human subjects protection program one that is highly regarded both locally and nationally.

## **National Accreditation for the TJU Human Subjects Protection Program**

The Thomas Jefferson University Human Research Protection Program received full accreditation from the Association for Accreditation of Human Research Protection Programs (AAHRPP) on June 13, 2008. Previously we had attained “qualified” accreditation. The qualified appellation was because

there were several minor items we needed to address along with the development of a policy for Research Device acquisition and tracking. AAHRPP accepted our response, and we will enjoy full accreditation until renewal time in 2011. AAHRPP was founded in 2001 and began accepting applications for accreditation in 2002. Currently there are 173 AAHRPP accredited organizations. To put this into perspective, there are over 3,200 organizations in the US and its protectorates with at least one IRB Committee registered with the Office of Human Research Protections (OHRP), 168 of these are in Pennsylvania. Thus, TJU is in a fairly elite group regarding its human subjects protection program!

What does accreditation mean for TJU? It provides sponsors with evidence that TJU has adopted the highest ethical and professional standards that can be applied to human subjects research. It means that Jefferson not only safeguards study participants but that our data is reliable and credible and that we are committed to continuous quality improvement. It provides sponsors, faculty, and regulatory agencies with assurance that we have an efficient operation with comprehensive protections for researchers and subjects. It is documented that Federal inspectors find fewer problems with accredited programs than with non-accredited programs. Accreditation also enhances our ability to attract high quality innovative clinical trials. Increasingly, accreditation is becoming a condition for research support. Finally, it enhances Jefferson's reputation in the community and indicates to potential research subjects that they can place their trust in Jefferson.

**IRB Transactions (information reflects calendar year 2008)**

The TJU IRBs review and oversee Phase I-IV clinical trials, epidemiological and behavioral research, basic research involving use of human tissues, and human translational and gene transfer research. This report encompasses the time period from January 1, 2008 through December 31, 2008. During this reporting period, the on-campus IRBs reviewed a total of 695 new submissions. The convened Boards reviewed 270 of the studies (38.8%). Three hun-

dred twenty two (322) studies were reviewed using the expedited process (46.3%), and 81 studies qualified for classification as exempt (11.7%). During the year, the DHSP conducted a total of 3,047 IRB transactions including 658 SAE reports. The TJU DHSP participates with the National Cancer Institute (NCI) Central IRB (CIRB) that reviews cooperative group studies sponsored by the NCI. During this reporting year we reviewed, in conjunction with the CIRB, 10 new protocols.

The Methodist Hospital convened IRB reviewed four Phase I studies for Wyeth Pharmaceuticals. The Methodist Board completed two continuing reviews, approved 10 amendments to protocols, received and reviewed 15 final reports, nine reports of adverse events, and reviewed four advertisements. The Methodist IRB completed 44 transactions during the reporting period.

The following table provides a breakdown of the activities of the 3 on-campus IRBs for calendar year 2008.

Submissions	Number Reviewed
New Submissions - Full Board Review	270
New Submissions - Expedited Review	322
New Submissions - Meeting Exempt Criteria	81
Continuing (annual) Reviews	708
Amendments	746
Studies Qualifying as Exempt	82
Adverse Event Reports	658
Final Reports	240
Disapproved Studies	22

There are currently 1,079 active studies in the TJU Clinical Trials Repository. Funding sources are as follows:

- Departmental Funds 32%
- Industry Sponsored 29%
- Federally Funded (mostly cooperative group studies) 19%
- State, Foundation, and other grants 20%

Of 345 departmentally funded studies, 68 received full Board review. Eighteen (18) of these involved drug intervention, six were device studies and 17 involved non-drug/non-device experimental procedure interventions.

### Personnel Changes - IRB Administrative Staff and Boards

Courtney Tirri Clemente, BS, Continuing Review and Quality Improvement Auditing left the DHSP and is now overseeing human subjects research at Paoli Memorial Hospital.

Personnel changes in the Boards are as follows:

**Brock Board:** No longer serving on the Board are Drs. Valerie Armstead, James Galvin, Parya Singh, Jacqueline Sullivan and Mr. Jeffrey Benowitz. New members are Shelley Burcat, MSN, RN (Bone Marrow Transplant), Margy Grasberger, MS (Information Services), Mitchell Maltenfort, PhD (Neurosurgery), Alex Meiji, MD (Pharmacology and Experimental Therapeutics), David Reiter, MD (Otolaryngology), Michal Anne Whiton, MD (Radiation Oncology), William Short, MD (Infectious Diseases), and Lisa Wus, RN, MSN (Cardiac Care, Family Medicine).

**Chambers Board:** No longer serving on the Board are Drs. Gloria Morris, Jianping Gong, Mary Bowen, and Hwyda Arafat, and Mr. Samuel Hutchins (community Member).

**Weinstein Board:** Coy Purcell, JD, and Doctors Thomas Force, Greg Russo, and George Lewis are no longer serving on this Board. New members are Meg Ryan, MD (Radiation Oncology), Prema Krishna, MD (Neurosciences), Emily Shafer (Public Relations), and Stephen Workman (Unaffiliated member).

**Mokrynski Board (Methodist Hospital):** Towanda Woodall, Secretary to the Board resigned her position and is working at Children's Hospital of Philadelphia. We wish her success in her new position. Dr. Larry Caputo and Stephanie Gaber, PharmD are no longer serving on the Board. Allison Zibelli, MD (Oncology) is a new member of the Methodist Board.

Doreen Kornrumpf, MSN, JD of the Office of University Counsel regularly attends all TJU IRB meetings as a voting member. She provides valuable advice regarding real or potential conflicts of interest of investigators and key personnel listed on human subjects research protocols and on relevant federal and state laws as they relate to human subjects research. She has extensive experience in health and research-related law.

We wish to extend our sincere appreciation for the hard work and dedication exhibited by those who have left the Boards. We also welcome the new members and trust they will find IRB membership an educational and rewarding experience.

### Quality Improvement Program

The mission of the DHSP Quality Improvement/Education Program is to augment and facilitate continuing review of ongoing clinical trials, enhance protection for research subjects, and ensure compliance with regulations and ethical guidelines. Danielle Papeika is the DHSP Quality Improvement Specialist. The program's goals are to: 1) develop a collegial relationship with clinical investigators and study coordinators and 2) to assist them in developing effective procedures to conduct and monitor all aspects of their human subjects research. In this way DHSP has encouraged a culture of compliance within the institution and a partnership between the research community and the DHSP. The DHSP Audit Team completed 31 audits of randomly selected trials between January 1, 2008 and December 2009. Consent interview by individuals who are not listed as Key Personnel was the most common non-compliance issue found.

## Education and Other Activities

The federal government mandates formal training regarding the ethics and regulations that govern human subject research for all those engaging in research involving humans. The number of investigators and key personnel who have completed the certification program in order to be eligible to conduct human subject research continues to expand. Since 2000, more than 5,000 individuals have been certified through our education program. In the past year, 1,399 individuals completed the self-study training program and passed the certifying examination, and 965 individuals completed the required annual training. The one-time mandatory HIPAA training was completed by 1,342 individuals.

The mandatory course for clinical research coordinators has been in existence for more than four years. Two-hundred-sixteen (216) individuals have now completed the course. Responses from attendees have been generally positive and we have made changes to the course to accommodate constructive criticisms.

The Director and Associate Director of the DHSP participate in numerous educational activities for TJU faculty and staff regarding protection of human subjects in research. These include participation in ongoing faculty improvement seminars, the new faculty orientation program, presentations to coordinator groups and presentations to Departments and Divisions. They also organize and participate in the mandatory Research Coordinator Course. Dr. Smith coordinates a 12-week summer course in the College of Graduate Studies (GC-690), entitled "Regulatory Issues in Human Subjects Research." Mr. Conner also participates as a lecturer in that course.

Four DHSP staff members, the three IRB chairs, two of the co-chairs and the Associate Director attended the annual IRB national meetings organized by Public Responsibility in Medicine and Research (PRIM&R) held in November 2008 in Orlando Florida. These meetings provide education and insight about historical and current issues regarding protection of research subjects.

Data collected from the initial year (2007) of use of the electronic adverse events reporting system (eSAEy™) revealed a significant decrease in the time between the event and the submission of the SAE report to the DHSP. The median time between the event and the submission by the Principal Investigator was less than two days (mean  $7 \pm 0.7$  days). For a similar reporting period using the paper-based system, the median time between event and submission was 24 days (mean of  $45 \pm 5.7$  days). Also, with eSAEy™, reports on adverse event characteristics (type, grade, etc.) were easily obtained and had consistent values based on standard terminologies.

## DHSP Web Site

The content of the DHSP Web site is updated on a regular basis. The *IRB Training Manual*, certifying examination, and annual update requirements can all be reviewed and completed online. The DHSP Web site has links to important University Policies and Procedures such as those for Conflict of Interest and Noncompliance. The DHSP Policy and Procedure Manual was completely upgraded during the course of the year and the book-marked searchable manual is also available on the DHSP Web site.

## Division of Clinical Trials Support

The Clinical Trials Support Office was established to foster clinical research and to hold such research to the highest standards. The Associate Director of the Division of Clinical Trials Support is Roseann Talarico. The Office of Clinical Trials Support has three main missions. These are 1) supporting faculty members involved in clinical trials research by providing administrative infrastructure support services 2) framing policy and operating issues surrounding clinical trials and 3) providing education and training to the research community at TJU. The Clinical Trials Support Office hosts the Jefferson Clinical Research Forum (JCRF), a very well attended monthly meeting of research coordinators and research administrators at which timely topics in clinical research are presented and discussed. The office also supports the Liaison Committee of

Clinical Coordinators (LCCC), a group of senior research coordinators who meet on a monthly basis with Ms. Talarico and the Director, DHSP, to discuss and plan implementation of programs that will improve the clinical research effort at TJU.

The Division of Clinical Trials Support has been very active in support of educational outreach to the Philadelphia Community. Jefferson participated in the Third Annual AWARE for All-Philadelphia Clinical Research Education Day on Saturday, March 28, 2009, held at the Bossone Center at Drexel University and sponsored by the Center for Information & Study on Clinical Research Participation (CISCRP). Roseann Talarico, Associate Director of the Clinical Trials Support Office in the OHR, was the prime organizer from TJU and did an excellent job as usual. Collaborating institutions in generating the program were Abington Memorial Hospital, Doylestown Hospital, Drexel University, Fox Chase Cancer Center, CHOP, and TJU/TJUH. The program hosted over 450 individuals from the local community who learned about participating in clinical research, informed consent, and who received clinical updates concerning research in cancer, infectious diseases and HIV/AIDS, cardiovascular disease and stroke, neurological diseases, diabetes, obesity and metabolic diseases, participation of children in clinical research studies, and personalized medicine. The very excellent keynote address was given by Liz and Jay Scott, parents of Alex of Alex's Lemonade Stand Foundation for Childhood Cancer. TJU/TJUH was well and ably represented by Drs. William Short, Walter Kraft, Edith Mitchell, Bonita Faulkner, Eugene Kennedy, Stephen Peiper, Rodney Bell, and Mr. John Furlong. All did a tremendous job and we are grateful to them. A number of Jefferson employees also participated at information booths and we are grateful for the help and commitment of Leslie Padron-Massara, Dora Posey, and Deborah Weingard from the Diabetes Prevention Program, and Jennifer Contipodero and Edie Fletcher from Cardiology.

During the coming year, the Division of Clinical Trials Support will continue to be involved in

the Medicare Clinical Trials Billing Project Working Group to establish sound and compliant practices regarding billing for standard of care and clinical trial-related activities. The Division will also continue to provide a valuable liaison function between Research Coordinators and PIs and the various TJU research support offices.

### **Research Biosafety Program**

The Research Biosafety program involves the inspection and certification of laboratories and investigators conducting research with risk group 2 or higher agents that require biosafety level 2 or higher laboratory physical containment conditions. All proposals for research using the above listed agents are reviewed and approved by the Institutional Biosafety Committee (IBC) prior to the start of the research.

The Institutional Biosafety Officer (BSO), Sue Gotta, MS, is also a member of the IBC. She conducts laboratory inspections, certifies investigators for work in the biosafety level-3 (BL-3) laboratories, conducts biosafety training, reviews protocol submissions and acts as a resource person for investigators.

### **Institutional Biosafety Committee**

Under the NIH Guidelines for Research Involving Recombinant DNA Molecules, each institution conducting or sponsoring recombinant DNA research covered by these Guidelines is responsible for ensuring that the research is carried out in full conformity with the provisions of the Guidelines. The institution must establish and implement policies that provide for the safe conduct of recombinant DNA research and ensure compliance with the Guidelines. The institution must also establish an IBC whose responsibilities need not be restricted to recombinant DNA. If the institution is engaged in recombinant DNA research requiring BL-3 containment, it must appoint a Biological Safety Officer (BSO) who shall be a member of the IBC.

The IBC functions as a critical component of TJU's Research Biosafety Program. The Commit-

tee's actions are detailed in an annual report filed with the Office of Biotechnology Activities of the National Institutes of Health. The following paragraphs summarize the major responsibilities and actions of the IBC during the past year.

Under the Occupational Safety and Health Agency (OSHA) Bloodborne Pathogens Standard (29 CFR 1910.1030), the University is obliged to ensure that employees whose work requires them to come into contact with human blood or other potentially infectious material shall be adequately protected. The IBC inspects and monitors, through the BSO, those research laboratories conducting research using human blood and tissues and body fluid contaminated with human blood.

The IBC is also responsible for working with the Institutional Animal Care and Use Committee (IACUC) to ensure that animal experiments in which biohazardous agents are used are conducted in a manner commensurate with the above guidelines and/or regulations.

The IBC is also responsible for interacting with University Health Services to ensure that investigators conducting research involving biohazardous agents are offered immunization against the agent being studied, in so far as immunization is available.

On behalf of the Institution, the IBC is responsible for:

- Reviewing recombinant and pathogens research for compliance with the NIH Guidelines for Research Involving Recombinant DNA Molecules and the NIH/CDC Guidelines for Biosafety in Microbiological and Biomedical Laboratories and approving those research projects that are in conformity.
- Reviewing research and inspecting laboratories using human blood, cells or tissues for conformity with the provisions of the OSHA Bloodborne Pathogens Standard.

- Keeping abreast of mandated guidelines and other sources of good safety practice (GSP).

- Establishing laboratory compliance and inspection guidelines that facilitate documentation that the IBC has met GSP requirements.

- Making an independent assessment of the containment levels required for the proposed research and of the facilities, procedures and practices of the investigator proposing to carry out the research.

- Setting containment level.

- Initially, and periodically, inspecting and certifying the laboratories conducting research which requires containment and practice at the BL-2 level or higher.

- Adopting emergency plans covering accidental spills and personnel contamination resulting from such research.

- Reporting to the appropriate institutional official and to the NIH Office of Biotechnology Activities any significant problems with, or violations of, the Guidelines and any significant research-related accidents or illnesses.

- Review of animal protocols submitted to IACUC for biosafety issues.

- Review of protocols submitted to the Institutional Review Board involving gene transfer for biosafety issues.

- Serving as a resource to provide guidance for investigators who are designing their biosafety plans.

The IBC comprises 13 members, so selected that they collectively have experience and expertise in recombinant DNA (RCDA) technology and/or pathogenic organisms, biological safety and physical containment and the capability to assess the safety of experiments utilizing recombinant DNA and/or pathogens and any risk to public health and to the environment.

Two of the members are not affiliated with the Institution and represent the interests of the sur-

rounding community with respect to health and protection of the environment. The Biological Safety Officer (BSO) is a member and Vice Chair of the IBC.

This past year, the IBC reviewed and classified a total of 36 new and revised research proposals. In addition, the Biosafety Officer performed 19 inspections to certify laboratories for work at the BL-2 or higher containment level. Laboratories functioning at the BL-2 are reinspected every two years, BL-2/3 are inspected annually, and those at the BL-3 level are reinspected bi-annually.

One of the protocols reviewed this year was a gene transfer protocol entitled "A Phase II study of HyperAcute-Pancreatic Cancer Vaccine in Subjects with Surgically Resected Pancreatic Cancer" under the auspices of Dr. Eugene Kennedy, Assistant Professor of Surgery. The research involves the use of human pancreatic cancer cell lines that have been engineered to express a mouse gene that will elicit a strong immune response when injected into the patient. The goal is to determine if adding this vaccine to the post-operative standard of care for patients with surgically resected pancreatic cancer will result in either greater disease free survival and/or overall survival.

The protocol was approved by both the IBC and IRB.

The IBC continued to improve the internal form for submission of studies to the IBC, partitioning the subsections of the original form into separate documents so only the pertinent sections need be submitted to the IBC for review (IBC-1 through IBC-6). Submission of the internal forms may now be done electronically.

A new and more comprehensive data base has been established for IBC protocol tracking. Thanks to Jack London, Research Associate Professor in the Kimmel Cancer Center, the database is up and running and we are working to transfer information to the new database.

## **Volunteers in Research Laboratories**

Individuals such as high school and college students volunteering to work in the research laboratories of the Medical College and any individual (such as a post doctoral fellow or other researcher) whose salary is not paid by the University, must register with the Office of Human Research and have their project reviewed by the IBC if their research involves biohazardous agents. This is required for risk management. During the year, the IBC and OHR processed 86 volunteers.

## **Select Agent Program**

The "Public Health Security and Bioterrorism Preparedness Response Act of 2002" requires that the United States improve its ability to prevent, prepare for, and respond to bioterrorism and other public health emergencies. Congress designated the CDC as the responsible agency to oversee 42 CFR Part 73, Possession, Use and Transfer of Select Agents and Toxins. This document builds on and greatly strengthens the earlier Select Agents Regulations presented in 42 CFR 72 for the possession, use and transfer of select biological agents.

Thomas Jefferson University is registered with the CDC under 42 CFR 72 to possess, use, and transfer botulinum toxin. The institution's three-year certificate will be coming up for renewal January 20, 2010. Consequently, preparations are under way to review the entire program to ensure the continued compliance with the CDC select agent program. We anticipate that we will receive a new three year license in January.

### **J. Bruce Smith, MD, CIP**

Professor of Medicine  
Director, Office of Human Research  
Director, Division of Human Subjects Protection

### **Gerald B. Grunwald, PhD**

Professor of Pathology, Anatomy and Cell Biology, JMC  
Senior Associate Dean, JCGS  
Chair, IBC