CLINICAL GROUP

Barry L. Gause, M.D., Director

CLINICAL RESEARCH DIRECTORATE

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DIRECTORATE OVERVIEW

The Clinical Research Directorate (CRD) was established in November 2006 by bringing together the Clinical Monitoring Research Program (CMRP) and the Quality Assurance Programs of the Vaccine Pilot Plant (QA-VPP) and the Biopharmaceutical Development Program (QA-BDP). The major purpose for establishing a new directorate was to bring those programs at the clinical end of the translational spectrum under an umbrella that fosters interactions in areas of overlap and provides clinical supervision of such activities. In addition, assigning the QA programs to this directorate was necessary to provide the required autonomy and transparency.

The overall objective of the directorate is to provide clinical research support for clinical trials and quality assurance for the production of vaccines and biological agents at the National Institutes of Health (NIH). This support includes clinical trials management and regulatory support for clinical research. The directorate accomplishes its mission by providing comprehensive, dedicated clinical research support to major clinical programs within the National Cancer Institute (NCI), the National Institute of Allergy and Infectious Diseases (NIAID), the National Heart, Lung, and Blood Institute (NHLBI), and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). In addition, the directorate establishes quality systems at VPP and BDP before the initiation of manufacturing and follows through on all regulatory aspects of production, including providing support for Investigational New Drugs (INDs). Detailed descriptions of QA activities will be presented under the sections for VPP and BDP.

CLINICAL MONITORING RESEARCH PROGRAM

Beth Baseler, M.S., Director

OVERVIEW

The primary mission of the Clinical Monitoring Research Program (CMRP) has been to provide comprehensive, dedicated clinical research support to major programs within NCI, including the Office of the Director, the Center for Scientific Strategic Initiatives, the Center for Cancer Research (CCR), the Division of Cancer Control and Population Sciences (DCCPS), the Division of Cancer Treatment and Diagnosis (DCTD); and within NIAID, including the Division of Clinical Research (DCR) and the Division of Intramural Research (DIR). To support the diverse research requirements of the clinical research community, CMRP provides an integrated range of quality services that are functionally organized within CRD. CMRP represents a comprehensive resource for NCI's and NIAID's Intramural Clinical Research Programs. CMRP staff continues to provide high-quality programmatic and clinical trials management support, as well as regulatory support to an extensive variety of high-profile NCI and NIAID initiatives. Our services have continued to expand and now include regulatory and clinical trials management support to NHLBI and NIAMS.

The creation of CMRP in late 2001 produced a unique program that has dramatically expanded to include operations such as: (1) the Regulatory Compliance and Human Subjects Protection Program (RCHSPP), providing support to NIAID; (2) support to the NIAID-Mali HIV Research Initiative; (3) support to the Phidisa Project, a joint effort between the South African Military Health Service of the South African National Defense Force (SANDF), the U.S. Department of Defense (DoD), and NIH; (4) the Clinical Consulting and Support Group; (5) support to the India/Mali initiative; (6) support to biostatistics; (7) support to the India initiatives; (8) support to the Uganda initiatives; (9) support to NIAID clinical teams; (10) nursing and clinical/protocol monitoring support to CCR; (11) support to CCR's Protocol Re-engineering Project; (12) support to the Cancer Therapy Evaluation Program (CTEP) through the Translational Research Initiative (TRI); (13) support to the NCI Behavioral Research Branch (BRB) and the Cancer Information Service (CIS); (14) support to the Development of Clinical Imaging Drugs and Enhancers (DCIDE) program; (15) support to the Cancer Disparities Research Program; (16) support to the Health Communication and Informatics Research Branch (HCIRB); (17) support to the CCR/DCTD Chemical Biology Consortium through the Project Management

Office (PMO); (18) support to the NCI Community Cancer Centers Program (NCCCP) initiative; (19) support to the Office of Biorepositories and Biospecimen Research (OBBR); (20) support to the Coordinating Center for Clinical Trials (CCCT); (21) support to the Office of Latin America Cancer Program Development (OLACPD); (22) support to the H1N1 Influenza initiatives; (23) support to the Radiation Research Program (RRP) Patient Navigation Research Program to include NCI's Cancer Disparities Research Partnership (CDRP) Program and the planning efforts for the Cancer Experts Corp; (24) support to the NIAID Institutional Review Board (IRB) Pilot Program; (25) support to the American Recovery and Reinvestment Act of 2009 (ARRA) through the NCCCP and cancer Human Biobank (caHUB) initiatives; (26) support to the Protocol Navigation/Protocol Development initiative; (27) support to NHLBI; and (28) support to NIAMS.

Major efforts include the management of regulatory, clinical trials, pharmacovigilance, and protocol development/navigation programs to monitor an extensive variety of clinical trials being conducted by the Intramural Research Program within NIAID and NCI. CMRP continues to expand its regulatory and clinical trials management support; during the reporting period staff was requested to provide its highly esteemed services to NHLBI and NIAMS. CMRP's ability to provide rapid responses and high-quality solutions, and to recruit and retain experts with a variety of backgrounds has allowed the program to meet NCI and NIAID's growing portfolios, while offering innovative solutions to the institutes.

CMRP is one of the first within the NIH community to offer and use electronic common technical document (eCTD) submissions for IND applications sent to the Food and Drug Administration (FDA). The eCTD method of submittal is an efficient and effective method that is preferred by the FDA. Recently, staff began providing the ability for other NIH users to discuss and collaborate with RCHSPP about the process of transitioning paper IND applications to an electronic format, including discussions of the lessons that have been learned and progressing from beta testing to full implementation using the new format.

As a program, CMRP has provided high-quality clinical research support services to meet the expanding and new challenges faced by NIH researchers. CMRP has recognized that there are numerous barriers to conducting clinical research not only domestically, but particularly in an international setting. Successful completion of our mission directly benefits the mission of NCI, NIAID, and other institutes, and has contributed to improving the overall standards of public health globally. The repertoire of support services provided to clinical researchers throughout the world has expanded dramatically over the last 10 years, assisting researchers in providing clinical research of the highest quality, which is compliant with applicable regulations and guidelines, and maintaining data integrity, with the overall goal of protecting human subjects. CMRP continues to provide regulatory, clinical trials management, pharmacovigilance, and project/program management services to support over 350 domestic and international clinical trials involving cancer, avian flu/severe human influenza, HIV, malaria, parasitic diseases, and other infectious diseases.

The year 2011 was marked by accomplishments across CMRP's portfolio of services and programs. CMRP has been instrumental in launching several major program initiatives in support of the evolving research and development mission of NCI-Frederick and NIAID. The program continually looks at new and innovative ways to enhance its service. Protocol navigation/protocol development pilot programs were established for both NCI and NIAID; the programs took off rapidly and were met with tremendous interest from principal investigators. The pilot programs have reduced the administrative and regulatory burden on investigators, so that they can now spend more time on science.

CMRP provided clinical trials management and regulatory and logistics support in the expansion of the H1N1 influenza network, including the initiation of two new multi-center influenza studies with seven sites in Australia. In addition, CMRP provided logistics and operational support to OLACPD, a pilot initiative and partnership to develop and implement beneficial cancer research programs in Latin America. During the reporting period, a number of sites were activated and subjects were enrolled in the first study of this new initiative. CMRP has supported the goal of increasing the capability of international locations to participate and partner in cancer research and has assisted in the critical development of clinical trials networks across the world.

CMRP staff has continued to play an active role in NCI-Frederick community outreach programs, including participation in the Elementary Outreach Program and Take Your Child to Work Day. In collaboration with Frederick Community College, CMRP presented a half-day seminar in October 2010, which featured speakers and posters to raise awareness of clinical research as a career path for nurses.

Significant Achievements

In collaboration with Frederick Community College, CMRP staff presented a half-day seminar in October 2010, which featured speakers and posters to raise awareness of clinical research as a career path for nurses. Planning is underway to expand this half-day seminar to additional Maryland community colleges.

A public-facing web site was developed and released to highlight the diverse clinical research service and support functions provided by CMRP. The site provides information about the many high-profile NIAID and NCI initiatives to investigators, clinicians, prospective job seekers, and the general public. As additional initiatives are supported, the web site will be updated. Statistical web tools and speed and search engine optimization

features were integrated into the site to enhance page delivery and improve visibility, while ensuring appropriate security safeguards were in place to comply with NIH standards. Flexible and configurable web development tools were also employed, which allow program staff, rather than web developers, to perform content updates.

CMRP's clinical training manager, a newly hired ARRA-funded training specialist, a training specialist/instructional designer, and an administrative support staff member supported an internal CMRP initiative to provide a wide range of trainings for recently hired ARRA staff. In an effort to identify/develop training resources that address client-identified training needs, the Clinical Training Group (CTG) worked with a number of subject matter experts to design and conduct training presentations for this program, including ARRA Inspection Awareness, Section 508 Awareness, Prime Contract Oversight, Financial Management (e.g., budgeting and procurement), research subcontracting, contracting officer's technical representative (COTR), property management, and Training Database Overview.

The magnetic resonance imaging/CT/radiology technologist (MRI/CT/RT) supporting NCI's Molecular Imaging Clinic is credentialed in three modalities and is a candidate for positron emission tomography (PET) certification training, an outstanding accomplishment. This technologist is responsible for developing and implementing standard operating procedures (SOPs) related to MRI contrast and delivery.

CMRP staff responded to an expedited request from CCR to provide a qualified person to serve as chair of the NCI IRB. A research subcontract was executed within a two-week timeframe to accommodate this high-priority request.

In collaboration with Biovest International, CMRP staff has been involved with the design, planning, and implementation of the Phase III vaccine trial for non-Hodgkin's lymphoma. CMRP staff assisted with developing the protocol and case report forms, tracking and maintaining study-related files, and assisting with conducting internal site visits to ensure compliance with clinical protocol and overall trial objectives.

A CMRP staff member serves as the associate investigator on 11 protocols for NCI's Experimental Transplantation and Immunology Branch, seven of which are actively recruiting and transplanting patients. Staff members have been involved in the development of the first double-cord blood transplant protocol at NIH, which is open and recruiting patients (three patients have received transplants). The group also identified and transplanted suitable cord units for seven aplastic anemia patients at NHLBI for the haplo/cord protocol. Of note, this group has played an integral role in negotiating the Data Transmission Agreements between the Center for International Blood and Marrow Transplant Research (CIBMTR) and NCI, NHLBI, and NIAID. This group also drafted the CIBMTR Data Repository Submission protocol for the Experimental Transplant and Immunology Branch (ETIB) and the Pediatric Oncology Branch (POB).

The CMRP senior nurse practitioner supporting the Developmental Therapeutics Clinic contributed to the successful development and undertaking of new trial designs, such as the single-agent Phase II trial with ADZ2171 (Cediranib), which is one of the most promising regimens for a rare form of sarcoma (alveolar soft-part sarcoma), and a multi-histology Phase II trial with R788.

Staff members supporting NCI's Urologic Oncology Branch have participated in the design and planning of a Phase II trial for advanced malignant melanoma, in collaboration with Genzyme Corporation, a subsidiary of Sanofi-Aventis, to build on the Phase I study closed in the previous year. CMRP staff members are assisting with the development of a protocol and consent as well as facilitating submissions to IRB.

Staff members supporting NCI's Vaccine Branch have participated in the design and planning of a Phase II trial for advanced malignant melanoma, in collaboration with Genzyme Corporation, to build on the Phase I study closed in the previous year. CMRP staff members are assisting with the development of a protocol and consent as well as facilitating submissions to the IRB.

At the direction of The Cancer Genome Atlas (TCGA) management team, CMRP modified all of the extended subcontracts to collect additional tumor types—beyond the three pilot-phase tumor types—including breast lobular carcinoma, hepatocellular carcinoma, pancreatic ductal adenocarcinoma, stomach adenocarcinoma, esophageal adenocarcinoma, cervical cancer squamous cell carcinoma and adenocarcinoma, uterine corpus endometrial carcinoma grade 3 and serous, head and neck squamous cell carcinoma, thyroid papillary carcinoma, acute myeloid leukemia, diffuse large B-cell lymphoma, cutaneous melanoma (including metastatic samples), lung adenocarcinoma, lung squamous cell carcinoma, bladder muscle invasive (high grade, nonpap), kidney papillary carcinoma, prostate adenocarcinoma, and sarcoma (de diff lipo, undiff pleiomorphic, leiomyo). Of special note is a subcontract that was awarded to the National Cancer Center (NCC) of Korea. This subcontract offers NCI the opportunity to collect rare samples from non-U.S. source sites where the standard of care in the U.S. would preclude the use of samples in the TCGA program. The Department of State approved a memorandum of understanding, creating a mechanism for the NCC of Korea to provide TCGA with rare pancreatic and gastric adenocarcinoma cancer tissue types at minimal cost. In addition to the tissue samples, the NCC of Korea will provide clinical and follow-up data, adding value to the specimen.

CMRP staff continued to support program expansion activities and provide project management services to NCCCP. Efforts included: (1) comprehensive communication support to all site representatives, including the coordination of approximately 30 monthly meetings and documentation (recurring subcommittee,

working group, and ad hoc meetings, and educational webinars); (2) maintaining the NCCCP private intranet site and its content, and providing network-developed resources/tools that are applicable to a broad range of community-based cancer programs to the NCCCP public web site; (3) overseeing more than 30 NCI listservs; (4) management of the NCCCP wiki content; (5) coordinating the two-day 2011 NCCCP Annual Meeting for nearly 400 participants, including venue comparisons, facility arrangements, budget oversight, travel and logistical support, agenda development, guest speaker arrangements, documentation and presentation management, and post-meeting activities to obtain and collate feedback from participants; and (6) facilitating efforts to write, edit, and publish white papers for each of the program's major focus areas.

This last task involved several levels of coordination, beginning with CMRP staff preparing an overview document that included guidelines for the white paper development process. As the seven individual NCCCP subcommittees gathered content and drafted material, CMRP managed the review and revision process to ensure that final drafts contained the sites' overall experiences with developing and implementing projects and tools, key success factors, and lessons learned. CMRP staff also made sure that all papers met with the approval of all NCCCP principal investigators (PIs). Once the seven white papers were complete, CMRP staff reformatted the documents for a consistent presentation style and posted them to the NCCCP intranet. In order to share the NCCCP experience, tools, and resources with other community cancer centers working toward similar goals, CMRP staff facilitated discussions with *Oncology Issues* and secured agreement from the journal to feature the NCCCP white papers in an ongoing series about the program. To date, 11 articles have been published in *Oncology Issues;* CMRP coordinated the article development process with the magazine's editorial staff, white paper authors, PIs, and NCI advisors, and made all articles section-508 compliant before posting them to the NCCCP public and private web sites.

CMRP programmatic support to NCCCP has also included ongoing management of 45 individual research subcontracts. Dedicated CMRP staff manages the relationships between the awarded organizations, SAIC-Frederick, and NCI to support project objectives and activities.

CMRP continued to provide a cost-effective and efficient support mechanism to reimburse the efforts of the clinical, scientific, and advocate experts serving on scientific steering committees (SSCs) in support of the NCI Clinical Trials Working Group (CTWG). In collaboration with SAIC-Frederick's Research Contracts and Accounts Payable offices, CMRP staff streamlined processes by replacing 417 consulting agreements with vendor agreements. This led to increased efficiency and has resulted in a decrease of nearly five months in processing time; a process that previously required six months is now averaging three days. CMRP's support of the 16 SSCs includes project management, program analysis, and management of the massive and growing vendor agreement effort.

During the reporting period, CMRP successfully completed filing of the first ever NCI new drug application (NDA) on behalf of NCI's Cancer Imaging Program. Even though CMRP provided full regulatory support to CIP in the submission of a marketing application (NDA) for [^{18}F]-NaF in 2008, this is the first time NCI filed an NDA with the FDA. FDA approval was received in late January 2011. This effort was spearheaded by the CMRP regulatory team and CMRP/CIP leadership, and the entire CIP support team contributed their varied skill sets to meet stringent and extensive FDA requirements in addressing this need.

The IT management support provided to NCI's Cancer Imaging Program has been a major contributor to initiatives across NCI in support of its imaging informatics plan. Collaboration with multiple NCI-wide committees and major imaging informatics initiatives have proven to be extremely important in NCI's development of an infrastructure that supports higher-level compatibility with the Center for Biomedical Information and Information Technology's (CBIIT) cancer Biomedical Informatics Grid (caBIG®) and other NIH Roadmap Initiatives. During the past year, the IT manager oversaw the development and population of an archive of in vivo radiology image sets to address needs of the image processing community; by providing submission, curation, and hosting services, a new vision has come to fruition as The Cancer Imaging Archive.

CMRP behavioral scientists and project administrators have been pivotal in researching the various causes, prevalence, and prevention of cancers, and have worked closely with Behavioral Research Program (BRP) staff to generate the research necessary to inform evidence-based practice and policy. CMRP staff also plays a critical role in BRP's national surveillance efforts, observing and communicating cancer trends to the public, developing web-based smoking cessation interventions and research tools for the extramural research community, and providing program and scientific support to BRP research networks and collaborations. In support of intramural research efforts, CMRP staff members have presented numerous scientific presentations at leading conferences and have published more than 90 articles in peer-reviewed journals on subjects ranging from tobacco use and other multiple risk factor behaviors (e.g., physical activity, dietary behaviors, and sun safety) to genetic susceptibility and breast cancer screening practices.

In a leadership role, CMRP staff contributed scientific content to four of NCI's DCCPS BRP surveillance efforts to examine trends in cancer communication and cancer prevention behaviors, and seek to better understand the mechanisms and theories of behavior change. CMRP led the development of the Health Information National Trends Survey (HINTS) 4 and managed the HINTS grid-enabled measures (GEM) web site, which allows the extramural community to contribute and comment on

HINTS 4 items. In addition, by serving as scientific content experts (or "HINTS Champions") and vital members of the HINTS III Management Team, CMRP staff has been a key source of information for health care providers, researchers, cancer patients, and survivors within these surveillance efforts.

One of CMRP's behavioral scientists serves as project leader of the Science of Team Science Toolkit. This is a web site, built on a wiki platform, which supports information exchange and knowledge sharing to promote the growth and unification of the interdisciplinary field called the "Science of Team Science." Under this capacity, the behavioral scientist has worked with a multidisciplinary team made up of computer programmers, social and clinical psychologists, and experts in business, communications, education, and informatics, to develop the structure and content of the toolkit, solicit public contributions, and promote the toolkit through a wide variety of high-profile avenues, including internal NIH meetings of interested groups, national and international conferences, listservs, web sites, and social media. As a result of the leadership of the behavioral scientist, the Team Science Toolkit had its public debut at the second annual International Science of Team Science Conference, in Chicago, IL, in April 2011. The web site is currently being refined based on usability testing, and a revised version was to be debuted at the exhibitors' hall of the October 2011 American Public Health Association conference—the largest annual international public health professional's conference.

CMRP staff is leading a study to evaluate lessons learned from the Transdisciplinary Research on Energetics and Cancer (TREC) Initiative. This study focuses on gleaning expert knowledge about strategies for successfully engaging in, facilitating, and studying team science. The TREC Initiative is one of the largest and highest profile of the grant initiatives supported by BRP. It represents a trend of large center grant initiatives that fund teams of collaborators to work together within and across centers at different academic institutions, to embark on a program of cross-disciplinary research.

CMRP and CCS Associates, Inc. (CCSA), worked collaboratively to establish the founding principles of a Data Monitoring Committee (DMC) for NCI's OLACPD United States–Latin American Cancer Research Network (US-LACRN). These principles will provide the important foundation for the first study conducted in the network, ensuring the quality of implementing the molecular profiling of breast cancer study and other studies to be conducted by US-LACRN. The CMRP program director and CCSA chief executive officer drafted the data monitoring and data sharing policies on behalf of the NCI program director and presented the policies at the second annual meeting in November 2010. A draft study monitoring plan is currently under development, which, upon NCI approval, will form the basis for study monitoring by investigators, NCI, and DMC. Work to establish the study monitoring team, DMC, and related processes has been initiated and will be finalized within the next several months.

In an ongoing effort to provide the clinical researchers with additional avenues to support quality clinical studies, the NIAID clinical director requested that CMRP establish a new team within the Regulatory Compliance and Human Subjects Protection Program (RCHSPP) that could provide protocol navigation and protocol development activities. Over the past year and a half, the Protocol Navigation/Protocol Development Program (PN/PDP) has become very well-known and successful in providing the investigators with medical/technical protocol writing and facilitating the logistical aspects of protocols.

CMRP's RCHSPP is on the forefront of new and innovative regulatory technologies. Most recently, the Regulatory Affairs Group successfully prepared and submitted the first NIAID Regulatory Compliance and Human Subjects Protection Branch (RCHSPB)–sponsored IND in eCTD format to the FDA. The eCTD method of submittal is a more efficient and effective process that provides cost/resource savings, is more environmentally friendly, and is preferred by the FDA. Following approval of an electronic submission gateway production account in August 2010, staff members prepared a pilot submission of an existing initial IND application that had been converted to an eCTD. This pilot submission was delivered to the FDA for validation in December 2010 and the Regulatory Affairs Group received a response in mid-January 2011 that the application was guidance compliant. In February 2011 and May 2011, staff held two meetings with PIs from separate DCR laboratories to explain the transition from a paper IND to an eCTD, the development and processes of an eCTD versus an IND, and the Regulatory Affairs Group progress to date.

In April 2011, the first RCHSPB eCTD IND for a new drug study (a Phase II study of DAS181 in parainfluenza) was submitted to the Center for Drug Evaluation and Research (CDER) at the FDA; the application was given safe-to-proceed status in May 2011. Since then, the Regulatory Affairs Group has submitted two additional eCTD INDs to CDER, delivered the first vaccine eCTD IND to the Center for Biologics Evaluation and Research (CBER), and has an additional four eCTD INDs in development for delivery to the FDA prior to the end of fiscal year (FY) 2011.

The RCHSPP Clinical Safety Office (CSO) has developed a comprehensive template for the "Assessment of Safety" section of IND protocols, which included changes required by new IND regulations and the need to identify and report "Unanticipated Problems." The CSO has revised the "Serious Adverse Events (SAE) Report Form," which is now the "SAE/UP Report Form," to accommodate the need to report "Unanticipated Problems."

The RCHSPP Clinical Trials Management Team is involved with the management and/or monitoring of approximately 155 clinical research studies conducted at sites throughout the U.S. and in several foreign countries.

The studies the team is responsible for monitoring vary and include Phase I/II IND and IDE studies, natural history studies, pediatric studies, and research studies that are noninvasive and are not under an IND. During FY2011, the team conducted one pre-study site assessment visit, 70 study initiation visits, 151 interim monitoring visits, and 22 study close-out visits. International trial monitoring included various international clinical sites in Africa (Mali, Uganda, and Kericho), Korea, Taiwan, Thailand, India, Vietnam, Cambodia, Peru, Mexico (Mexico City), and other countries across the world. The Clinical Trials Management Team also conducted international site-initiation visits in Thailand, China, Australia, Mexico City, and Mali, and conducted seven study-site audits in hospitals in Korea.

The Clinical Trials Management Team continues to provide sponsor-related clinical trials management for several newly established NIAID networks, including the H1N1 Network, the International Network for Strategic Initiatives in Global HIV Trials (INSIGHT [Strategic Timing of Antiretroviral Treatment study (START)]), and the Mexico Flu networks. The team also initiated several new studies in the D.C. area that are part of the D.C. Partnership for HIV/AIDS Progress (DC-PFAP) program. The Clinical Trials Management Team manages the sponsor's essential document files for the 30 active clinical sites within all three networks, as required by FDA and the Department of Health and Human Services (HHS), and conducts sponsor site audits. The team monitored four of the INSIGHT (START) protocol sites in FY2011. The Clinical Trials Management Team also expedited the initiation of two new multi-center influenza studies this fiscal year for IRC-003 and IRC-004, which also included the expansion of the IRC-003 study to seven Australia sites in the H1N1 network.

The RCHSPP PN/PDP consists of protocol navigators and medical writers, as well as CMRP staff who are involved with aspects critical to protocol implementation. Since September 2010, two additional protocol navigators and one additional medical writer were hired to support the increasing number of projects using PN/PDP. During the reporting period, the PN/PDP team was involved with the development of 16 initial protocols. Of these, five projects were from investigators who have never submitted a protocol, six were from investigators who were new to the PN/PDP process, and five were repeat customers. The program facilitated five international protocols. Protocols for these studies have varied in phase, type, and sponsorship, and have also spanned several NIAID intramural labs.

The RCHSPP PN/PDP serves as a pilot for other NIH institutes that continue to investigate the implementation of similar navigation programs. During the reporting period, the senior protocol navigator was asked to consult on program issues related to protocol navigation training. This person has also been involved in a collaborative effort across institutions, and at the request of and in conjunction with the Office of Protocol Services and the Office of Human Subjects Research Program office, is drafting a revised protocol application for across-the-board use by all institutions to meet the requirements of the Association for the Accreditation of Human Research Protection Programs (the credentialing body NIH is seeking to apply for in the upcoming months). At the request of OHSPR, this effort includes editing SOPs to provide insight into protocol logistics and current administrative and regulatory requirements.

The RCHSPP Project Management Team (PMT) established an Integrated Strategic Project Management Framework (ISPMF) to identify, assign, and align current projects with available human resources using historical data to develop resource utilization reports to periodically plan and identify resource allocations needed to support approved projects. Through preliminary reports, which were based on historical data, the team was able to demonstrate how the program management capability, which combines standard project management methodology and protocol lifecycle methodology, can be used to streamline research support processes and align budget and labor resources across all functional groups and protocol projects involving both domestic and international clinical research sites. The preliminary reports demonstrated the alignment of budget and labor resources with protocol development and regulatory projects, which has enabled program management staff to enhance existing clinical research support processes by monitoring, tracking, and reporting progress; optimizing and aligning resources across functional groups for each lab and/or site involved in the clinical research; and establishing forecast criteria for projecting budget and labor resource requirements for each fiscal year. Four regulatory service offering models, including natural history, screening, training, and intervention, were developed, and a list of resource utilization reporting templates (along with standard reports) was established. These reports will be generated on a biannual and annual basis and provided to senior management for review.

In collaboration with PN/PDP representatives, the RCHSPP Informatics Team was able to complete the conceptual design phase of a new TrackWise® (TW) project– protocol navigation. In this phase, the functional requirements of the project were assessed, a workflow with key milestones in the lifecycle of a navigational protocol was drafted, and a developmental model was completed for feasibility analysis. The next phase of the build is pending prioritization of additional TW objectives.

A Basic Ordering Agreement (BOA) was established with the Rakai Health Sciences Program in Uganda to support additional clinical research protocols. Task Order 1, the first protocol, "A Randomized, Double-Blind, Placebo-Controlled Trial of Acyclovir Prophylaxis versus Placebo among HIV-1/HSV-2 Co-Infected Individuals in Uganda," studied the role of HSV-2 in facilitating both HIV-1 acquisition and transmission. Interventions that slow HIV-1 disease progression among persons with $CD4^+$ counts above 250 cells/L could postpone the need

for antiretroviral therapy and prolong life expectancy for HIV-infected persons. Due to the lack of human resource capacity, health care infrastructure, cost, and supply chain management structures required for antiretroviral therapy delivery in resource-limited settings, strategies to retard the development of clinical AIDS and requirements for HAART are urgently needed. The above-mentioned protocol addressed this issue and was completed in January 2011.

A BOA was established with the Infectious Disease Institute (IDI) in Uganda to support clinical research protocols. IDI is an Uganda-registered, non-governmental, independent teaching, research, and clinical organization owned by Makerere University, whose mission is to build capacity in Africa to deliver sustainable, high-quality care and prevention of HIV/AIDS and related infectious diseases through training and research. IDI trains health workers from Uganda and 26 other countries on HIV/AIDS, malaria, pharmacy, lab, and data management. The first protocol, titled "A Comparison of the Development of Thymidine Analogue Mutations (TAMS) with CD-4 Monitoring Alone Versus CD-4 Monitoring Plus Viral Load Monitoring in Naïve HIV-1 Individuals on First Line ART in Africa," was a cross-sectional comparison of the rate of thymidine analogue mutations in treatment-naïve patients following 36 months of HAART; comparing 500 patients in the cohort with 1,000 additional clinic patients not enrolled in the cohort. The results of this study have had a positive impact on the clinical monitoring of HIV-infected patients and the choice of second-line antiretroviral therapy drug regimes.

CMRP's QA specialist provided initial and follow-up reviews of NIAID International Centers for Excellence in Research (ICER) sites in terms of their adherence to Good Laboratory Practices (GLPs), College of American Pathologists (CAP) or equivalent standards, and implementation of QA/QC programs for laboratories, as appropriate. The QA specialist made substantial contributions to the continued CAP accreditation of the Mali ICER Clinical Laboratory; performed initial site visits to the South Korea and China sites; provided quality management training administered to three international sites (Tanzania, China, Cambodia); supported the path to ISO 15189 accreditation for the SEREFO Laboratory at the Mali ICER; and provided overall guidance on the roll-out of the NIAID enterprise electronic biospecimen management system (BSI-II) to international and domestic DIR laboratories, and quality management of biorepositories.

CMRP continues to provide support to NIAID's Laboratory of Immunoregulation (LIR) for the recombinant human interleukin-15 (rhIL-15) project, working in collaboration with NCI's DCTD. In November 2010, a Phase III pharmacodynamic study was completed on five of the original male rhesus monkeys that had received IL-15 via 10-day continuous dose of Low-D IL-15 (at 20 μg/kg/day). There were no apparent long-term effects on clinical, cage-side, and post-dose observations, or on body weights, body weight changes, or qualitative food consumption. As a result of the successful completion of the pharmacodynamic and pharmacokinetic studies, CMRP, in collaboration with LIR, initiated a new research support contract with Avanza Laboratories to perform another study to evaluate the immunologic and virologic effects in rhesus monkeys infected with simian immunodeficiency virus (SIV). Completion of the final report for this study, including all data analysis,is anticipated by the end of the fourth quarter of calendar year (CY) 2011.

The CMRP director and clinical trials director participated in a Strategic Planning Workshop for the Phidisa Project held in late September 2010 to further refine the three strategic goals and develop draft operational plans. At the workshop, the CMRP director served as a strategic facilitator working with the U.S. and South African scientific goal leaders to develop a draft operational plan and scientific agenda relevant to the South African military. The clinical trials director participated as a team member on the development of the goal and draft operational plan to more effectively integrate Phidisa into the South African Military Health System (SAMHS)/SANDF/SA DOD. During the second strategic planning workshop held in May 2011, the CMRP director served as a facilitator to discuss and refine the three goals from the perspective of the laboratory and pharmacy working groups.

NIAID's DIR requested programmatic support from CMRP for its ICER sites in Uganda, India, Mali, and other international sites in South Korea, Cambodia, China, Peru, and Thailand to assist with the integration of the DataFax® clinical data system into several of the ICER clinical research sites supported by DIR, DCR, and the Office of Cyber Infrastructure and Computational Biology. The CMRP protocol coordinator supporting the Rakai Health Sciences Program in Uganda has been actively engaged in integrating the DataFax® data management system in the Uganda clinical research studies as part of support for the ICER site in that country. Furthermore, CMRP Clinical Consulting and Support and RCHSPP staffs were involved in several of these sites where the DataFax® system was being integrated by providing a wide range of administrative, logistical, regulatory, clinical trials management, and travel support. DIR requested support from the CMRP protocol coordinator to provide direction and training to the Office of Cyber Infrastructure and Computational Biology study staff in the operation and configuration of DataFax®, with the goal of integrating the technology into other international protocols being developed by DIR.

CMRP staff continued to enfranchise the Infectious Diseases Clinical Research Program (IDCRP) steering committee by helping re-write the interagency agreement that outlines steering committee functions and objectives and develop agendas for steering committee meetings. In addition, CMRP staff worked with NIAID staff to clarify steering committee membership to best reflect those parties with knowledge of areas of military relevance for

clinical research. The staff also facilitated the development of research capacity by aiding IDCRP staff in developing and implementing protocols for infectious diseases of military relevance.

In 2008, the D.C. Department of Health and NIH launched a new partnership to make D.C. a leader in the response to the HIV/AIDS epidemic. CMRP has played a major role in implementing this partnership, beginning with initial navigation by the clinical research nurse III, who helped to bring the D.C. HIV provider community and NIH together, and assisted in recruiting the medical director and a medical affairs scientist II for the DC-PFAP subspecialty clinics. Significant accomplishments during this reporting period have advanced the program from initial care implementation into the research phase. These accomplishments included recruiting a recent infectious disease trained physician who is on a clinician scientist pathway; caring for patients in D.C. with hepatitis B and hepatitis C; developing a laboratory-based research program in hepatitis C resistance; recruiting a recent NIAID nurse case manager to become a research coordinator in the D.C. community-integrated hepatitis clinics; implementing the first clinical trial for the program; enrolling patients directly in the D.C. clinics; submitting a clinical trial for one of the newly approved agents for hepatitis C to IRB; comparing persons with hepatitis C monoinfection and HIV coinfection; and submitting a novel interferon-sparing hepatitis C agent to IRB.

In keeping with the mission of support to NIAID clinical teams, the senior protocol nurse coordinator II assisted the NIAID nursing administration with formulating a nursing orientation competency form to meet Joint Commission requirements. The competency check-off sheet has been finalized and will soon be initiated.

H1N1 influenza presents challenges to global health security because many foreign nations, especially less developed countries, may not have preparedness plans and/or the capabilities/capacity to respond to the pandemic. CMRP staff provides a breadth of clinical research support services to NIAID's H1N1 influenza initiative, including administrative and programmatic coordination, scientific and technical guidance, clinical trials management, and regulatory and safety support. Two CMRP physicians serve as associate investigators for a number of NIAID DCR influenza trials. Numerous RCHSPP and CMRP staff members are providing ongoing regulatory, clinical trials management, and pharmacovigilance oversight to the trials. These protocols are supported by a multitude of multimillion-dollar research subcontracts. During Phase I, CMRP provided support for an observational study to characterize persons infected with H1N1 during the 2009–2010 pandemic on five continents. Enrollment occurred in 50 clinics located in North America, South America, Western Europe, Australia, Thailand, Japan, and Africa; currently 800 patients are enrolled. An additional study, FluPro, has been approved and will begin enrolling this fall when the flu season begins. The NIAID Influenza Research Collaboration (NIRC) is a NIH/NIAID-sponsored clinical trials network dedicated to finding new treatments for seasonal and pandemic flu. Currently there are four ongoing NIRC studies supported by SAIC-Frederick:

1. IRC 001 - H1N1 Plasma Collection Study: enrolls healthy volunteers who have had the flu or received the H1N1 flu vaccine and are found to have high levels of H1N1 antibodies in their blood; this study is currently being conducted at 10 domestic sites with 469 subjects enrolled.
2. IRC 002 - H1N1 Plasma Therapy Study: evaluates the safety of using human plasma containing high-titer antibodies in addition to standard care antiviral medications in treating subjects with severe influenza; 12 sites are active and seven subjects are enrolled. For the upcoming flu season, it is anticipated that 20 sites will be open to enrollment and will enroll children, pregnant women, and other adults with severe influenza.
3. IRC 003 - Combination Therapy Study: focuses on enrolling subjects who are at risk of developing severe influenza, and evaluating whether combination therapy with three antivirals (compared to the standard one antiviral) will help symptoms resolve faster and with fewer complications; seven domestic sites are active, six additional domestic sites will be activated in fall 2011, and seven Australian sites are in the process of being activated; one subject has been enrolled at this time. The protocol will launch in Mexico in October 2011 and Thailand in late fall 2011. Argentina is expected to start enrolling subjects in 2012.
4. IRC 004 - Tamiflu (Oseltamivir) Versus Placebo Study seeks to understand if subjects on Tamiflu show decreases in the amount of virus detected in the nose or throat, and if the change in the amount of virus is associated with changes in symptoms; five sites have received IRB approval and the study expects to enroll 800 patients.

CMRP staff began supporting clinical research operations of Phase I and Phase II clinical trials conducted within the NIAMS' Intramural Clinical Research Program. The initial emphasis of the support provided to NIAMS was focused on protocol navigation, regulatory compliance through IND support (three new INDs are estimated per year), and clinical trials management to assist with developing case report forms and monitoring studies under an IND/IDE. CMRP has also created template monitoring language for the NIAMS support group to use when it starts a new study and wants to request CMRP trial monitoring. The clinical trials director also provided monitoring language to be considered for all studies that CMRP may monitor for the NIAMS team. In addition to the above, the clinical trials director provided NIAMS staff with a "notes to file" template and site SOP templates. The regulatory affairs

director met with NIAMS leadership in March 2011 to discuss requirements for developing a new protocol using IL-1 Trap in deficiency of the interleukin-1 receptor antagonist (DIRA). The regulatory affairs director wrote a draft protocol document and forwarded it to NIAMS for review in April 2011.

During the reporting period, NHLBI requested support for the rapid deployment of clinical services for time-sensitive critical clinical research. To meet the request of this new initiative, CMRP hired one clinical project manager I, two clinical research associate IIIs and one regulatory associate II. Recruitment activities are in process for a clinical research associate II to support the rest of the NHLBI team. Support staff members will be located at the NIH Clinical Center in Bethesda, MD, and will perform the activities assigned by their CMRP management team as requested through the NHLBI Office of Clinical Affairs. The clinical trials director presented an overview of the services that will be offered during three NHLBI QA meetings during the month of June. In addition, a clinical research associate III created a case report form packet and the first site-initiation visit occurred in July 2011. As of the end of the fiscal year, two site initiation visits took place for new studies and one monitoring visit occurred.

CMRP Recognitions/Awards/Distinctions

- Forty CMRP employees were mentioned in the *Coordinator's Report*: Beth Baseler, John Beigel, Melissa Borucki, Molly Buehn, Lana Cross, Tracy Dean, Michelle Eby, Dawn Fishbein, Taree Foltz, Millie Gapara, Jiwan Giri, Craig Gladden, Mariana Gonzalez del Riego, Jessie (Wenjuan) Gu, Jen Imes, Sara Jones, Laurie Lambert, Yin Li, Joshua Lorenzo, Maryellen McManus, Tracey Miller, Tamika Mitchell, Kevin Newell, CK Osburn, Anu Osinusi, Michelle Paulson, John Powers, Silvana Rivera, Alice Rosenberg, Val Sevastita, Joseph Shott, Rachel Silk, Shelly Simpson, Mary Spinelli, Sharat Srinivasula, Sara Stallings, Barbara Van der Schalie, Julia Welch, Susan Yi, and Kristin Young.
- One CMRP employee received a NCI 2010 Merit Award: Barry Eagel.
- Seven CMRP employees received an Outstanding Achievement Award/SAIC-Frederick 14th Annual Achievement Award: Michelle Eby, Laurie Lambert, Daphne Mann, Tracey Miller, Irene Mueller, Vali Sevastita, and Barbara van der Schalie.
- Three CMRP employees received a Customer Relations Award/SAIC-Frederick 14th Annual Achievement Award: Carissa Haney, Tamika Magee, and Shelly Simpson.
- Thirteen CMRP employees received a 2010 NIAID Merit Award: Molly Buehn, Barry Eagel, Michelle Eby, Scott Garrand, Jiwan Giri, Angel Gonzalez-Rodriguez, Laurie Lambert, Tracey Miller, Irene Mueller, Cynthia K. Osborne, Hope Salvo, Vali Sevastiti, and Shelly Simpson.
- Four CMRP employees received a FY2011 Annual Performance Award: Rocco Caldararo, Maryellen McManus, Kathryn Spates, and Jessica Springer.
- Four CMRP employees received their master's degrees in science: Jennifer Farrell (biotechnology specializing in biosecurity and biodefense), Leah Giambarresi (biomedical science with a concentration in regulatory compliance), Lisa Timmer (information systems engineering, with a focus in distributed programming), and Robert Eackles (biomedical science with a concentration in regulatory compliance).
- One CMRP employee received a master's degree in business administration: Luis Cordeiro.
- One CMRP employee obtained certification in clinical laboratory accreditation inspection by the College of American Pathologists: Joe Shott.
- Three CMRP employees passed the certified administrative professional exam: Brenda Fevrier-Sullivan, Melinda Hohnke, and Lynda Huber.
- One CMRP employee attained her regulatory affairs certification from the Regulatory Affairs Professionals Society: Michelle Chakrabarti.

CMRP Products and Services

CMRP staff provides a wide variety of services as outlined below:

- Provides comprehensive clinical trials monitoring/management and regulatory support encompassing clinical trials monitoring, IND management, regulatory support, and other operational support;
- Maintains regulatory surveillance of clinical trials to ensure that trials are conducted in accordance with HHS/FDA/NIH regulations and International Conference on Harmonization (ICH) Good Clinical Practices (GCP) guidelines;
- Develops, assembles, maintains, and submits IND applications to sponsors and interim/annual reports to the FDA; offers regulatory guidance (assists in determining whether an IND is needed; IND application document review for new protocols); offers consultation, preparation, and submission of IND applications (investigator's brochure; protocol review; informed consent form review; and pre-IND meetings with the FDA); provides IND maintenance (maintains IND, prepares IND amendments, annual reports, IND safety reports); and serves as a communication link with the FDA;
- Reviews adverse event (AE) reports and prepares safety reports, provides instruction and guidance to staff, and prepares and submits IND safety reports for sponsored INDs; provides a dedicated safety fax and phone line for PIs to report SAEs; develops uniform SAE reporting forms;

- Acts as a liaison for regulatory issues with the FDA, the pharmaceutical industry, and the Office for Human Research Protection while initiating and conducting a clinical trial;
- Develops training programs in the principles of GCPs and the regulations pertaining to the standards of clinical research for clinical research personnel;
- Provides pre-IRB protocol and informed consent review of protocol templates based on the clinical center *Protomechanics Guide*; reviews consents for adherence to the *Code of Federal Regulations* and ICH/GCP;
- Evaluates IND requirements, makes recommendations regarding monitoring/Data Safety and Monitoring Board (DSMB) plans, and evaluates case report form needs;
- Performs clinical trials monitoring: develops guidelines on monitoring requirements; provides investigator study binders for new protocols; provides study manuals for study staff; provides protocol and informed consent review prior to submission of the IRB application/approval; initiates protocol monitoring to protect the well-being of human subjects, reports accurate trial data (i.e., safety/efficacy and adherence to clinical protocol), compliance with regulatory authorities (i.e., NIH/HHS and/or FDA), and compliance with ICH/GCP; and meets with PIs to conduct and review/outline monitoring plans and discuss study initiation visits, routine monitoring visits, study close-out visits, and tools to assist study staff with conducting the trial;
- Provides medical personnel (e.g., physicians, clinical research nurses, protocol nurse coordinators, physician assistants, clinical assistants) to support various NCI and NIAID intramural clinics;
- Provides protocol development and navigation services in support of the NCI CCR Protocol Service Center and NIAID intramural PIs;
- Provides management of domestic and international clinical operations, including study initiation, document design, preparation, submission, distribution, and tracking; development of guidelines, investigator meetings, and site training, initiation, and monitoring; and preparation for FDA audits;
- Provides scientific administration to oversee establishment of subcontracts and professional services agreements/consultants for clinical/hospital sites, correlative studies, laboratory services, consultants, and clinical research organizations;
- Provides logistical and operational support to a variety of clinical projects, including document control, informatics support, quality assurance/compliance, laboratory supplies and renovations, and capacity building;
- Provides project management support to a variety of domestic and international clinical studies and NIH programs;
- Provides medical and scientific writing that supports the development of clinical/scientific materials;
- Evaluates regulatory documents to ensure consistency and accuracy from a quality control perspective.

CMRP Personnel

CMRP staff resides in Frederick, MD, and the surrounding greater Washington, D.C., area. The current CMRP staff (positions filled) located at Industry Lane and Grove Road in Frederick, MD, consist of 96 staff members, including 25 professionals, 26 technical, 44 administrative/computer support, and one shuttle bus driver. CMRP is consistently recruiting to fill additional professional, administrative, and technical positions to meet the needs of NCI-Frederick. Included in CMRP, but working off-site, are 130 staff members who support the Bethesda, Rockville, and D.C. operations: 37 professionals, 62 technical, 30 administrative/computer support, and one shuttle bus driver. Several employees are approved for full-time telecommuting, including professional employees who reside in North Carolina, Minnesota, and New Hampshire. Support to several international initiatives requires employees to be detailed to the following international locations: one professional employee in Uganda, one professional employee in India, and one administrative employee in Mali.

CMRP Initiatives

CMRP staff members frequently take part in activities that promote and teach about NCI and NIAID projects, including volunteering in the NCI-Frederick-sponsored Take Your Child to Work Day, participating in each bi-weekly New Employee Orientation program, and presenting “Clinical Trials 101” for senior nurses at Frederick Community College to increase the visibility of the clinical trials arena as a career option. CMRP staff, in collaboration with Frederick Community College, presented a half-day seminar in October 2010, featuring speakers and posters to raise awareness of clinical research as a career path for nurses. Planning is underway to expand this half-day seminar to additional Maryland Community Colleges.

Moreover, CMRP staff is greatly involved in creating and maintaining an atmosphere with a strong sense of team work and high employee morale. Two important projects that staff organized, planned, and participated in were the annual diversity day potluck luncheon in May 2011 and the fourth annual office olympiad, held during the summer of 2011, in which 78 percent of the staff participated. Several CMRP members were also recognized by their peers through the RESPECT (Recognizing Excellent Service Promotes Employee Commitment and Teamwork) employee recognition program for their service to others.

Many CMRP team members were designated to participate in NCI and NIAID projects within FY2011. Team members prepared, participated, and presented at a monthly seminar series, provided seminars at the NIH Clinical Center and Rockledge, and presented several posters in various forums held at Fort Detrick and NIH.

To encourage innovation and cost savings, several CMRP staff members submitted suggestions to the "APennySaved" initiative, as well as to the "Ask Beth" mailbox.

During CY2011, the CMRP team continued to expand its technical and professional skill competencies. Coursework in clinical research, current Good Clinical Practice (cGCP), and regulatory affairs was completed by some team members. Seventeen members of the CMRP administrative team participated in a year-long class to prepare for the International Association of Administrative Professionals certification examinations. Three administrative staff members passed the certification examination and other administrative staff continues to pursue the certification.

At the request of the staff, the second annual CMRP Training Retreat was held in September 2011. This event included more than 30 sessions organized into six major areas: communication, compliance, health, professional development, managerial/supervisory, and IT applications. The event also featured a poster session highlighting the diverse activities of CMRP staff and a webinar on data management that provided continuing education units.

CMRP Program Management

CMRP continues to provide high-quality clinical trials/regulatory and programmatic/project management support to NCI and NIAID initiatives. The ability to provide rapid responses, high-quality solutions, and to recruit and retain diverse subject matter experts is evidence of CMRP's success. CMRP programmatic management support was launched to offer a complete approach to clinical support services. The CMRP Program Management Office contributes to NCI and NIAID clinical research activities by providing centralized services that facilitate high-quality clinical research through program guidance and support, strategic planning and direction, project management, technical direction, learning and professional development, and general assistance to various government entities. The CMRP Program Management Office includes an administrative group, a training group, and a clinical informatics group.

CMRP Project Management

The CMRP Project Management Office (PMO) provides operational support to all overarching CMRP initiatives. PMO comprises two level I clinical project managers, one medical writer, and one document coordinator.

Working in conjunction with the administrative group and NIAID, NCI, NHLBI, and NIAMS support groups, PMO staff prepares and submits budgets and responses for Yellow Task (YT) inquiries. Once YTs have been approved, PMO works with the respective CMRP group to track the status of tasks (including hiring staff and establishing research subcontracts) required to fulfill the needs of the YT. When budget revisions are requested, PMO staff works with the appropriate CMRP personnel to revise the budget and submit it through the YT webmail system.

PMO staff is also responsible for coordinating the submission of several reports throughout the contract year. Every six months, the staff collects information regarding each CMRP group's goals and objectives; each goal has specific and measureable elements with associated target dates. Staff works with the corresponding CMRP group to monitor the progress made towards the goals. PMO also collects information for the Operational Contract Performance Status Report, which highlights significant work conducted in the previous six-month time period. Additionally, PMO staff coordinates the efforts of generating and submitting the NCI Annual Report, the CMRP Annual Report, and the International Efforts Report each fall.

PMO provides overall project management support for internal CMRP initiatives, as well as the external high-profile HIV/AIDS collaboration between NIH and the Washington, D.C., Department of Health. During CY2011, PMO launched a new CMRP web site that allows both CMRP staff and the public to see the specific projects CMRP staff support. PMO staff also contributed to the development of policies and procedures related to the federal Health Information Technology for Economic and Clinical Health (HITECH) Act, initiated the publication of a monthly internal newsletter, reorganized CMRP's electronic filing system, developed and implemented a new electronic signature process, provided background research for projects, assisted with creating and editing presentations, and provided management and oversight for CMRP organizational charts. In addition, the PMO staff developed a directorate-specific process for future potential government shutdowns and began to develop the CMRP strategic plan. Supporting the CMRP director, PMO provides medical writing services to prepare presentations, edit statements of work (SOWs), generate and distribute meeting minutes, and write internal procedures.

During the reporting year, PMO also assisted multiple CMRP programs in the establishment of research subcontracts, including assisting in the preparation of SOWs, shepherding contract documents through the research contracts process, and performing a critical review of proposals and budgets; developed a YT metrics spreadsheet to assist in summarizing and tracking all tasks associated with each CMRP YT; worked with management and the YT coordinator to develop and refine YT templates to assist the government customer in requesting or eliminating CMRP support and in establishing research contracts; compiled a database of all staff publications that can be accessed to provide report data; initiated the development of a CMRP intranet site

that will allow both on- and off-site staff to access forms and provide a central location for all documents (PMO staff assumed responsibility for uploading documents associated with multiple projects to the CMRP subcontracts SharePoint site); and worked with management to redesign the new employee orientation presentation that provides an overview of CMRP support.

In addition, a PMO clinical project manager I attended a three-day course in Orlando, Florida, on developing a project management office and portfolio management, and a document specialist II completed four software training courses: Microsoft Word 2010 Levels II and III and Microsoft Excel 2010 Levels II and III. The knowledge gained in these courses will be especially important as the CMRP group transitions from Microsoft 2007 to Microsoft 2010.

CMRP Document Control

CMRP Document Control provides administrative and clerical support related to documentation requirements and system management of documents to support the program.

To simplify the process for collecting and storing data for tracking employee publications, the group implemented Manutrak, a document management software system. The software is used and maintained by the document coordinator to gather and summarize data to prepare reports that are in compliance with NIH requirements. Internal audits are performed to ensure the effectiveness of the software and CMRP compliance with NIH requests.

During the reporting period, CMRP electronic file data storage was organized to ensure information was deposited intuitively, thus simplifying navigation of the folder and files held within the internal CMRP shared drive. Any duplication of material was evaluated and either deleted or archived to eliminate issues concerning document version history. Document Control staff created or updated internal procedures detailing the purpose, function, and requirements of a process and created easy-to-follow flow diagrams to be used in conjunction with written internal procedures. In collaboration with staff, internal forms were created, edited, updated, or reformatted to be electronically fillable and user-friendly.

The document coordinator also assisted in the maintenance of a CMRP subcontracts database by uploading the appropriate documentation into a SharePoint document library and tracking updates received from new invoices in the form library. In addition, a spreadsheet was developed to track historical YT data to be used as a reference tool.

CMRP Financial Management Group

The CMRP Financial Management Group continues to expand its capabilities and take on new challenges in support of NCI and NIAID. In an effort to meet the increasing demand for cost accountability and to monitor budgets to ensure funding availability, CMRP established a Financial Management Working Group. This group collaborates with other SAIC-Frederick directorates, managers, and inner departments, as well as with NCI and NIAID officials, and manages the following 78 cost centers: two for CRD, 13 for the NCI Office of the Clinical Director, three for the Clinical Center/Agency, two for other clinical centers/institutions, 16 for the NCI Center for Clinical Research, six for NCI's DCTD, one for the NCI Division of Cancer Epidemiology and Genetics, one for the NCI DCCPS, 17 for the NIAID DIR, and 17 for the NIAID DCR.

During this period, the Financial Management Working Group developed two internal operations management administrative standard procedures, which are included in the CMRP Administrative Policy Manual. This manual allows for process consistency, which increases the efficiency of SOPs that support the program.

In addition, the Financial Management Working Group completed the migration of all information to a central CMRP SharePoint site to manage all CMRP research subcontracts, professional service agreements, and consultant agreements. This site provides quick access from one location to all source documents and financial information, allowing the program to increase efficiency when responding to customer inquiries.

The Financial Management Group received recognition in the *Coordinator's Report* in December 2010 and March 2011 for their support to RCHSPP in support of NIAID's DCR, and for their dedication to all of the H1N1 subcontract budgets.

Within the reporting period, the Financial Management Group continued to manage and develop cost estimates for new YTs and work scopes, provide monthly financial report information, anticipate estimates-at-completion deadlines, and track project costs for all budgets to ensure accuracy and cost accountability. In addition, as a result of excellent planning for the collection and assembly of information, the group responded to the submission of the CY2012 budgets to meet the contractual deadline.

CMRP Clinical Training Group

CMRP training support is provided by the Clinical Training Group (CTG), which is composed of a clinical training manager, training specialist/instructional designer, an ARRA training specialist, and an administrative support staff member. CTG supports RCHSPP, the Office of Planning and Operations Support (OPOS), CMRP, and the ARRA program. In supporting these various clients, CTG participates in activities that fall into five categories: (1) identify/develop training resources to address client-identified training needs; (2) provide training and professional development subject matter expertise; (3) provide administrative support for activities with training components; (4) ensure compliance and continuous improvement of training processes and initiatives; and (5) conduct professional development sessions to ensure that staff members maintain their subject matter expertise, including

providing training sessions, presenting at conferences, and participating on advisory committees.

During this reporting period, the group has implemented the following activities to serve specific needs:

Identify/Develop Training Resources to Address Client-Identified Training Needs

CTG facilitated a monthly seminar series on topics of interest to CMRP staff. These seminars are available via webinar to all staff and cover diverse topics, including specific diseases, compliance/regulations, and professional skills. The two most recent presentations were The Long and Winding Road to Drug Development and The Yin and Yan of Effective Communication, each provided by SAIC-Frederick colleagues.

The instructional designer completed a 14-month program to prepare the administrative team to complete the International Association of Administrative Professionals certification; this effort resulted in a 75 percent pass rate on the first testing.

CTG assembled a three-part training series on the ABCs of clinical research from an administrative perspective, hosted the CMRP Annual Administrative Professionals' Day, and served on the CMRP Administrative Professionals' Retreat Planning Committee.

The clinical training manager continued to provide the Communication Style Preference Training to new managers biannually. This effort was in addition to the numerous sessions provided to diverse SAIC-Frederick training audiences, including Giving and Receiving Constructive Feedback, ARRA Audit Awareness, Generations in the Workplace, and the Myers-Briggs Type Indicator.

This year, the clinical training manager received an SAIC-Frederick Outstanding Achievement Award, as part of the SAIC-Frederick Internal Training and Development Team.

Provide Training and Professional Development Subject Matter Expertise

In October 2010, CTG facilitated the Community College Outreach Program, a half-day program designed to raise the visibility of clinical research as a career option for nurses.

One of the CTG training specialists developed a presentation on the Foreign Corrupt Practices Act.

Additionally, the clinical training manager served on the Workforce Development Board of Frederick, the Science Technology and Engineering Steering Committee for Frederick County Public Schools, and the Scientific Publications, Graphics & Media Advisory Board.

Provide Administrative Support for Activities with Training Implications

CTG facilitated five installments of the monthly seminar series for CMRP staff while ensuring WebEx access for off-site staff. The group also facilitated 22 training sessions on various topics; each session included presentation evaluation and attendance documentation for each participant.

In addition, CTG facilitated 15 New Employee Orientation sessions for 44 new employees. Efforts included scheduling presenters, compiling information into a reference binder for each new employee, and presenting the Clinical Training Presentation and Training Management Policy Presentation sections of the session. Furthermore, the team facilitated seven weekly sessions of the Ethical and Regulatory Aspects of Clinical Research via video conferencing for 14 CMRP employees, including attendance monitoring, administering pre- and post-tests, and transferring information to a liaison at the Department of Bioethics.

The CTG team also provides administrative support to the FDA Inspection Readiness Teams, and the CMRP Training Work Group.

Ensure Compliance and Continuous Improvement of Training Processes and Initiatives

CTG is heavily involved with the CMRP Gallup Poll Impact Plan, assisting authors, collecting data, and facilitating delivery on actions. The group is also administering the 2011 résumé/CV and signature log review project for all CMRP staff, which includes sending a current résumé/CV and signature log to each employee, instructing the employee to update, if needed; and tracking the return of all résumé/CVs and signature logs to ensure 100 percent compliance.

CTG also conducted a Value of CMRP New Employee Orientation survey. The results were favorable; new employees find great value in the New Employee Orientation session whether they are off-site or located at Industry Lane.

The training records, maintained in both hard copy and electronic formats, are audited annually, both hard copy to electronic and electronic to hard copy. As in the past, this effort ensures that CMRP training records are at least 97 percent accurate; this year's records were 98 percent accurate.

Conduct Professional Development Activities

CTG provided extensive facilitation services for the 2011 CMRP Training Retreat, including venue and speaker identification, participant communication, retreat day logistics, and post-retreat evaluation and thank you letters. The event involved over several sessions from 22 presenters and 160 participants from all CMRP locations.

The clinical training manager served on a team that presented at the Association of Biomedical Communications/Directors, Health Sciences Communications Association, and BioCommunications Association's annual meeting. The title of the presentation was Manager as Communicator: A Case Study in the Development of a Strategic Corporate Communication Plan for SAIC-Frederick, and was video cast to the conference in Phoenix, Arizona.

One of the training specialists is a regular contributor to the monthly CMRP newsletter, *The CMRP Insider*, supplying articles designed to help CMRP staff better

understand the role of CTG, how to better use CMRP support services, and to increase participation and compliance with requests for information that maintain inspection readiness in regards to training records and other training documentation.

CMRP Clinical Informatics Group

The CMRP Information Technology (IT) group provides software development, computer, network, application, and disaster recovery support to NCI, NIAID, NHLBI, and NIAMS initiatives. Members of the IT group specialize in evaluating core business processes, utilizing simple and flexible methodologies to transform business needs into suitable, cost-effective technical solutions while maintaining focus on both customer satisfaction, and meeting the unique operational requirements for management of clinical trial, regulatory, and clinical safety data.

In the past year, the IT group was involved in several key technical initiatives for the program, including:

A public-facing web site was developed and released to highlight the diverse clinical research service offerings and support functions provided by CMRP. The site provides information about the many high-profile NIAID and NCI initiatives to investigators, clinicians, prospective job seekers, and the general public. As additional initiatives are supported, the web site will be updated. Statistical web tools and speed and search engine optimization features were integrated into the site to enhance page delivery and improve visibility while ensuring appropriate security safeguards were in place to comply with NIH standards. Flexible and configurable web development tools were also employed, which allow program staff, rather than web developers, to perform content updates.

Several programmatic and operational enhancements were introduced for the research subcontracts' SharePoint release, which was launched in late 2010 to centrally store, manage, and track program-specific subcontract information via custom form and document library integrations. Programmatic changes included the addition of several new fields, including an estimate-at-completion date field that allows for an enhanced forecasting of expenditures for individual subcontracts. The reporting web interface was expanded to provide a more detailed view of research subcontract data and, based on input from the project's stakeholders, new reports were created to provide advanced performance-tracking metrics such as the ability to review research subcontracts from several predefined performance period date ranges. These views expanded the tracking capabilities of the COTR, which allowed them to better respond to and take necessary action for ensuring successful completion of the subcontract. Operational changes included the build-out of several new reporting platforms to provide the software development group with the ability to assess new versions of the Microsoft® SharePoint Services platform and to determine the most suitable upgrade path, as well as to separate development and production environments. In addition, the working group membership expanded to include appointed accountable representatives from each program area. This was necessary to support a change request process developed by the group to manage system changes, to ensure proper communication channels are open, and to ensure changes are made in a consistent and uniform manner.

Members of the IT group continue to be involved in multiple facets of technical service delivery for the ARRA initiatives awarded to SAIC-Frederick, ranging from the specification and technical evaluation of IT equipment requirements to the management of data systems, application support, and participation in training initiatives for the design and construction of standardized framework. This allows for the rapid delivery of IT and business-related training to program staff.

The IT group completed the integration of a new communications network, in close collaboration with SAIC-Frederick telecommunications and network operations staff. The group was responsible for evaluating and developing a network design to provide high-speed wide-area connectivity to the NCI-Frederick campus, as well as interoperability between the leased space and the Industry Lane location. Hardware specification for both local and wide-area network operations was conducted and reviewed for compatibility and integration into existing infrastructure, and a run of fiber optic cabling was installed between each endpoint in mid-2011. Efforts are underway to transition the primary wide-area connection over to the fiber optic link.

The IT group acquired, installed, configured, and provided support for smart card equipment and middleware software for CMRP program staff to ensure compliance with smart card authentication requirements and standards set forth by the Homeland Security Presidential Directive 12 (HSPD-12) Act of 2004, and associated Federal Information Security Management Act regulations, Office of Management and Budget memoranda, and NIH policy.

In addition, with logical access to the NIH network and with HHS-verified Public Key Infrastructure software certificates embedded on individual personal identity verification (PIV) cards, an initiative was undertaken to utilize electronic signatures in lieu of paper-based wet signatures for approvals of designated program documents. The initial document type selected was a mobile device usage certification form and corresponding monthly invoice. A program review and analysis was conducted to evaluate the current process of managing and distributing these documents to appropriate staff members. Based on this evaluation, a more efficient and modularized mechanism was developed using scripting methods to manage the workflow and e-signature capabilities provided by the PIV cards. This initiative has significantly reduced not only the time required to route these documents, but also the paper footprint of the original process. This process also eliminates the potential of a paper invoice or usage certification form being lost or misplaced. The initiative has been well received by the

program staff involved and efforts are underway to expand the capability to other document types.

The IT group continually assesses the goals and objectives of CMRP and uses leading-edge technology to provide the best return on investment, while ensuring compliance with all applicable regulatory and security best practices, policies, and standards.

SUPPORT TO AMERICAN RECOVERY AND REINVESTMENT ACT OF 2009 (ARRA) INITIATIVE, NCI

During the reporting period, CMRP continued to provide support to numerous ARRA initiatives within NCI.

Cancer Human Biobank (caHUB) ARRA Initiatives

Originally, eight ARRA YTs were approved to support new initiatives within caHUB. The eight initiatives are divided into three main components: (1) tissue procurement; (2) caHUB coordination; and (3) biospecimen research and development. CMRP provided dedicated staff and managed numerous research subcontracts and professional/consulting agreements to address these initiatives from September 2009 through January 2011.

Several changes occurred over the past year due to the change in NCI leadership. In January 2011, the Office of Biorepositories and Biospecimens Research (OBBR) announced that the goals and objectives for caHUB were being redesigned. The 'repurposing' of caHUB also included a reduction in funds from $60 million to approximately $36.5 million. The original purpose of caHUB was to create a benchmark biospecimen collection process to be used for future unspecified work. The premise was that OBBR would build this collection so that investigators/researchers could apply for the right to receive biospecimens with specific attributes to use in their own research projects. Because the collection was not intended for particular, defined research projects at the time of biospecimen acquisition, the NCI director asked that changes be made so that biospecimens would be collected for specific, meaningful research purposes. Thus, over the past year, caHUB has evolved into a foundation of collecting biospecimens driven by the development of standards to generate products for the public domain.

In April 2011, oversight of and support for OBBR initiatives were transferred from CMRP to the Information Systems Program (ISP). The transfer included staff, equipment, and supplies. CMRP senior management created a transition plan, taking the following aspects into consideration: document control and chain of custody, subcontracts management, equipment and sensitive property, cost center and financial management, and personnel. Steps were taken to conduct official transfers of property accountability, cost center signature authority, personnel supervision, COTRs, etc. Additionally, all project documents were transferred from CMRP servers to one of the OBBR SharePoint sites. These efforts provided for a seamless transition between directorates.

NCCCP ARRA Initiatives

CMRP provided extensive program management and administrative support to the NCCCP network that was expanded in April 2010 to include 30 community hospitals located in 22 states. Dedicated CMRP staff continued to manage and support the comprehensive communications infrastructure of the expanded program, and the 45 research subcontracts awarded to the NCCCP community hospitals and collaborating institutions.

Cancer Diagnosis Program (CDP) ARRA Initiatives

CMRP provided ad hoc administrative and subcontract management support to the Patient Characterization Center/Clinical Assay Development Center subcontracts for a specimen retrieval system to collect cases for validation of NCI-supported clinical assays. NCI is establishing a system that will provide sets of appropriate specimens to facilitate the evaluation of an assay's analytical performance and initial assessment of clinical utility. The specimen sets will be assembled rapidly to meet assay development needs identified during the review of clinical trial concepts and emerging technologies, and will be associated with clinical and outcome data.

CMRP ARRA Training Support

In addition to providing project management, logistical, and subcontract support to NIH programs and initiatives, CMRP infrastructure support to ARRA initiatives includes assistance with training as detailed below. CMRP's clinical training manager, a newly hired training specialist, a training specialist/instructional designer, and an administrative support staff member support ARRA training initiatives.

In an effort to identify/develop training resources that address client-identified training needs, CTG designed a number of training presentations for this program, including ARRA Inspection Awareness, Section 508 Awareness, and Training Database Overview.

CTG provided training and professional development subject matter expertise by collaborating with the ARRA Training Program Steering Committee to design and implement the ARRA Training Program. This program, which falls under the CMRP training policy, involved an extensive training needs assessment, including a risk analysis; identification of qualified subject matter experts; training session configuration, review, approval, and evaluation; and documentation of all training events. CTG also participated in the instructional design and review of several of the ARRA training sessions, including the OBBR program overview, IT security, budget/funding, an NCCCP program overview, and signature authority and property accountability.

CTG has managed and coordinated all mandatory ARRA trainings, in order to ensure a 100 percent completion by all ARRA staff. These trainings allowed newly hired and newly dedicated staff to quickly transition into their roles to support the ARRA activities. This resulted in staff performing their duties and responsibilities in a rapid and proficient manner. Documentation of the ARRA trainings has been recorded and maintained in an audit-ready state.

In addition, CTG provided administrative support for activities with training implications such as configuring the training program and training records, tracking components, and developing training modules.

To help ensure compliance and continuous improvement of training processes and initiatives, CTG conducted extensive research on auditable elements of the ARRA Training Program to develop an audit awareness training module. The ARRA training records are maintained in an audit-ready state. TW training manager is currently being developed to monitor compliance with training requirements.

Infrastructure Administrative Group ARRA Initiatives

The CMRP Infrastructure Financial Management Group continued to maintain budgets and staffing for all ARRA projects. Other functions include preparing project reports and performing data analyses; monitoring new subcontract awards; recruiting staff; providing document control management support of all ARRA source documents; providing review of Statements of Work; providing medical writing support for the review of scientific, technical, and administrative documentation; supporting project meetings that included internal (e.g., NCI, SAIC-Frederick) and external stakeholders (e.g., advisors, subcontractors); providing subject matter expert training to employees regarding processes and procedures; providing information technology backbone support services, including acquiring, installing, and configuring equipment; developing/implementing software and disaster recovery services; creating new reports to maintain accurate accounting of ARRA records and the Transition Plan to phase out ARRA projects; and performing internal audits to ensure adherence to proper procedures. In addition, the back office infrastructure team managed space requirements for CMRP back office infrastructure, caHUB, and NCCCP staff to support efforts based on location requirements. This group worked collaboratively with other SAIC-Frederick directorates, managers, and inner departments, as well as with NCI officials.

The Financial Management Group working in collaboration with technical support services developed and implemented a central CMRP ARRA SharePoint site to manage all CMRP ARRA-related research subcontracts, professional service agreements, and consultant agreements. This site provides quick access from one location to all source documents and financial information, allowing the program to increase efficiency when responding to customer inquiries.

Within the reporting period, the Financial Management Group continued to manage and develop cost estimates for new revised work scopes, provided monthly static financial report information, anticipated estimates-at-completion, and tracked project costs for all budgets to ensure accuracy and accountability of all costs. In addition, as a result of excellent planning and documenting static financial worksheets, the group responded to multi-year spending predictions, which was used to quickly generate the information needed as part of the submission of the CY2012 budgets.

Support provided by the IT Group spanned an array of technical service areas, ranging from authoring technical guidance documents and modeling\prototyping software solutions to acquiring and managing end-user computing equipment and back-office support. Several key initiatives and efforts were undertaken and completed during the year, including the following:

The acquisition, installation, configuration, and support for smart card equipment and middleware software to program staff to ensure compliance with smart card authentication requirements and standards set forth by HSPD-12 and associated Federal Information Security Management Act regulations, Office of Management and Budget memoranda, and NIH policy.

A public-facing web site was developed and released to highlight the diverse clinical research service offerings and support functions provided by CMRP. The site provides information about the many high-profile NIAID and NCI initiatives to investigators, clinicians, prospective job seekers, and the general public. Speed and search engine optimization features were integrated into the site to enhance page delivery and improve visibility.

The functional requirements were evaluated for the development of an electronic method to deliver mobile device invoices to program staff. The solution replaced a paper-based process by embedding digital signature capabilities into electronic invoices and utilizing a tiered workflow to route invoices for review, approval, and storage.

Additional details for ARRA support are presented in the respective sections of this report.

SUPPORT TO NCI

Support to the Molecular Imaging Program (MIP), NCI

Barry L. Gause, M.D., Clinical Director
Beth Baseler, M.S., Director
Revia Wade, MSN, C.R.N.P.
Stephen Adler, PhD, Laboratory Director

The mission of the Molecular Imaging Program (MIP) is to develop and test targeted imaging agents for cancer

detection and treatment. This program performs translational research in targeted cancer imaging for purposes of early tumor detection and characterization, treatment monitoring, and drug development. CMRP provides a dedicated team of individuals to support the operations of the NCI Research Imaging Clinic in the most efficient, effective, and compassionate way.

CMRP staffs a PET physicist to work with the National Institute of Standards and Technology (NIST). This support has been instrumental in determining the accuracy of the program's PET/computed tomography (CT) scanner; performing radiation dosimetry for clinical trials; credentialing the PET/CT scanner for clinical trials experiments; performing quantitative analysis; and solving technical image quality problems. In the absence of the nuclear medicine dosimetry calculations physician, the PET physicist is responsible for solving technical problems with imaging and quantitative analysis.

A senior nurse practitioner supports MIP by participating in the screening of human subjects for research by conducting history and physical exams for all participating subjects. The senior nurse practitioner also assists NCI's Gastrointestinal Stoma Clinic with biannual assessments.

The MIP PET/CT technologists perform highly skilled PET/CT scans for patients involved in clinical trials. The technologists are instrumental in writing policy relevant to PET/CT and maintaining quality assurance (QA) for radiation safety. Staff members have met all rigorous credentialing requirements necessary to function as authorized users of radiopharmaceuticals. This accomplishment provides support directly to the PI, as well as to the entire department.

The MRI/CT/radiology technologist (RT) is credentialed in three modalities and is a candidate for PET certification training, an outstanding accomplishment. This technologist is responsible for developing and implementing SOPs related to MRI contrast and delivery.

The patient care coordinator is responsible for scheduling patients who visit the molecular imaging clinic for participation in clinical trials. Other responsibilities include serving as an interpreter for Spanish-speaking patients and interfacing with other branches, such as urology, to coordinate referrals into the department. The coordinator provides administrative support to the PI, as well as to the patient clinical trials clinic.

During the reporting period, the laboratory director submitted a paper for publication titled "A Method for Statistical Image Quality Normalization." It was the culmination of a project involving the NIH Clinical Center and physicists from NIST. The project involved studying how patients could be scanned on different PET/CT scanners and attaining data of similar statistical image quality. This is important work needed to help harmonize data sets for multi-center clinical trials involving protocols requiring PET/CT scans of subjects under study. The director is currently waiting to hear if the paper has been accepted for publication. A poster presentation of this work was given at the Society of Nuclear Medicine's annual meeting in June 2011 in San Antonio, Texas.

The director was also involved in qualifying the preclinical PET/CT scanner (scanner for mice and rats), which will be a key instrument used by Dr. Peter Choyke's (program director, Molecular Imaging Program) preclinical program. Qualification tests were conducted during the summer. The results were published in a peer-reviewed journal and a presentation was given at the World Molecular Imaging Congress in September 2011.

Support to the Metabolism Branch, NCI

Barry L. Gause, M.D., Clinical Director
Beth Baseler, M.S., Director
Lamin Juwara, MSN, Senior Nurse Practitioner

The primary focus of the Metabolism Branch is to combine basic research with preclinical investigation and drug development to provide innovative therapeutic clinical trials in immune response and immunoregulation disorders that underlie immunodeficiency and neoplastic diseases. CMRP provides a clinical research associate II to support these efforts.

In support of the Metabolism Branch, CMRP staff perform many integral functions, such as developing several collaborative relationships with investigative sites and client personnel; performing and coordinating assigned aspects of the clinical monitoring process in accordance with GCPs and global SOPs to assess the safety and efficacy of investigational products; conducting internal audits to determine protocol compliance; preparing required documentation; and providing assistance with close-out visits.

During the reporting period, CMRP staff performed a QA/quality improvement review of various studies and provided data to PIs to analyze for presentations, posters, and publications.

In collaboration with Biovest International, CMRP staff has been involved with designing, planning, and implementing the Phase III vaccine trial for non-Hodgkin's lymphoma. CMRP staff assisted with developing the protocol and case report forms, tracking and maintaining study-related files, and assisting with conducting internal site visits to ensure compliance with clinical protocol and overall trial objectives.

Staff members tracked patients, patient follow-up appointments, and overall patient outcomes in addition to assisting with the preparation and production of documents for FDA submission regarding approval of this study.

Support to the Protocol Support Office (PSO), NCI

The Center for Cancer Research (CCR) re-engineered its processes regarding the development, review, and opening of clinical trials in order to decrease the time

from scientific review to opening clinical trials for patient accrual, while maintaining or increasing quality and safety. As a result, CCR established a Protocol Service Office (PSO) and a Protocol Review Office (PRO) (described below). PSO oversees services in three major areas: (1) writing and editing, (2) regulatory and compliance, and (3) protocol navigation and administration. CMRP is responsible for assisting with the preparation of new proposals/protocols and progress reports for IRB meetings. CMRP assists PSO staff in reviewing and making recommendations/changes to protocol amendments and other documents related to research studies. This team also assists with training new staff and has been involved in creating the electronic document management system. CMRP staff is required to attend the IRB meetings and assists with contacting PIs for the review board, as needed.

In support of PSO, CMRP hired two protocol coordinators to serve as liaisons between CMRP and CCR/NCI staff to initiate and complete tasks related to protocol support; a regulatory associate II to prepare and review submissions to FDA and ensure that all documents are in compliance with FDA regulations; and a medical writer III to attend IRB and branch meetings, take minutes, create and edit SOPs and templates, and review and edit protocol amendments and continuing reviews. Staff also edited or created associated documents, such as informed consents.

Support to the Protocol Review Office (PRO), NCI

PRO is under the direction of the CCR Clinical Director's Office, and provides administrative support for the NCI intramural IRB. Currently, IRB has approximately 400 protocols under its review. PRO staff provides assistance by reviewing all protocol actions designated for expedited review by the IRB chair and protocol actions that require full board review.

The IRB administrator assists PRO staff with the review of documents submitted for IRB review by the PIs and study coordinators and extracts relevant technical information to include in the IRB packets and database. The administrator is also responsible for distributing correspondence to PIs and study contacts and distributing amendments approved by the IRB chair and Clinical Director's Office. Other duties include processing and distributing documents (deviations/violations, closure to accrual, and outside IRB documents) to the IRB chair using iRIS; preparing and distributing IRB and Safety Monitoring Committee (SMC) meeting packets in a timely manner; receiving all internal calls regarding protocol submissions using iRIS; monitoring the task box in iRIS and routing issues to the appropriate analyst; and maintaining hard copies of protocols and IRB meeting minutes.

CCR made an expedited request through the YT system for CMRP to provide a qualified person to serve as chair of the NCI IRB. CMRP staff responded quickly and was able to accommodate the high-priority request within a two-week timeframe through a research subcontract.

Support to Clinical Core (Transplantation), NCI

Lamin Juwara, MSN, Senior Nurse Practitioner
Jennifer Wilder, Clinical Research Nurse III

The Experimental Transplant and Immunology Branch (ETIB) is dedicated to coordinating efforts for basic, preclinical, and clinical investigations in the area of transplantation science. The goal of this program is to generate information from basic and preclinical investigations leading to the development of novel, curative therapies for cancer. Information from new treatment protocols (including novel endpoints generated in the course of basic and preclinical research) is used to generate new questions and studies in basic and preclinical research efforts. CMRP provides a nurse practitioner I, a clinical coordinator, a clinical research nurse III, a physician assistant, and a senior nurse practitioner to support the transplantation clinical efforts.

CMRP serves as the associate investigator on 11 protocols, seven of which are actively recruiting and transplanting patients. Staff members have been involved in the development of the first double-cord blood transplant protocol at NIH, which is open and recruiting patients; three patients have received transplants. The group also identified and transplanted suitable cord units for seven aplastic anemia patients at NHLBI for the haplo/cord protocol.

Staff is responsible for coordinating all clinic-related functions and administrative support for ETIB. The group has coordinated graft-versus-host disease patient recruitment; processed patient intakes; facilitated patient accrual into clinical trials; worked closely with patients, donors, and families through a protocol screening process; and maintained communication with patients and referring physicians' offices.

Notably, the Clinical Core group has played an integral role in negotiating the Data Transmission Agreements between the Center for International Blood and Marrow Transplant Research (CIBMTR) and NCI, NHLBI, and NIAID. This group also drafted the CIBMTR Data Repository Submission protocol for ETIB and POB.

CMRP staff members are preparing to submit the National Marrow Donor Program (NMDP) Cord Blood IND protocol to IRB to comply with new cord blood FDA licensure requirements, which went into effect in October 2011. Staff members are also coordinating the effort to amend the Clinical Center agreement with NMDP to reflect the new regulations.

During the reporting year, CMRP also facilitated, coordinated, and managed all unrelated donor product/ research activity at NIH. Staff assisted in the development of standards and processes to support this initiative and

continue to perform searches and advise on donor selection for all unrelated donor products and patients. The team has worked with clinical staff to schedule and coordinate appointments with patients and donors; coordinate the processing of human leukocyte antigen (HLA) kits (including obtaining HLA packages from patients and donors, filling out forms, and submitting blood samples to the HLA lab); obtain HLA typing results; inform transplant coordinators and patients of HLA typing results, when required; and maintain an updated tracking database. The CMRP nurse practitioner has worked on NCI's inpatient transplant unit, directing, scheduling, and planning the care of these patients. Staff members also provide outstanding leadership by participating and leading weekly HLA meetings for NCI unrelated donor patients. This effort has resulted in improved communication among all parties involved in a transplant and has aided in problem solving.

The Clinical Core Group created and updated databases, ran queries, and participated in the creation of educational material for NIH graft-versus-host disease patients, transplant patients, donors, and NIH regarding stem cell transplantation to help patients and donors understand a transplant and what to expect during the transplant process. The group also wrote letters requested by patients, donors, and/or caregivers, such as visa- and work-related letters, and completed documents such as patient health insurance and work disability forms.

Support to the Developmental Therapeutics Clinic (DTC)/Phase 0, NCI

Barry L. Gause, M.D., Clinical Director
Beth Baseler, M.S., Director
Lamin Juwara, MSN, Senior Nurse Practitioner

The overarching mission of the Developmental Therapeutics Clinic (DTC) is to evaluate innovative anticancer compounds in early phase clinical trials, while providing outstanding clinical care for patients with different types of cancer. An important focus of the clinic is first-in-man clinical trials, particularly those that incorporate pharmacodynamic and pharmacokinetic endpoints, with the goal of informing subsequent clinical development. CMRP provides a senior nurse practitioner and a clinical research nurse II to support these efforts.

During the reporting period, the senior nurse practitioner contributed to the successful development and undertaking of new trial designs such as the single-agent Phase II trial with ADZ2171 (Cediranib), which is one of the most promising regimens in a rare form of sarcoma (alveolar soft-part sarcoma), and a multi-histology Phase II trial with R788.

CMRP staff continues to perform protocol-required skin punch biopsies to facilitate the research process for the Phase I LMP776 protocol and continues to collaborate with other cancer centers in multiple trials, including a Phase I 5FdCyd +THU trial and a Phase I ABT-888+Cytoxan trial. Staff also participates extensively in the Phase I oral Topotecan trial of tumors that are positive for hypoxia-inducing factor-1 alpha (HIF-1 alpha), under the direction of the DTP-Tumor Hypoxia Laboratory.

The clinical research nurse supporting DTC's early drug development team under the Medical Oncology Branch is currently involved in coordinating eight research protocols and capturing research data to assist the team in fulfilling its mission. The clinical research nurse supports the Medical Oncology Branch thoracic team, which reports to the Medical Oncology Branch branch chief. The team is involved in various research projects using targeted agents alone and in combination with conventional chemotherapeutic agents like SNX-5422 RML, which is an HSP-90 inhibitor that inhibits the division and replication of cancer cells. A combination therapy of ADZ 2271 (a targeted agent) with Gemzar+Cisplatin is being used for refractory solid tumors in a Phase I trial.

The clinical research nurse received recognition for initiatives during the past year.

Support to the Surgery Branch, NCI

The main objective of the Surgery Branch is to conduct laboratory and clinical research focused on improving the care, management, and outcomes of patients by developing innovative surgical and adjunctive approaches.

The CMRP Surgery Branch support team consists of seven team members, including a clinical project manager I, a clinical research nurse II, two clinical research associates (level II and level III), a clinical coordinator, a protocol coordinator I, and a documentation specialist I.

Staff members currently support 14 clinical investigators, which conduct approximately 40 active clinical protocols. Staff has been instrumental in maintaining and improving the Surgery Branch's reputation for high-quality work. In particular, this branch has been the coordinating center for a high-profile Phase III trial, which has entered its final phase of data analysis; this effort is primarily managed by the clinical research associate III. The clinical research associate III has also been readily available to assist external data analysts, providing them with comprehensive and accurate information.

The Hepatobiliary Team has seen a sharp increase in workload, with multiple new complex surgical protocols actively accruing. Support staff has easily adapted to assisting the new patient population and continued to provide the highest quality of work and, as a result, has received excellent client feedback. Both clinical research associates and the clinical coordinator are heavily involved in maintaining the integrity of the data and the well-being of the patients. Both clinical research associates also assist the Hepatobiliary Team with preparing both internal and external presentations.

The clinical research nurse currently coordinates four trials (one additional trial awaits approval) for the Endocrine Oncology Section of the Surgery Branch. The

clinical research nurse has been praised by the client, clinical fellows, and designated patients as a caring and highly competent individual.

The increase in active protocols being reviewed by the Surgery Branch PSO as well as the complexity of these protocols has also created an increase in workload. The protocol coordinator and documentation specialist played key roles in processing 40–60 protocols for submission and maintained databases to track all submissions to various regulatory agencies, such as IRB, FDA, the Office of Biotechnology Activities, and the Institutional Biosafety Committee. The protocol coordinator also supervises the documentation specialist. Between mid-May and mid-August, the documentation specialist was out on maternity leave and the protocol coordinator performed most of her duties. With assistance from the clinical project manager and the rest of the team, the protocol coordinator was able to maintain the same quality of service and submit all deliverables on time or ahead of time, including the challenging task of simultaneously updating 21 immunotherapy protocols with new Surgery Branch fellows by July 2011.

The clinical project manager is responsible for providing regulatory and scientific support to PSO and has been instrumental in directly assisting two PIs with the successful submission and maintenance of five separate clinical protocols, including two gene therapy protocols. In addition, the clinical project manager assists other PSO staff as needed with submission and maintenance of an additional 20 clinical protocols. The clinical project manager has also prepared four new INDs and more than 10 annual reports for the FDA during this reporting period.

Support to the Urologic Oncology Branch (UOB), NCI¶

Barry L. Gause, M.D., Clinical Director
Beth Baseler, M.S., Director
Lamin Juwara, MSN, Senior Nurse Practitioner

The Urologic Oncology Branch (UOB) conducts clinical and basic research designed to develop better methods for detection, prevention, and therapy of patients with genitourinary malignancies. The primary focus of UOB is the study of the genes associated with initiation and progression of kidney and prostate cancers. CMRP provides a clinical research nurse II to support these efforts.

Staff members have developed collaborative relationships with many investigative sites and client personnel. They have also coordinated and collaborated with multi-clinical teams, including internal medicine, pre-anesthesia, and outside primary care providers to successfully manage 196 preoperative cases (comprising 65 patients for robotic radical prostatectomy/cystectomy and 131 patients for MRI-guided prostate fusion biopsy).

Additionally, CMRP staff manages 450 active patients, routine follow-up patients, and patients on active surveillance protocols within agreed-upon time frames. Staff members have conducted internal audits to determine protocol compliance and have prepared required documentation and assisted with close-out visits.

During the reporting period, CMRP staff efficiently recruited and enrolled an additional 152 new patients into tissue procurement protocol 97-C-0147 and screening protocol 01-C-0129 to meet patient needs for early cancer detection and early treatment of prostate/bladder cancer.

CMRP staff continues to coordinate and collaborate with the MIP study on C-Acetate PET and 3 Tesla MRI in Men with Prostate Cancer Undergoing Prostatectomy (08-C-0226) and the study on the Electromagnetic Tracking of Devices during Interventional Procedures (05-CC-0091).

In addition, CMRP staff supports UOB collaborative efforts with external prostate cancer outreach programs and physician referrals.

Support to the Vaccine Branch, NCI

Barry L. Gause, M.D., Clinical Director
Beth Baseler, M.S., Director
Lamin Juwara, MSN, Senior Nurse Practitioner

The Vaccine Branch combines basic research with preclinical investigation and drug development to provide innovative therapeutic clinical trials in the area of immune response and to recruit the body's own immune system to fight diseases, including cancer. CMRP provides a clinical research nurse II to support these efforts.

In accordance with GCPs and global SOPs, CMRP staff has coordinated the clinical monitoring process to assess the safety and efficacy of investigational products, conducted internal audits to determine protocol compliance, prepared required documentation, and facilitated audits of clinical trial records.

Staff members have participated in the design and planning of a Phase II trial for advanced malignant melanoma, in collaboration with Genzyme Corporation, a subsidiary of Sanofi-Aventis, to build on the Phase I study closed in the previous year. CMRP staff members are assisting with the development of a protocol and consent as well as facilitating submissions to IRB.

CMRP staff also assist in the daily operations of two active Vaccine Branch protocols by recruiting and enrolling patients, tracking and maintaining study-related files, scheduling patient follow-ups, monitoring overall patient outcomes, and compiling and sending correspondence to a patient's local physician.

Staff members also assist in producing and preparing documents for FDA submission, for IND annual reporting, and with amendments related to sponsor-investigator-held INDs.

Support to the HIV/AIDS Malignancy Branch (HAMB), NCI

The HIV/AIDS Malignancy Branch (HAMB) is instrumental in focusing on AIDS-related malignancies

that are positive for Kaposi's sarcoma–associated herpesvirus (KSHV). Therefore, pathogenesis of KSHV, a causal agent of Kaposi's sarcoma, primary effusion lymphoma, and multicentric Castleman disease, research efforts are ongoing.

The CMRP patient coordinator is responsible for providing administrative support to HAMB. This staff member currently assists three investigators and two research nurses with approximately 120 patients who are in enrolled on seven active protocols. In addition, the patient coordinator works with the team on the recruitment process to increase patient referrals for new protocols.

Through this assignment, the patient coordinator has implemented a new coding system for storing research specimens and cataloging old protocols (dating from 1984 to present). This system is used to gather clinical information from research specimens that describe previously unknown syndromes cited in journals written by the investigators.

Additionally, the protocol coordinator works with patients and staff from doctors' offices to obtain medical records and other pertinent documents prior to a patient's appointment or admission. This effort includes coordinating patients' appointments, making travel/lodging arrangements, and providing patients with information (dates, times, and hospital maps) about their appointments.

The benefit of a patient coordinator on staff allows HAMB researchers to concentrate on the scientific aspect of their jobs, while patients continue to receive excellent service.

During the reporting period, the HAMB team opened four new protocols and saw three patients complete response to treatment (showing no disease); saw a reduction in off-study treatment regimen, which can be interpreted as low disease progression; and demonstrated a low incidence of death in HAMB clinical trials, with only two deaths of protocol participants over the last two years. In addition, the patient coordinator was recognized in the SAIC-Frederick *Coordinator's Report* for the reporting period.

Psychometrician Support to the Pediatric Oncology Branch (POB), NCI

Barry L. Gause, M.D., Clinical Director
Beth Baseler, M.S., Director
Mary Ann Tamula, M.A., Psychometrician
Nia Billings, M.S., Psychometrician
Ken Tercyak, Ph.D., Behavioral Scientist

In 2010, CCR's POB established a Behavioral Sciences Core that consists of two separate but interrelated components: (1) the neurobehavioral program and (2) the psychosocial program. While the two programs have been in existence for many years, the Behavioral Sciences Core was created to facilitate the development of studies investigating the neuropsychological and psychosocial effects of chronic illness; provide specialized research support to clinical trials using neuropsychological and quality of life outcome measurements; and offer clinical services to the patients and families enrolled in studies throughout NCI.

The main objectives of the neurobehavioral program are to conduct research to: (1) investigate the effects of disease and treatment on the neurobehavioral functioning of children and adults with chronic medical illness through comprehensive, state-of-the-art longitudinal assessments; and (2) examine the pathogenesis of central nervous system dysfunction by exploring the relationships of neuropsychological measurements with disease parameters, neurological abnormalities, biomedical and genetic variables, and environmental and psychological factors.

In addition, the neurobehavioral group offers clinical services to patients, including providing assessment results to families, making recommendations and coordinating at-home psychoeducational services, and implementing clinical interventions based on patient needs. The neurobehavioral group also conducts a training program, providing valuable clinical and research experience in a medical setting to psychology students.

CMRP psychometricians primarily work with the neurobehavioral program to conducting longitudinal neurobehavioral assessments of children, adolescents, and adults with medical conditions on collaborative research protocols or in response to clinical referrals.

The psychometricians conduct comprehensive neuropsychological research evaluations of patients and prepare comprehensive clinical reports to help families, schools, and/or mental health agencies locally manage the child's educational services and psychological care. The psychometricians also provide clinical interventions to children enrolled in protocols who have developmental delays, problems with medication adherence, severe emotional disturbances, or other behavioral issues, in an effort to improve the child's well-being and help the patient remain in the study and comply with treatments.

The psychometricians are integrally involved in training incoming employees and students, where appropriate, and also completing data entry, administrative, and other research-related tasks. On a part-time basis, one of the psychometricians works with the psychosocial group and provides support on protocol development and implementation of novel therapeutic tools such as games and workbooks.

During the reporting period, both psychometricians participated in the collaborative development of research posters that were accepted for the 2011 Children's Tumor Foundation to be held in Jackson Hole, WY. One of the psychometricians will be presenting the poster at the conference.

Support to the Office of the NCI Director

Support to the Office of Biorepositories and Biospecimen Research (OBBR), NCI

Joy Beveridge, M.S., Clinical Project Manager III
Beth Baseler, M.S., Director

Since April 2008, CMRP has supported multiple initiatives within the Office of Biorepositories and Biospecimen Research (OBBR). During the past year, CMRP continued to add project managers and technical experts to the OBBR project team to address the comprehensive needs of the program. CMRP provides dedicated project and procurement management and logistical support to OBBR's initiative to develop a common biorepository infrastructure that promotes resource sharing and team science to facilitate multi-institutional, high-throughput genomic and proteomic studies.

During the past year, CMRP supported the following major OBBR initiatives: the Biospecimen Research Network (BRN), the caHUB pilot, and the Genotype-Tissue Expression (GTEx) NIH Common Fund project. The staff dedicated to each of these initiatives assisted NCI with the coordination of activities and the comprehensive communication plan for all stakeholders in the mission of OBBR.

In recent years, advances in biomolecular technology have significantly increased the power and precision of analytical tools used in cancer research. Human biospecimens are a critical resource for basic and translational cancer research because they are a direct source of molecular data from which targets for therapy, detection, and prevention are identified. The reliability of molecular data derived from these new analysis platforms depends on the quality and consistency of the biospecimens being analyzed; therefore, the standardization of biospecimen resources, using state-of-the-science approaches, has become a critical need across the research enterprise. The lack of standardized, high-quality biospecimens is widely recognized as a significant roadblock to cancer research.

In this context, NCI began a comprehensive due-diligence process in 2002, consisting of NCI surveys, community forums, and publications (e.g., the National Biospecimen Network Blueprint and Case Studies of Existing Human Tissue Repositories) to understand the state of its funded biospecimen resources and the quality of biospecimens used in cancer research. In 2005, OBBR was established to lead and coordinate a strategic plan to confront and resolve the issues identified in a stepwise fashion. In 2006, NCI successfully published *First-Generation Guidelines for NCI-Supported Biorepositories*, a first-iteration document that was subsequently revised based on public comment and input from content experts, and renamed *NCI Best Practices for Biospecimen Resources* (NCI Best Practices). The second version of this document was released in late 2010.

In addition to developing principles of best practices for biospecimen resources, NCI took a stepwise, multifaceted approach to address the needs of biospecimen resources across the cancer research community.

Due to changes in NCI leadership, several adjustments have occurred to the OBBR support provided by CMRP. In January 2011, OBBR announced that the goals and objectives for caHUB had to be redesigned. The 're-mission' of caHUB also included a reduction in funds from $60 million to approximately $36.5 million. The original purpose of caHUB was to create a benchmark biospecimen collection to be used for future unspecified work. The premise was that OBBR would build this collection so that investigators/researchers could apply for the right to receive biospecimens with specific attributes to use in their own research projects. Because caHUB collections were not intended for particular, known research projects at the time of biospecimen acquisition, Dr. Harold Varmus, NCI director, requested changes to the caHUB model. NCI leadership supported the collection of biospecimens for specific, meaningful research purposes. Thus, over the past year, caHUB has evolved into a foundation for collecting biospecimens driven by the development of standards to generate products for the public domain.

In April 2011, ownership of and support for OBBR initiatives was transferred from CMRP to ISP within SAIC-Frederick. The transfer included staff, equipment, and supplies. An annual summary of the various initiatives supporting OBBR and caHUB will be provided under ISP's report.

Support to The Cancer Genome Atlas (TCGA), NCI

Joy Beveridge, M.S., Clinical Project Manager III
Lenny Smith, M.S., Clinical Project Manager II

In 2005, NCI and NHGRI established The Cancer Genome Atlas (TCGA) as a comprehensive and coordinated effort to accelerate an understanding of the molecular basis of cancer through the application of genome analysis technologies, including large-scale genome sequencing. By 2006, a collaborative three-year TCGA pilot project was launched to assess the feasibility of a full-scale effort to systematically explore the entire spectrum of genomic changes involved in select human cancers. Support to TCGA currently continues beyond the original pilot phase of the project.

CMRP staff assist with the oversight and management of 26 new or extended tissue source site (TSS) subcontracts for the three pilot-phase tumors: brain, lung, and ovarian. Together, these tumor types account for more than 250,000 cancer cases in the U.S. each year. The comprehensive and integrative efforts of four program components contributed to the pilot phase efforts: a Biospecimen Core Resource (BCR); the Cancer Genome Characterization Centers; the Genome Sequencing Centers; and a Data Management, Bioinformatics, and Computational Analysis Core.

Along with NCI's and NHGRI's existing infrastructures, knowledge, and resources, the data from the TCGA pilot project is being used to determine whether it is possible to cost-effectively characterize the genomes of a few cancer types and to determine the feasibility of an atlas of all major cancer types. The project also supports the development of new technologies. Critical to the success of TCGA is the supply of qualified and adequately annotated biospecimens. Since its inception, the TCGA pilot project has subcontracted with academic medical institutions to obtain actively and retrospectively collected biospecimens through the SAIC-Frederick prime contract. The project also selected, through subcontracts with SAIC-Frederick, the services of two BCRs: International Genomics Consortium and Nationwide Children's Hospital.

During the reporting period, the CMRP project team determined the status of the remaining open subcontracts, gathering information on the potential to collect additional specimens and the ability to provide clinical data for specimens collected. Using information obtained from BCR site tissue qualification and clinical data from the sites, CMRP was tasked with identifying the sites that could be closed for the following reasons: (1) the work could be completed and goals of the subcontract could be met, or (2) the sites were unable to provide the tissue types approved by TCGA. During the past year, many subcontracts were modified to collect from an expanded list of tumor types, but many collection sites had difficulty identifying and obtaining the required tissue types. As a result, the period of performance for those subcontracts was extended.

The portfolio of TSS subcontracts was evaluated and 11 received no cost extensions and are still active with work in progress. These sites will complete clinical data collection, submit final invoices, ship final tissue samples, and/or provide a new tissue type other than those originally contracted. An additional 23 subcontracts will be closed after the completion of final billing and a financial audit.

Of special note is a subcontract that was awarded to the National Cancer Center of Korea (NCC of Korea). This subcontract offers NCI the opportunity to collect rare samples from non-U.S.-source sites where the standard of care in the U.S. would preclude the use of samples in the TCGA program. The Department of State approved a memorandum of understanding, creating a mechanism for the NCC of Korea to provide TCGA with rare pancreas and gastric adenocarcinoma cancer tissue types at minimal cost. In addition to the tissue samples, the NCC of Korea will provide clinical and follow-up data, adding value to the specimen.

CMRP continues to manage two subcontracts awarded to NCI Community Cancer Centers Program (NCCCP) hospitals to collect prospective biospecimens for the initial TCGA pilot tumor types as well as the expanded list of tumors. During the next few months, CMRP will support the tentative plan to offer the NCCCP sites another opportunity, via a limited competition among the 30 NCCCP cancer centers, to provide specimens to TCGA. It is hoped that these community cancer centers will be able to contribute additional specimens from the current list of TCGA tumor types.

TCGA has satisfied specific expectations for several tissue types. Ovarian, clear cell renal kidney, endometrial grades 1-2, colon, rectal, breast ductal, and glioblastomas have all been discontinued from further TSS collection (with notification) at the request of NCI.

During the reporting period and at the direction of the NCI TCGA management team, CMRP modified all of the extended subcontracts to collect additional tumor types—beyond the three pilot-phase tumor types—including: breast lobular carcinoma, hepatocellular carcinoma, pancreatic ductal adenocarcinoma, stomach adenocarcinoma, esophageal adenocarcinoma, cervical cancer squamous cell carcinoma and adenocarcinoma, uterine corpus endometrial carcinoma grade 3 and serous, head and neck squamous cell carcinoma, thyroid papillary carcinoma, acute myeloid leukemia, diffuse large B-cell lymphoma, cutaneous melanoma (including metastatic samples), lung adenocarcinoma, lung squamous cell carcinoma, bladder muscle invasive (high grade, nonpap), kidney papillary carcinoma, prostate adenocarcinoma, and sarcoma (de diff lipo, undiff pleiomorphic, leiomyo).

During the past year, CMRP project managers and subcontract specialists continued to coordinate weekly and biweekly project meetings with TCGA leadership and subcontractors, providing subcontract progress reports and managing the communications and site closure plans for all TCGA subcontractors.

Support to the NCI Community Cancer Centers Program (NCCCP), NCI

Beth Baseler, M.S., Director
Joy Beveridge, M.S., Clinical Project Manager III

Administrative clinical services support has been provided to NCCCP since May 2006, beginning with the original NCCCP request for proposal. NCCCP is a network of hospital cancer centers that serves as a community-based platform to support basic, clinical, and population-based research initiatives across the cancer care continuum—from prevention, screening, diagnosis, treatment, and survivorship through end-of-life care. NCCCP began in 2007 as a three-year pilot program with 16 community cancer centers. In 2010, stimulus funding allowed program expansion with the addition of 14 sites to the network and additional work for the original 16 NCCCP community cancer centers.

NCCCP is a network of 30 community cancer centers located in rural, suburban, and inner-city communities in 22 states. The sites see 53,000 new cancer patients per year and serve a population of 23 million Americans. NCCCP hospitals are addressing ways to offer patients state-of-the-art coordinated care and to support a wide range of basic, clinical, and population-based cancer research. Partnerships among the 30 NCCCP hospitals,

and with other NCI programs and national cancer research organizations, have been instrumental in the network's success. CMRP's strategic support services are helping the network sites achieve the following overarching goals of the program: enhancing access to care, improving the quality of care, and expanding research.

During the reporting period, CMRP continued to support program expansion activities and provide project management services to NCCCP. Efforts included: (1) comprehensive communication support to all site representatives, including the coordination of approximately 30 monthly meetings and documentation (recurring subcommittee, working group, and ad hoc meetings, and educational webinars); (2) maintenance of the NCCCP private intranet site and its content, and provision of network-developed resources/tools that are applicable to a broad range of community-based cancer programs to the NCCCP public web site; (3) oversight of more than 30 NCI listservs; (4) management of the NCCCP wiki content; (5) coordination of the two-day 2011 NCCCP Annual Meeting for nearly 400 participants, including venue comparisons, facility arrangements, budget oversight, travel and logistical support, agenda development, guest speaker arrangements, documentation and presentation management, and post-meeting activities to obtain and collate feedback from participants; and (6) facilitation of efforts to write, edit, and publish White Papers for each of the program's major focus areas to share lessons learned with other community cancer centers working toward similar goals (to date, 11 articles in *Oncology Issues*).

CMRP programmatic support to NCCCP has also included ongoing management of 45 individual research subcontracts. Dedicated CMRP staff manages the relationships between the awarded organizations, SAIC-Frederick, and NCI to support project objectives and activities. There are four sets of subcontracts, each with its defined scope of work and specific deliverables:

- 10 original pilot awards that address the comprehensive and overarching NCCCP activities (7/2007–6/2012)
- 10 ARRA awards to the original pilot organizations to conduct 18 additional individual projects in support of the NCCCP mission (4/2010–3/2012)
- 11 ARRA awards to academic institutions to support the NCCCP sites with two specific projects; this is a collaboration of NCCCP with two NCI programs—the Community Networks Program and the CTEP Early Drug Development Program (4/2010–3/2012)
- 14 ARRA awards to additional organizations to address the comprehensive and overarching NCCCP activities (4/2010–3/2012)

During the reporting period, staff continued to assist with NCCCP evaluation efforts. This assistance included: (1) collaborating with RTI International, Inc., for an external, formal evaluation of the pilot network (7/2007–6/2010), including the facilitation of a cost study, patient surveys and focus groups, data outcomes, and clinical trials accrual analyses; (2) identifying data analysis requirements and establishing, executing, and monitoring an online quarterly reporting tool to enable efficient data collection and analysis; (3) directing and coordinating all data collection efforts to ensure the comprehensive collection of high-quality data; (4) reviewing and analyzing data to measure and document programmatic progress, and sharing results with NCI and NCCCP stakeholders; and (5) administering and analyzing baseline and final assessment surveys.

CMRP assisted NCI with formal presentations of NCCCP data and accomplishments to highlight the program's unique features and to demonstrate the work necessary to build a national network of community cancer centers that are fully engaged with the research community and that provide the latest evidence-based, multidisciplinary care and treatment to all cancer patients. CMRP staff continued to provide qualitative, fiscal, and quantitative data to the NCI project officer to keep the newly appointed NCI leadership apprised of NCCCP activities.

The CMRP NCCCP team continued to facilitate the outstanding efforts being conducted by the NCCCP network as outlined below.

Reducing Cancer Health Care Disparities

A major focus of NCCCP is to reduce cancer health care disparities and ensure that patients from underserved populations have the same access to quality cancer care and research studies as provided to cancer patients from the general population with similar disease burdens. With 40 percent of total funding dedicated to disparities, this is a cross-cutting theme for all NCCCP awards. Each cancer center has identified at least one underserved population from a racial or ethnic minority group, or from a rural population, and improved outreach activities tailored for those populations. In addition, the network sites have:

- Implemented standardized tracking of race and ethnicity data
- Increased community and research partnerships focused on ways to address health care inequities for underserved populations;
- Increased community outreach activities and screening events;
- Increased patient navigation services to improve the coordination of cancer care, especially for underserved populations; and
- Increased the utilization of policies that incorporate cultural considerations related to donating tissue and other biospecimens.

Increasing Patient Participation in Clinical Trials

NCCCP sites are supporting cancer research by enhancing infrastructure to increase patient accrual to clinical trials, with an emphasis on the accrual of patients from underserved populations. Network-developed tools

have allowed the sites to document accrual challenges, measure program improvements, and collectively focus efforts on strategies to expand the clinical trial infrastructure.

Many of the sites partnered with NCI-designated cancer centers to offer their patients access to Phase I and Phase I/II clinical trials. Additionally, NCCCP sites have broadened their clinical trials portfolio, increased supportive care/cancer control and prevention trials, increased cooperative group membership, and increased the number of local physicians accruing patients to clinical trials.

The network is focused on ways to increase clinical trial accrual rates for underserved populations. The NCCCP sites use tools to assess barriers to clinical trial participation as they continue to devote efforts to improve accrual rates for underserved populations. The sites are:

- Increasing the engagement of patient navigators who educate patients about clinical trials and serve as liaisons between the patients and the research team;
- Providing continued cultural awareness training programs for hospital and cancer program staff;
- Sharing best practices among the network sites and using resources from external experts in underserved accrual to promote the expansion of the clinical trials infrastructure; and
- Identifying specific underserved populations in local communities and developing program resources to reach patients from those populations.

Expanding Community-Based Informatics Infrastructure

With project oversight from CMRP, NCCCP sites worked with and participated in caBIG®—NCI's nationally networked research IT platform—to leverage standards-based best practices and provide insight into the nuances of community-based informatics programs while helping to build documentation more suited to the community segment. The 30 sites gained access to a network of oncology informatics expertise to solve both common and unique technology issues, while also receiving guided access to the tools through caBIG® and other program solutions. The sites continue to work on a number of efforts to implement informatics tools to support improved cancer care in the community and to facilitate data sharing activities in support of research efforts. A few of these include:

- Participation in a collaborative project to network with and exchange technology and informatics best practices with the NCI-designated cancer centers through the NCI caBIG® Deployment Program;
- Collaborations with the NCI Cancer Imaging Program (CIP) and CBIIT to demonstrate electronic data submission for clinical trial imaging data through annotated image exchange using the National Biomedical Imaging Archive (NBIA); and
- Initiation of a project with NCI's CBIIT to define community-based oncology outcomes data elements to support data warehousing and outcomes data analysis capabilities (NCCCP sites are working to create data warehouses, build longitudinal patient records, and develop strategies to engage private practice oncology providers in data sharing).

Integrated electronic health records are essential to supporting quality cancer care due to the longitudinal nature of the cancer continuum. Leveraging the Clinical Oncology Requirements for electronic health records documentation created by NCCCP sites in collaboration with the American Society of Clinical Oncology (ASCO) and NCI, the expanded NCCCP network is working to improve platforms for oncology care.

Promoting High-Quality Biospecimen Collection

To advance cancer research, NCCCP sites are actively participating in the collection of high-quality biospecimens using standardized collection and storage procedures. This is helping to build a community-based research platform where patient data and high-quality blood and tissue samples are collected to support genomically informed medicine. Sites that collect and store high-quality biospecimens follow NCI Best Practices for the collection and storage of high-quality biospecimens. Several NCCCP sites are participating in biospecimen research programs such as Moffitt Cancer Center's Total Cancer Care program and TCGA, a collaboration of NCI and NHGRI.

Promoting Evidence-Based Cancer Care

The sites are committed to improving the quality of cancer care they deliver by following evidence-based practice guidelines developed by national cancer organizations. With NCI support and CMRP oversight, the NCCCP network has created a platform for community cancer centers to make significant progress in their efforts to promote and deliver evidence-based care. Accomplishments include the following:

- The 30 cancer centers and their affiliated oncology practices have more than doubled their participation in ASCO's Quality Oncology Practice Initiative (QOPI®)—a program that collects data and reports on measures from evidence-based guidelines, such as conducting pain assessments, providing smoking cessation support, tracking timeliness of chemotherapy administration, and providing psychosocial support. By fall 2010, oncology practices from 25 NCCCP sites were participating in QOPI® and five sites achieved QOPI® certification through ASCO's national certification program.
- The 16 original pilot sites continued participation in the beta-testing of the Commission on Cancer's Rapid Quality Reporting System. The system allows real-time reporting using existing cancer registry operations to measure concordance with breast and colorectal cancer measures and supports ongoing QA

programs. A comparative analysis of NCCCP sites' performance with non-NCCCP sites is currently underway.

- The network continued to add disease-specific multidisciplinary care conferences, where oncologists, surgeons, radiologists and support staff meet to discuss individual cases to determine personalized, optimal treatment plans.
- All network sites are promoting the use of evidence-based approaches for the integration of genetic and molecular testing into the model of cancer care in their centers and they are using the *NCCCP-Cancer Genetic Counseling Assessment Tool* to evaluate their cancer genetic programs, set improvement goals, and exchange information with other NCCCP sites.

Expanding Cancer Survivorship and Palliative Care Programs

To improve cancer treatment and follow-up care, the NCCCP network is expanding survivorship, palliative care, and psychosocial programs and services for all cancer patients. Sites are increasing the use of patient treatment summaries to facilitate communication among the cancer treatment team, the patient, and the patient's other health care providers. The sites developed and utilized psychosocial and palliative care assessment tools to evaluate their respective center's ability to provide quality care in these areas.

NCCCP: Partnerships Drive Progress

The NCCCP network provides a platform for collaboration with a number of national cancer organizations to enhance the goals of the organizations as well as NCCCP; partnerships include:

- American College of Surgeons Commission on Cancer, ASCO
- NCI-designated cancer centers
- NCI Center to Reduce Cancer Health Disparities, Community Networks Program
- NCI Cancer Therapy Evaluation Program, Early Drug Development Program

NCCCP: Expanding Research through Federal Stimulus Funding

In addition to supporting the 2010 expansion of NCCCP from 16 to 30 cancer centers, government stimulus funds have been used to retain staff and create new positions. ARRA funds have also been used to develop several research programs at the original pilot sites by funding additional projects. A few of the key activities are outlined below:

- Create additional partnerships with NCI's Center to Reduce Cancer Health Disparities, Community Networks Program, to increase cancer screening events in racial/ethnic minorities and other underserved populations.
- Improve the coordination of care for underserved populations across the cancer care continuum.
- Participate with NCI-designated cancer centers in the preliminary validation of the patient reported outcomes – common terminology criteria for AE measurement tool.
- Improve the navigation of patients during the transition from cancer care to survivorship.
- Expand access to evidence-based smoking cessation programs for cancer survivors and their family members.
- Conduct a study on the impact of multidisciplinary care on processes and outcomes of cancer care.
- Facilitate access to early phase trials through collaborations with NCI's Early Drug Development Program.
- Engage community physicians in minority communities to enhance clinical trial accrual.
- Research breast cancer biomarker practice changes.
- Identify strategies to enhance clinical trial participation among Native Americans.
- Partner with state cancer coalitions to implement mutual objectives in state cancer plans.

Communications and Patient Advocacy: Connecting Patients with Care

For many patients, cancer treatment advances are limited because they are out of reach or patients don't know they are available. Each NCCCP site is working to enhance community awareness of cancer-related issues and the role of NCCCP in their communities. Communications efforts include:

- Supporting initiatives to increase cancer screening and early detection with a focus on underserved populations;
- Developing lay language educational materials and programs to promote increased accrual to cancer clinical trials; and
- Educating local oncologists about NCCCP to increase participation in multidisciplinary care conferences, clinical trials, and other program components.

This advocacy association ensures the perspective of cancer patients is considered in all aspects of NCCCP. The connections with the patient and community perspective continue to provide ongoing direction to NCCCP to support its central purpose of improving patient outcomes and research opportunities for patients in diverse communities across the United States.

Support to the Coordinating Center for Clinical Trials (CCCT), NCI

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Geoffrey D. Seidel, R.N., M.S., Clinical Project Manager II

During the past year, CMRP continued to provide a cost effective and efficient support mechanism to reimburse the efforts of the clinical, scientific, and advocate experts serving on SSCs in support of the NCI CTWG. In addition, CMRP staff supported the Biomarker, Imaging and Quality of Life Studies Funding Program (BIQSFP) and assisted with planning for the Special Translational Research Acceleration Program (STRAP).

Two clinical project managers are detailed to the CCCT office in Bethesda, MD, to provide on-site support for these programs. Two additional support staff members are assigned to the Fort Detrick, Frederick office. The clinical project managers maintain enhanced and streamlined communication between CMRP and CCCT program directors in addition to BIQSFP and SSC responsibility and accountability.

Between 2008 and 2011, the SSC program increased from six SSCs and 140 consulting agreements to the current 16 SSCs and 417 vendor agreements. In collaboration with SAIC-Frederick's Research Contracts and Accounts Payable offices, CMRP staff streamlined processes by replacing consulting agreements with vendor agreements. This led to increased efficiency and has resulted in a decrease of nearly five months in processing time—a process that previously required six months is now averaging three days. CMRP's support of the SSCs includes project management, program analysis, and management of the massive and growing vendor agreement effort. The Clinical Imaging Steering Committee is expected to begin this year, which would bring the total number of SSCs to 17, while also adding new vendors.

The support provided by CMRP staff has matured to include the design and maintenance of the CTWG contracts database, which maintains conflict of interest and confidentiality disclosure agreement documents, as well as term dates for the SSC vendors. Clinical project manager I support also includes maintaining and updating the CCCT and BIQSFP web sites, supporting weekly CCCT program director meetings, designing slide presentations for CCCT program directors, and ensuring Section 508 compliance of CCCT documents.

During the reporting period, the BIQSFP program continued to grow in scope and effort, with nine BIQSFP applications being submitted and reviewed. Support efforts have entailed collaborating with several NCI programs, including CTEP, the Division of Cancer Prevention (DCP), CIP, CDP, and the various SSCs, as appropriate. Support also included facilitating the identification and coordination of expert external reviewers.

NCI approved seven BIQSFP study applications, with two more pending final review and approval. In addition, nine new BIQSFP subcontracts were awarded this year.

CMRP staff facilitated and supported the April 2011 solicitation of a revised BIQSFP announcement, which included the addition of cost-effectiveness analysis and revisions to the official BIQSFP web site. The BIQSFP web site received over 3,500 visitors during the first nine months of the fiscal year. In addition, the BIQSFP bookmark was revised and is now being distributed via CTEP, DCP, CIP, and CDP program directors. This bookmark describes BIQSFP and directs recipients to the BIQSFP web site. CMRP staff presented the BIQSFP program at the NCI Meet-the-Expert booth at the ASCO conference in June 2011 and facilitated a Clinical Biomarker Speed poster session at the Translational Science Meeting III in July 2011. A BIQSFP poster designed by CMRP staff was presented at the meeting.

In the fall of 2010, NCI decided to fund the STRAP awards via an NCI supplement rather than through SAIC-Frederick subcontracts. This resulted in the elimination of the clinical project manager position supporting STRAP. The STRAP program has seen continued success with the review of 23 submitted proposals and the award of supplements for two projects. The success of the program was due in part to the program start up and project management support of the CMRP staff member hired in February 2009. It is anticipated that the STRAP program will continue with the supplement model of funding.

As CMRP and SAIC-Frederick program support scope has broadened, there have been more opportunities to present with a BEDSIDE focus. In March 2011, CMRP, working with Scientific Publications, Graphics & Media, formed the BEDSIDE-Focused SAIC-Frederick Slide Templates Working Group. The goal of the group is to develop a set of SAIC-Frederick corporate slide templates that can be used when staff present at BEDSIDE-focused vs. BENCH-focused venues. The effort will be completed by the end of FY2011 and the plan is to have it available on the SAIC-Frederick web site for presenters to use, alongside the current BENCH-focused corporate slide templates.

Strategic planning efforts are underway as the program's future beyond the current subcontract period is considered. Various budget options and program scenarios are being discussed, along with new request for proposal considerations for a possible fall 2011 competition.

SUPPORT TO DCTD

Support to the Cancer Imaging Program (CIP), NCI

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G. Craig Hill, Ph.D., Medical Affairs Scientist I
Marc Teitelbaum, M.D., Medical Affairs Scientist II
John Freymann, Systems Program Technical Manager

Overview/Summary

Since 2002, overarching support to CIP has included the oversight of regulatory affairs, medical imaging agent availability, and imaging informatics. Regulatory support has been related to the IND process for the imaging agents and managing the subcontracts awarded to facilitate preclinical and clinical activities. These IND efforts have enabled wider availability of investigational agents for exploratory clinical trials—by contract, in the research community, and within the Joint Early Phase Therapeutics Development Program and the Imaging Drug Group, now part of the NCI Experimental Therapeutics (NExT) Program.

The IT management support provided to CIP has been a major contributor to initiatives across NCI in support of its imaging informatics plan. Collaboration with multiple NCI-wide committees and major imaging informatics initiatives have proven to be extremely important in NCI's development of an infrastructure that supports higher-level compatibility with CBIIT's caBIG® and other NIH Roadmap Initiatives. During the past year, the IT manager oversaw the development and population of an archive of in vivo radiology image sets to address needs of the image processing community; by providing submission, curation, and hosting services, a new vision has come to fruition as The Cancer Imaging Archive.

Since January 2006, the CMRP manager, in support of CIP, has collaborated with other NCI programs, with groups within NIH at the Clinical Center and in Frederick, MD, with scientific societies, and with FDA. These efforts have supported CIP's goals of promoting the wider use of medical imaging in diagnosis, response to therapy monitoring, therapeutic drug development, and medical decision making. Since May 2009, a chemist-medical affairs scientist has provided oversight to the group. This person serves both a radiopharmaceutical-scientific and administrative role and as a resource for the development of the recently opened SAIC-Frederick radiopharmacy.

A new leader for IND-related regulatory affairs joined the CIP support team in November 2009 and oversees numerous regulatory submissions related to the CIP IND portfolio. A physician-medical affairs scientist provides clinical trials monitoring and regulatory support related to imaging agent development, including IND work and subsequent late-stage development toward commercialization to include clinical trials, and oversees the QA team that has been in place since June 2009. Over the past year, the QA team has shifted from a CIP auditing program, conducting site visits for most of the program's IND agents, to providing significant day-to-day oversight for the American College of Radiology Imaging Network (ACRIN) QA, monitoring and audit programs, and protocol review of advanced imaging activity with the CTEP Protocol Information Office.

During the past four years, CIP program emphasis continued to shift toward development and delivery of a variety of imaging products, requiring new strategies, resources, and cross-division, cross-institute, cross-agency, and external outreach activities. The Phase 0 initiatives and the dissemination of short-lived tracer technology are two prominent examples of initiatives resulting from this shift in CIP focus.

The NExT Program integrated the activities of several cross-institute imaging drug activities into two decision-making committees; CIP continues to be involved in NExT projects.

CMRP staff also serves in an advisory role with CCR's MIP, the Small Animal Imaging Program (SAIP), and the Nanotechnology Characterization Laboratory. This has resulted in additional on-site CMRP support to CIP.

Last year, bench chemistry expertise was added to the team to support medical imaging agent development activities. This expertise was in addition to the expertise provided by the medical affairs scientist. CIP's chemistry program was recently expanded to include a senior scientist and a postdoctoral fellow. These positions primarily support the goals of the Imaging Drug Group, providing development of new imaging agents and backup testing of currently administered agents. This groundbreaking work may eventually lead to increased availability of types of agents for clinical trials. Maturation of this effort is documented by the fact that the original space designated for this work will soon be turned into a United States Pharmacopeia (USP)-level radiopharmaceutical production center capable of delivering clinical-grade human doses for use in preclinical and clinical evaluation efforts by a certified pharmacist.

In April 2009, a radiopharmaceutical chemistry lab was set up in Frederick, MD, (in Building 325 at Fort Detrick) to develop PET/SPECT tracers for NCI's CIP and the Small Animal Imaging Program. This lab became fully operational in August 2009. In early 2010, CIP decided to establish a USP lab for early phase clinical trials of radiotracers. A plan was implemented to convert the Building 325 laboratory into a USP laboratory and to create a new tracer developmental laboratory in Building 376. These two labs are mainly for the development of existing and new radiotracers for preclinical studies. The Radiochemistry Laboratory in room 132 is now fully functional. Radiochemical projects and experiments using 18F, 89Zr, 111In, and 99mTc isotopes occur regularly. Several doses of PET and SPECT tracers have been provided recently to SAIP for mice studies and future animal doses will continue to be produced in this space. All nonradioactive chemical manipulations (protein

purifications, bio-conjugation, and assay development) are performed in the room 233 cold chemistry laboratory.

This USP laboratory's previous space (Building 325) was placed under development and converted into the SAIC-Frederick Radiopharmacy. Installation of a sterile hood was critical to the success of this conversion. A nuclear clinical pharmacist and a technician were recruited to staff the radiopharmacy. The nuclear pharmacist worked with the Maryland State Board of Pharmacy, the SAIC-Frederick radiation safety officer, and the Nuclear Regulatory Commission to meet the regulatory requirements and compliance issues for human dose production. The USP Radiopharmacy became functional in April 2011 and should deliver product to the Clinical Center in Bethesda shortly.

During the past year, substantial progress was made with the ACRIN/American College of Radiology to provide SOP development and qualification of Cancer Centers as Centers of Quantitative Imaging Excellence. The primary objective of this agreement was to establish a resource of trial-ready sites within approximately 59 cancer centers across the nation. These sites require capabilities to conduct clinical trials that have an integral molecular and functional advanced imaging endpoint; for example, PET, volumetric computed tomography or magnetic resonance, and dynamic contrast-enhanced magnetic resonance imaging. To date, 22 such centers have completed full qualification, with many more having completed partial qualification. Most centers are expected to be fully qualified by fall 2011. This resource supports the development and clinical implementation of quantitative imaging to measure response to therapy. The potential exists to extend this effort to other NCI Clinical Trial System participating sites within other groups, such as SPOREs and CTEP Cooperative Groups.

The physician-medical affairs scientist, experienced in IT systems and regulatory affairs, assists the clinical trials branch chief to administer the procedures covering the research, design, development, alteration, and improvement of new and existing protocols, and helps direct and manage these clinical trial efforts. Over the course of several years, this position has evolved and now serves as the lead CIP contractor representative on various NCI committees and working groups. In June 2009, two clinical research associates were hired in anticipation of inaugurating an on-site audit program, which was implemented later that year and concluded its first round of on-site audits in mid-2010. This expansion greatly increased the amount of support to the program by enabling new and expanded clinical trials contracts to be placed through NCI and additional related subcontracts to be placed through SAIC-Frederick. This addition to the CMRP team has provided invaluable expertise in the auditing and oversight functions for managing trials within CIP. Departure of the second clinical research associate for an internal SAIC advancement opportunity in early 2011 conveniently coincided with a hiatus in the site visit program. This fortuitous shift in workload permitted remaining team members to manage the maturing QA function at the requisite level through remote monitoring procedures and systems introduced in 2010–2011.

The CIP support team works with the ACRIN program director and branch chief at CIP and with ACRIN senior staff to provide significant day-to-day oversight for the ACRIN QA, monitoring, and audit programs. ACRIN operational (QA, monitoring, and audit) reports are reviewed primarily by the CMRP CIP QA support team. Audit tracking schedules are reviewed in advance and evaluated against actual audit performance. Preliminary audit reports are sent to the QA team for review immediately post-audit, thus providing an early warning opportunity to CIP. Should prompt action be necessary, the CMRP QA team works hand-in-hand with CIP and ACRIN to define and implement a course of timely intervention to mitigate a suboptimal site situation. Along with these preliminary reports, the medical affairs scientist is responsible for final approval and sign off on audit reports and corrective action plans. Items requiring immediate action are brought to the attention of the ACRIN program director at CIP and the branch chief. The QA team handles much of the day-to-day communication with ACRIN in pursuit of resolution, and offers new drafts and/or modifications to existing ACRIN documents towards this end. Federal staff and the CIP CMRP QA team conduct ongoing reviews of several ACRIN guidance documents, such as the Adverse Event Guide and the Audit Manual. Strategic support is provided to ACRIN to assist in improving regulatory, IRB, and protocol compliance.

Upgrades continue to systems and processes for the receipt and tracking of AEs and auditing reports at CIP for the ACRIN trials. CMRP staff completed modifications and evaluation of existing AE reporting systems designed for therapeutics, so that they now meet the needs of imaging clinical trials. Additional regulatory projects include: (1) the ongoing co-monitoring of some trial sites within ACRIN to gather sufficient information to permit a comprehensive process audit of the cooperative group, and (2) a project to amend the cooperative group guidelines so that ACRIN can be managed under the same policies as the other cooperative trial groups.

During the past year, additional support was provided to the informatics team to accommodate the heightened level of maturity of the National Cancer Imaging Archive. The existing project manager was assigned to accommodate most of the administrative functions performed by this team. This change proved advantageous to all involved and greatly facilitated progress, especially on the Washington University contract. Additional projects in support of the ACRIN cooperative group have provided new opportunities for the growth and maturity of valuable cross-discipline projects in informatics to become a reality.

The IT team has been instrumental in CIP's efforts to develop and populate an archive of in vivo radiology image sets to address the needs of the image processing

community. The team provides submission, curation, and hosting services. As a result, an $806,000 contract was signed with Washington University of Saint Louis to put this resource into production with the IT team's assistance. It is provided as a public resource to advance computer-aided diagnosis and hybrid man-machine detection of disease, and to distribute images for measuring response to therapy in clinical trials. The NBIA software, developed in concert with caBIG®, is a scalable, web-accessible image repository. The image repository contains more than 2.5 terabytes of curated image data and more than four million images from a range of clinical imaging instruments, including CT, MRI, and PET/CT and radiation therapy.

The 10 members of the CMRP CIP support team provide comprehensive scientific and administrative support to the program. More than 20 procurements (including subcontracts and consulting agreements) have been executed to meet the needs of the CIP principals. Subcontracts have been established with major medical institutions, experts in the field of cancer imaging, and with commercial companies that are assisting in the analysis and development of CIP's portfolio of radiopharmaceuticals. Additional details of this support and are outlined below.

Regulatory Support

During the past year, comprehensive regulatory support was provided to CIP activities related to the IND process for imaging agents. Subcontracts with extramural sites were coordinated to facilitate the formal clinical trials performed at the CIP Phase I and II NCI contract sites. CIP facilitates the development of promising diagnostic agents that are not otherwise likely to undergo adequate preclinical testing to warrant an IND application or early phase clinical testing in the conventional industrial development/sponsorship process.

Seven INDs are currently held by CIP and management is supported by CMRP staff:

1. IND 71,260 ([18F]-fluoro-L-thymidine), proliferation agent
2. IND 68,556 (ferumoxytol), blood pool MR agent
3. IND 70,900 (ferumoxtran-10), lymph node MR agent
4. IND 76,042 ([^{18}F]-fluoro-misonidazole), hypoxia agent
5. IND 79,005 ([^{18}F]-fluoroestradiol), estrogen receptor agent
6. IND 100,429 [^{111}In]-Herceptin, Her2 receptor agent
7. IND 103,429 [^{18}F]-NaF, bone scanning agent

Multiple protocols, the majority of them Phase II trials, are being conducted under each of the CIP-sponsored INDs. Twelve trials are active and enrolling patients. Many of the trials have inherent regulatory complexities due to the involvement of multiple investigators, sites, and contract organizations located in the United States, Canada, and Korea. One additional IND is still in the later stages of preparation, F-deoxycytidine, for patients receiving deoxycytidine with THU and is expected to be completed in fall 2011.

During the reporting period, CMRP successfully completed the filing of the first ever NCI New Drug Application (NDA) on behalf of CIP. Even though CMRP provided full regulatory support to CIP in the submission of a marketing application (NDA) for [^{18}F]-NaF in 2008, this is the first time NCI filed an NDA with the FDA. FDA approval was finally received in late January 2011. This effort was spearheaded by the CMRP regulatory team and CMRP/CIP leadership, and the entire CIP support team contributed their varied skill set to meet stringent and extensive FDA requirements in addressing this need.

Chemistry and Imaging Agent Availability

Efforts to make promising radiopharmaceutical agents available to the research community for clinical investigation have been significantly broadened. Because the aforementioned PET tracers have no intellectual property associated with them, commercial entity investment is viewed as risky. Even so, this effort has been realized through patient and sustained effort, made over the course of several years. CMRP personnel negotiated a letter of reference to the full toxicology data in an IND held by a commercial firm for the therapeutic (nonradioactive) fluoro-L-thymidine. Additional activities included: (1) several meetings between FDA, NCI, Radiological Society of North America, and the Society of Nuclear Medicine, culminating in an Imaging Workshop in April 2010; (2) making FDA-accepted documents to manufacture three PET agents: fluoro-L-thymidine, fluoro-misonidazole, and 16alpha-[^{18}F]fluoro-17beta-estradiol, available on the CIP web site; (3) issuing letters of authorization to CIP's INDs (more than 10 this reporting period) to allow outside clinical researchers to file INDs of their own; and (4) ongoing activities related to the May 2005 contract award to Ion Beam Applications S.A. (IBA), a major supplier of cyclotron-produced isotopes and radiopharmaceuticals, for implementing fluoro-L-thymidine tracer synthesis and applying for a drug master file (DMF) so the tracer could be supplied to NCI trials and other sites. This effort stimulated the two other main fluoro-L-thymidine manufacturers, Cardinal Health and PETNET, to file DMFs to CIP's fluoro-L-thymidine IND, and now these companies are supplying from 19 sites across the country. Every six monthsm these same companies are queried as to their new DMF sites brought on line and also of what their sites of expansion might be.

Additionally, a company investigating a therapeutic drug contracted with PET agent manufacturer Cardinal Health to make fluoro-misonidazole, a PET tracer for which CIP holds INDs. The CIP manufacturing documents for this tracer were transferred to the company under an MTA. The trial of the therapeutic with the tracer is ongoing. Other entities are planning trials using this agent and the company has filed a DMF to allow use of

the agent. Cardinal Health filed a DMF on fluoro-L-thymidine and provided a cross-file letter in the CIP IND so that CIP can use this company, as well as IBA and PETNET, to supply its trials. Cardinal Health has also been awarded two additional task orders: the transfer of synthesis of alpha-[^{11}C] methyl-L-tryptophan from Wayne State University to Moffitt Cancer Center (which Cardinal is operating) and the transfer of synthesis of fluoroestradiol from the University of Washington to their Beltsville, MD, production facility. These three main PET manufacturers have agreed to supply their imaging agents for expanded NCI-sponsored multicenter clinical trials in the areas that they currently serve as part of the widening projects funded by ARRA. The companies communicate through the CMRP contractors to avoid commercial conflicts.

Additional tracers are being investigated under SAIC-Frederick subcontracts, whereby the vendor holds the IND or obtains Radioactive Drug Research Committee approval. These include: (1) synthesis and exploratory clinical study of three PET tracers (1-(2'-deoxy-2'-fluoro-beta-D-arabinofuranosyl) uracil [FAU], now at five patients; 3'-deoxy-3'-18F -fluorothymidine, now at five patients; and 18F -1-(2'-deoxy-2'-fluoro-beta-d-arabinofuranosyl) thymine [FMAU], now at four patients) in breast cancer patients who will be receiving capecitabine as part of their standard of care; (2) evaluation of alpha-[^{11}C] methyl-L-tryptophan as a probe to assess tryptophan metabolism in extra-cranial tumors by performing total body PET imaging with alpha-[^{11}C] methyl-L-tryptophan in a small cohort of human subjects to assess the feasibility of using imaging as a potential tool to select, direct, and monitor future trials with the immunomodulator 1-methyltryptophan (due to slow accrual according to the enrollment criteria, this study will be moved to the Moffitt Cancer Center); and (3) a pilot study of ^{11}C-SN-38 uptake and retention in patients who will be receiving irinotecan as part of their standard of care, now at six patients.

Informatics support

During the reporting period, informatics support initiatives included: (1) responding to a CIP request to stimulate imaging integration with genomics/molecular analysis by developing and managing a project to correlate imaging characterizations with molecular data from the TCGA project; (2) providing technical direction, including the creation and management of an extensive documentation wiki to major CIP-sponsored research data accrual activities (e.g., the Reference Image Database to Evaluate Response to Therapy, Lung Image Database Consortium, Imaging Databases Resource Initiative projects, radiotherapy data, PET/CT studies), and providing logistical support for data transfer and data manipulation; (3) providing policy and technical leadership for accelerated development and deployment of the NBIA web site; and (4) providing leadership guidance for caBIG® Imaging Workspace activities through successful community-building and project-implementing activities.

The IT manager serves on the NBIA and caBIG® Imaging Workspace steering and technical committees and coordinates the implementation by the NCI CBIIT team. This activity is a CIP-funded collaboration between CIP and CBIIT. The IT manager also coordinates data-gathering activities and outreach with cancer centers and clinical trial PIs, and participates in developing design documents for workspace-funded software and standards development activities.

The premise of NBIA and caBIG® Imaging Workspace efforts is that reliable image data can lead to smaller clinical trials with fewer patients, earlier go/no-go decisions on compounds, faster regulatory approval, and shorter time to market for new drugs and therapies, which in turn would lead to improved efficiencies in the cost of NCI clinical trial operations.

The Imaging Informatics resources are divided about equally between the development of NBIA and the Imaging Workspace. NBIA is a web-based infrastructure (http://imaging.nci.nih.gov) that supports submission, curation, storage, and access to cancer clinical and research-relevant image data and image-related data. By providing standards-based, controlled collections of data using NBIA, CIP is able to leverage a central resource rather than funding the endless replication of ad-hoc data systems from new grant resources. NBIA is actively supporting three ongoing CIP projects, and working with others. NBIA has proactively engaged with industry to provide free or low-cost data to populate the system. Through NBIA, CIP is leveraging resources at CBIIT, which is providing space and management staff for the project. NBIA leverages CBIIT infrastructure and technology support as well. NBIA has collaborated with commercial off-the-shelf software developers (Cedara) to provide central-read support at a greatly reduced cost. Additionally, NBIA leverages the Radiological Society of North America, which provides significant technology support for the data submission component of NBIA.

The Imaging Workspace is designed to address the lack of imaging standards and quantitative tools by providing support for 15 funded subject matter experts and through funding of focused technology development projects. Participation by the subject matter experts is complemented with 60–80 regular voluntary expert participants. Telephone conferences occur regularly and several face-to-face meetings are scheduled throughout the year. Active projects include developing an Extensible Imaging Platform by Washington University in St. Louis and Siemens CR. The Annotation and Image Markup project, an effort to associate standard-based human and computer analysis with images, leverages participation of Integrating the Healthcare Enterprise and other standards organizations. Another project, caGRID Imaging Middleware, will allow disparate image archive systems and algorithms to interoperate over the NCI Grid, representing a major efficiency in using data and analytical resources. The Imaging Workspace and NBIA

activities are complementary, closely coordinated, and integrated.

Major informatics projects that continued during the past year include:

Integration of Imaging with Genomics

CMRP continued to manage a project that included developing feature characterizations of brain MR images, collecting image data from three cancer centers from cases included in a TCGA project within NCI/NHGRI, guiding a team of six neuroradiologists in the use of custom-built workstation software to score the images, and working with biostatisticians to provide analysis. The intent is to determine if any characteristics of the images will correlate with any of the genomic or survival data for any of the tumor types. This activity will increase with additional data and tumor types.

Support for Radiation Therapy (RT)/Multi-modality Trial Research

RT planning images and FDG-PET/CT images used to evaluate patient responses to chemo-radiation were acquired. The images were in a completely different format and required substantial effort to bring into the archive. Once the image sets are fused, RT dose planning should improve. CMRP participated in the strategic planning subgroup for this project.

The team also managed the development of proposals for a clinical trial image management system and infrastructure for tumor tracking and managed the implementation of RECIST 1.1 for support from CBIIT through caBIG® Imaging Workspace. A coordination team was established to develop recommendations for de-identification of in vivo images for the imaging community.

Cancer Diagnosis Program (CDP), NCI

Joy Beveridge, M.S., Clinical Project Manager III
Rhona McVicker, R.N., O.C.N., CMRP Administrator

Since January 2008, research subcontracting support has been provided to CDP to assist with its mission to improve the diagnosis and assessment of cancer by effectively moving new scientific knowledge into clinical practice. To date, six initiatives have been supported: (1) construction of statistically designed tissue microarrays using pre-existing breast cancer tissue; (2) just-in-time accession of clinically annotated pathology specimens for molecular marker research; (3) calibration of the BCR-ABL assay; (4) Phase II calibration of the BCR-ABL assay; (5) creation of a specimen retrieval system to collect cases for validation of NCI-supported clinical assays; and (6) implementation of a Clinical Assay Development Program focused on supporting the development and optimization of clinical-grade assays. As of July 2011, 20 research subcontracts were awarded to 14 different institutions for a total award amount in excess of $2.1 million.

During the contract year, the research subcontract with Harvard University continued. This organization functions as a test site for the evaluation of a peer-to-peer informatics system to locate and retrieve specimens and pertinent clinical/outcome data on an as-needed (just-in-time) basis from community health care settings, including health maintenance organizations (HMO) and community hospitals. Specifically, Harvard continues to test and adapt their previously developed de-identification protocol at local community health care settings, evaluating its performance on even larger numbers of cases. Additional modifications and an extension were issued to Harvard in support of the just-in-time accession of clinically annotated pathology specimens for molecular marker research. The work on this subcontract will continue into FY2012, with CMRP staff continuing to manage the open and pending subcontracts and monitoring the work being conducted at multiple subcontract sites.

During the reporting period, CMRP staff also provided part-time support to the Patient Characterization Center/Clinical Assay Development Center, an ARRA-supported subcontract for a specimen retrieval system to collect cases for validation of NCI-supported clinical assays. This subcontract was awarded to Kaiser Permanente. A second subcontract supporting this initiative was awarded in August 2011 to Marshfield Clinic Research Foundation. NCI is establishing a system that will provide sets of appropriate specimens to facilitate the evaluation of an assay's analytical performance and initial assessment of clinical utility. These sets of specimens will come from community settings and will be associated with clinical and outcome data. The specimen sets must be assembled rapidly to meet the assay development needs identified during the clinical trial concept review and the continued review of emerging technologies.

Initially, two member organizations of the Cancer Research Network, a subset of the HMO Research Network, participated in a pilot study that indicated that previously developed software could identify cases that meet defined assay development needs. The software, developed by a group at Harvard as part of an earlier NCI initiative, was designed to interact with existing medical records at the participating institutions, to strip the records of protected health information, and to use natural language processing to collect specified data related to treatment and outcomes.

The current subcontract with Harvard supports the collection of specimens from 1,000 to 1,500 cases each of defined tumor types. The cases will be evaluated for their completeness, and appropriate paraffin blocks will be submitted to a repository in Frederick, Maryland, for subsequent distribution to laboratories participating in the Clinical Assay Development Program. Demographic and clinical data will be assembled into a database established by NCI with contractor support. Before using specimens, a pathologist will review each case to ensure that it meets the requirements of the study in which it will be used.

Additional subcontracting support is being performed for the Clinical Assay Development Program. NCI

initiated this program to focus on support for the development and optimization of clinical-grade assays. The intention of this program is to select from submitted applications the specific assays that are determined to have scientific merit and feasibility that will have the most impact on clinical decision making. As part of the effort, a group of eight Clinical Laboratory Improvement Amendment–accredited laboratories was selected to provide the needed assay development and optimization services. CMRP staff supported the selection and award of the BOAs with institutions that will have the opportunity to submit proposals in response to specific assay-related SOWs.

In March 2011, NCI approved two applications and initiated the subcontracting process to select and award task orders. The two applications are: (1) Development and Optimization of an Assay for Detection and Quantitation of 2-hydroxyglutarate (2HG) Metabolite Derived from Somatic Mutations of IDH1 and IDH2; and (2) Development, Optimization of an Assay for Detection of Somatic Mutations of IDH1 and IDH2. CMRP staff serves as the assistant COTR by preparing SOWs; participating in and supporting SEG meetings where proposals from the BOA sites are reviewed, critiqued, and scored; preparing the SEG Evaluation Report to recommend subcontract awards; and tracking all awarded subcontracts. Continued support is anticipated into FY2012.

Support to the Cancer Expert Corps (CEC) within the Radiation Research Program (RRP), NCI

Joy Beveridge, M.S., Clinical Project Manager III
Rhona McVicker, R.N., O.C.N., CTEP Administrator

Beginning in December 2005 and continuing through July 2008, high-level administrative support was provided to the Cancer Expert Corps (CEC), a unique Radiation Research Program (RRP)-based initiative that helps provide the infrastructure, technical assistance, and coordination of public and private organizations necessary to establish a regional, national, and international knowledge and mentoring network of expert cancer professionals. Through the development and implementation of research, education, and communications platforms, CEC would enable applicant organizations to become active and networked members of the global cancer research community and, thereby, help generate, benefit from, and disseminate new knowledge and support best practices related to cancer research, prevention, diagnosis, and treatment to health-disparaged communities that have historically been on the periphery.

Unfortunately, dedicated funding from NCI was not allocated, so the full-time staff assigned to support CEC resigned. No support was provided to CEC until December 2008, when a part-time effort was provided for the program's ongoing efforts to identify potential private partners, such as ASCO, the International Agency for Research on Cancer, and the International Union against Cancer.

As reported for FY2010, only modest support has been provided to collaborate and assist in developing a plan of action to contact previous mentors who were willing to help develop relevant research projects and access NIH funding through the grant process. RRP continues to work with the mentors, offering assistance with NIH grant application tasks. The list of participating individuals was continually updated and forwarded to RRP.

In addition, several of NCI's CTEP personnel expressed interest in volunteering their time and talent in this venture. The Oncology Nursing Society offered to assist in providing expert nursing resources. All corresponding spreadsheets and documents were forwarded to RRP in order for these to be incorporated into their database(s).

NCI persisted by investigating potential funding sources for CEC and for hiring full-time NCI staff. In August 2010, NCI hired full-time support for this initiative. During the reporting period, CMRP successfully transitioned all support to the NCI counterpart. No additional support to this program is anticipated.

Support to the Division of Cancer Control and Population Sciences (DCCPS) Behavioral Research Program (BRP), NCI

Beth Baseler, M.S., Director
Mary Spinelli, Clinical Program Administrator
April Oh, Ph.D., M.P.H., Senior Behavioral Scientist, On-Site Supervisor
Lila Finney-Rutten, Ph.D., M.P.H., Behavioral Scientist
Amanda Vogel, Ph.D., Behavioral Scientist
Giovanna Zappala, Ph.D., Medical Affairs Scientist
Heather Edwards, Ph.D., M.P.H., Behavioral Research Associate II
Allison Rose, M.H.S., Clinical Project Manager I
Paul Courtney M.S., Clinical Project Manager II

The primary goals of the Division of Cancer Control and Population Sciences (DCCPS) are to reduce risk, incidence, and deaths from cancer and to improve the quality of life for survivors. Over the past 10 years, CMRP has assisted DCCPS in its mission by providing programmatic and scientific support services to all branches within the DCCPS Behavioral Research Program (BRP), including the Tobacco Control Research Branch (TCRB), the Health Communication and Informatics Research Branch (HCIRB) (formerly the Applied Cancer Screening Research Branch [ACSRB]), the Office of the Associate Director, the new Science of Basic and Biobehavioral Research Branch, and the Health Behaviors Research Branch.

CMRP behavioral scientists and project administrators have been pivotal in researching causes, incidence, prevalence, and prevention of cancers, and have worked closely with BRP program staff to generate the research necessary to inform evidence-based practice and policy. CMRP staff also plays a critical role in BRP's national surveillance efforts, observing and communicating cancer trends to the public, developing web-based smoking cessation interventions and research tools for the extramural research community, and providing program and scientific support to BRP research networks and collaborations.

In support of intramural research efforts, ranging from tobacco use and other multiple risk factor behaviors (e.g., physical activity, dietary behaviors, and sun safety) to genetic susceptibility and breast cancer screening practices, CMRP staff members have presented numerous scientific presentations at leading conferences and have published more than 90 articles in peer-reviewed journals.

The passing of legislation granting the FDA authority to regulate tobacco products also brought new responsibilities and an increased workload to CMRP as staff drafted responses to a number of HHS, FDA, and White House inquiries. In addition, as the FDA Tobacco Products Scientific Advisory Board evaluated the role of menthol cigarettes in the public health burden of tobacco-induced death and disease, CMRP staff worked closely with NCI program directors to build the evidence surrounding this public health burden by developing and disseminating findings from a journal supplement on this topic, published by *Addiction* in November 2011.

In a leadership role, CMRP staff contributed scientific content to four of NCI's DCCPS BRP surveillance efforts to examine trends in cancer communication and cancer prevention behaviors, and to seek to better understand the mechanisms and theories of behavior change. CMRP led the development of the Health Information National Trends Survey (HINTS) 4 and managed the HINTS GEM web site, which allows the extramural community to contribute and comment on HINTS 4 survey items. In addition, by serving as scientific content experts (or "HINTS Champions") and vital members of the HINTS III Management Team, CMRP staff has been a key source of information for health care providers, researchers, cancer patients, and survivors within these surveillance efforts.

During the reporting period, staff also supported the dissemination of the Food, Attitude, and Behaviors survey, and the development of a web site and related fact sheets to disseminate the survey and results to the extramural research community. CMRP staff also contributed to the conceptualization, framing, and development of new surveys consistent with BRP's mission to understand and promote research on the mechanisms of behavior change to prevent cancer. Staff also served as project leaders and managers on several priority initiatives and as resources for key products supporting BRP's scientific content areas.

CMRP provided a central leadership role in developing, maintaining, and evaluating several NCI web sites, including http://smokefree.gov, http://women.smokefree.gov, and http://meetings.smokefree.gov. The Team Science Toolkit is the first web-based toolkit and resource for Team Science. CMRP staff supported the conceptualization, development, launch, and maintenance of this web-based tool, http://www.teamsciencetoolkit.cancer.gov.

Similarly, CMRP staff led the development, conceptualization, launch, evaluation, review, and maintenance of the Classification of Laws Associated with School Students (C.L.A.S.S.) web site. This web site, http://class.cancer.gov, offers an online tool for evaluating laws in schools that target obesogenic behaviors such as physical activity and diet.

CMRP staff provided administrative and scientific support to various BRP/TCRB research networks, including the Tobacco Research Network on Disparities (TReND) and the Tobacco Harm Reduction Network. CMRP staff has also played key management roles and contributed to the scientific content of high-level BRP meetings, workshops, and conferences, including the final culmination meeting of TReND, "Making the Difference in Tobacco-Related Health Disparities Science: TReND Progress, Process, and Opportunities for Future Investment"; The International Smokeless Tobacco Meeting, held in partnership with NCI and the Centers for Disease Control and Prevention; and another groundbreaking meeting sponsored by ACSRB, "Multilevel Interventions in Health Care: Building the Foundation for Future Research Goals."

Recognizing the growing needs of CMRP's support to DCCPS, a clinical program administrator position was requested and approved via YT 08-220. The CMRP clinical program administrator serves as an essential communication liaison between NCI's DCCPS and CMRP management and staff. This position provides administrative support to various branches within the program and works closely with the on-site supervisor, CMRP personnel, and the customer to coordinate and participate in the planning and implementation of new and ongoing initiatives. These activities also include recruiting and hiring for various technical positions; assisting with creating and maintaining budget assumptions and cost estimates for all existing and new positions and activities within the group; serving as the CMRP COTR on numerous subcontracts; coordinating the planning and support for various conferences and seminars for the program; and serving as the point of contact on these efforts.

During the reporting period, a clinical project manager II was hired to lead the efforts related to the PopSciGrid. The PopSciGrid is an initiative to use and expand on the resources of caBIG® to develop tools for behavioral health scientists. Specifically, PopSciGrid aims to develop resources that allow researchers to combine and analyze large datasets, including population-based health surveys, such as the National Health and Nutrition Examination

Survey, the National Health Interview Survey, and HINTS. This initiative includes addressing the technical details of mounting data sets, harmonizing data elements, and developing analytic tools.

In addition, CMRP was requested to provide additional support to BRP to develop new areas of research and to expand its research portfolio. During the past year, SAIC-Frederick hired a medical affairs scientist to fulfill this need. The medical affairs scientist contributed to the development of a biobehavioral research network and assisted in planning a one-day seminar, "Stress-Mediated Effects on Cancer Biology: A Primer on Cancer Biology and Plausible Mechanisms."

Support to the Health Behaviors Research Branch, NCI

April Oh, Ph.D., M.P.H., Senior Behavioral Scientist, On-Site Supervisor

The mission of the Health Behaviors and Research Branch is to plan, develop, and coordinate research on non-tobacco behavioral prevention, including diet, physical activity, sleep, sedentary behaviors, energy balance, virus, and environment and sun exposure. Activities include providing leadership in developing methodologies for the measurement of health behaviors and psychosocial correlates of behaviors; examining the interaction between the environment and psychosocial factors; evaluating interventions and policies; and promoting training and dissemination in behavioral health research.

Several key program initiatives surrounding energy balance include the Food, Attitude, and Behaviors survey, the C.L.A.S.S. web site, and the Food, Activity, Sedentary, Sun-safety, and Tobacco survey. CMRP's senior behavioral scientist provides programmatic leadership and management for these initiatives.

The senior behavioral scientist has provided key leadership and conceptual and scientific content for the development, launch, evaluation, and dissemination of the Health Behaviors Research Branch C.L.A.S.S. web site, http://class.cancer.gov. This web site includes features developed specifically for researchers, policy makers, practitioners, and the lay audience. Specific tools managed by the senior behavioral scientist include a policy mapping tool and state policy profiles. During the reporting period, the senior behavioral scientist presented web site information at several national and local conferences/meetings. In addition, a symposium focused on the web site and related analyses was selected by the Society of Behavioral Medicine for media attention through a press release at a recent Society of Behavioral Medicine Annual Meeting in Washington, D.C.

The Food, Attitude, and Behaviors survey is a survey that examines national fruit and vegetable intake. SBS has assisted in developing and reviewing the final survey documentation and related materials to make the data publically available for the extramural research community. The senior behavioral scientist has been integral in developing a new web site to share these materials, as well as to manage Food, Attitude, and Behaviors survey data distribution.

The Food, Activity, Sedentary, Sun-safety, and Tobacco survey seeks to examine psychosocial, generational, and environmental correlates of cancer preventive behaviors. The survey's goal is to advance the understanding of the dynamic relationship between the environment, psychosocial factors, and behavior from an intergenerational perspective (e.g., assessing adolescent-parent dyads). The senior behavioral scientist led and managed the development of this survey, including facilitating partnerships with Centers for Disease Control and Prevention staff and the National Collaborative on Childhood Obesity Research; identifying survey items; coordinating cognitive interviewing and related protocols; submitting Office of Management and Budget and IRB applications; performing literature reviews; and preparing manuscripts. The senior behavioral scientist has written, presented, and submitted over 12 scientific abstracts and manuscripts.

Support to the Basic Biobehavioral and Psychology Sciences Research Branch (BBPSB), NCI

Giovanna Zappala, Ph.D., Medical Affairs Scientist
Mary Spinelli, Clinical Program Administrator

CMRP staffs a medical affairs scientist and a clinical program administrator to support the newly established Basic Biobehavioral and Psychology Sciences Research Branch (BBPSB). The purpose of the network is to stimulate transdisciplinary research on biological and behavioral mechanisms that underlie the interactions of the mind, brain, body, and social context, and contribute to the pathogenesis, course, and treatment of cancer. The network includes a diverse discipline of researchers whose goals are: (1) to encourage collaborations among multiple research disciplines; (2) to serve as a forum for generating new ideas and research projects focused on understanding social regulation of tumor biology; and (3) to serve as a knowledge-transfer conduit for basic, clinical, and translational scientists.

In addition to monthly conference calls, the network meets three to four times per year. During the reporting period, CMRP staff provided scientific communications and administrative support, meeting and travel coordination, and established four consulting agreements and one YT to support BBPSB efforts.

CMRP staff supported and participated in the first BBPSB meeting, "Epidemiology of Psychological and Social Influences on Cancer Outcome," held in Los Angeles in late September 2010. The medical affairs scientist, working with the BBPSB chief, presented "From the Clinic, to the Bench, to the Genome: Evidence that Psychosocial Experiences Matter in Biologically Relevant Ways." The meeting focused on how the

analysis of findings is relevant to understanding the epidemiology of psychological and social influences on cancer outcome.

The medical affairs scientist and the clinical program administrator also supported and participated in the second BBPSB meeting, held in San Diego in January 2011. The title of the meeting was: "Neural and Physiological Mechanisms underlying Cancer and Cardiovascular Diseases: A Basic and Biobehavioral Research Branch Think Tank." The meeting focused on discussions relative to the understanding of the common background and communalities between cancer and cardiovascular diseases.

The medical affairs scientist and clinical program administrator supported the third BBRN meeting held in July 2011, titled "Building Bridges: A Conversation between the Biobehavioral Research Network and the National Cancer Institute." During this meeting, the network's mission, vision, focus, and research were exposed to a larger NCI audience.

Support to the Tobacco Control Research Branch (TCRB), NCI

April Oh, Ph.D., M.P.H., Senior Behavioral Scientist, On-Site Supervisor
Allison Rose, M.H.S., Clinical Project Manager I

CMRP staff continued to participate in a wide range of TCRB support activities during this reporting period. Activities included reviewing abstracts for scientific conferences and manuscripts submitted to scientific journals; authoring multiple manuscripts published in scholarly journals; and presenting original work at scientific meetings. In addition to the general scientific and administrative support CMRP provided to TCRB, staff members also provided mentoring to fellows, interns, and graduate students, and continued to be actively involved in more than a dozen research projects.

With the help of a behavioral research associate, CMRP continues to support, promote, and maintain NCI's smoking cessation web sites: http://smokefree.gov and http://women.smokefree.gov. The Smokefree.gov web site has been rated by peers in published manuscripts as one of the two most trusted and credible web sites in the world for smoking cessation. It continues to maintain the number one ranking on both Google™ and Yahoo!®, using the search term "quit smoking," without any commercial advertising or promotion. CMRP's behavioral research associate manages the global Smokefree.gov task list, works with team members to ensure that deliverables are completed, and helps determine priorities to ensure proper implementation of selected revisions to the site. Mother's Day 2011 marked the second anniversary of the Smokefree Women campaign, a multimillion-dollar smoking cessation campaign targeted at women. The centerpiece of this effort is the Smokefree Women web site, http://women.smokefree.gov, which offers a special focus on topics important to women. Along with the founding team, the behavioral research associate was responsible for launching the initial concept for Smokefree Women. The team received an NCI Director's Group Scientific Award for the Smokefree Women web site in November 2010.

The passing of legislation granting FDA authority to regulate tobacco products brought new responsibilities and an increased workload to TCRB. The behavioral research associate helped draft a number of responses to HHS and FDA inquiries and created presentations for the DCCPS division director and the TCRB chief. One of the noteworthy responses was the NIH Priority Setting, "Tobacco Goal on Youth Smoking Prevalence." HHS selected the area as one of their high-priority goals and designated NIH, the Centers for Disease Control and Prevention, FDA, and the Administration for Children and Families as contributors to the performance goal. These goals will also become goals of the Obama presidential administration. The CMRP behavioral research associate participates in communication liaison meetings as the TCRB representative; one at the division level and the other at the program level. Both the BRP and the DCCPS communication liaison meetings facilitate the transfer of best practices, protocols, and project updates among BRP and DCCPS communication staff.

The CMRP behavioral research associate also continues to expand NCI visibility by publishing and preparing presentations, manuscripts, and *NCI Cancer Bulletin* articles. The CMRP behavioral research associate coordinates the dissemination of TCRB publications at national and international conferences, such as the American Psychological Association, Society for Research on Nicotine and Tobacco, National Conference on Tobacco or Health, National Conference on Health Communication, Marketing, and Media, and the World Conference on Tobacco or Health. The behavioral research associate was also involved in disseminating the NCI Tobacco Control Monograph No. 20, titled "Phenotypes and Endophenotypes: Foundations for Genetic Studies of Nicotine Use and Dependence," which involved revising fact sheets, creating summary presentations, and distributing copies of the publication to NIH leadership and various organizations.

The subcontract initially established to support the network and several conferences was terminated. In its place, two additional subcontracts have been established to support TReND efforts, including support to numerous conferences. CMRP staff has been involved with providing administrative and scientific support to the various TReND research projects, dissemination efforts, and investigator conference calls and meetings, including the TReND Final Meeting.

The CMRP clinical project manager I participated in a number of research activities involving the dissemination of critical tobacco-related findings at international and domestic conferences and meetings. The clinical project manager I provided support to the International Smokeless Tobacco projects and the Tobacco Harm Reduction Network by attending meetings, drafting

meeting reports, updating web site content, and coordinating network activities. In addition, the clinical project manager I provided technical support for the NCI/Center for Disease Control and Prevention Global Smokeless Tobacco Report by coordinating communications and report development with over 20 scientists. This staff member recently began providing administrative support to the TobPRAC/Research and Development contract by assisting with meeting planning, and coordinating communications between NCI and study investigators. The clinical project manager I has also authored, co-authored, and presented various scientific, peer-reviewed posters and publications.

CMRP staff continues to assist TCRB in support of TReND. TReND's mission is to understand and address tobacco-related health disparities by advancing science, translating the scientific knowledge into practice, and informing public policy. As a member of the TReND meeting planning committee, the clinical project manager I was involved in nearly all aspects of planning and coordinating the TReND Final Meeting. This effort included program development, management, and maintenance of a database with over 500 TReND network members. The clinical project manager I also helped to redesign the NCI TReND web sites, provided content for all 19 TReND projects, and contributed to their design, content, and usability in conjunction with TReND's web site, http://www.tobaccodisparities.org.

The clinical project manager I also worked closely with editorial teams to develop two journal supplement proposals and call for papers and secured the journal contracts. In addition, the clinical project manager I co-authored two publications featured in the Menthol Special issue, worked with the editorial team to finalize the dissemination list, and coordinated electronic and hard copy dissemination efforts. Additionally, the clinical project manager I created a new TReND project webpage to feature the journal supplement.

Support to the Health Communication and Informatics Research Branch (HCIRB), NCI

Sarah E. Evans, Ph.D., Senior Behavioral Scientist, On-Site Supervisor
Lila Finney-Rutten, Ph.D., M.P.H., Behavioral Scientist

A CMRP behavioral scientist supports and leads several initiatives within BRP's HCIRB, including serving on the HINTS (http://hints.cancer.gov/) management team. Duties during the last fiscal year have included leading weekly planning meetings for the program; developing program publications; supporting HINTS data users and responding to their questions; updating and providing content to the HINTS web site; and working to develop and implement the next iteration of the HINTS survey, which included developing and implementing an online infrastructure for item solicitation and rating (HINTS GEM: http://secure.mmgct.com/hints-gem/) and developing a series of four instruments to be fielded during the upcoming three-year field period.

The behavioral scientist serves on the Steering Committee for the Center for Excellence in Cancer Communication Research (CECCR). CECCR duties include participating in monthly calls, working with the center grantees to develop and implement an evaluation of the Cancer Survival Query System developed by NCI's Statistical Research and Applications Branch, and briefing the center leadership on opportunities for collaboration in HCIRB initiatives. The behavioral scientist is also actively involved in the Cancer Research Network Patient-Centered Communication Special Interest Group, participating in monthly calls and meeting in person at the annual Health Maintenance Organization Research Network conference held in Boston, MA, in April 2011.The behavioral scientist also serves on the HINTS Guam Planning Committee, helping inform efforts to implement HINTS in the Pacific Islands using the Behavioral Risk Factor Surveillance System infrastructure in Guam.

The behavioral scientist works on many HINTS writing projects and other DCCPS data resources. Since September 2010, the behavioral scientist published seven manuscripts in peer-reviewed journals and submitted an additional seven articles for publication. These articles are currently under review in a variety of journals including: *Journal of Health Communication*, *Journal of Cancer Education*, and *Preventing Chronic Disease*. Additionally, the behavioral scientist has published three book chapters and three technical reports during this time.

The behavioral scientist also served as the lead editor on a Hampton Press volume *Health Communication*, which was published in December 2010. The volume is dedicated to analyses of HINTS data, with a focus on methodological issues, the changing communication landscape, health disparities, and the role of health information technology in promoting health communication. The behavioral scientist served as lead editor on a special issue of the *Journal of Health Communication* published in December 2010. The special issue documents the use of HINTS data to inform the science and practice of health communication so that other scientists, public health planners, and medical practitioners can benefit from the national data collection.

The behavioral scientist actively participates in and presents work at national meetings. The behavioral scientist presented more than 10 papers at the following meetings since September 2010: American Public Health Association, Denver, CO, 2010; American Association for Cancer Research Cancer Health Disparities, Miami, FL, 2010; American Medical Informatics Association, Public Health Informatics section, Orlando, FL, 2011; American Public Health Association, Washington, D.C., 2011; International ACM Web Science Conference 2011, Koblenz, Germany; Society for Behavioral Medicine, Washington, D.C., 2011; and National Cancer Institute

Cancer Control P.L.A.N.E.T. Cyber-Seminar, Bethesda, MD, 2011.

The behavioral scientist serves on an expert panel for BRP in its effort to develop a longitudinal survey to assess and compare the extent to which certain health behavior theories and related constructs are predictive of health behavior change relevant to cancer. The behavioral scientist also serves as an expert consultant to BRP efforts to develop a cross-sectional survey of children and adolescents' food attitudes and behaviors.

During the reporting period, the behavioral scientist served as an invited discussant in a session on methods and measurement at an Institute of Medicine (IOM) Workshop on Understanding the Relationship between Food Insecurity and Obesity in Washington, D.C., November 2010. The institute also invited the behavioral scientist to serve as a consultant to develop a chapter on social marketing and front-of-package nutrition labeling for an Institute of Medicine report to be published in late 2011 or early 2012.

The behavioral scientist has served as a reviewer for the following journals since September 2010: *Journal of Cancer Education*, *Annals of Behavioral Medicine*, *Cancer Detection and Prevention*, *Journal of Health Communication*, and *Preventive Medicine*. In the fall of 2010, the behavioral scientist wrote a developer challenge for Health 2.0 and challenge.gov titled, "Enabling Community Use of Data for Cancer Prevention and Control" to promote the integration and visualization of publicly available federal data resources. This challenge resulted in two winning applications that were showcased at the Hawaii International Conference of System Sciences.

Support to the Office of the Associate Director and Science of Research and Technology Branch, NCI

April Oh, Ph.D., M.P.H., Senior Behavioral Scientist, On-Site Supervisor
Amanda Vogel, Ph.D., M.P.H., Behavioral Scientist
Paul K. Courtney, Clinical Project Manager II

The behavioral scientist supporting the Office of the Associate Director and the newly developed Science of Research and Technology Branch joined CMRP in August 2010 and immediately played a tremendous role in program efforts. The behavioral scientist serves as project leader of the Science of Team Science Toolkit. This is a web site, built on a wiki platform, which supports information exchange and knowledge sharing to promote the growth and unification of the interdisciplinary field called the "Science of Team Science." Under this capacity, the behavioral scientist works with a multidisciplinary team comprising computer programmers, social and clinical psychologists, and experts in business, communications, education, and informatics, to develop the structure and content of the Toolkit, solicit public contributions to the Toolkit, and promote the Toolkit through a wide variety of high-profile avenues, including internal NIH meetings of interested groups, national and international conferences, listservs, web sites, and social media. As a result of the leadership of the behavioral scientist, the Team Science Toolkit had its public debut at the Second Annual International Science of Team Science Conference, in Chicago, IL, in April 2011. The behavioral scientist led four sessions highlighting the Team Science Toolkit, during three days of this five-day conference. The sessions included a scientific poster session, as well as three interactive demonstration sessions where visitors could use laptop computers to engage with the Toolkit and discuss their experiences with the behavioral scientist and BRP staff. These sessions were extremely well attended; out of a total conference attendance of 350, approximately 100 visitors attended the behavioral scientist's sessions. The behavioral scientist has provided leadership for the testing and evaluation of the Team Science Toolkit, and to obtain NIH funding for these activities through internal applications for Evaluation Set-Aside funds. The web site is currently being refined based on usability testing, and a revised version will be debuted at the exhibitors' hall of the October 2011 American Public Health Association conference—the largest annual international public health professionals' conference.

In addition to the demonstration sessions described above, the behavioral scientist co-authored 11 oral presentations and posters during the reporting period.

The behavioral scientist is leading a study to evaluate lessons learned from the TREC Initiative. This study focuses on gleaning expert knowledge about strategies for successfully engaging in, facilitating, and studying team science. The TREC Initiative is one of the largest and highest profile of the grant initiatives supported by BRP. It represents a trend of large center grant initiatives that fund teams of collaborators to work together within and across centers at different academic institutions, to embark on a program of cross-disciplinary research. The behavioral scientist's study includes interviews with over 40 participants in TREC, including center directors, senior and junior investigators, and NCI staff members. It capitalizes on the lessons learned from TREC to develop a scientific manuscript that will share generalizable lessons learned that can support the activities of other investigators, academic institutions, and government agencies that are interested in supporting and facilitating team science.

The behavioral scientist is part of a team that is leading a study to assess the impact of the Center for Population Health and Health Disparities (CPHHD) Initiative to create research collaboration networks among investigators participating in the ten funded CPHHD centers. Like the TREC Initiative, CPHHD is one of the largest and highest profile of the grant initiatives supported by BRP, and represents the trend toward support for large center grants supporting cross-disciplinary team research. This study uses survey methods in combination with cutting-edge social network mapping techniques to assess the impact of CPHHD on

the development of social networks. This work will also be disseminated in a scientific manuscript.

The behavioral scientist is leading a group process, among members of the new Science of Research and Technology Branch (SRTB), to develop the official mission statement and scientific priorities of the branch. Engaging with a collaborator in BRP, the behavioral scientist is crafting the language for this document, and facilitating a complex iterative process to ensure that all stakeholders' contributions are reflected.

The behavioral scientist is working with the BRP director to develop a new study to assess physicians' attitudes and practices related to referrals of patients to clinical trials. This is a priority topic area for BRP and NCI. As challenges related to meeting quotas for clinical trials participation continue, research is needed to understand the factors that influence enrollment. One critical factor is physician referrals to trials. This study will use a physician survey to explore attitudes and practices related to referring patients to cancer clinical trials.

The behavioral scientist is leading a group of co-authors, drawn from across the nation, to develop a manuscript on web-based technologies to support collaborative team science. Web-based technologies for collaborative research are a high-priority area for NCI and more broadly, NIH, as evidenced by the caBIG® initiative, and other major investments in cyber infrastructure to support collaboration. This manuscript will document the recent boom in these technologies, highlight leading technologies in the field, and explore the implications of this trend for the future of collaborative team science.

The clinical project manager II provides leadership, coordination, and guidance to multiple biomedical informatics projects across the division. These efforts are related to BRP's GEM, PopSciGrid, and Team Science Toolkit; the Applied Research Program's Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events, Population-Based Research Optimizing Screening through Personalized Regimens, and Breast Cancer Surveillance Consortium; the Surveillance Research Program's Surveillance, Epidemiology, and End Results (SEER)-Rx and web site redesign; and the Epidemiology and Genetics Research Program's Cohort Consortia.

The support provided demonstrates the value of integrating disparate datasets; exploring novel sociotechnical approaches to harmonizing items and measures; ensuring that projects are constructed using best practices of data standards and the semantic interoperability of systems (as exemplified by NCI's CBIIT and partners); and investigating ways to encourage the dissemination of NCI-funded study metadata and data with innovative software and incentives.

It is vital to tracking institute/center and division initiatives regarding informatics infrastructure and maintaining awareness of other cyber infrastructure initiatives in the field of biomedical research. The clinical project manager II travels nationally and internationally to facilitate dialogue and meetings between institutes/centers, divisions, and CBIIT leadership, and advises the Office of the Director on how best to adopt technologies from various resources. The clinical project manager II works with national organizations to develop standards on tools and techniques available to support population-based cancer control research.

The clinical project manager II was part of the GEM team that received the NCI Director's Group Scientific Award for the Grid-Enabled Measures portal on November 4, 2010. This staff member is also the lead author on a review paper, "Data Liquidity in Health Information Systems," published in the July/August 2011 issue of *The Cancer Journal* and was co-author on two papers, "Grid-Enabled Measures: Using Science 2.0 to Standardize Measures and Share Data," (published in *American Journal of Preventive Medicine* in May 2011) and "Supporting implementation of evidence-based behavioral interventions: the role of data liquidity in facilitating translational behavioral medicine," (published in the inaugural issue of *Translational Behavioral Medicine* in March 2011).

The clinical project manager II continues to collaborate with DCCPS and CBIIT to gain a better understanding of the larger CBIIT initiatives, and how DCCPS could engage more productively with them.

Support to the Process of Care Research Branch (PCRB), (formerly the Applied Cancer Screening Research Branch – ACSRB), NCI

Allison Rose, M.H.S., Clinical Project Manager I, On-site Supervisor
Heather Edwards, Ph.D., M.P.H., Behavioral Research Associate II

ACSRB planned, implemented, and maintained a complete program of social and behavioral research that promoted the adequate use of cancer screening tests and strategies for informed decision-making regarding cancer screening technologies in the community and clinical practices. The branch employed interdisciplinary teamwork and collaboration with relevant organizations and constituencies to establish a national research agenda for cancer screening. ASCRB addressed gaps in cancer screening research and served as a national model for supporting the development and testing of new and innovative methods, theories, and strategies that may increase the understanding, and utilization of cancer screening technologies.

In May 2011, ACSRB evolved into a new branch, the Process of Care Research Branch (PCRB). Along with the name change, a new mission statement and priorities were established. The new branch supports and encourages behavioral research on how individuals, teams, and health care organizations can act and interact more effectively to improve health through health care delivery. PCRB

focuses on behavioral health issues in health care settings across the cancer continuum, from prevention and screening through diagnosis and treatment. The branch focus encourages a broad array of studies and methodological approaches that increase understanding and promote behavioral interventions that affect health through health care delivery.

A behavioral research associate was hired to provide scientific support to PCRB. This position provides data and portfolio analyses, writes manuscripts, and supports other research-related projects. The behavioral research associate provides leadership and guidance for many large scale projects, spanning the scope of the branch and involving a multidisciplinary group of scientists external to BRP and NIH. The behavioral research associate serves as HINTS Champion, making recommendations and also acting on informal subcommittees to consider survey items, and serves as a project manager for the Multilevel Intervention Project, by planning conferences, leading meetings and serving as an internal editor for a project-related journal supplement. During the reporting period, the behavioral research associate authored and co-authored manuscripts, and presented posters, papers, and abstracts at several meetings and conferences. The behavioral research associate also coordinated and monitored a panel session at the American Public Health Association Annual Meeting in November 2010.

Support to the Office of Latin American Cancer Program Development (OLACPD), NCI

Beth Baseler, M.S., Director
Silvina Frech, Ph.D., Scientific Program Manager
Mariana González del Riego, Clinical Project Manager II
Jennifer Imes, Program Manager
Irene Mueller, MPH, Clinical Project Manager I

OLACPD is a pilot initiative and partnership between NCI and the Fogarty International Center designed to develop and implement mutually beneficial cancer research programs in Latin America. The goal of this program is to increase the capability of these countries to participate and partner in cancer research, including the critical development of clinical trials networks, advanced technology centers, and personnel to deliver state-of-the-art cancer care to patients.

The U.S.–Latin America Cancer Research Network (US-LACRN) currently comprises six study sites in five countries (i.e., Mexico, Argentina, Brazil, Chile, and Uruguay). The potential inclusion of additional countries is being considered. Each country has a specific formal agreement with the NCI through a ratified letter of intent, which outlines joint efforts in cancer research projects, project-specific training and capacity building activities, as well as other research-related activities that support these projects.

The first phase of the Latin America initiative features a multi-site breast cancer molecular profiling study titled, "Molecular Profiling of Stage II and III breast Cancer in Latin American Women Receiving Standard of Care Treatment." During this reporting period, CMRP support included the following:

1. Monitoring of the FY2011 budget and assisting with FY2012 budget preparation;
2. Planning and coordinating eight scientific conferences, seminars, and workshops and associated support;
3. Preparing approximately 19 CMRP international travel packages, 74 non-employee travel packages, and two non-employee national travel packages;
4. Receiving two letters of intent to participate in the molecular profiling of breast cancer study from two Latin American countries: Chile and Uruguay (Note: The other four letters of intent were received in FY2010);
5. Establishing formal agreements between SAIC-Frederick and the participating countries to implement the breast cancer study;
6. Renewing a task order (under an existing BOA) with a clinical pathologist who has expertise in human tissue banking;
7. Establishing an agreement for a Latin American onsite research coordinator;
8. Exercising option year one of the research subcontract with Information Management Services (IMS) to continue supporting the Biological Specimen Inventory (BSI)-II system instances across sites;
9. Modifying and exercising the scope of work of Task Order 1 under an existing BOA with CCS Associates, Inc. (CCSA), a clinical research organization, to continue providing technical and scientific guidance and infrastructure support to collaborating investigators, researchers, and the US-LACRN Steering Committee in the implementation of the clinical study protocol as well as in data analysis and monitoring;
10. Establishing two new agreements with microarray technology subject matter experts (molecular pathologist and molecular biologist) to support the breast cancer molecular profiling study and related training; and
11. Establishing a new agreement with a biostatistician who has experience analyzing breast cancer clinical data.

CMRP also successfully recruited a scientific program manager and an operational clinical project manager to provide dedicated support to OLACPD as the program plans for expansion in the upcoming year. The scientific program manager provided scientific expertise to the molecular profiling of breast cancer study while the clinical project manager supported day-to-day operations for the same. A senior program coordinator has supported

US-LACRN since fall 2010. This person has contributed to monitoring and ordering of Dako reagents and instrumentation for the sites and provided study site subcontract and budget support as well as scientific conference, seminar, and workshop and travel support. In addition, an SAIC-Frederick biobanking expert conducted site visits to 11 biobanks and more than 20 biospecimen collection sites to provide guidance on biospecimen collection, processing, and storage and the establishment of new repositories as well as to assess operations at already existing ones. Finally, an SAIC-Frederick subcontractor and clinical pathologist, with expertise in human tissue banking, gave multiple presentations at the 2010 US-LACRN Annual Meeting held in Rio de Janeiro, Brazil, in plenary, breakout, and media sessions. This staff member also contributed to the development of tissue collection and processing, proficiency testing, and other relevant SOPs.

Two SAIC-Frederick subcontractors played an important role in the progress achieved during the current reporting period: CCSA and IMS. In the past year, IMS constructed and deployed six BSI-II databases (one for each study site) across five participating Latin American countries for the tracking of blood and tissue samples obtained during the breast cancer molecular profiling study. Data entry, requisition, and report templates as well as workflow documents were developed based on study SOPs. In addition, IMS contributed to the design of a study dashboard maintained by CSSA. IMS staff participated in meetings, conferences, and workshops as appropriate; demonstrated system capabilities; offered BSI training to sites in conjunction with CCSA training sessions on OpenClinica® (see below), as well as on an ad-hoc basis; and provided help desk support via email and Squish.

In turn, CCSA provided expert support in the design and development of the molecular profiling of breast cancer study protocol, an extensive epidemiology survey, and other clinically relevant documents as well as associated revisions. CCSA developed the LACRN Manual of Operations comprising SOPs, guidelines, workflows, checklists, and responsibility descriptions in the following general areas: clinical operations, biospecimen management, molecular biology, pathology, quality assurance and quality control, and informatics data management. Efforts to revise, edit, and translate these (and related documentation) from English to Spanish were completed. CCSA provided scientific and technical assistance for preliminary data analyses, and was responsible for scientific and technical issues related to the supply of Dako kits, Agilent reagents, and instrumentation to study sites.

CSSA successfully installed OpenClinica®, a clinical trials software system for electronic data capture and clinical data management, and established training and production instances of OpenClinica® for each study site. Case report forms were developed and incorporated into the system in English, Spanish, and Portuguese. In-person and webinar OpenClinica® training sessions were scheduled or offered on an ad hoc basis, often in conjunction with BSI-II training. For example, a Bioinformatics Workshop was held in November 2010 and a subsequent webinar for local administrators in January 2011. Access to the production sites were granted upon completion of the site activation process (i.e., development and application of a site activation checklist, calls with the sites to discuss plans and readiness, and deployment of production version of OpenClinica® and BSI-II), also supported by CCSA. Access to the production sites were granted upon completion of the site activation process and were also supported by CCSA. OpenClinica® help desk support was offered via email and Squish. Furthermore, periodic reports on data entered into OpenClinica® were produced for NCI. The subcontractor designed and began to develop a study dashboard with contributions from IMS and feedback from NCI and CMRP.

CCSA staff coordinated the development of materials and presentations as well as technical logistics associated with the 2010 LACRN Annual Meeting held in Rio de Janeiro, Brazil, and training workshops, such as the Residual Cancer Burden Training (MD Anderson, March 2011) and the Microarray Training Workshop (Montevideo, Uruguay, June 2011). Support to scientific committees included the preparation of minutes and meeting materials for the US-LACRN Steering Committee, the Basic Research and Advanced Technology Committee, Pathology Committee, and Epidemiology Committee. CCSA staff also attended and often presented at professional meetings and conferences as requested by NCI OLACPD and CMRP, such as the OpenClinica® annual conference and the San Antonio Breast Cancer Symposium.

CMRP and CCSA worked collaboratively to establish the founding principles of a Data Monitoring Committee (DMC) for NCI's OLACPD's US-LACRN. These principles will provide the important foundation for the first study conducted in the network, assuring the quality of implementing the molecular profiling of breast cancer study and other studies to be conducted by US-LACRN. The CMRP program director and CCSA chief executive officer drafted the Data Monitoring Policy and Data Sharing Policy on behalf of the NCI program director and presented the draft policies and guiding regulatory and GCP guidelines at the second annual meeting in November 2010. A draft study monitoring plan is currently under development, which, upon NCI approval, will form the basis for study monitoring by investigators, NCI, and DMC. Work to establish the study monitoring team, DMC, and related processes has been initiated and will be finalized within the next several months.

SUPPORT TO NIAID

Support to the Regulatory Compliance and Human Subjects Protection Program (RCHSPP), NIAID

Beth Baseler, M.S., Director
Molly Buehn, Director of Regulatory Affairs
Shelly Simpson, M.S., Clinical Trials Director
Barry Eagel, M.D., Director, Clinical Safety Office
Laurie Lambert, Clinical Project Manager III
Barbara van der Schalie, M.S., Clinical Training Manager
Michael Galcik, M.S., IT Manager
Kathy Simpson, M.B.A., Document Control Manager

OVERVIEW/SUMMARY

Since January 2002, CMRP has played a major role in developing a regulatory environment to support the work of the NIAID Intramural Research Program. CMRP established and managed RCHSPP, which included development of the Regulatory Affairs Group, Clinical Trials Management Team, and Clinical Safety Office (CSO). The objectives of RCHSPP are to continue to provide a unique resource for comprehensive clinical trials monitoring and management, regulatory support, and clinical safety oversight encompassing clinical trial monitoring; clinical research organization oversight; IND/IDE/DMF application development and management; compliance with clinicaltrials.gov reporting requirements; regulatory surveillance over clinical trials; AE reporting; safety reporting; protocol and informed consent development and review; investigational product oversight; Data and Safety Monitoring Board (DSMB) and Safety Monitoring Committee (SMC) management; IRB support; IT systems maintenance; QA compliance; document management, and training program support. All of these efforts are to ensure that the clinical protocols are conducted in accordance with HHS, FDA, and NIH regulations and ICH/GCP guidelines. Additionally, RCHSPP provides scientific administration oversight to the establishment and maintenance of subcontracts, logistical/project management, and operational support to a variety of clinical projects.

CMRP's mission is to provide regulatory support to the PIs within NIAID to meet the requirements of the *Standards of Clinical Research* established by NIH in 2000. Before RCSHPP existed, PIs were required to manage and coordinate all of the regulatory/monitoring oversight for their individual clinical studies. With the establishment of RCHSPP, the regulatory compliance, clinical monitoring, and medical monitoring aspects of clinical research are now supported. This has given the PIs more opportunity to focus on the main objectives of their clinical protocols.

In an ongoing effort to provide the clinical researchers with additional avenues to support quality clinical studies, the NIAID clinical director requested that CMRP establish a new team within RCHSPP that could provide protocol navigation and protocol development activities. Over the past year and a half, the PN/PDP has become very well-known and successful in providing investigators with medical/technical writing of protocols as well as assisting the investigators with facilitating the logistical aspects of protocols.

RCHSPP provides dedicated regulatory, safety, clinical monitoring, and protocol navigation/protocol development support for a variety of clinical trials conducted by the Intramural Research Program within NIAID. These Phase I, II, and III trials run the gamut from natural history to interventional studies, including gene therapy, and cover a wide range of infectious disease states. The studies may involve IND or IDE applications. While many of the clinical studies are conducted at NIH, Johns Hopkins University's satellite site, the Washington Hospital Center, Unity Clinic, and the Walker Clinic in Washington, D.C., the staff is also currently traveling to remote sites, such as Mali, Kenya, India, Uganda, Cambodia, Peru, China, Indonesia, Thailand, Vietnam, Singapore, Korea, Mexico City, Australia, and South Africa. Staff also monitor domestic sites, including Children's Hospital in Seattle, University of Vermont, University of Rochester, Yale University, and Tufts University. RCHSPP also continues to play a significant role in the regulatory/clinical trials support for the U.S. Department of Defense (DoD) HIV, general infectious diseases, and Acute Respiratory Infections Consortium clinical protocols, including H1N1.

RCHSPP is also in the forefront of expanding to new and innovative regulatory technologies. Most recently, the Regulatory Affairs Group successfully prepared and submitted the first RCHSPB-sponsored IND in eCTD format to the FDA. The eCTD method of submittal is a more efficient and effective process, providing cost/resource savings, is more environmentally friendly, and is preferred by the FDA.

Key management staff members within RCHSPP serve as technical experts on a variety of committees and task forces within NIAID, including the NIAID Clinical Research Subcommittee, the Learning and Professional Development Group, the Strategic Planning Working Group, the Protocol Navigation Working Group, and the steering committee for the Office of Science Planning and Assessment.

Regulatory Affairs Group (Investigational New Drugs/Biologics/Devices)

The RCHSPP Regulatory Affairs Group prepares, submits, and maintains IND applications, IDEs, and DMFs to ensure that these documents are in compliance with FDA regulations, GCPs, GLPs, GMPs, and the ICH/GCP guidelines. Regulatory Affairs staff consists of a regulatory affairs director, a senior IND manager, seven RAs, and a regulatory submissions coordinator.

The Regulatory Affairs Group, in collaboration with RCHSPB IND clinical research oversight manager, is responsible for overseeing IND, IDE, and DMF

sponsorship. Staff provides overall regulatory support and guidance to the intramural investigators; interacts with industry collaborators; and serves as a liaison to FDA. The Regulatory Affairs Group supports investigators in the NIAID Intramural Research Program, which includes multiple laboratories within DIR, as well as investigators within DCR and the Vaccine Research Center (VRC).

Staff members provide comprehensive protocol reviews to the PIs; interact with various FDA divisions; work closely with investigators to prepare IND, IDE, and DMF applications and other regulatory documents; and interact with various pharmaceutical companies and other outside contractors to obtain information required to support RCHSPB-sponsored projects. Other important responsibilities include preparing, compiling, and submitting various documents to maintain and ensure regulatory compliance of RCHSPB-sponsored INDs, IDEs, and DMFs. These documents include, but are not limited to, protocol amendments, information amendments, annual reports, safety reports, responses to FDA comments and requests for additional information. In addition, staff members are also responsible for ensuring compliance with the mandated reporting requirements for the clinicaltrials.gov web site.

Currently, the group provides support for 60 active IND applications, two active IDEs, and five active DMFs, several of which include protocols conducted at international sites. During the contract year, the group prepared and submitted 13 new IND applications. Additionally, there are approximately 15 INDs/IDEs in various stages of development. As part of the ongoing maintenance for these new and existing applications, staff developed and submitted approximately 200 IND, IDE, and DMF serial submissions, and three pre-IND or pre-IDE meeting requests and information packages to FDA. Staff also participated in three teleconferences with FDA to discuss IND and IDE issues.

Other IND, IDE, and DMF support provided by the Regulatory Affairs Group during the contract year includes: (1) participating in numerous teleconferences and face-to-face meetings with NIAID scientific investigators, PIs, collaborating industry representatives, and other stakeholders to discuss ongoing scientific issues and IND management strategies (e.g., anti-H1N1 plasma studies, HPIV3cp45 IMPAACT study, MedImmune pandemic influenza CRADA projects); (2) participating in multiple meetings with investigators from the Laboratory of Infectious Diseases to review current and proposed projects and project timelines; (3) and providing cGMP guidance to RCHSPB about product storage, labeling, and manufacturing issues.

The Regulatory Affairs Group also successfully prepared and delivered the first RCHSPB-sponsored IND in the eCTD format to FDA. Following approval of an electronic submission gateway production account in August 2010, staff members prepared a pilot submission of an existing initial IND application that had been converted to an eCTD. This pilot submission was delivered to FDA for validation in December 2010 and the Regulatory Affairs Group received a response in mid-January 2011 that the application was guidance compliant. In February and May 2011, staff held two meetings with PIs from separate DCR laboratories to explain the transition from a paper IND to an eCTD, the development and processes of an eCTD versus an IND, and the Regulatory Group progress to date. In April 2011, the first RCHSPB eCTD IND for a new drug study (a Phase II study of DAS181 in parainfluenza) was submitted to the Center for Drug Evaluation and Research (CDER) within the FDA; the application was given safe-to-proceed status in May 2011. Since then, the Regulatory Affairs Group has submitted three additional eCTD INDs to CDER, delivered two vaccine eCTD INDs to CBER, and submitted a pre-IND meeting request to CDER for a new expanded access protocol.

During the reporting period, staff provided ongoing maintenance for three high-profile IND applications, two of which are evaluating the potential therapeutic use of H1N1 hyperimmune plasma for immunotherapy, and one that is evaluating combination antivirals to treat influenza. The first IND supports two protocols and involves a coordinated effort among 12 study sites to collect high-titer anti-influenza H1N1 plasma from human volunteers. The second IND evaluates the safety and efficacy of treatment with this collected investigational anti-H1N1 hyperimmune plasma in subjects who are likely to have H1N1 influenza and are at risk for severe disease. The third IND is to assess whether combination antiviral therapy is beneficial in resolving symptoms with lesser complications in the treatment of subjects with confirmed influenza infection. To provide management for these IND applications, the group developed and submitted more than 30 IND amendments and participated in weekly teleconferences with DCR, NIH PIs and study coordinators, representatives from DoD, and other external contractors to discuss site recruitment, document flow from the clinical site to FDA, and the data capture process for the studies. The Regulatory Affairs Group also submitted information on these protocols and the combined, active 32 study sites to the clinicaltrials.gov web site in accordance with the federal regulations. The regulatory affairs director, senior IND manager, and two RAs were among those honored in January 2011 with a NIAID 2010 Merit Award for their work on these important influenza studies.

The senior IND manager continued to direct the ongoing processes related to the RCHSPP Inspection Readiness Program. General inspection awareness training was provided to select Industry Lane–based RCHSPP staff in January 2011 and to Bethesda-based RCHSPP PN/PDP staff in May 2011. A live training on the inspection process, entitled "Regulatory Inspections: Meeting with Inspectors," was developed and is currently in the final stages of approval. This training will be provided to all RCHSPP staff that may be called for interview during an inspection. The Inspection Readiness program underwent a semi-annual audit in May

2011. This audit was conducted to ensure that all inspection-related materials, processes, and staff trainings are up-to-date. Several areas of improvement were identified and current procedures and processes will be revised or initiated to enhance and streamline the program.

Staff continues to work closely with the TW developers and serve as a member of the TW Working Group to improve the capture of process details and information, define new work processes and reports, and ensure that all TW notifications are appropriate. Fifteen TW change requests were submitted for review in this past year; of these, 12 were completed, and formal trainings were conducted to ensure understanding and proper implementation of the system changes. Examples of important TW modifications include:

- Creating a new record to capture the recently established review of investigator brochures by the Clinical Safety Group;
- Adding a field to the IND record to select and report on the INDs under the FDA Office of Vaccines Research and Review; and
- Developed and generated a new report that allows users to comply with a November 2010 request from FDA to provide a quarterly report on prior and anticipated IND submissions.

In addition, a regulatory associate played a large role in creating a TW-integrated training application and presented this training to functional group users in November and December 2010. This training will provide awareness to all RCHSPP functional area groups currently using TW about the benefits of the application to group processes.

The regulatory affairs director worked with the RCHSPB IND clinical research oversight manager to update the "NIAID Division of Clinical Research Practices and Guidelines for the Management of Investigational New Drug Applications." The regulatory affairs director reviewed and substantially edited this 55-page document to reflect current FDA regulations/guidance and any changes in RCHSPB practices as well as to add new hyperlinks and update over 40 web page addresses. The document was then passed through multiple branch and division reviews, finalized, and distributed to RCHSPB for posting on the DCR web site within three months of assignment.

Clinical Trials Management Team

The Clinical Trials Management Team is an integral part of RCHSPP. The team plays a key role in the success of performing well-controlled clinical research for non-IND and Phase I and Phase II trials sponsored by the RCHSPB/NIAID Intramural Research Program at NIH. The Clinical Trials Management Team's main focus is to facilitate and oversee clinical research studies. The team's responsibilities are to monitor studies to ensure that the rights, safety, and well-being of human subjects are protected; ensure that the reported study data are accurate, complete, and verifiable from source documents; ensure that the study conduct is in compliance with IRB/ethics committee-approved protocol, ICH/GCP guidelines, and all other applicable regulatory requirements; detect, report, and assist with site quality management planning and resolve discrepancies that occur during the study period; and communicate all site-monitoring reviews and observations to PIs and clinical research oversight managers. The team also ensures that the sites maintain study agent in compliance with study protocols that are under an IND.

Currently, the Clinical Trials Management Team is involved with the management and/or monitoring of approximately 155 clinical research studies conducted at sites throughout the U.S. and in several foreign countries. The studies the team is responsible for monitoring vary and include Phase I/II IND and IDE studies, natural history studies, pediatric studies, and research studies that are noninvasive and are not under an IND. During FY2011, the team conducted approximately one pre-study site assessment visit, 70 study initiation visits, 151 interim monitoring visits, and 22 study close-out visits. Trial monitoring included various international clinical sites in Africa (Mali, Uganda, and Kericho), Korea, Taiwan, Thailand, India, Vietnam, Cambodia, Peru, Mexico (Mexico City), and other countries across the world. The Clinical Trials Management Team also conducted international site-initiation visits in Thailand, China, Australia, Mexico City, and Mali, and conducted seven study-site audits in hospitals in Korea.

The team continues to provide sponsor-related clinical trials management for several newly established NIAID networks, including the H1N1 Network, INSIGHT (START), and the Mexico Flu networks. The team also initiated several new studies in the D.C. area that are part of the DC-PFAP program. The Clinical Trials Management Team manages the sponsor's essential document files for the 30 active clinical sites within all three networks, as required by FDA and HHS, and conducts sponsor site audits. The team monitored four of the INSIGHT (START) protocol sites in FY2011. The Clinical Trials Management Team also expedited the initiation of two new multi-center influenza studies this fiscal year for IRC-003 and IRC-004, which also included the expansion of the IRC-003 study to seven Australia sites in the H1N1 network. The large kickoff meeting for Australia occurred in June 2011. RCHSPP and the Clinical Trials Management Team activated the first site in August 2011.

The team reviewed clinical research protocols and informed consent forms, and provided commentary to NIAID, DoD, and IDCRP PIs. The group also reviewed, created, and revised IDCRP protocol study manuals, source documents, and case report form edits on various new studies and studies that were previously activated. The Clinical Trials Management director and clinical project manager II assisted the IDCRP management with review and implementation of their QA program. They

received and commented on several IDCRP SOPs and report templates for this group. The two teams (Clinical Trials Management and IDCRP) have excelled this year in their communication pathways. IDCRP management solicited the team's guidance on some of their new initiatives more frequently this year and included some of the Clinical Trials Management Team members in their new study planning activities. Several team members also received invitations for an investigators meeting. These efforts allow CMRP to excel and enhance the level of efficiency for this group.

The Clinical Trials Management Team provided input for the updated NIAID unanticipated problem language and the RCHSPP (CSO) sponsor, reporting SAE and unanticipated problem template language. In addition, the team helped to revise NIAID monitoring guidelines and the informed consent guidance document to now include topics on pediatric consenting and guidance on telephone consenting, all of which are posted on the RCHSPB web site. In addition, the screening and enrollment terminology document was posted. A new protocol violation guidance document was created for the Mexico Network. The group also initiated the first draft of an *Investigator Study Start Up Guidance Manual*, which will be a reference for PIs within NIAID who are conducting domestic studies outside of the Clinical Center.

A clinical project manager I and clinical research associate II will present a poster at the NIH Fall Poster Session on tracking protocol violations and corrective and preventive action plans resulting in expanded training initiatives for study teams. The team continues to review all protocol amendments that affect the activated DoD/IDCRP general infectious diseases and HIV studies and will monitor the second IND study activated within IDCRP. The clinical trials director and the clinical project manager II continue to review and comment on the goals/objectives of the RCHSPP PMT, in addition to working with the group to enhance the protocol project life cycle and milestones. The clinical trials director also worked with PMT to continue to enhance the project management models used to help assess the resources needed to complete future studies within certain models. CMRP staff members helped to meet several of the RCHSPP strategic planning goals and assess key performance indicators in order for the team to follow the RCHSPP Strategic Plan.

The entire team completed the new Gallup Poll survey and continues to discuss areas of enhancement and improvement for team processes and communications. Clinical Trials Management staff members also completed a two-day training, which gave the team an opportunity to brainstorm ideas to improve monitoring in the field. The team implemented several new tools to enhance monitoring, including the creation of a tool for the sites to use when obtaining a subject's consent and a concise monitoring checklist tool for the clinical research associates to use in the field. In addition, staff members updated the clinical trials management policies and procedures to include 8.0 TW screens and the new terminology required for protocol violations per NIH. In addition to this list, the clinical project managers met to discuss ways to improve the report review process carried out within the team.

The Clinical Trials Management Team continues to provide oversight of PPD Thailand and Quintiles Korea for monitoring functions that are carried out in Korea, China, and Southeast Asia. The team worked with NIH PIs and the Southeast Asia network to close several protocols still opened at the end of 2010. To date, one new study is planned for the Southeast Asia network; NIH PI staff added one new study in Korea this year and may add another by the end of CY2011. The increase in protocol-related activities and the closure of other protocols has impacted the clinical research organization's efforts for the contracts that are currently in place. The plan for FY2011 is for two new studies to be opened in Thailand and one to be opened in Vietnam at several sites. The Clinical Trials Management Team will continue to work with NIH staff and the PPD clinical research organization to ensure that new studies under the new Southeast Asia network contract are executed in a timely manner and within all applicable guidelines. In addition to the activities in Korea, CMRP contracted PPD, Inc., to serve as the clinical research organization and monitor activities for a study conducted at Henan Provincial Chest Hospital in Zhengzhou, China.

The team continued to review and provide extensive comments on several draft documents for RCHSPB, including monitoring guidelines, RCHSPP SOPs, draft outlines for TW trainings, the *Clinical Trials Management Policy and Procedures Manual* updates to version 4.0, and other Clinical Trials Management Team computer-based trainings. The clinical trials director assisted the RCHSPB clinical research oversight manager with revising several sections of the clinical trials management protocol template language per a request from the NIAID IRB and the new NIH policy on unanticipated problem reporting.

Several team members wrote and received approval from RCHSPB on guidance documents this fiscal year, such as the "Subject Study Status Definitions including Screening and Enrollment Terms," and the "Investigator Study Start Up Guidance." In addition, the Clinical Trials Management Team continued to maintain 11 approved SOPs specific to major processes for clinical site monitoring and internal procedures, and has revised six of the 11 active SOPs. A new SOP is also in development.

The clinical trials director participated in the review of several of the safety group's and training group's SOPs.

Additionally, a clinical project manager I attended and presented at a vendor training conference. The presentation was titled "Site Visit Follow-Up: Visit Reports, Notes to File, and Corrective and Preventive Action Plans."

The Clinical Trials Management Team performed a comprehensive review and developed monitoring plans in support of the H1N1 Network and Mexico Network initiative. In addition, the clinical trials director continued

to perform a comprehensive review by providing comments on site visit reports in support of the Phidisa South Africa initiative and continued to attend regulatory working group calls and conferences for the Phidisa project. The Clinical Trials Management Team designees continued to perform comprehensive revisions of Southeast Asia monitoring reports produced by the clinical research organization that monitors the SEA001 and SEA034 protocols.

The team created and updated lessons learned and items observed from monitoring visits for the IRC/H1N1, DoD, and Johns Hopkins University studies, and the Southeast Asia Network.

The team also developed and provided approximately six study case report forms to PIs for data collection for various studies, and reviewed approximately 30 initial clinical research protocols/informed consent forms, 60 amendment reviews, and 12 site-specific informed consent forms.

The decrease in case report form development was related to the improvement of other data collection tools, which have been implemented for new studies during the reporting period. Some of the international study PIs started to use a system called DataFax® as well as electronic case report form data systems. The Clinical Trials Management Team will be trained on creating case report forms that are adoptable to this new data system. The clinical trials director updated the RCHSPP Protocol Review and Amendment Review reference tool and supported the review efforts by making significant revisions to the Clinical Trials Management Team's policy and procedure manual for clinical research associate/clinical trials management reference. The clinical trials director also participated in bi-weekly calls to review/discuss the timelines associated with the protocols under the protocol navigation process that were implemented in FY2011.

This year, the clinical project manager I helped to implement three new studies in the CRIMSON data collection system outside of NIH; studies are currently conducted at Johns Hopkins University, the University of Vermont, and Rocky Mountain Laboratories.

One of the new challenges that the Clinical Trials Management Team is facing is helping to manage the data in CRIMSON for studies that were conducted at Johns Hopkins University that have since closed. Since the implementation of CRIMSON system at the Johns Hopkins University site, this is the first time the Clinical Trials Management Team is experiencing closing these types of studies. A working group has been established to include several members of the Clinical Trials Management Team, CRIMSON staff, and Johns Hopkins University staff, as well as the Clinical Trials Management clinical research oversight manager. The working group plans to map a process for all Johns Hopkins University CRIMSON studies.

Designees from the Clinical Trials Management Team are also working with the CRIMSON staff and Clinical Trials Management clinical research oversight manager to develop CRIMSON to allow for electronic monitoring. Recently, the Clinical Trials Management Team created a monitoring visit procedure document for the CRIMSON staff to review. The document detailed each step of the Clinical Trials Management Team monitoring process, including preparing, conducting, and following up on monitoring visits. It details how the monitoring visits are currently managed and how they could be managed if electronic monitoring is added as a function of CRIMSON.

A clinical research associate, who was hired to monitor in Mali, also performed approximately two GCP training sessions at the request of the site PIs in Mali, Africa.

The clinical trials director and several Clinical Trials Management Team designees continue to participate in a steering committee and working group to enhance the SOP on FDA inspection readiness and assisted with the staff training tools for compliance with this SOP.

During the contract year, the team worked internally to revise the customer-specific site initiation visit templates for studies. The templates continue to help the team facilitate timely and focused presentations for study protocols for PIs from IND, non-IND, and pediatrics-only studies. The team also updated the Johns Hopkins University/DoD/VRC templates for other non-IND studies that may be initiated domestically and internationally. The clinical project manager I updated the monitoring visit, site initiation visit, and study close-out visit reports to include entry fields for project codes to allow for easy reference. A working group assisted by developing the instructions for completing the study close-out visits and site initiation visit reports. Team members were also trained on each of these tools this year.

The Clinical Trials Management Team continues to enhance the field training program for newly hired clinical research associates. A clinical research associate II also worked on a case report form training tool that allows new clinical research associates to review a set of fictitious source documents and compare them to the data on a case report form as a training tool. In addition, the clinical research associates worked with management to help ensure that monitoring plans are written and sent to PIs shortly after the activation of their studies. This has allowed PIs and the Clinical Trials Management Team to make better assessments of resources and schedule timely monitoring visits.

The team updated several clinical trials management template forms for further enhancement/function, made suggestions to Johns Hopkins University staff on revising some of their template forms, and participated in several face-to-face meetings with IDCRP key staff and NIH coordinators to streamline clinical trials processes. Staff members assisted with providing training topics for the two-day in-house quarterly regulatory updates training session, to be presented by an outside vendor to NIAID staff, and planned for the fall 2011 at NIH.

The team updated and distributed a work distribution flow chart to the Clinical Trials Management Team for reference so all members will know who primarily works on each group's projects, including VRC, NIH, Johns Hopkins University, DoD/IDCRP, and international projects. This has allowed the clinical research associates to reach out within the team for more assistance when needed. The DoD/IDCRP work flow chart was also updated and distributed to IDCRP to use as a reference.

The clinical trials director and the clinical project manager I worked together to create a monitoring plan tracker data file in the TW system and edited the monitoring plan templates for clinical research associates to use for many of the IND and DoD/IDCRP studies. The clinical project manager I worked with the team and the TW support designee to streamline clinical trials management process entry screens and helped to create and test reports that are generated out of TW. This effort also helps to update, on a quarterly basis, the Program Management Team, the DCR clinical director, the RCHSPB clinical research oversight manager, and the branch chief on many items, including any significant protocol violations that occur. These efforts have successfully streamlined the project updates for the Regulatory Affairs Group and Clinical Trials Management Team and have been essential in developing other reports for clinical trials management. The Clinical Trials Management Team requested and implemented several new reports that are distributed to the Clinical Trials Management clinical research oversight manager at regular intervals. These reports include some of the activities the team performs for NIH PIs, and summary tables for easy tracking and trending of data.

The clinical trials director and the clinical project manager II continue to work with the RCHSPB clinical research oversight manager to identify ways for PIs to inform the group about upcoming projects in a timely manner. This information helps the clinical trials director assess new projects in the pipeline and ensure proper resources are in place within the RCHSPP Clinical Trials Management Team.

The Clinical Trials Management Team continues to collaborate with the medical monitors, clinical project managers, and regulatory director to improve the protocol/consent form initial review process, as well as the PI review process and checklist. To meet an RCHSPP strategic plan goal, a medical writer and a Clinical Trials Management mini-group continue to meet quarterly to review the timelines, completed protocols reviews, and IRB stipulations.

The Clinical Trials Management staff consists of one clinical trials director, three clinical project managers, 12 clinical research associates, and a program coordinator. A clinical research associate located in Benin, Africa, is also part of the team and is seamlessly involved with monitoring studies in Mali and Kericho, Africa. In addition, a clinical research associate was hired this year to help continue the support of RCHSPB, NIAID, and NIH activities. Due to the continually increasing number of clinical studies supported by CMRP staff, recruiting is active for one additional Clinical Trials Management Team position.

Members of the Clinical Trials Management Team participate in calls involving the H1N1 Network and the Australia Network. The monthly H1N1 calls involve the clinical research organization for Southeast Asia and RCHSPB members for updates on the networks. Members also participate in quarterly program-related calls with RCHSPB and IDCRP staff. In addition, Clinical Trials Management Team members participate in disease-specific calls for the IDCRP group (HIV/general infectious diseases/Acute Respiratory Infections Consortium), as well as case report form development calls that involve the IDCRP data management team.

Projects that Clinical Trials Management Team members have continued to initiate or collaborate on include assisting with strategic planning activities and IRB stipulation monthly protocol enhancement meetings; finalizing and assisting in the development and beta testing of computer-based training, covering TW database fundamentals and proficiency; participating in the protocol development project; implementing CRIMSON at clinical sites outside of NIH; and writing approval documents related to CRIMSON.

Clinical Safety Office (CSO)

CSO provides primary professional support to the (RCHSPB/ RCHSP Program) in three distinct functional areas: (1) CSO support for RCHSPB; (2) data and safety oversight committee support; (3) and medical writing support. Additional support functions include pharmacologic, scientific, and clinical support to other RCHSPP groups and to the RCHSPB, as well as serving as primary protocol medical monitor on specific protocols.

CSO also provides surveillance, monitoring, and regulatory reporting of SAEs occurring on NIAID intramural clinical trials, including all trials where RCHSPB is the IND sponsor. CSO ensures compliance with the *Code of Federal Regulations*, NIH policies, ICH/GCP guidelines for protocols, informed consent documents, and case report forms. During the contract year, 31 SAEs were processed and completed with continuing correspondence with the reporting investigators. AE tables were reviewed for SAE reconciliation and standard (MedDRA) AE terminology in preparation for IND annual reports to FDA.

The medical monitors and clinical safety associates reviewed 126 clinical research protocols over the contract year, consisting of 41 PI reviews, 70 amendment reviews, 15 site-specific informed consent form reviews, along with the associated informed consent documents. Comments and edits were suggested to the PI regarding safety and regulatory compliance prior to submission to the NIAID IRB. For the initial pre-IRB reviews, medical monitors performed a final review of the entire protocol for subject safety concerns, data integrity, and clinical trial design. As part of the review process, the reviewer

often participated in numerous conference calls with investigators to discuss and resolve regulatory or safety concerns with the protocol, which may have forestalled approval by the NIAID IRB or FDA. Nearly universally, PIs have commended these reviews as being useful in addressing concerns prior to IRB submission.

CSO staff participated in the PN/PDP, providing medical monitoring and clinical safety support to assist in the development of 16 protocols. This task included weekly meetings and close cooperation between the medical monitor and protocol navigators.

CSO provides administrative and logistical support to the NIAID intramural DSMB. A clinical safety associate serves as the DSMB executive secretary, and is responsible for arranging all teleconferences and face-to-face meetings, distributing review materials to the DSMB, recording and moderating the review sessions, preparing the DSMB summaries for the reviews, communicating with the members of DSMB, and maintaining records associated with DSMB membership. In the past contract year, the DSMB executive secretary arranged and facilitated 20 teleconferences involving 13 PIs for 18 protocols. The DSMB executive secretary also arranged and facilitated two face-to-face meetings where 17 protocols were presented by 13 PIs. Following each meeting, the DMSB executive secretary prepared summaries of the reviewed protocol discussions and recommendations and distributed them to the PIs and DSMB members. A total of eight new data table templates were developed to improve the efficiency and accuracy of the data submitted to the DSMB for review.

The standard AE data tables that were developed by CSO last year were programmed into CRIMSON and were used by the DSMB in the past two face-to-face meetings. The initial use of the tables revealed several data consistency and logistical issues that are being addressed. The implementation of these tables has enhanced the ability of reviewers (PIs, oversight committees, medical monitors) to analyze AE data that is entered into CRIMSON. These tables are also being programmed or created in other databases (i.e., Frontier Science for the IRC protocols). Since NIH has limited experience using CRIMSON to generate comprehensive data tables for analysis of AEs, this initiative has been groundbreaking.

CSO was responsible for oversight, support, and facilitation of five protocol-specific SMCs and 28 Independent Medical Monitor (IMM) teleconferences during the past contract year. The SMC executive secretary is responsible for arranging all teleconferences, distributing review materials to the SMC members, moderating the review sessions, preparing the SMC minutes for the reviews, and maintaining records associated with SMC membership.

CSO also collaborates with the Regulatory Affairs Group and the Clinical Trials Management Team, providing guidance, instruction, and expertise to the staff. CSO reviewed Monitoring Visit Reports and collaborated with the clinical research associates to resolve any safety discrepancies found during these reviews.

In FY2011, the CSO medical writer provided grammatical, formatting, and content review for 18 PI review protocols, and associated informed consent documents. The medical writer drafts original documents, edits, and reviews documents generated by or received from CMRP sources. Also, as a whole, CSO developed documents for both internal and external use.

Consistent with the RCHSPP operational plan for 2010–2012 to improve the review of protocols, the medical writer has presented a monthly review of the IRB stipulations from 13 individual protocols to representatives of the RCHSPP functional groups (CSO, Regulatory Affairs, and Clinical Trials Management). Summary tables of lessons learned and IRB suggested language have been created. A database of 1,600 IRB stipulations for all initial protocol reviews (56 protocols) during 2010–2011 was created and is updated monthly. A line listing of stipulations exclusively related to safety has been identified and compiled from the database. A subset of safety stipulations for select topics (e.g., withdrawal, halting, pausing, and stopping) has also been prepared and distributed for the purpose of refining safety template language. Work has started with the Clinical Trials Management Team to provide a similar database of monitoring stipulations and line listings on select topics. A draft poster and slide presentation to summarize the significant trends in IRB stipulations for all functional groups has been prepared.

Consistent with the pharmacovigilance initiative, CSO is working on improved methods of internal review of AE/SAE data from specific protocols (i.e., IRC 002). This work has uncovered important AE data recording/ reporting/database issues that are being addressed to enhance the quality of AE data. The availability of comprehensive, accurate, and appropriately labeled AE tables has expanded the role of CSO beyond that of processing and reconciling SAEs. As these AE tables become available for other protocols, CSO will become the core component of the pharmacovigilance process.

CSO has developed a standard SAE narrative template to be used for all SAEs. This will allow reviewers (e.g., oversight committees) to review SAEs in a concise and standard clinical summary format as opposed to raw data contained in a lengthy "SAE Report Form" and multiple pages from various source documents.

CSO has developed a comprehensive template for the "Assessment of Safety" section of IND protocols, which included changes required by new IND Regulations and the need to identify and report "Unanticipated Problems."

CSO has revised the "SAE Report Form," which is now the "SAE/Unanticipated Problems Report Form," to accommodate the need to report "Unanticipated Problems."

CSO participates in training and develops educational and procedural programs for both internal and external groups. Over the course of the contract year, 40 New Employee Orientation presentations were given by four

members of the team; both CSO and the medical writer provide presentations.

In support of RCHSPB, CSO staff members have participated in NIAID/NIH programs, projects, and committees that expand the scope and visibility of their respective positions beyond the confines of their usual positions. CSO physicians, at the request of PIs, have served on protocol teams as IND sponsor medical monitors on eight clinical trials.

CSO staff members have collaborated with other RCHSPP staff to implement the 2010–2012 RCHSPP Operational Plan. CSO staff members play active or leadership roles in the Products and Services, Protocol Enhancement, and Resources Working Groups. A CSO staff member has assisted in creating, writing, and presenting TW Integrated Training Applications.

CSO staff consists of one CSO director/medical monitor, one medical monitor, one medical affairs scientist, one medical writer, one clinical safety associate/SMC executive secretary, one clinical safety associate/DSMB executive secretary, and one secretary III.

The CSO team continues to expand their technical and professional skill competencies. During FY2011, an NIH Clinical Center Certificate in Principals of Clinical Pharmacology was obtained by a member of CSO.

Awards and distinctions presented to the CSO director/medical monitor during FY2011 include a 2010 NIAID Merit Award for support to the H1N1 Plasma Treatment protocol and a 2010 NCI Merit Award for serving on the cancer.gov editorial board.

RCHSPP Protocol Navigation/Protocol Development Program (PN/PDP)

The Protocol Navigation/Protocol Development Program (PN/PDP) comprises protocol navigators and medical writers, as well as CMRP staff who are involved with aspects critical to protocol implementation. This is a high-priority initiative for NIAID, who requested support from CMRP. There are two aspects of this program. The Protocol Navigation (PN) aspect facilitates the research logistics of studies being conducted at the NIH Clinical Center, collaborative clinical sites, and international investigative sites while the Protocol Development Program (PDP) aspect is critical to study start-up activities.

Since September 2010, two additional protocol navigators and one additional medical writer were hired to support the increasing number of projects using PN/PDP. Current staff includes a senior protocol navigator (program manager), two protocol navigators and three medical writers.

During the reporting period, the PN/PDP team was involved with the development 16 initial protocols. Of these, five projects involved first-time PIs and five were with repeat customers. The program facilitated five international protocols. Protocols for these studies have varied in phase, type, and sponsorship, and have also spanned several intramural labs, including, the Laboratory of Clinical Infectious Diseases, Laboratory of Immunoregulation, Laboratory of Parasitic Diseases, Laboratory of Allergic Diseases, Laboratory of Immunogenetics, and Laboratory of Infectious Diseases. Recently, the Laboratory of Molecular Immunology, a lab that has not been involved in clinical research previously, requested PN/PDP assistance on two clinical research protocols. CMRP support staff has also assisted in amendments and consent re-writes for six other protocols that have been approved through IRB.

The PN/PDP team has consulted with other offices to improve logistics handling; specifically, staff met with a NHGRI representative to review the genetics issues involved in protocol and consent development. The team will meet with Office of Protocol Services, the Office of Technology Development, and the point person for the genome-wide association studies' process to discuss ways in which navigation can improve research processes within NIAID.

Meetings are held, as needed, with the NIAID clinical director, the RCHSPB branch chief, and various oversight managers (from the safety, regulatory, monitoring, and IRB offices) to keep each party apprised of the workload and upcoming projects, to troubleshoot issues, and to promote the future growth of this program. A bi-weekly status call is held between RCHSPB and RCHSPP staff (who are involved in protocol development) so all members are aware of timelines, areas of concern, and action items. This call is also used to assist the teams with planning and evaluating the future workload the protocol would place on these groups. Less frequent meetings were instituted because the program is staffed and has operations in control which are under its purview.

NIAID's PN/PDP serves as a pilot for the other institutions that continue to investigate the implementation of similar navigation programs. During the reporting period, the senior protocol navigator was asked to consult on program issues related to protocol navigation training. This person has also been involved in a collaborative effort across institutions and at the request of and in conjunction with Office of Protocol Services and the Office of Human Subjects Research Program office, is drafting a revised protocol application for across-the-board-use by all institutions to meet the requirements of the Association for the Accreditation of Human Research Protection Programs (the credentialing body NIH is seeking to apply for in the upcoming months). At the request of OHSPR, this effort includes editing SOPs to provide insight into protocol logistics and current administrative and regulatory requirements.

A reference manual of resources and guidance that may be referred to by the PN/PDP team was created. This document is available in hard copy and electronic format and serves as an orientation manual for new staff. A protocol development writing guide was also developed and is being used as a reference tool for medical writers and protocol navigators regarding specific writing guidance. This guide is updated when new or improved language is provided by various entities. Informed

consent templates were developed and are used as a guide for the medical writers when drafting a consent document. The informed consent templates outline essential elements and provide pointers for the type of information that may be required in each section as well as available template language. An internal QC checklist for protocol review of navigation projects was developed to outline the information a second reviewer is responsible for when reviewing the primary author's document. Since September 2010, the team attended five webinars to keep abreast of relevant topics such as communication in multidisciplinary teams, trends in research, FDA perspective on avoiding common mistakes in research, project management, and regulatory science. In addition, the team attended video casts related to HIV/AIDS and hepatitis to enhance their knowledge of the infectious diseases.

The program continues to collect metric data, which includes tracking milestones dates and categorizing stipulations from IRB reviews to identify areas needing quality improvement. Program staff reviewed IRB stipulations, both from navigation and non-navigation protocols, and developed a frequently encountered issues document for all team members to reference. This document is available on a shared drive; it provides a history of issues and is also beneficial for new staff. Specific information per logistical entity (i.e. radiation safety, ethics) is maintained in the shared drive for convenient reference and to decrease any duplication of efforts should a similar situation arise in the future.

By tracking milestones such as cycle time data, the navigation program appears most beneficial in keeping the investigator engaged and facilitating the time between scientific review to IRB submission. The process flow map created in the previous year was modified to shorten the review timeframe by taking advantage of employee "down-time" and to minimize the redundancy in comments and the assessment of issues, which have previously been discussed and resolved.

Spreading the word on this very exciting initiative is a top priority. During the contract year, the PN/PDP team presented a poster entitled "The Evaluation Methodology for the NIAID Protocol Development Program" at the NIH Research Festival in Bethesda, MD, and the Association of Clinical Research Professionals Annual Global Conference in Seattle, WA. The team also presented an overview of services at the RCHSPB/RCHSPP retreat, NIAID QA meeting, and IRB Quarterly Meeting for study coordinators. The protocol navigation manager worked with IT to announce the program and provide contact information for the NIAID IRB and RCHSPB offices. In conjunction with the RCHSPB branch chief and IRB oversight manager, the protocol navigation manager presented at the NIAID Evaluation Forum in July 2011.

A feedback tool to gauge customer satisfaction was developed and has been distributed to investigators. The highest rating was received for overall satisfaction with the protocol development process, which included the highest ratings for using the PN/PDP to improve the IRB submission; overall assistance provided by the PN/PDP staff during the entire process; communication provided by the PN/PDP staff; issue resolution during protocol development; and availability of PN/PDP staff.

Project Management Team

RCHSPP's PMT provides program management, operational management, and logistical support to enhance the capacity of RCHSPB in conducting its mission and maintaining the infrastructure needed for CMRP to fulfill contractual requirements. PMT works in collaboration with all program support team members and functional groups to strategically link their operational and project activities with the tactical goals and objectives required to achieve overall success within RCHSPB/P. PMT's Project Management (PM) team provides expertise and logistical support for developing and implementing RCHSPP's strategic plan in support of its mission, goals, and objectives.

PMT Accomplishments

Within the project management function, a list of significant accomplishments and key milestones were achieved during FY2011. PMT established an Integrated Strategic Project Management Framework (ISPMF) and collaborated with functional group leaders to identify, assign, and align current projects with available human resources, using historical data to develop resource utilization reports to periodically plan and identify resource allocations needed to support approved projects. PMT presented ISPMF to the NIAID clinical director and RCHSPB/OPOS senior management.

Through preliminary reports, which were based on historical data, the team was able to demonstrate how the program management capability, which combines standard project management methodology and protocol lifecycle methodology, can be used to streamline research support processes and align budget and labor resources across all functional groups and protocol projects involving both domestic and international clinical research sites. The preliminary reports demonstrated the alignment of budget and labor resources with protocol development and regulatory projects, which has enabled program management staff to enhance existing clinical research support processes by monitoring, tracking, and reporting progress; optimizing and aligning resources across functional groups for each lab and/or site involved in the clinical research; and establishing forecast criteria for projecting budget and labor resource requirements for each fiscal year.

During the ISPMF implementation stage, four regulatory service offering models, which included natural history, screening, training and intervention, were developed, and a list of resource utilization reporting templates (along with standard reports) was established. These reports will be generated on a bi-annual and annual basis as requested by the branch.

Working in collaboration with the functional group leaders and senior managers, PMT also developed an operational plan for implementing RCHSPP's strategic plan. The operational plan is currently in effect and is being used to track and monitor progress on the defined strategic goals and objectives. PMT is facilitating implementation and providing support with the use of additional tools and templates used for monitoring, tracking, and reporting progress on major strategic goals, objectives and associated key performance indicators.

PMT submitted two poster presentations and two conference presentations for sharing outcomes of the project management implementation within RCHSPP/RSCHPB. The posters for the September 2011 Society of Clinical Research Associates (SoCRA) Conference and the October 2011 NIH Fall Research Festival have already been accepted for presentations.

In addition, the 2010 NIAID Merit Award was presented to PMT in recognition of how regulatory support models were used to predict resource requirements.

Current PMT Activities

The team continues to collaborate with RCHSPP senior management and functional group leaders to leverage their knowledge and expertise in project management and to heighten program management success by implementing flexible, customizable, repeatable, and extendable service offering models to fit RCHPSB's strategic/project needs. These models have been accepted by the RCHSPB. PMT is working with functional groups to implement the models through a pilot list of nine selected clinical protocols. While using ISPMF to pilot test these, PMT has been able to identify areas where additional resource and process alignment (along with proper data entry, lab coding, and report interfacing between TW and time card management systems) must be integrated and completed. It is imperative that these steps are configured and streamlined to adequately retrieve, analyze, review, monitor, track, and report progress on key performance indicators at each major milestone during the protocol lifecycle stage.

During the pilot testing phase, PMT identified several areas for improvement and proactively worked with RCHSPB/P on streamlining the process to address some of the data entry errors, to reconcile inconsistencies, and to add/refine/realign tracking lab codes with the budget flow for each protocol that RCHSPP supports.

This pilot program will enable project leaders to plan, execute, monitor, track, control, and report progress on protocol projects in a timely manner. This will also allow RCHSPB/P to establish baseline program plans and gather meaningful project data for senior management to use to make informed decisions that address the growing program management requirements related to budget and labor resources and promptly respond to RCHSPB inquiries.

Furthermore, PMT is developing two new posters. Staff members expect to present the first poster at the SoCRA conference in September 2011 and the second poster at NIH Fall Research Festival in October 2011.

Institutional Review Board (IRB) Support

RCHSPP provides administrative support to NIAID's IRB. In this role, RCHSPP works in collaboration with RCHSPB to process documents for IRB submission. Support efforts include processing protocol actions for IRB meeting reviews via iRIS; generating the agenda and minutes templates; preparing meeting packages; tracking protocol submissions from initial submission through the approval phase; preparing tracking reports, as needed; and maintaining protocol-specific records.

During the contract year, RCHSPP provided administrative support for the following ongoing IRB-related activities: processing incoming submissions and submission approvals, including reviewing submission components, identifying deficiencies, and providing administrative stipulations and guidance to investigators to assist them in successfully completing their submissions; processing final approvals incoming from the Office of Protocol Services (including logging and filing); updating the Action Tracker, a manual log of protocol renewals; responding to inquiries and providing advice to investigators and study staff; participating in regular staff meetings; contributing to procedure discussions regarding new/changing NIH policies that affect NIAID IRB; writing meeting agendas and minutes shells; and writing SAE Reports to the clinical director and the acting director of the Office of Human Subjects Research. All deadlines for submissions, inquiries, and reports were met for the contract year.

In addition, RCHSPP provided support to special projects, including the utilization of iRIS (iMedRIS) web-based IRB submission software (where submissions from the NIAID labs are received and processed) by serving on the iRIS development work group, which collaborates with iRIS developers to identify and troubleshoot methods for optimal use; and writing and presenting quarterly trainings to keep study coordinators informed on IRB activities and changes to NIH policies. In addition, efforts have been focused on developing quality management standards by identifying process improvement opportunities. During the contact year, RCHSPP initiated the review and update of the IRB office SOPs. Seven SOPs/tools were updated/developed to increase the efficiency with which submissions are processed, to enhance communication, and to develop transparency among the IRB office team.

RCHSPP Training Group

Support for RCHSPP is provided by a clinical training manager, a training specialist/instructional designer, a training specialist, and an administrative support staff member. The activities supporting RCHSPP are listed below.

Identify/Develop Training Resources to Address Client-Identified Training Needs

During CY2011, the instructional designer identified and developed training resources in support of RCHSPP, including the following trainings: Travel Guidance, TrackWise® (TW) Training Protocol Review for Managers and Reviewers (TW8 revision), What's New in TW8, TW Training All Users Module (TW8 revision), TW Training Regulatory IND/MF Record for Managers Module, TW Training Regulatory IND/MF Record for Regulatory Associates Module, TW Training Regulatory Serial Submission Record Module, TW Training Clinical Trials Management Site Record Module (TW8 revision), TW Training Clinical Trials Management Site Visit Record (TW8 revision), and Clinical Trials Management Monitoring Visits.

The instructional designer also provided instructional design assistance in the development of several training presentations, including TW Integrated Team Applications, Regulatory Inspection Readiness Interviewing Techniques, Adverse Event Reporting in Drug Development 101, SmartStream, and Investigator Brochure Review Record.

Provide Training and Professional Development Subject Matter Expertise

CTG provided support to RCHSPP Operational Plan teams, including Products and Services and Core Competencies.

CTG participated in the TW Working Group and worked with the IT Group to develop a TW Training Manager.

Provide Administrative Support for Activities with Training Implications

CTG facilitated 20 audio conferences on technical topics, including obtaining approval for the session, as well as implementation, evaluation, and documentation for each participant. The titles of these audio conferences include: Device and Drug Clinical Development; FDA Clinical Trial Holds; Informed Consent, More than Just a Signature; Introduction to MedRA; Pharmacovigilance, Medical Affairs, and Risk Management; Safety Reporting: the Final Rule on INDs; Biosimilars, Biobetters, Biogenerics: A Closer Look; Clinical Research: An FDA Perspective; Learning to Communicate Effectively in Multidisciplinary Teams; Drug Master File in eCTD Format; FDA Discusses Latest eCTD Updates; GCP: Practical Application and Implementation; Good Clinical Practice: The Sponsor, Monitor, Investigator; Use of Notes to File; Clinical Trials Forecasting for Finance Professionals; and The Trial Master File: Mastering Regulatory Standards.

CTG provided administrative support to the TW® Working Group, including scheduling the meetings and providing meeting minutes.

Ensure Compliance and Continuous Improvement of Training Processes and Initiatives

CTG wrote and is currently circulating four SOPs and 23 forms outlining the training process to ensure consistency throughout RCHSPP. These SOPs include: "Identification of Training Requirements"; "Development and Maintenance of Training Materials"; Facilitation, Documentation, and Evaluation of Training Events"; and "Configuration, Maintenance, and Management of Training Records."

CTG continued to provide guidance on FDA inspection readiness and participated in the development and implementation of "Regulatory Inspection Interview Strategies." In order to ensure compliance of the RCHSPP functional groups with all mandatory SOPs, CTG reviews training completion data on each new SOP as it is issued with consideration of technical revisions to existing SOPs. CTG is also working with the IT Group to implement TW Training Manager, a program that will enhance CMRP training compliance efforts and will also allow each employee to monitor their own training record.

CTG continued to maintain a spreadsheet identifying FDA Warning Letters citing GCP issues. This data was the basis of a presentation at the Cambridge Healthcare Institute's Clinical Auditing Forum in Boston in June 2011.

Conduct Professional Development to Ensure that Staff Members Maintain Their Subject Matter Expertise

CTG facilitated a two-day training seminar on special topics in clinical research management for NIAID study coordinators. This initiative highlighted critical areas of scrutiny by FDA, including revisions to 21CFR312 and NIAID-specific discussions of critical compliance topics from a sponsor's perspective. CTG also worked closely with the OPOS training clinical research oversight manager on the DSMB training CBT, which will provide a unique online resource to NIH and non-NIH DSMBs.

RCHSPP Document Control (DC)

CMRP's RCHSPP DC group is at the core of RCHSPP's quality system. The DC group maintains and archives critical documents, including RCHSPP-controlled documents and clinical research's trial master files. DC offers many services to assist with the document control needs of the various RCHSPP groups. These services include: (1) the protocol review process; (2) paper and electronic file storage and maintenance of various documents; (3) creation of CDs, various databases, and logs; (4) document scanning and archiving; and (5) training on the DC system and the various electronic documents maintained in the system.

Currently, DC is involved with the management of files in support of approximately 150 active protocols, 83 active IND/IDE/MF, 1,300 SAEs, and various other regulatory documents RCHSPP is required to maintain. DC is also responsible for assigning project codes and has assigned over 30 new project codes this year. To date, DC has processed approximately 100 protocol reviews (this includes amendments, site-specific informed consents, letters of amendment and navigational reviews).

The team has been working on developing the protocol review process to utilize TW and Livelink®.

During the last year, the first phase of this process, which included developing a folder structure and a means to utilize Livelink® and TW together, was completed. Each functional area designated two representatives, who have been subsequently trained. The appropriate folder structure has been developed for Livelink® and phase two has been initiated. This process includes developing standard naming conventions for the folders and standard minimal metadata requirements, using hyperlinks to link the Livelink® location to the TW record, creating user manuals for each stakeholder, and testing the system. The use of Livelink® will provide an audit trail and a more consistent way to access protocol reviews. This will provide a tight control for the electronic documents.

Another project DC participated in was the migration to eCTD submission format. DC, in conjunction with the Regulatory Affairs Group, has started to process eCTD submissions for archival. DC worked closely with the Regulatory Affairs Group to develop an archiving process that would meet the needs of both groups as well as the requirements of the *Code of Federal Regulations*. To date, DC has processed six eCTD submissions and drafted a direction sheet on how to process this new document type.

This year, the majority of Southeast Asia protocols were closed and archived. In March 2011, DC assisted with boxing and archiving these protocols. During the reporting period, 37 boxes (equal to approximately 82 cubic feet of documents) were moved to Iron Mountain.

As well as performing daily duties, the DC group participates in numerous committees to support the needs of RCHSPP.

RCHSPP Information Technology (IT)

The RCHSPP IT Group provides software development, computer, network, application, and backup/disaster recovery support services for NIAID initiatives. Staff members include an IT manager, secretary, three program analysts, a systems administrator, and a network specialist. In the past year, the IT group was involved in several key technical initiatives for the program.

The IT group provided technical guidance and direction for acquiring and deploying an eCTD authoring and publishing software package for submitting regulatory documents to FDA by the RCHSPP Regulatory Affairs Group via the FDA's electronic submission gateway. The IT group, along with project stakeholders from the Regulatory Affairs Group and the Office of Cyber Infrastructure and Computational Biology, evaluated several commercial off-the-shelf products for suitability and best fit for program operations; the OmniSUITE™ product line from Omnicia, Inc., was chosen as the preferred product. Following the vendor selection process, the IT group served as the technical liaison for the Regulatory Affairs Group and was used to evaluate system specifications, ensure that software interoperability existed with United States Government Configuration Baseline group policies, and determining the appropriate implementation path. Dedicated eCTD publishing kiosks were successfully configured and deployed, as were template management tools to workstations used by each regulatory staff member. To transmit the rendered and complied eCTD submission to the FDA, the IT group worked closely with the Regulatory Affairs Group to establish a certificate authority that would provide third-party authentication services to FDA that the identity of all eCTD packages and content submitted by RCHSPP via the FDA's electronic submission gateway were original, verifiable, and unchanged.

To ensure compliance with smart card authentication requirements and standards set forth by the HSPD-12 Act of 2004 and associated Federal Information Security Management Act regulations, Office of Management and Budget memoranda, and NIH policy, smart card equipment and middleware were installed and configured for each RCHSPP workstation.

The IT group also completed soliciting, reviewing SOW for professional services configuration management of the TW Training Manager component by Sparta Systems, Inc®, and allocating internal and external program-related resources for initial prototype construction. Within the scope of this project, an upgrade to the latest service release of the current application build occurred, resulting in additional enhanced functionality, including visual workflows and usability improvements, being available to the user community. Program requirements for the application from the RCHSPP CTG were assessed and existing processes used by the group to manage training sessions, both curricular and non-curricular, were evaluated and selected as the basis for the generation of TW Training Manager projects, field types, and workflows. A functional prototype was developed and is being refined to incorporate additional elements and notification functionality.

The integration of Livelink® and TW to manage content for clinical protocols undergoing an initial or amendment review by the RCHSPP has entered the pilot phase. A re-structuring of the project plan occurred midstream because it was determined that the application programming interface packaged with the TW system contained limitations that would prevent a successful production release. The move required many changes, such as creating new TW field types and transferring document workflow and permissions engine responsibilities to the Livelink® document repository rather than the TW state machine. All efforts have been successful to date. The project team was expanded to include RCHSPP staff involved in the review process. Stakeholders from the Livelink® team have generated end-user documentation and guides that are currently in technical review and will be available to the user community for the final production release.

In collaboration with PN/PDP representatives, the IT group was able to complete the conceptual design phase of a new TW project—protocol navigation. In this phase, the IT group assessed the functional requirements of the project, drafted a workflow with key milestones in the

lifecycle of a navigational protocol, and completed a developmental model for feasibility analysis. The next phase of the build is pending prioritization of additional TW objectives.

The initial phase of the expansion of the wide-area network telecommunications infrastructure from a copper-based DS-3 to a fiber-optic solution has been completed. Fiber-optic cabling, traversing over a 10 km path from Industry Lane to Fort Detrick, was finished in May of 2011, and the next phase of patching in the demarcation points to the NIAID network via NIAID's Integrated Research Facility is in progress. A cutover of the primary data backbone responsibility from the DS-3 to the fiber-optic/dark-fiber run will follow, with the topology providing redundancy and fault tolerance as two, high-speed independent paths will be available.

Ongoing core IT functions provided to the program and program staff span a broad spectrum of technologies and service offerings, including: (1) application of whole-disk encryption to all new laptop computers, encryption key recovery services, and conduction of routine audits to ensure continued compliance with the Office of Management and Budget/HHS directive for protection of sensitive information; (2) evaluation, specification, acquisition, integration, and management of computer hardware/software; (3) system administration, technical support, and backup/disaster recovery services for program staff in both domestic and international settings; (4) standardization of government-furnished Microsoft Windows® personal computers in compliance with the United States Government Configuration Baseline mandate via technical analysis and review of federal policies/procedures, establishment of project plans, analysis of software impact, dissemination of communications to program staff, categorization of resources into applicable security containers, development and submission of waivers, and generation and allocation of secondary administrative accounts; (5) installation and monitoring of McAfee ePolicy Orchestrator® for the management of site antivirus and related security software and BigFix™ for hardware inventory and software patch management; (6) collection, evaluation, design, and implementation of change requests for TW, the quality and process tracking system for the program; (7) development, unit testing, and maintenance of custom Crystal® reports for correlative analysis, qualitative and quantitative process/data measurements, and end-of-month/quarter/year summaries from TW; (8) participation in RCHSPP strategic planning sessions, Section 508 compliance, TW, Livelink® Working Groups, and FDA inspection readiness teams; (9) evaluation, procurement, and deployment of encrypted USB key chains to staff in adherence with HHS policies; (10) development of IT training materials and presentation at New Employee Orientations; (11) providing management, maintenance, and support services to the core site network and data services infrastructure; (12) design, development, hosting, integration, and maintenance of a Microsoft® SharePoint Services platform; (13) serving as a member of and key contributor to several technology-related project teams, including the SAIC-Frederick, Inc., IT Steering Committee and Microsoft® Active Directory Working Group; and (14) providing video conferencing and video collaboration support services for both near and remote locations.

CMRP Support to the Rakai Project, NIAID

Beth Baseler, M.S., Director
Jennifer Imes, Program Manager
Irene Mueller, M.P.H., Clinical Project Manager I
Melissa Borucki, M.S., Senior Special Projects Administrator

The Rakai Health Sciences Program initiative is an ongoing project sponsored by the Laboratory of Immunoregulation's (LIR) DIR, to establish the provision of antiretroviral drugs in rural villages in the Rakai District, Uganda, Africa. Since 2004, CMRP has provided support to Rakai Health Sciences Program by providing timely assistance with subcontracting, purchasing, consolidating, and shipping instrumentation and supplies to assist in this effort. The Rakai Program is a NIAID International Center for Excellence in Research (ICER). ICER is a laboratory-oriented grant that funds many of the laboratory studies to be conducted on biospecimens. The primary purpose of ICER has been to build infrastructure in Rakai, Uganda, to conduct collaborative biomedical research with Ugandan scientists.

CMRP staff members have collaborated on a project specifically involving a subcontract with Rakai Health Sciences Program in support of NIAID. LIR, DIR, NIAID, Makerere University, Johns Hopkins University, Columbia University, and the Walter Reed Army Institutes of Research are studying, on a population-based level, the effect of U.S. President's Emergency Plan for AIDS Relief (PEPFAR)-provided antiretroviral drugs. This collaboration is in a unique position to assess multiple potential effects of PEPFAR-derived antiretroviral drugs because of the wealth of historical data of the cohort in Rakai, Uganda. For the past 10 years, the collaborative efforts in Rakai have collected linked interviews and biological specimens from 44 communities, representing approximately 12,000 individuals, 15 percent of whom are positive for HIV. Collaborative efforts from this cohort have produced more than 60 peer-reviewed manuscripts and influenced the public health practices involving HIV treatment and care in the developing world.

A BOA was established with the Rakai Health Sciences Program to support additional clinical research protocols. Task Order 1, the first protocol, "A Randomized, Double-Blind, Placebo-Controlled Trial of Acyclovir Prophylaxis versus Placebo among HIV-1/HSV-2 Co-infected Individuals in Uganda," studied the role of HSV-2 in facilitating both HIV-1 acquisition and transmission. Interventions that slow HIV-1 disease

progression among persons with $CD4^+$ counts above 250 cells/L could postpone the need for antiretroviral therapy and prolong life expectancy for HIV-infected persons. Due to the lack of human resource capacity, health care infrastructure, cost, and supply-chain management structures required for antiretroviral therapy delivery in resource-limited settings, strategies to retard the development of clinical AIDS and requirements for Highly Active Antiretroviral Treatment (HAART) are urgently needed. The above-mentioned protocol addressed this issue and was completed in January 2011.

In addition, a BOA was established with the Infectious Disease Institute (IDI) to support clinical research protocols. IDI is an Uganda-registered, non-governmental, independent teaching, research, and clinical organization owned by Makerere University, whose mission is to build capacity in Africa to deliver sustainable, high-quality care, and prevent HIV/AIDS and related infectious diseases through training and research. IDI trains health workers from Uganda and 26 other countries on HIV/AIDS, malaria, pharmacy, lab, and data management. The first protocol, titled "A Comparison of the Development of Thymidine Analogue Mutations (TAMS) with CD-4 Monitoring Alone versus CD-4 Monitoring Plus Viral Load Monitoring in Naïve HIV-1 Individuals on First Line ART in Africa," was a cross-sectional comparison of the rate of thymidine analogue mutations in treatment-naïve patients following 36 months of HAART, comparing 500 patients in the cohort with 1,000 additional clinic patients not enrolled in the cohort. The results of this study have had a positive impact on the clinical monitoring of HIV-infected patients and the choice of second-line antiretroviral therapy drug regimes.

Rakai Health Sciences Program and IDI are collaborating on a study titled "Hepatitis B and HIV Co-infection." The study examines liver disease and hepatoxicity in participants with HIV and hepatitis B. Data from Africa on the prevalence and clinical implications of HIV/hepatitis B co-infection are sparse or unavailable. Upon completion of this collaborative study, information for understanding the complex interaction of HIV and hepatitis B will be provided, as well as a plan for optimizing the benefits while mitigating the potential consequences of antiretroviral drug programs in Africa.

A new study was initiated in FY2011; a task order under the Rakai BOA was executed in FY2011 to conduct "Malaria Surveillance in Rakai," a one year study to determine the epidemiology of malaria infection in children and adolescents/adults by conducting surveillance in approximately 320 households selected from two of the 10 clusters under the Rakai Community Cohort Study. This study will enhance the investigators' understanding of the epidemiology of pediatric and adolescent/adult malaria infection in the Rakai district in preparation for future malaria vaccine trials. Investigators will be able to determine malaria rates and estimate the rates of uncomplicated and severe malaria in children and adolescents/adults.

The Rakai Project provides dedicated personnel, both on-site in Africa and off-site in Frederick, MD, to coordinate activities for the laboratories, manage administrative concerns, track and monitor dedicated budgets, assist with personnel logistics, provide project procurement support, and provide overall coordination of administrative program-level functions.

During the reporting period, a protocol coordinator, located in Johannesburg, South Africa, made regularly scheduled site visits to Uganda and assisted the Ugandan research teams in implementing and conducting QC procedures/processes required for research and clinical care and to ensure GCPs for existing and new protocols. The protocol coordinator assisted the research teams with data analysis and the preparation of manuscripts for peer-reviewed journal publications, and conducted the analysis for and contributed to the abstract for a presentation given by the PI at the 2011 Conference on Retroviruses and Opportunistic Infections.

The protocol coordinator also led a program-wide collaborative effort to upgrade clinical research data management operations by implementing the DataFax® system to create an independent team of data personnel. One of the first DataFax® studies managed by IDI in Uganda was commended by DSMB for the high quality of the trial, and specifically for the good quality of its data. This is an important demonstration that DataFax® users in partner institutions like IDI can be mentored to a high level of competence in this industry. These are positive steps for the recognition of IDI as an international center of excellence in the area of clinical research and data management.

A QA specialist, based at NIH in Bethesda, MD, made several visits to Rakai and provided QA/QC support for GLPs and assisted with implementing new laboratory tests and procedures, including HIV viral load testing, routine chemistry and hematology, expanding the current microbiology and molecular biology laboratories, and implementing the FreezerWorks® system for specimen inventories and tracking.

During the reporting period, support was also provided for logistical and administrative tasks related to daily international operations; budget preparation and monitoring; travel preparation for three nonemployees for training and collaboration visits; and procurement of miscellaneous laboratory items.

Support to the India/Mali International Centers for Excellence in Research (ICER), NIAID

Beth Baseler, M.S., Director
Jennifer Imes, Program Manager
Allison Eyler, Secretary III

The India/Mali ICER initiative is an ongoing project sponsored by NIAID to establish a research infrastructure that facilitates research relevant to the pathogenesis and control of lymphatic filariasis in both Indian and West

African populations. Because Africa and India disproportionately bear the burden of lymphatic filariasis, the study of these infections must be performed in these international locations. Since these countries have few resources, they require outside assistance to develop resources and strategies relevant to their local conditions. Since 2004, CMRP staff has assisted NIAID researchers with establishing research infrastructure and training investigators for both the Indian and Malian lymphatic filariasis research initiatives. NIAID has outlined three stages of this project: (1) NIAID will establish laboratory facilities, train personnel, and conduct several well-defined pilot projects; (2) NIAID will implement small-scale clinical trials; and (3) NIAID will facilitate multiple trials conducted by both intramural and extramural investigators.

The India/Mali effort provides dedicated personnel off-site in Frederick, MD, and through a subcontract on-site in India to coordinate activities for these state-of-the-art laboratories, manage administrative concerns, track and monitor dedicated budgets, assist with personnel logistics, provide project procurement support, and provide overall coordination of administrative program-level functions. A scientific director located in Chennai, India, oversees the research projects conducted at the Laboratory of Parasitic Diseases at the Tuberculosis Research Center. The collaborative program has recently:

- Started a new protocol examining the pre- and post-treatment immune responses in pulmonary tuberculosis (TB) while also using biomarkers to predict the occurrence of relapse after treatment;
- Demonstrated that pulmonary and extra-pulmonary manifestations of TB are characterized by differences in multi-functional T cells elicited in response to TB antigens;
- Characterized the presence of multifunctional T and NK cells in filarial pathology in comparison to asymptomatic infection in lymphatic filariasis;
- Examined biomarkers of pathogenesis in filarial lymphatic pathology;
- Examined the impact of helminth infection on TB-antigen-specific immune responses in latent TB;
- Examined the numbers and function of T cells, B cells, NK cells, inflammatory monocytes, DC subsets, and Tregs in filarial infections and related these parameters to pathological consequences of filarial infections; and
- Examined the role of immune complexes and complement system in filarial infections and tuberculosis.

CMRP's overall goal is to facilitate communication and continuity for the clinical researchers located in India and Mali. During the reporting period, CMRP provided logistical and administrative support for daily international operations; budget preparation and monitoring; travel preparation for three nonemployees; procurement of two pieces of capital equipment; and more than 800 pieces of miscellaneous laboratory items, including the establishment of service agreements for equipment located in India and Mali, and the coordination and tracking of 14 perishable, 10 bulk, and two dangerous goods.

CMRP Support to Malian Malaria Research, NIAID

Beth Baseler, M.S., Director
Melissa Borucki, M.S., Senior Special Projects Administrator

In 2005, NIAID began a research initiative investigating the cellular and molecular bases of the acquisition and maintenance of malaria immunity. NIAID maintains laboratory facilities, trains personnel, and conducts several well-defined projects and small-scale clinical trials by both NIH intramural and extramural investigators through the Malaria Research and Training Center. The overall goal is to take advantage of the research infrastructure to facilitate research that is relevant to the acquisition and maintenance of malaria immunity in Mali.

Mouse models for malaria infections exist but these do not faithfully recapitulate the human disease, particularly with regard to the immune response. Because African scientists have few resources, they require outside assistance to develop resources and strategies relevant to their local conditions. NIAID is planning both basic and applied research to address needs in Africa to develop new malaria vaccines and biomarkers for disease outcome. In order to meet this need, CMRP was requested to provide administrative assistance for the management of a subcontract in support of the NIAID-Malian Malaria Immunology Research Program, which is part of the NIH/NIAID ICER program. An agreement with Immport Therapeutics was executed to procure malaria protein microarray chip fabrication, probing, and analysis on serum and/or plasma samples. Also, an agreement with Stanford University was executed to perform multiplex Luminex cytokine assays on samples collected from volunteers enrolled in a NIAID-sponsored observational cohort study of naturally acquired malaria immunity in Mali. The results of these analyses will allow NIAID to address needs in Africa to develop new malaria vaccines and biomarkers for disease outcome.

CMRP Support to Division of Intramural Research (DIR) – South Africa, NIAID

Beth Baseler, M.S., Director
Jennifer Imes, Program Manager
Melissa Borucki, Senior Special Projects Administrator

The Laboratory of Virology within DIR recently initiated a collaborative research program with the

National Institute for Communicable Diseases in Johannesburg, South Africa, to study hemorrhagic fever viruses and other emerging infectious disease viruses. The collaborative research initiative will involve ecological field studies of hemorrhagic fever viruses, pathogen discovery and sequencing of viral isolates collected in the field, and studies on potential animal intermediate hosts and vectors of these viruses, including African fruit bats. The studies will include establishing field research sites in the Democratic Republic of the Congo, Kruger National Park in South Africa, and other potential sites to be determined in the future. Laboratory of Virology investigators will work closely with counterparts at the National Institute for Communicable Diseases in training and execution of the research objectives.

In support of the NIAID–National Institute for Communicable Diseases collaborative research initiative, CMRP will provide rapid deployment of a range of services in support of this initiative, including procuring and arranging the shipment of laboratory and field research equipment, arranging to subcontract full-genome sequencing (including 454 sequencing) of noninfectious viral isolates, and arranging travel services.

Support to the Division of Intramural Research's International Centers for Excellence in Research Core, NIAID

Beth Baseler, M.S., Director
Jennifer Imes, Program Manager
Irene Mueller, M.P.H., Clinical Project Manager I
Joseph Shott, Quality Assurance Specialist for International Research

CMRP staff continues to provide critical research support to NIAID's ICER initiatives in Mali, Uganda, Tanzania, Cambodia, China, South Korea, Thailand, and India. The primary goal of this support is to facilitate new research program sites in geographic areas of high infectious disease burden through partnerships with scientists, and to evaluate and improve established international research sites throughout Africa and Southeast Asia in order to perform clinical research in accordance with NIAID guidelines and U.S. government–mandated regulatory requirements.

The QA specialist provided initial and follow-up reviews of the aforementioned sites in terms of their adherence to GLPs, College of American Pathologists (CAP) or equivalent standards, and implementation of QA/QC programs for laboratories, as appropriate.

Significant accomplishments include the continued CAP accreditation of the Mali ICER Clinical Laboratory; initial site visits to the South Korea and China sites; quality management training administered to three international sites (Tanzania, China, and Cambodia); supporting the path to ISO 15189 accreditation for the SEREFO Laboratory at the Mali ICER; roll-out of the NIAID enterprise electronic biospecimen management system (BSI-II) to international and domestic DIR laboratories; and quality management of biorepositories.

CMRP's Clinical Consulting and Support staff and RCHSPP have been actively involved in supporting the operations of several of these sites by providing an extensive range of administrative, QA, and logistical services, including the establishment of subcontracts for clinical study implementation, regulatory support for clinical trials, study monitoring to ensure GCP, and comprehensive travel support for personnel.

Support to the NIAID-Mali HIV Research Initiative, NIAID

Beth Baseler, M.S., Director
Jennifer Imes, Program Manager

The U.S.-Mali HIV Research Initiative is an ongoing project sponsored by NIAID to establish clinical research projects investigating the effects of HIV and its treatment in West African populations. Since 2003, CMRP staff has assisted NIAID researchers in establishing laboratory facilities and training Malian investigators for Project SEREFO (Centre de Recherche et Formation), located at the University of Bamako in Bamako, Mali, West Africa. The overall goal of this operation is to help establish a research and administrative infrastructure that facilitates research relevant to the African HIV epidemic. Phase III of this project is ongoing, whereby clinical research protocols are developed and initiated with the Malian clinical research team.

A clinical research associate located in Benin, West Africa, provides support through an employment agency. This clinical research associate travels one week of each month to Bamako and works closely with CMRP staff to ensure NIAID clinical trials are effectively monitored and the rights, safety, and well-being of human subjects are protected. The clinical research associate also works to ensure that the reported study dates are accurate, complete, and verifiable from source documents; to ensure the study conduct is in compliance with the protocol, ICH/GCP guidelines, and applicable regulations and standards; and to detect, report, and resolve discrepancies that occur during the conduct of the study.

The Mali HIV effort provides dedicated personnel, both on-site in Africa and off-site in Frederick, MD, to coordinate activities for state-of-the-art laboratories, manage administrative concerns, track and monitor dedicated budgets, assist with personnel logistics, provide project procurement support, provide translation services to researchers and guests visiting the research facility, and participate in the overall coordination of administrative program-level functions. Dedicated staff permanently located in Bamako, Mali, includes a senior program coordinator. The overall goal is to help establish a research infrastructure and to provide training to the Malian collaborators that facilitates research relevant to the African HIV epidemic, a necessary step to advance the global fight against AIDS.

Due to an decrease in work scope for the Mali HIV project, the NIAID DIR submitted a YT to eliminate the senior program coordinator permanently detailed in Bamako, Mali. CMRP coordinated efforts with SAIC-Frederick Human Resources for a reduction in force and repatriation to the United States, including the purchase of return transportation and shipment of personal/household goods.

During the reporting period, efforts provided include: (1) logistic and administrative support for daily international operations; (2) budget preparation and monitoring; (3) continued on-site training of the senior program coordinator; (4) travel preparation for seven Malian investigators to attend various international conferences; (5) procurement of two pieces of capital equipment and more than 1,000 pieces of miscellaneous laboratory items, including training and establishing service agreements for equipment located in Bamako; (6) coordination and tracking of 13 perishable, 10 bulk, and 15 dangerous goods from CMRP; (7) coordination and tracking of two hazardous sample shipments from Mali to Frederick, MD, for testing; (8) continuation of contracts to provide transportation service for the CMRP employees temporarily detailed to Bamako; (9) maintenance of the agreement with Johns Hopkins School of Public Health to provide training and mentoring to the Malian investigators; and (10) technical experts for maintenance and recertification of the BioSafety Level-3 (BSL-3) laboratory.

The renovation of the BSL-3 laboratory, including procurement, shipment, installation and operation, was successfully completed this year.

Support to the IL-15 Project, NIAID

Laurie Lambert, Clinical Project Manager III
Craig Gladden, M.B.A., Program Manager

CMRP continues to provide support to NIAID's LIR for the recombinant human interleukin-15 (rhIL-15) project, working in collaboration with NCI's DCTD.

CMRP's Administrative Support Group continues to provide project management support in concert with the SAIC-Frederick Research Contracts Department to oversee coordination with a subcontractor (Biological Consulting Group), the Clinical Services Program (CSP), and Avanza Laboratories (formerly Bridge Laboratories) to perform pharmacodynamic and pharmacokinetic studies. Since September 2010, CMRP staff has successfully completed the following activities in support of this effort:

In November 2010, a Phase III pharmacodynamic study was completed on five of the original male rhesus monkeys that had received IL-15 via 10-day continuous infusion of low-D IL-15 (at 20 μg/kg/day). Parameters evaluated included mortality, cage side observations, physical examinations, post-dose observations, body weights, body weight changes, food consumption, clinical pathology (clinical chemistry and hematology), cytokine analysis, FACS analysis, immunogenicity analysis, and pharmacokinetic analysis. There were no apparent long-term effects on clinical, cage-side and post-dose observations, body weights, body weight changes, or qualitative food consumption.

At NIAID's request, CMRP assisted with the modification of the existing contract to draw additional blood samples from the 12 surviving monkeys from Phase I of the IL-15 pharmacodynamic/pharmacokinetic studies. This amendment allowed Avanza Laboratories to draw approximately 25 ml of blood on each animal to send to the SAIC-Frederick Clinical Support Laboratory for additional immunologic studies. In addition, the amendment included the housing and maintenance of the 12 surviving monkeys for an additional six months, until it was decided if they would not be needed for future studies related to IL-15. A modification of the contract was completed to hold the six monkeys until December 2010. Upon expiration of the contract for housing the additional monkeys, they were all returned to the colony in January 2011. The 12 monkeys from the previous study were also returned to the colony.

As a result of the successful completion of the pharmacodynamic and pharmacokinetic studies, CMRP, in collaboration with LIR, initiated a new research support contract with Avanza Laboratories to perform another study to evaluate immunologic and virologic effects in rhesus monkeys infected with SIV. This study involved administration for two 10-day cycles of IL15 (rhIL-15). This study was in concert with the SAIC-Frederick Research Contracts Department, a subcontractor (Biological Consulting Group), the Clinical Services Program, and Avanza Laboratories. The SIV study protocol was finalized and the animals were quarantined. Surgeries to add ports for IL-15 administration were completed in March 2011. SIV infection of the nonhuman primates was conducted at the end of that same month. The first 10-day dosing using IL-15 began in late May 2011. Upon completion of the first dosing, an eight-week wash-out period was completed. The primate's SIV viral load was determined to be causing an impact on the health of the animals; the protocol was amended to allow for three antiretroviral drugs (Raltegravir, Tenofovir [PMPA], and FTC [Emtricitabine]) to be administered to the animals in September 2011.

Support to the Biostatistics Research Branch, NIAID

Laurie Lambert, Clinical Project Manager III
Sharat Srinivasula, M.S., Biostatistician II
Wenjuan Gu, M.S., Biostatistician II
Gyan Joshi, M.S., Biostatistician I

The Biostatistics Research Branch's (BRB's) mission is to develop collaborative relationships with intramural and extramural researchers and to conduct independent research in statistical methodology. CMRP staffs three

biostatisticians support this effort—one at level I, and two at level II.

The biostatistician I and biostatistician II provide statistical support as well as data management, programming, and statistical data analysis to many intramural clinical research protocols. This staff member is also involved in analyzing novel, high-dimensional immune assay data collected through the Phase I vaccine studies conducted at NIAID's VRC, including HIV, West Nile virus, and severe acute respiratory syndrome. During the reporting period, the biostatisticians were involved in a wide variety of projects, from the analysis plan development stage to performing complex statistical analysis and producing monthly reports for an H1N1 flu study, hepatitis B study, Taqman validation study, and influenza-like illness study. The biostatistician I also conducted various statistical tests and generated descriptive statistics and graphs for several VRC studies and Phidisa II projects. In addition, the biostatisticians were involved in developing new theories for researchers and training staff to use statistical software at various NIAID laboratories.

The biostatistician II provides statistical and mathematical programming support and aids in analyzing a broad range of clinical and laboratory studies, while assisting with the research in the experimental imaging of SIV/SHIV in rhesus macaques. In the present fiscal year, the biostatistician II is involved in a variety of projects, including noninvasive in vivo single-photon emission computed tomography imaging of SIV/SHIV-infected nonhuman primates; designing and analyzing ligand–receptor-binding studies; estimating the dual-phase HIV viral load decay rates in patients who started HAART therapy; and developing a mathematical model to explain the recovery of CD127 receptors and changes in interleukin-7 levels during the course of antiretroviral therapy for HIV-1 infection.

Support to the Southeast Asia Initiative, NIAID

Beth Baseler, M.S., Director
Julia Welch, M.S., Clinical Project Manager II

The CMRP director and other senior staff have provided valuable expertise and input into the development and implementation of protocols designed for the Southeast Asia Clinical Research Network, which is now in its sixth year. This clinical research network began in four countries (United States, Vietnam, Thailand, and Indonesia) and has expanded and contracted according to the needs of the studies underway. Originally established to address avian influenza, the network has enlarged its scope to include other emerging infectious diseases in the Southeast Asia region. This research is of highest priority for HHS, NIH, and NIAID. CMRP focuses on addressing and resolving the logistical challenges presented through conducting international clinical research, which includes complying with the multiple and varying regulations of different countries, identifying and improving unequal levels of readiness among sites to conduct research, and overcoming language barriers.

The Southeast Asia Initiative, which began in 2005, is one of several special projects in DCR. CMRP has facilitated research by developing and awarding several multimillion-dollar subcontracts. These subcontracts provided support and assistance to the network and provided site management for the clinical research sites in Indonesia. Fifteen protocols were written and implemented during the first five years, with all but one concluding prior to the end of the first contract. In September 2010, DCR reorganized its research support with a new funding mechanism that emphasized strategic planning and support of individual protocols while eliminating the overarching coordinating center. CMRP staff participated in the strategic planning initiative and its early stage implementation to assist with the transition. To increase network efficiency, DCR is further revising its funding strategy by creating separate support contracts for regional activities; one for work in Indonesia and one for the remaining countries in the region. NIAID is contracting with SAIC-Frederick to create and release a request for proposal in the fall of 2011 for a subcontractor to manage the Thai and Vietnam protocols and sites. This new subcontract will facilitate a new protocol to identify and enroll patients with fevers of unidentified etiology as well as provide coordination for a redesigned Network Operations Center.

In the past year, CMRP staff members spent several weeks in Southeast Asia supporting NIAID. Activities both abroad and domestically included: (1) assisting the DCR strategic planning staff with developing SOWs and strategic plans; (2) assisting with transitioning and mentoring new network personnel; (3) developing tools and procedures for project oversight; (4) creating and managing a request for proposal for a subcontractor to manage parts of the network; and (5) providing expertise on establishing working partnerships in the region. CMRP hired a local expert in Indonesia to provide in-country assistance to NIAID with developing the emerging Indonesia research network.

Additionally, CMRP staff worked closely with DCR leadership to develop a statement of work that was to be issued as a competitive research subcontract during August/September 2011. This new subcontract will facilitate the conduct of a new protocol to identify and enroll patients with fevers of unidentified etiology as well as provide coordination for the Network Operations Center.

CMRP will provide oversight of the additional support and assistance contracts in the continual development of the sites, training of site staff, and regulatory input.

Support to the Phidisa Project, NIAID

Beth Baseler, M.S., Director
Shelly Simpson, M.S., Clinical Trials Director
Melissa Borucki, M.S., Senior Special Projects Administrator

CMRP staff continues to be part of the U.S. team collaborating with NIAID DCR, the South African National Defense Force (SANDF) and the U.S. DoD to establish the necessary clinical research infrastructure needed to conduct clinical research to prevent and treat infectious diseases and disorders of the immune system, specifically HIV infection, in Africa. The Phidisa Project is an extension of the Masibambisane Program, a cooperative initiative to help prevent the transmission of HIV/AIDS among South African military and civilian employees and their families. Phidisa is designed to conduct clinical research within SANDF and its network of clinics, sick bays, and hospitals. The intent is to build important biomedical and public health research capacity that can be used in the future to address health issues of critical importance for military force preparedness. As a result of Phidisa, information has been and will continue to be generated to assist SANDF in its decisions about how best to manage the HIV/AIDS epidemic in military settings, to advise SANDF of combat readiness, and to expand knowledge regarding the best way to treat HIV infections.

A major focus for the Phidisa Project during 2011 was developing a five-year strategic plan. Working collaboratively with SANDF, SAMHS, U.S. DoD, and U.S. NIAID-DCR and SAIC-Frederick colleagues, significant progress was made in developing three major strategic goals and associated operational plans. The three major goals of the project are to: 1) more effectively integrate Phidisa into SAMHS/SANDF/SA DoD as a clinical infectious diseases research component; 2) build the capacity for sustainable clinical research within SAMHS/SANDF/SA DoD; and 3) conduct high-quality clinical research.

The CMRP director and clinical trials director participated in a Strategic Planning Workshop held in late September 2010 to further refine the three strategic goals and develop draft operational plans. At the workshop, the CMRP director served as a strategic facilitator, working with the U.S. and South African scientific goal leaders to develop a draft operational plan and scientific agenda relevant to the South African military, while the clinical trials director participated as a team member on developing the goal and draft operational plan to more effectively integrate Phidisa into the SAMHS/SANDF/SA DoD. During the second strategic planning workshop held in May 2011, the CMRP director served as a facilitator to discuss and refine the three goals from the perspective of the laboratory and pharmacy working groups.

As of August, the current draft of the strategic plan was working its way through the SAMHS/SANDF/SA DoD for approval. The formal plan will be presented and operational tracking will begin in earnest within the next six months.

The involvement of the clinical trials director and the CMRP director as active participants of the Phidisa Regulatory Working Group is of notable importance. This group provides expert advice and input on regulatory and clinical trials management issues, such as DSMB, SAE reporting, ICH/GCP, and South African GCP guidance related to accessing study files, and general monitoring issues for the Phidisa clinical trials. The clinical trials director participated in discussions related to the Phidisa benchmarks and helped to edit and finalize the revised monitoring plan for the Phidisa protocols. The clinical trials director continues to work with the group on a possible follow-up publication to benchmark paper, which would involve input from PIs and data management. Additional activities include periodically reviewing site reconsent tables, participating in discussions on possible satellite closure and strategies for subjects follow-up visits at lead site, and a continuing review of monitoring visit reports.

The CMRP director continues to be an active participate of the Phidisa Laboratory Working Group and serves as the COTR for the clinical monitoring (laboratory) research subcontract.

A number of subcontracts continued to support the Phidisa Project during this reporting period. Agreements with seven pharmaceutical companies, through two distributors, provide all antiretroviral drugs. SAIC-Frederick awarded a large clinical monitoring subcontract to the Lancet Corporation in South Africa on January 1, 2005, to provide courier support and clinical laboratory monitoring for the Phidisa protocols. In April 2008, a division of Lancet Corporation, Bioanalytical Research Corporation, took over the responsibility of Phidisa IA and II support. There was no difficulty in the transition to the Bioanalytical Research Corporation and no interruption of services provided because all contacts remained the same. A BOA was executed, effective April 1, 2008, and two task orders were issued. Task Order 1 continued supporting the Phidisa IA and II protocols for laboratory, shipping, sample storage, courier, etc. Task Order 2 completed an analysis of possible immunological indicators of early mortality in HIV infection and complications of hepatitis B infection in HIV-infected study participants who received the antiviral drug Lamivudine. This study added to the existing body of knowledge that explores the contribution of the infecting virus to the therapeutic outcome and evolution of the HIV-1 pandemic, provided valuable information in understanding the treatment outcomes observed in the Phidisa II protocol, and contributed to overall knowledge of the HIV-1 epidemic in South Africa.

Support to the Clinical Consulting and Support Group, NIAID

Beth Baseler, M.S., Director
Jen Imes, Program Manager
Melissa Borucki, M.S., Senior Special Projects Administrator

The Clinical Consulting and Support Group was established in the fall of 2004 to support NIAID's special initiatives and projects. The CMRP support group provides specialized administrative programmatic support for various NIAID, DCR, and DIR initiatives, including subcontracts, conference, travel coordination, and overall administrative support. This support group consists of 14 administrative staff members.

Over the contract year, this group has provided the following support: assisted in recruiting and hiring 27 positions; participated in four conference booth exhibits; established and maintained 57 subcontracts, consulting and professional service agreements; prepared 31 international and 186 domestic travel packages; coordinated arrangements for eight conferences, seminars, retreats, and training sessions; prepared 44 nonemployee travel packages to attend conferences, seminars, and training sessions; completed 520 courier runs; and provided acquisitions support, including purchasing and property.

Clinical Consulting and Support Group support includes the following:

Subcontracts Management

The support group administers and oversees the establishment of subcontracts in support of specific international and domestic NIAID research efforts. This support includes preparing SOWs, monitoring subcontractor progress, monitoring budgets, and collaborating with NIAID project officers to ensure the SOW goals are met in a timely and efficient manner. Throughout 2011, the Clinical Consulting and Support Group was active in preparing and managing subcontracts with Adamas Pharmaceuticals, United BioSource Corporation, Social and Scientific Services, and the University of Minnesota/Insight to support domestic and international influenza initiatives; preparing and managing PPD, Inc., to support continuing clinical monitoring efforts in Southeast Asia; managing a subcontract with the University of Pittsburgh to provide an additional clinical research site to conduct a clinical research protocol for NIAID; preparing and managing subcontracts for the Phidisa project to support clinical research protocols and substudies in South Africa; preparing and managing subcontracts with the Rakai Health Sciences Program and the IDI for hepatitis B and HIV co-infection studies in Uganda; and managing a subcontract with the HIV Resistance Response Database Initiative for modeling various antiretroviral therapy responses.

The Clinical Consulting and Support Group also administers and oversees subcontracts in support of the NIH Clinical Center's Critical Care Department for their Collaborative Program for AIDS Progress to provide support for HIV studies at NIH for DC-PFAP. Subcontracts were established for medical assistance support and phlebotomy services at three clinics: Whitman Walker, Unity, and Family Medical. Additionally, a professional services agreement with Howard University was created to provide medical support services for assistance with raising awareness and provider competency in HIV knowledge and testing, and facilitating communication about best practices in opt-out testing.

Conference and Travel Coordination

The Clinical Consulting and Support Group provides travel coordination for non-government and CMRP employees involved in major initiatives within NIAID. The support group coordinates international and domestic meetings, conferences, and training for non-government participants collaborating on many long-term, clinical research initiatives. The services include arranging visits by foreign/domestic scientists/officials to foreign countries and locations within the U.S. to attend meetings, conferences, planning sessions, and program discussions; developing detailed travel itineraries; providing guidance and assistance to U.S. and foreign travelers in obtaining passports and/or visas; arranging ground transportation as necessary; arranging hotel or other lodging accommodations; paying appropriate subsistence allowances in advance; making direct contact with the host and the traveler to ensure all arrangements are mutually understood; and providing reimbursement upon receipt of an expense statement for appropriate expenses relating to travel.

Administrative Support

The current scope of work supporting the DCR mission has resources located in Bethesda, MD. These resources are allocated to support initiatives in the areas of strategic planning, program operations, clinical research, biostatistics, and international collaborations. Staffing consists of two secretary IIIs, one administrative assistant, and one senior program coordinator, all of which support the Program Planning and Analysis Branch (PPAB), RCHSPB, the Collaborative Clinical Research Branch (CCRB), and the Office of the Director.

The Clinical Consulting and Support Group administrative staff services include, but are not limited to, managing program schedules, coordinating meetings, preparing agendas and disseminating meeting minutes, making conference arrangements (local and international), scheduling guest speakers, coordinating training sessions, preparing travel packages in accordance with all applicable government guidelines (both domestic and foreign), tracking action items related to branch initiatives and project milestones, coordinating with project teams to compile and distribute information as directed,

monitoring program operational plans, and developing progress reports.

CMRP Support to the Office of Cyber Infrastructure and Computational Biology, NIAID

Beth Baseler, M.S., Director
Jennifer Imes, Program Manager
Kevin Newell, M.Ed., M.P.H., Protocol Coordinator
Irene Mueller, M.P.H., Clinical Project Manager I

DIR requested programmatic support from CMRP for its ICER sites in Uganda, India, Mali, South Korea, Cambodia, China, Peru, and Thailand to assist with integrating the DataFax® clinical data system into several of the ICER clinical research sites supported by DIR, DCR, and the Office of Cyber Infrastructure and Computational Biology. The Office of Cyber Infrastructure and Computational Biology manages technologies that support NIAID intramural and extramural biomedical research programs and provides a wide range of management, technologies development, applications/software engineering, bioinformatics support, and professional development services for a global scientific network of biomedical researchers.

The CMRP protocol coordinator supporting the Rakai Health Sciences Program in Uganda has been actively engaged in integrating the DataFax® data management system in the Uganda clinical research studies as part of support for the ICER site in Uganda. Furthermore, CMRP Clinical Consulting and Support Group staff and RCHSPP were involved in several of these sites where the DataFax® system was being integrated by providing a wide range of administrative, logistical, regulatory, clinical trials management, and travel support. DIR requested support from the CMRP protocol coordinator to provide direction and training to the Office of Cyber Infrastructure and Computational Biology study staff in the operation and configuration of DataFax®, with the goal of integrating the technology into other international protocols being developed by DIR.

During the DataFax® initial planning stages, the protocol coordinator traveled to NIH in Bethesda, MD, and provided consulting, training, and support for implementing clinical protocols on the DataFax® server infrastructure, followed by a visit to the Mali ICER site to train on-site clinical research staff in DataFax® technology and to build on NIAID's long-standing malaria research collaboration with scientists in Mali, and a trip to the DIR collaborative malaria research program in Morogoro and Muheza, Tanzania, for DataFax® implementation.

At the end of the year, the protocol coordinator provided training in Bethesda, MD, to NIAID and CMRP clinical trials personnel and covered issues pertinent to DataFax® case report form development and the use of the DataFax® system for monitoring DIR clinical protocols.

Support to the Office of Planning and Operational Support, NIAID

Beth Baseler, M.S., Director
Laurie Lambert, B.S., Clinical Project Manager III
Cynthia K. Osborne, B.S., Clinical Project Manager II
Barbara van der Schalie, M.S., Clinical Training Manager
Mildred Gapara, M.B.A., PMP, Clinical Program Administrator

During FY2011, the CMRP clinical program administrator continued to serve as executive secretary for the NIAID Clinical Research Subcommittee. The clinical program administrator is the liaison to the Clinical Research Working Group to organize groups of subject matter experts to assist with facilitating NIAID Clinical Research Subcommittee initiatives through the approval process. This year, the clinical program administrator continued to directly support three key NIAID Clinical Research Subcommittee initiatives related to Barriers to Clinical Research: (1) identifying alternative models for IRB review; (2) identifying and resolving barriers produced by HHS, NIH, and NIAID policies and regulations; and (3) addressing barriers to international research caused by requirements of the European Union Clinical Trials Directive.

The clinical program administrator provides administrative support to these initiatives by creating and editing documents and reports, and provides programmatic support by tracking and reporting the progress of initiatives for NIAID Clinical Research Subcommittee leadership. In addition, the clinical program administrator serves as the logistical point of contact to coordinate and facilitate work group sessions (for subject matter experts and division representatives) to discuss progress and monitor performance.

The clinical program administrator is involved in planning and coordinating high-level complex division-wide meetings and collaborative forums. In June 2011, the clinical program administrator was recognized in the *Coordinator's Report* for expert ability to arrange DCR Branch Chief Meetings.

Since April 2011, the clinical program administrator has been involved in facilitating an effort to increase the efficiency at which the Clinical Research Working Group performs literature searches. The clinical program administrator reviews and categorizes scientific papers, then posts them to the NIAID Clinical Research Subcommittee SharePoint site. Users can maximize their search by selecting the category of interest. The clinical program administrator will be providing support to other SharePoint initiatives such as the European Union web-based matrix. This staff member is also responsible for maintaining the Clinical Research Working Group SOPs and performing quarterly progress report updates in conjunction with the Office of Planning and Operations Support (OPOS) Strategic Planning Group.

The clinical project manager II continues to provide support to the OPOS Strategic Planning Group throughout the strategic planning process. The group currently has plans in process for six DCR branches/offices: Office of Planning and Operations Support (OPOS), Program Planning and Analysis Branch (PPAB), NIAID Regulatory Compliance and Human Subjects Protection Branch (RCHSPB), Intramural Clinical Operations Branch (ICMOB), Collaborative Clinical Research Branch (CCRB), and the Integrated Research Facility. The Behavioral Research Branch (BRB), PPAB, and RCHSPB have started a new strategic planning cycle for the current reporting period.

The clinical project manager II develops and maintains a project management master system as well as the related processes/templates necessary for facilitating the planning, tracking, and execution of operational plans for DCR branches and offices. DCR has directed resources for operational planning in an effort to implement and execute a strategy for its branches and offices. During this reporting period, one operational plan was developed and implemented for OPOS to support its new strategic plan. Operational plans for ICMOB, RCHSPB, and PPAB remain deployed and monitored. An operational plan is in development for CCRB. In addition to DCR branches and offices, operational planning support was also provided to DCR projects and programs such as the La Red Network in Mexico, Phidisa, and IDCRP.

The clinical project manager II is also responsible for establishing, implementing, and maintaining a flexible reporting system for monitoring the progress of operational plans, which requires facilitating the ongoing review and maintenance of four DCR operational plans and preparing quarterly progress reports for each branch's leadership. During this reporting period, quarterly progress reports for OPOS, RCHSPB, PPAB, and ICMOB were reported for each branch. Annual strategy reviews for operational plans were facilitated for RCHSPB, PPAB, and ICMOB. During these sessions, goals, objectives, and key performance indicators were reviewed to ensure strategic alignment to the program's mission and to develop operational plans for the next year.

Utilizing project management concepts, the clinical project manager II performs a high degree of mentoring and knowledge/skills transfer within the subject area of operational planning. During the current reporting period, the clinical project manager II collaborated with the PPAB program specialist to facilitate the annual strategy review of the PPAB strategic plan as a means of encouraging staff to be more participatory and take ownership of the operational plan. As a result of this collaboration, the program specialist led the review and successfully engaged fellow colleagues to contribute to the operational planning process. A new reporting process, which incorporates a role for each staff member, was initiated.

The clinical project manager II also develops, implements, and maintains workforce alignment strategies throughout DCR, assisting various levels of staff with aligning performance initiatives to strategic goals and objectives and aligning operational accomplishments with performance targets. In the current reporting period, the clinical project manager II assisted 35 DCR staff members with workforce alignment strategies. In June 2011, the clinical project manager II was recognized in the *Coordinator's Report* for outstanding performance of aligning strategic plans to performance objectives and working with the DCR branches on their Performance Management Appraisal Programs.

The clinical project manager II was a NIAID 2010 Merit Award recipient for collaborations with the PN/PDP team; specifically for establishing the PN/PDP, which supports NIAID domestic and international research across the intramural program.

Management Support

In May 2011, a new administrative support plan was implemented as a result of a resource evaluation and time-to-task analysis. The new plan included sharing supervisory responsibilities with other CMRP positions supporting DCR, allowing the clinical program administrator to support the Clinical Research Working Group with project management activities. In addition, a centralized resource was identified to support the travel needs for projects/programs that require participation from multiple branches. Organizational tools, such as an organizational chart, roles and responsibility matrix, and employee coverage plan, have been updated and redeployed. Efforts are being directed to develop standards for job performance and service excellence. Through focus group sessions, which included the administrative and management staff, four key areas for improvement were identified: (1) professionalism, (2) communication, (3) policy and procedures, and (4) roles and responsibilities. Work groups have been formed for each area to define the skills, knowledge, and competencies necessary to provide excellent service and increased customer satisfaction.

OPOS Training Support

A clinical training manager provides training support for OPOS by serving as a member of the Learning and Professional Development Group.

Identify/Develop Training Resources to Address Client-Identified Training Needs

During the reporting period, most of the training requests within OPOS were initiated by DCR's ICMOB and PPAB. This year, the clinical training manager has provided training on communication style preference, assertive/aggressive communication, strengths-based leadership, group decision making, and active listening. CTG has also provided extensive organizational development support and facilitation services. Both ICMOB and PPAB have requested ongoing training, including one learning segment per month, through the end of CY2011.

The clinical training manager also presented multiple training topics at PPAB and ICMOB staff retreats, as well as designing and facilitating the PPAB Associate Branch Chiefs' retreat.¶

CTG facilitated a two-day training event for study coordinators, "Special Topics in Clinical Trials Management," provided by an external vendor.

Provide Training and Professional Development Subject Matter Expertise

ICMOB, OPOS, and PPAB requested assistance in human capital allocation, using succession planning tools supplied by CTG. This project will include job analyses, alignment of roles and responsibilities to their strategic plans, competency identification, and internal training resource identification.

The clinical training manager facilitated job satisfaction–centered focus groups with both the senior program specialists and junior program specialists within PPAB and also facilitated the work groups that followed.

CTG participated extensively in the development and review of DSMB CBT, which is currently under review and revision.

The Learning and Professional Development Group is leading the team responsible for implementing a leadership culture within DCR. A leadership model, based on the Baldrige leadership competencies, has been approved for implementation among the DCR senior leadership. The distribution plan is in progress; there were six participants in the initial roll out, and two more will join in six months.

Conduct Professional Development to Ensure That Staff Members Maintain Their Subject Matter Expertise.

This year, the clinical training manager presented three presentations at national conferences: "The Care and Feeding of Subject Matter Expert Trainers" (Barnett Clinical Training Forum, Philadelphia, PA, October 2010), "What Do We Know? A Review of Publically Available Information and Resources to Develop FDA Inspection Readiness" (Barnett Clinical Auditing Forum, Boston, June, 2011), "Who's Out There and Why Do We Care?" (SoCRA Annual Conference, San Diego, CA, September 2011).

The clinical training manager also published an article, "Why Train? Lessons Learned from FDA Warning Letters," in the *SoCRA Source*, April 2011; attended four courses on evaluation provided by The Evaluator's Institute of George Washington University's Graduate School; and became certified in the Kirkpatrick Evaluation Model.

OPOS Technical Solutions Group (TSG)

OPOS TSG provided support to the sixth and seventh CRIMSON Award Fee panel reviews to assess contract performance against the metrics outlined in SOW. TSG extracted data from monthly status reports and compiled the information into comparative spreadsheets. Excel templates were used to graphically depict the quantitative metrics from SOW. The current review period, as well as other review periods, were compared to SOW metrics. A qualitative summary was written and combined with the metric analysis into a detailed review narrative that the panel used to make their determination for the six-month period.

During this reporting period, the TSG group managed the installation of the PIV software on over 62 laptops located in 6700A and 6700B Rockledge facility. This project was completed one month ahead of schedule. The laptops are in compliance with federal regulations for two-factor authentication.

TSG serves as the central point of contact for ordering all technical equipment upgrades and replacements. This team also determines hardware and software specifications, provides IT support, and follows through to user satisfaction. TSG also completed ordering 76 computers for staff. The ordering, delivery, and installation of each piece of equipment was tracked, and the associated costs of the items were reconciled with the DCR Funding Report issued by the Office Of Cyber Infrastructure and Computational Biology.

Additionally, TSG played an integral part in the 2011 annual Acquisition Management and Operations Branch inventory of equipment. This includes tracking PDAs, laptops, and all equipment used for telecommuting. The group collaborated with the inventory team to reconcile property records and research the locations of missing and/or at-home equipment to resolution. Over 300 pieces of equipment were inventoried.

TSG also provided support in issuing approximately 52 long-term property passes for all portable and at-home equipment within DCR. This process is coordinated with the property custodian and includes verifying the equipment, NIH decal number, and manufacturer's serial number within the NIH Business System property database.

TSG was responsible for supporting 20 fellows in 2010 and 20 fellows in 2011, including 15 fellows in the NIAID Allergy and Infectious Diseases Fellowship Program, four Intramural Research Training Award fellows, and one presidential fellow. This effort required purchasing laptops, upgrading BlackBerries, and transferring equipment from previous year fellows.

Support to the Infectious Diseases Clinical Research Program (IDCRP), NIAID, DoD

John Powers, M.D., Senior Medical Scientist
Alice Rosenberg, R.N., Clinical Research Nurse III (Outreach)

Since 2005, CMRP has worked with NIAID to establish a collaborative effort between CMRP, NIAID, and DoD in IDCRP. With the senior medical scientist serving as the team leader for this project and the clinical research nurse III serving as project manager, the overarching goal of this collaboration has been to

facilitate high-priority, translational clinical research to address infectious disease problems of military relevance. Additional ambitions of this partnership include building research capacity, developing infrastructure, facilitating efficient clinical research, and leveraging scientific expertise within and outside of NIH.

During this reporting period, CMRP staff continued to enfranchise the IDCRP steering committee by helping re-write the interagency agreement that outlines steering committee functions and objectives and develop agendas for steering committee meetings. In addition, CMRP staff worked with NIAID staff to clarify steering committee membership to best reflect those parties with knowledge of areas of military relevance for clinical research. The staff also facilitated the development of research capacity by aiding IDCRP staff in developing and implementing protocols for infectious diseases of military relevance.

Currently, 66 protocols are in various stages of development within IDCRP; of those, at least 19 are approved. CMRP staff members have also helped develop research capacity by acting as points of contact for clinical research questions and standards, such as NIAID-specific protocol templates and SOPs. Administratively, CMRP staff organized regular meetings regarding function and vision of the IDCRP program and kept NIAID staff up-to-date on the progress of the program. CMRP's senior medical scientist serves on the Scientific Review Board, ensuring the scientific validity of protocols before sending them to IRB. The senior medical scientist has also lectured to groups of PIs to enhance their scientific understanding and has given the Preventative Medicine Grand Rounds.

CMRP staff aided DoD staff in developing an infectious disease–specific IRB. In addition, CMRP RCHSPP staff provides protocol pre-review for regulatory compliance and, when appropriate, provides protocol monitoring per GCPs. The clinical research nurse III has assisted in addressing monitoring and regulatory issues. Most recently, CMRP staff worked with IDCRP staff to develop an acute respiratory diseases program to address clinical research in novel influenza disease and in other respiratory diseases in the military.

In this period, the American Institute of Biological Sciences review submitted several recommendations for program improvement. A revised system for evaluating and prioritizing new protocol concepts has been developed and implemented, along with multiple suggestions for alternate funding sources. The system and implementation meetings were attended by the IDCRP senior medical scientist whose oversight and research knowledge led to a more concise system of instituting protocols. Currently, there are 45 active protocols at multiple DoD sites in the U.S. and internationally, with 11 more in development. Thirty-two articles have been published in peer-reviewed journals.

The CMRP RCHSPP support team has helped IDCRP develop an informed, independent staff for regulatory and monitoring functions. Under that mentorship, IDCRP staff now monitors some of its own protocols.

The senior medical scientist worked closely with the financial administration branch to develop an amendment to the interagency agreement to include additional funding for research support; creation and maintenance of data collection and analysis within the network; and addressing the backlog in case report forms. CMRP staff has been instrumental in developing and managing the subcontracts associated with this amendment to the interagency agreement.

The senior medical scientist also worked with NIAID staff to develop and implement an interagency agreement between Uniform Services University and the Biomedical Advanced Research and Development Authority to fund influenza-related clinical research.

Support to the District of Columbia Partnership for AIDS Progress (DC-PFAP), NIAID

John Powers, M.D., Physician III
Dawn Fishbein, M.D., M.S., Medical Director, Medical Affairs Scientist II
Rachel Newman, R.N., MPH, Clinical Nurse Administrator
Anu Osinusi, M.D., MPH, Physician II
Colleen Kotb, R.N., Clinical Nurse Coordinator
Erica Eaton, MPA, Clinical Program Administrator
Alice Rosenberg, R.N., Clinical Research Nurse III (Outreach)

In 2008, the Washington, D.C., Department of Health and NIH launched a new partnership to make D.C. a leader in the response to the HIV/AIDS epidemic. This is being referred to as DC-PFAP. For the first time, the nation's capital and leading health research institution joined together to work with the district's universities and community-based health care providers to bring new ideas, new services, and access to clinical research to D.C. residents. The partnership draws upon a diverse portfolio of academic institutions, community-based organizations, and stakeholder groups for the design and implementation of specific projects and activities. CMRP has played a major role in implementing this partnership, beginning with initial navigation by the clinical research nurse III who helped to bring the D.C. HIV provider community and NIH together, and assisted with recruiting the medical director, a medical affairs scientist II, from the DC-PFAP subspecialty clinics in May 2009.

During the reporting period, there have been multiple advances in the program's development, moving from initial care implementation into the research phase: (1) recruiting an infectious disease–trained physician who is on a clinician scientist pathway, caring for patients in D.C. with hepatitis B and hepatitis C and developing a laboratory-based research program in hepatitis C resistance; (2) recruiting a NIAID nurse case manager to become a research coordinator in the D.C. community-integrated hepatitis clinics; (3) implementing the first clinical trial for the program and enrolling patients

directly in the D.C. clinics; (4) poster presentation at the Conference on Retroviruses and Opportunistic Infections (CROI) 2011, about a retrospective study of fibrosis in African Americans with hepatitis C; distinct abstract submitted for the American Association for the Study of Liver Diseases, 2011; manuscript under development; (5) approving and implementing a Natural History Prospective cohort for persons with hepatitis C or hepatitis B, with and without HIV; (6) IRB submission of a clinical trial of one of the newly approval agents for hepatitis C, comparing persons with hepatitis C monoinfection and HIV coinfection; (7) IRB submission of a novel interferon-sparing hepatitis C agent; (8) screening and referring patients for other NIH research protocols; (9) evaluated over 200 new patients for subspecialty hepatitis care and treatment within three integrated HIV community clinics in D.C., totaling over 1,000 patient visits; (10) started a D.C. Hepatitis Research Network to promote clinical and research collaboration among academic institutions and young investigators in DC; (11) continued monthly educational webinars for HIV treatment/care providers, organized by the core team in collaboration with the D.C. Department of Health and the AIDS Education and Training Center; (12) established monthly NIAID Liver Disease research meetings.

The DC-PFAP Subspecialty Clinic program development is on target and is continuing to create an expanding number of new opportunities to address the high rate of HIV infection in Washington, D.C.

Support to NIAID and the Washington Hospital Center Collaboration to Enhance Clinical Research, NIAID

John Powers, M.D., Senior Medical Scientist
Alice Rosenberg, R.N., Clinical Research Nurse III (Outreach)

For the first time, an NIH intramural research protocol was taken off site to increase the scope of research training for fellows and the patient population available for study, and to make research protocol participation more accessible, resulting in a greater opportunity for inner-city resident participation.

As a result of this change, the protocol to evaluate the function of HgbA1C in the progress of diabetes enrolled 125 patients at Washington Hospital Center and was completed within one year. It was considered a great success and gave way to the program's next project.

A second protocol, in conjunction with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), was established to determine if proteinuria is a predictor of renal disease in HIV-positive patients. In January 2011, proteinuria study enrollment was completed; 118 patients participated at Washington Hospital Center. This protocol was completed in conjunction with NIDDK by NIAID and CMRP staff—another first for NIH. In June 2011, the final patient visit occurred. The study at Washington Hospital Center will be closed, with four long-term follow-up patients completing their visits over two years at NIH Clinical Center. The final monitoring visit with CMRP RCHSPP's Clinical Trials Management Team took place in July 2011. Afterwards, the protocol results will go to analysis and then be documented and submitted for publication. All aspects of this procedure are supported by CMRP departments.

In addition, a team at the Washington D.C. Veteran's Administration Hospital (DC VA Hospital) was formed to conduct a protocol that will determine the value of using pioglitazone to diminish steatosis in HIV-positive patients with hepatitis C complications. Under the supervision of the medical affairs scientist, CMRP's clinical research nurse III helped to organize these projects; recruited, consented, and enrolled patients; collected all patient samples; prepared and packed specimens for shipment; and prepared the necessary documentation for monitoring visits. The pioglitazone protocol was able to recruit only one patient at the DC VA Hospital and the study will not continue to enroll. CMRP staff members are in discussion regarding the next potential protocol to bring to the DC VA Hospital.

NIAID rents permanent office/exam space at Washington Hospital Center for NIH staff to use when seeing patients at this site. There are several extended projects being proposed for the site since CMRP has established a very positive collaboration with Washington Hospital Center.

Support to NIAID Clinical Teams

Taree Foltz, Program Manager
Michelle Paulson, Physician II
Daphne Mann, Nurse Case Manager III
Maryellen McManus, Protocol Nurse Coordinator III
Katherine Spates, Protocol Nurse Coordinator III

Support to the Intramural Clinical Management Operations Branch

The Intramural Clinical Management Operations Branch (ICMOB) oversees the logistical management of clinical research and all related clinical operations for the intramural laboratories (Laboratory of Immunoregulation, Laboratory of Host Diseases, Laboratory of Clinical Infectious Diseases, Laboratory of Parasitic Diseases, Laboratory of Allergic Diseases, and Laboratory of Immunology), with a major emphasis on patient-oriented research. ICMOB manages inpatient units and outpatient clinics in concert with the Clinical Center. It is also responsible for clinical protocol review and approval, assurance of scientific quality and human subject protection, the quality of care delivered to NIAID patients, and the quality of professional performance of the health care providers.

The intramural portfolio is constantly expanding as new research initiatives and projects are identified to help further the mission of NIAID. CMRP is actively involved with projects of a similar nature and similar support services where clinicians, study coordinators, and

administrative support personnel have been requested and provided. These staff members provide the necessary clinical support to handle this extensive effort.

Support to the Laboratory of Immunoregulation

CMRP provides study coordinator, case management, recruitment, laboratory, clinical, and research support to the Laboratory of Immunoregulation (LIR). During the reporting period, a clinical research nurse II was hired to assess and deliver care to study participants in the fast-paced treatment room of the Outpatient Eight Clinic. A research technician was also hired to provide technical assistance in research lab management, while responding to requests from scientists for sample information. Two additional positions, a case manager and protocol nurse coordinator II, were also hired. These positions provide regulatory and safety data management, as well as patient care-related activities.

The clinical research associate I, in support of LIR, was a co-author on an abstract presented at the prestigious Conference on Retroviruses and Opportunistic Infections Conference and serves as the lead author on a *strongyloides* paper that will be submitted for publication.

Several LIR staff members received an annual performance award for FY2011, and two staff members were recognized for their continuing support to the NIAID Clinical Teams in the SAIC-Frederick *Coordinator's Report*.

Support to the Laboratory of Host Diseases

CMRP provides nurse case management support to the Laboratory of Host Diseases (LHD). A nurse case manager II provides direct nursing care to an assigned caseload of patients by facilitating patient visits and supporting both clinical and research needs. A clinical research nurse was hired to assist with implementing clinical protocols, documenting and tracking requirements for adverse events, and corresponding with patients. The group's protocol coordinator provides support for protocol regulation, patient screening, and patient enrollment.

Support to the Laboratory of Clinical Infectious Diseases

CMRP provides clinical and protocol support to the Laboratory of Clinical Infectious Diseases (LCID), a group that is interested in a wide spectrum of diseases, including primary immunodeficiencies, hyper IgE syndrome, mycobacterial, viral, and tick-borne infections, and autoimmune lymphoproliferative syndrome. CMRP staffs four nurse practitioners to provide direct patient care to patients enrolled in LCID protocols.

A physician II provides support for clinical and research efforts related to mycobacterial diseases, including a recently discovered mutation that leads to MonoMac syndrome and the development of a clofazimine protocol. CMRP staffs four protocol nurse coordinators to support protocols implementation, data and regulatory management, and safety data monitoring. Two of the protocol nurse coordinators are co-authors in research publications this year. CMRP provides additional direct clinical support through three nurse case managers. These case managers coordinate patient care-related activities. Additionally, CMRP staffs one patient care coordinator and a clinical research nurse II to LCID to facilitate chart reviews, patient enrollment, and specimen processing.

During the reporting year, two staff members received a 2010 SAIC-Frederick Annual Achievement Award; one for Customer Relations (Scientific) and one for Customer Relations (Technical). In addition, a nurse practitioner presented an abstract at a national conference.

Support to the Laboratory of Parasitic Diseases

CMRP provides nurse case management support and study coordination services to the Laboratory of Parasitic Diseases (LPD). During FY2011, the senior protocol nurse coordinator II was actively involved in the orientation of two new protocol coordinators. The protocol coordinators serve as liaisons with personnel at clinical and laboratory sites, participate in clinical trials protocol development, develop procedure manuals for clinical trials protocols, train staff, and visit off-site collaborative centers as needed. This year, the senior protocol coordinator II advocated for LPD protocol coordinators to play a more active role in each of the studies they oversee. As a result, the three LPD protocol coordinators are now associate investigators on at least five protocols supported by LPD and contribute significantly to data collection for each study. The role of the LPD protocol coordinator is expanding to include data collection that will be used for future publications.

In keeping with the mission of support to the NIAID clinical teams, the senior protocol nurse coordinator II assisted the NIAID nursing administration with formulating a nursing orientation competency form to meet Joint Commission requirements. The competency check-off sheet has been finalized and will soon be initiated.

The senior protocol nurse coordinator II received an annual performance award for FY2011.

Support to the Laboratory of Allergic Diseases

CMRP provides nurse case management support to the Laboratory of Allergic Diseases (LAD), supporting protocols that study various aspects of mastocytosis, idiopathic anaphylaxis, urticaria and atopic dermatitis, asthma, and systemic capillary leak syndrome. A nurse case manager II provides direct nursing care to an assigned caseload of patients, utilizing the nursing process to assess, plan, intervene, and follow-up on disease-related features as outlined in the clinical protocols. Additionally, the nurse case manager II provides procedure support through skin punch biopsies, antigen skin testing, and pulmonary function testing.

Support to the Laboratory of Immunology

CMRP provides clinical trial coordination/ implementation and clinical protocol/data management to the Laboratory of Immunology (LI). A protocol nurse coordinator II was hired to manage QA and quality improvement initiatives; manage implementation, tracking, data abstraction, collection, and data reporting; liaise with referring physicians and patients; and coordinate a screening protocol clinical trial. These studies will assist in determining the biochemical and genetic causes of inherited childhood immune diseases that affect lymphocyte homeostasis.

H1N1 Influenza Support to the Division of Clinical Research (DCR), NIAID

John Beigel, M.D., Medical Affairs Scientist II
John Powers, M.D., Senior Medical Scientist

Influenza Support to NIAID (IRC protocols)¶

CMRP continues to provide support to the H1N1 Influenza initiative. H1N1 influenza presents challenges to global health security because many foreign nations, especially less developed countries, may not have preparedness plans and/or the capabilities/capacity to respond to the pandemic. For these reasons, NIAID's DCR requested that CMRP provide support in the following areas: (1) associate investigator activities including development, management, and oversight of the conduct of these studies; (2) clinical trials management and support; (3) regulatory support, including clinical monitoring, safety reporting, and IND management; (4) clinical site preparation and study/trial operational assistance; (5) handling of clinical specimens; (6) training; (7) data management; (8) management and oversight of three multimillion-dollar subcontracts, including several task orders; (9) general logistical and administrative services, such as conference, travel, and meeting planning and organization; (10) protocol development and review; (11) web site development and maintenance; (12) personnel; and (13) biostatistics support.

NIAID Influenza Research Collaboration is a NIH/NIAID-sponsored clinical trials network dedicated to finding new treatments for seasonal and pandemic flu. Currently, there are four ongoing NIAID Influenza Research Collaboration studies supported by SAIC:

IRC 001 - H1N1 Plasma Collection Study - A plasma collection study that enrolls healthy volunteers who have had the flu or received the H1N1 flu vaccine and are found to have high levels of H1N1 antibodies in their blood. This protocol was launched in September 2009 and is currently being conducted at 10 domestic sites. In the reporting period, six sites have been activated, 378 subjects enrolled, and 490 units of human plasma with high-titer H1N1 antibody collected. In addition, 13 submissions have been made to FDA under an IND.

IRC 002 - H1N1 Plasma Therapy Study evaluates the safety of using human plasma containing high-titer antibodies in addition to standard care antiviral medications in treating subjects with severe influenza. This protocol was launched in December 2010. In the reporting period, 12 sites were activated and seven subjects were enrolled. There was also one DSMB meeting and seven submissions to FDA under an IND.

IRC 003 - Combination Therapy Study focuses on enrolling subjects who are at risk of developing severe influenza based on criteria set by the Centers for Disease Control and Prevention. The purpose of the study is to evaluate whether combination therapy with three antivirals (compared to the standard one antiviral) will help symptoms resolve faster and with fewer complications. This protocol was launched in January 2011. In the reporting period, the protocol was finalized with a subsequent amendment, seven domestic sites were activated, six additional domestic sites received IRB approval and will be activated in the fall, seven Australian sites are in the process of being activated, one subject was enrolled, one investigator meeting was held in Sydney, Australia, and there were five submissions to the FDA under an IND. Future sites will launch in Mexico in October 2011 and Thailand in late fall 2011. Argentina is expected to start enrolling subjects sometime in 2012.

IRC 004 - Tamiflu (Oseltamivir) Versus Placebo Study seeks to understand if subjects on Tamiflu show decreases in the amount of virus detected in the nose or throat, and to understand if the change in the amount of virus is associated with changes in symptoms. Subjects at low risk for developing complications will be randomized to receive either Tamiflu or a placebo. In the reporting period, five sites received IRB approval.

Influenza Support to NIAID (Symptoms Scale)

During Phase I, CMRP provided support for an observational study to characterize persons infected with H1N1 during the 2009–2010 pandemic on five continents, also known as the Acute Respiratory Infections Consortium protocol. The primary objectives of this study were to: (1) characterize individuals with influenza or influenza-like illness in terms of demographics, co-morbid conditions, and prior influenza vaccinations; (2) describe the clinical course and treatment provided; (3) assess the outcome 28 days after diagnosis of influenza A; and (4) establish a repository of samples to determine a precise diagnosis and to characterize, on a molecular level, the virus from different sites. CMRP provides management of a multimillion-dollar subcontract in which enrollment began in September 2009 from 50 clinics located in North America, South America, Western Europe, Australia, Thailand, Japan, and Africa; currently, 800 patients are enrolled. An additional study, FluPro, which was awarded under a separate subcontract, was approved and began enrolling in fall 2010 when the flu season began; 14 patients are enrolled. Investigators meetings will be held to discuss analysis of patient data collected to date.

During the reporting period, plans were made for studies that will take place during the 2011–2012

influenza season at Washington Hospital Center. CMRP will continue to offer support to these projects as described above. Four influenza studies, including FluPro, are being proposed at Washington Hospital Center, thus bringing the opportunity to participate in research to a community with limited options for this. The CMRP senior medical scientist (acting as associate investigator) will establish a contact system for identifying patients and organizing the screening, enrolling, and consent process. The senior research nurse III will be responsible for operationalizing these studies according to established GCP principles. These studies will be required to undergo the usual IRB review at Washington Hospital Center and comply with any restrictions placed by this governing group.

Support to National Institute of Arthritis and Musculoskeletal and Skin Diseases

Overview

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) requested programmatic and logistical support for the clinical research operations of Phase I and II clinical trials. NIAMS' Intramural Clinical Research Program conducts studies in natural history and treatment as well as basic investigations into the etiology and/or pathophysiology of disease, including rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, vasculitis, scleroderma, myositis, osteoarthritis, or other inflammatory/rheumatic diseases. Currently, NIAMS has approximately 23 active studies that vary from screening and training to natural history and Phase I and II clinical trials. Approximately five of these protocols are conducted under IND applications.

NIAMS requested SAIC-Frederick support for the rapid deployment of clinical services for time-sensitive critical clinical research. Acquiring these services through CMRP will help to streamline protocol development time, provide flexibility for emerging/fluctuating needs, eliminate costly time delays, and ensure the success of the NIAMS clinical mission. These services complement those that CMRP already provides to other NIH clinical research programs. CMRP contributes a unique resource to NCI's and NIAID's intramural clinical research teams by providing regulatory support to their PIs to help meet the requirements of the NIH Standards of Clinical Research established in 2000. This support gives PIs more opportunity to focus on the main objectives of their clinical research portfolios.

The initial emphasis of this request is focused on protocol navigation, regulatory compliance through IND support (three new INDs are estimated per year), and clinical trials management to assist with developing case report forms and monitoring studies under an IND/IDE.¶

CMRP met with NIAMS leadership in March 2011 to discuss the support needed for the studies below. Since then, CMRP staff has had various conversations or meetings, including the following:

- For another IND Study, 05-AR-0014 (IND 100567), NIAMS staff provided copies of the data collection tools and sources for the CMRP clinical trials director to review. CMRP staff held a call with the study coordinator to discuss the data collection process used for this study. The plan is for the data collection process to be monitored and a study close-out visit to be performed in FY2012. The site staff may write a final study report or manuscript to be submitted to FDA. PI sent a memorandum to FDA in October 2010 stating that the protocol had been closed and that there were no plans for additional studies under IND; however, a new protocol is currently being developed by CMRP and the NIAMS team, which will be submitted to IRB and FDA under the existing IND 100567 upon completion.
- The regulatory affairs director met with NIAMS leadership in March 2011 to discuss requirements for developing a new protocol using IL-1 Trap in DIRA. The regulatory affairs director wrote a draft protocol document and forwarded this to NIAMS for review in April 2011.
- A regulatory associate III met with a protocol manager in April 2011 to review the IND files (specifically any regulatory communication and interactions with FDA concerning IND) and to evaluate next steps required for proper IND maintenance for IND Study, 03-AR-0298. The CMRP Regulatory Affairs Group will prepare the IND annual report for FDA submission.
- The regulatory affairs director met with NIAMS regarding Study 03-AR-0173, a natural history study that does not require IND regulatory support. They met in April 2011 to discuss the recent IRB stipulations received for this protocol. Following that meeting, the regulatory affairs director updated the protocol, three associated informed consent documents, and the IRB amendment memo to address those stipulations. The documents were returned to NIAMS that month.
- NIAMS submitted IND Study 10-AR-0182 to FDA in August 2010 to establish IND 109649. A regulatory associate III met with the NIAMS protocol coordinator in April 2011 to review documents related to IND 109649 and the associated protocols. This protocol was never initiated due to issues with drug availability, and was terminated with IRB that month. Following a subsequent June 2011 meeting with the NIAMS protocol coordinator, the regulatory associate and regulatory affairs director, working with the rest of the Regulatory Affairs Group staff, prepared a submission package requesting withdrawal of IND 109649 and delivered this to FDA in June 2011.

- The regulatory affairs director and a CMRP regulatory associate met with the NIAMS protocol coordinator in June 2011 to discuss the status of protocol T-AR-0081, "A Pilot Study of Anakinra in Behcet's Disease." The protocol was submitted to FDA under IND 11138, which also supports protocol 03-AR-0298. The NIAMS protocol coordinator responded to IRB stipulations and is expecting IRB approval for the protocol. The CMRP Regulatory Affairs Group will begin working on the IND annual report for submission to FDA. The Clinical Trials Management Team was asked to review the new set of draft case report forms.

CMRP has also created template monitoring language for the NIAMS support group to use when they start a new study and request CMRP monitoring of the trial. The clinical trials director also provided monitoring language to be considered for all studies that CMRP may monitor for the NIAMS team. In addition to the above, the clinical trials director provided NIAMS staff with a "notes to file" template and site SOP templates.

SUPPORT TO THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Overview

During the reporting period, the National Heart, Lung, and Blood Institute (NHLBI) requested support for the rapid deployment of clinical services for time-sensitive critical clinical research. Acquiring these services through CMRP will streamline protocol development time, provide flexibility for emerging/fluctuating needs, eliminate costly time delays, and ensure the success of the NHLBI clinical mission. These services complement those that CMRP already provides to other NIH clinical research programs.

With an initial emphasis on regulatory compliance, clinical trials management, protocol navigation, and data management, NHLBI support will include data/document collection and compilation for regulatory filing (pre-IND, IND, IDEs) with FDA and other regulatory authorities; technical review and report preparation; clinical site monitoring activities; final container packaging, purchasing, labeling, storage, distribution, and tracking of investigational products; storage of biological samples; implementation and maintenance of computer information systems; data management support; administrative coordination and general logistical support for regulatory activities; training; and other services as required.

In addition, NHLBI requested CMRP provide QA and QC oversight, including, but not limited to: (1) GCP monitoring of non-IND protocols; (2) IND and IDE clinical trial monitoring; (3) study monitor support by personnel with appropriate training and educational credentials; (4) data safety monitoring board formulation and management; (5) general QA for data acquisition; (6) ad hoc review formulation and management; (7) scientific pre-reviews on protocols prior to IRB submission; (8) logistic and secretarial support for IRB submissions: (9) interfacing between biostatistics staff and investigators; and (10) the development and maintenance of a database to track and tabulate adverse events and unanticipated adverse device effects.

To meet the request of this new initiative, CMRP hired one clinical project manager, two clinical research associate IIIs and one regulatory associate II. Recruitment activities are in process for a clinical research associate II to support the rest of the NHLBI team. Support staff will be located at the NIH Clinical Center in Bethesda, MD, and will perform the activities as assigned by their CMRP management team as requested through the NHLBI Office of Clinical Affairs.

The clinical trials director presented an overview of the services that will be offered during three NHLBI QA meetings during the month of June. In addition, a clinical research associate III created a case report form packet and the first site-initiation visit occurred in July 2011. The goal is to have one study activated by this new group and perhaps two monitoring visits scheduled by the end of the FY2011.

Prior to hiring the staff to support this YT, RCHSPP staff and the clinical trials director spoke with several PIs about their programmatic needs. CMRP contacted the first PI and informed him that the team is available for support when he begins his new IDE study. The clinical trials director also spoke with a PI who is also looking for regulatory support for a unique IDE. Another PI from this group plans to begin work on a new IND and spoke with the clinical trials director in March 2011 about assisting his team.

CMRP has started to meet with several PIs and their protocol navigators to review study files and draft tools that will be used by the team while monitoring NHLBI studies. The tools include a site visit log, an attendance log, and a delegation log. Staff members are creating monitoring and regulatory guidance documents/tools for NHLBI, including an executive summary that can be presented at a branch meeting. The team has also received an overview of the group's IRB tracking system and completed several CMRP training activities over the first few weeks of being hired.

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