CLINICAL GROUP

Barry L. Gause, M.D., Director

CLINICAL RESEARCH DIRECTORATE

Barry L. Gause, M.D., Clinical Director

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 required of GMP quality assurance operations.

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, regulatory, pharmacovigilance, protocol development and navigation, and operational support for clinical research. The directorate accomplishes its mission by providing comprehensive, dedicated clinical research support to major clinical programs within the National Institutes of Health (NIH), including but not limited to, 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 the Division of Cancer Epidemiology and Genetics (DCEG); within NIAID, including the Division of Clinical Research (DCR), the Division of Intramural Research (DIR), and the Division of AIDS (DAIDS), and the National Heart, Lung, and Blood Institute (NHLBI), and the National Institute for Arthritis and Musculoskeletal and Skin Diseases (NIAMS). 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 the Intramural Clinical Research Programs of NCI, NIAID, NHLBI, and NIAMS. CMRP staff continues to provide high-quality programmatic and clinical trials management, regulatory, pharmacovigilance, and protocol development/navigational 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) support to the Cancer Therapy Evaluation Program (CTEP); (2) support to the NCI Behavioral Research Branch (BRB) and the Cancer Information Service (CIS); (3) support to the NCI Community Cancer Centers Program (NCCCP); (4) support to the NCI Community Cancer Centers Program (NCCCP); (5) support to the American Recovery and Reinvestment Act of 2009 (ARRA) through the NCCCP initiative; (6) support to The Cancer Genome Atlas (TCGA); (7) support to the Coordinating Center for Clinical Trials (CCCT); (8) support to the NCI Center for Global Health (CGH); (9) nursing and clinical/protocol monitoring support to the Center for Cancer Research (CCR); (10) support to the CCR's Protocol Support Office; (11) the Regulatory Compliance and Human Subjects Protection Program (RCHSPP), providing support to NIAID; (12) support to the NIAID-Mali HIV Research Initiative; (13) 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; (14) the Clinical Consulting and Support Group; (15) support to the India/Mali initiative; (16) support to biostatistics; (17) support to the India initiatives; (18) support to the Uganda initiatives; (19) support to NIAID clinical teams; (20) support to Influenza initiatives; (21) support to the NIAID Institutional Review Board (IRB) Pilot Program; (22) support to the Protocol Navigation/ Protocol Development initiative; (23) support to the DC-Partnership for HIV/AIDS Progress (DC-PFAP); (24) support to NHLBI; and (25) support to 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 the growing portfolios of NCI, NIAID, NHLBI, and NIAMS, while offering innovative solutions to the clinical research programs within these four institutes.

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 11 years, assisting researchers in providing the highest-quality clinical research, 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, protocol development and navigation, and project/program management services to support more than 400 domestic and international studies involving cancer, avian flu/severe human influenza, HIV, HCV, TB, malaria, heart, lung, and blood diseases and conditions, parasitic diseases, rheumatic and inflammatory diseases, arthritis, and musculoskeletal and skin diseases.

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 trial networks across the world. In support of the NCI director, CMRP staff provided logistical and technical support for the Inaugural Global Health Conference; a two-day, high-profile conference featuring world leaders in cancer research, for the purpose of establishing NCI's scientific and public health priorities and building capacity for global cancer research.

In conjunction with supporting the goal of increasing international location capability, CMRP provided capacity-building contributions to multiple international networks, including the US-Latin American Cancer Research Network (LA CRN) and the influenza network in Mexico; CMRP is preparing for an upcoming capacity-building need in China.

In addition, CMRP provided expanding logistical and operational support to the NCI Center for Global Health, a collaborative initiative and partnership to develop and implement beneficial cancer research programs in Latin America; specifically, support was provided to the US-LA CRN Molecular Profiling Study, in which 25 of the 27 recruitment sites were activated and are enrolling participants. Under the leadership of the CMRP scientific program manager and clinical project manager, expert guidance was provided to US-LA CRN partners in meeting the project's scientific objectives. Staff led the coordination of the scientific agenda for the first meeting of virtual Data Coordinating and Analysis Teams (vDCAT) in Buenos Aires and Argentina, and the annual meeting in Guadalajara, Mexico, and provided agendas, minutes and meeting materials for the Steering Committee, the Basic Research and Advanced Technology Committee, Pathology Committee, Clinical Oncology and Breast Cancer Surgeons Committee, vDCAT Committee, and Epidemiology Committee. Two additional US-LA CRN committees were recently added: the Data Monitoring Committee and the Data Sharing and Publications Committee.

CMRP high-profile influenza support includes a research contract with the United BioSource Corporation, which was executed September 1, 2009, and renewed in 2012, to develop a standardized measure of influenza symptoms for defining the baseline severity of illness and providing uniform, valid measures of outcomes that are meaningful to patients in studies in interventions to treat or prevent influenza.

During the past year, CMRP provided clinical trials management and regulatory and logistics support in the expansion of NIAID's initiatives, including DCR's influenza, influenza-like-illness (ILI), and emerging infectious diseases (EID) initiatives. CMRP staff facilitated the conduct of International Network for Strategic Initiatives in Global HIV Trials (INSIGHT) clinical research studies through a research subcontract with the University of Minnesota. This network enrolls subjects with influenza, ILI, and/or other EID within southern hemisphere sites in Australia, South America, Asia, and Africa.

At the end of this contract year, CMRP began working to establish a new agreement with the University of Minnesota to facilitate the conduct of additional research in support of NIAID's influenza, ILI, and EID platforms. CMRP also provided support for the activation of 37 domestic and 16 international clinical trials sites; the enrollment of more than 430 subjects across one FLU-PRO and three IRC protocols; and the development of manuscripts for publication on the initial findings of the Acute Respiratory Infections Consortium (ARIC) protocol.

At the end of FY2012, CMRP was also requested to provide assistance to DAIDS, NIAID, with the establishment of a sustainable Chinese research network/consortium to perform tuberculosis studies. Support will include capacity building at several sites in

China to develop an effective and organized infrastructure of network facilities, central laboratories, specimen repositories, central coordinating and data management centers, and other network resources.

An additional end-of-contract-year request was received by the NCI Division of Cancer Epidemiology to initiate the development of a subcontract with the Cancer Institute of the Chinese Academy of Medical Sciences (CICAMS) to support an esophageal cancer precursor lesion genomics study in the northern Henan and southern Hebei provinces of China.

Domestic support included specific chemistry management support from CMRP staff within the Cancer Imaging Program to the SAIC-Frederick United States Pharmacopeia (USP)-level radiopharmacy in Frederick, MD, ensuring wider availability of investigational agents for exploratory and Phase I—III clinical trials. CMRP staff assisted in the development and fabrication of F18-labeled Fluoroestradiol within the radiopharmaceutical facility; six doses were supplied and administered to three subjects at the Clinical Center in Bethesda under CIP's IND during the reporting period.

CMRP was one of the first within the NIH community to offer and use electronic common technical document (eCTD) submissions for IND applications sent to the U.S. Food and Drug Administration (FDA). The eCTD method of submittal is an efficient and effective method that is preferred by the FDA. The Regulatory Affairs Group has fully implemented the eCTD format and now prepares and submits all new IND applications in this format. Of special significance is the Regulatory Affairs Group's effort to share this eCTD knowledge with staff in other NIH divisions and institutes. In December 2011 and January 2012, the regulatory affairs director and eCTD subject matter experts gave presentations to members of the regulatory teams in the Division of AIDS (DAIDS), NIAID, and the Cancer Therapy Evaluation Program, NCI, sharing information about the development of our eCTD program and lessons learned in the process, gave a demonstration of the eCTD software, and showed examples of finalized, FDA-accepted documents. In early March 2012, a meeting was hosted for the DAIDS regulatory group to provide them with additional, more directed eCTD training. Staff has also shared eCTD experiences and information with members of the Cancer Imaging Program and the Surgery Branch of NCI. All of these presentations were well received and greatly appreciated. Staff also developed and presented a poster describing our experience transitioning from paper INDs to an eCTD program at the Frederick National Laboratory (FNL) NCI Spring Research Festival on Fort Detrick.

The year 2012 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 the FNL and NIAID. The program continually looks at new and innovative ways to enhance its services.

Protocol navigation/protocol development programs were expanded and enhanced to support NCI, NIAID, and NHLBI clinical researchers; the programs took off rapidly and were met with tremendous interest from principal investigators. The programs have reduced the administrative and regulatory burden on investigators, so that they can now spend more time on science.

In support of The Cancer Imaging Archive (TCIA) within NCI's Cancer Imaging Program, CMRP developed state-of-the art image de-identification methodologies and tooling by partnering with standards organizations and professional societies. TCIA was highlighted on the whitehouse.gov federal government fact sheet as one of two NCI programs leading "the big data revolution."

CMRP staff plays a critical role in the Behavioral Research Program's (BRP) national surveillance efforts, observing and communicating cancer trends to the public, developing web-based smoking cessation interventions and tools, and research tools for the extramural research community, and providing program and scientific support to BRP research networks and collaborations. During the reporting period, CMRP staff members published and presented more than 90 papers and abstracts in peer-reviewed journals and leading scientific conferences in support of intramural research efforts ranging from tobacco use and other behavioral risk factors (e.g., physical inactivity, poor dietary behaviors, and sun safety) to genetic susceptibility and breast cancer screening practices, and measurement and methods related to cancer prevention and control research.

In a leadership role, CMRP staff contributed scientific content to the NCI Division of Cancer Control and Population Sciences' BRP surveillance efforts to examine trends in cancer communication and cancer prevention behaviors, and to seek better understanding of the mechanisms and theories of behavior change. CMRP led the development of the Health Information National Trends Survey 4 (HINTS 4) and managed the HINTS GEM website, which allows the extramural community to contribute and comment on HINTS 4 survey items.

In addition, CMRP played a central leadership role in developing, maintaining, and evaluating several NCI websites, including http://smokefree.gov; http://women.smokefree.gov; and http://meetings.smokefree.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.) website. This website, http://class.cancer.gov, offers an online tool for evaluating state laws that target obesogenic behaviors, such as physical activity and diet, in the school environment.

In support of The Cancer Genome Atlas Project (TCGA), CMRP staff assisted 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 United States each year. During the reporting period, TCGA actively augmented their network of TSSs to provide tumor specimens that are

collected retrospectively or prospectively. Up to 35 different tissue types need to be procured from the new TSS. By mid-August 2012, 32 proposals were received, and 164 Basic Ordering Agreements (BOA) and more than 30 Task Orders were negotiated.

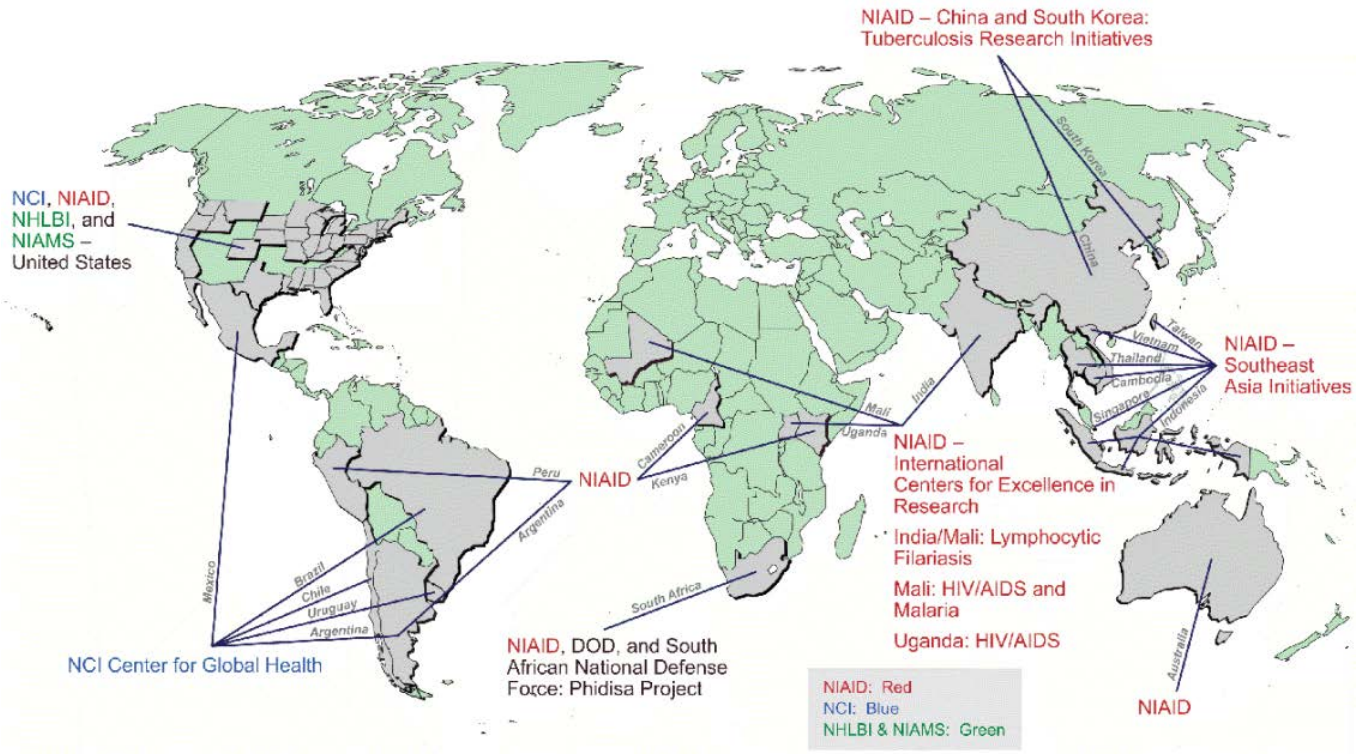
CMRP's support to government infrastructure included the Learning and Professional Development Group's leading the team responsible for implementing a leadership culture within NIAID's Division of Clinical Research. A leadership model based on the Baldrige leadership competencies is in progress, with a 360-degree feedback survey completed, aggregate data, as well as individual feedback data provided, and six leader-participants selected to work with leadership coaches to improve leadership areas of their choice. The second phase of this initiative, which includes DCR "emerging leaders," is under development.

CMRP infrastructure support included staff developing and presenting training materials on compliance with the Health Information Portability and Accountability Act (HIPAA) and the Health Information Technology for Economic and Clinical Health (HITECH) Act. Staff created a compliance guide to accompany the training and developed a fillable protected health information/personally identifiable information incident reporting form. Between June and August 2012, five HIPAA/HITECH compliance trainings were presented and one discussion forum was held by the CMRP Compliance Working Group; all CMRP staff attended the training by the end of the contract year.

Other CMRP projects included the launch of a new intranet site in response to the need for a central location for resources, including tools and links that can be easily accessed by all CMRP employees to assist them in their daily activities. The site will further enhance internal communications among CMRP staff members working at multiple Frederick and Bethesda/Rockville locations.

Additional efforts in which CMRP staff has continued to support and play an active role include the FNL community outreach programs, specifically participation in the Elementary Outreach Program and Take Your Child to Work Day.

CMRP World Map



Clinical trials management support to NCI, NIAID, NHLBI, and NIAMS comprise more than 400 studies in cancer, influenza, HIV, and other infectious diseases (such as HCV, TB, and malaria); heart, lung, and blood diseases and conditions; parasitic infections; and rheumatic and inflammatory diseases. CMRP provides medical and clinical research professionals to support numerous NIH Clinics.

Significant Achievements

During FY2012, CMRP reported the following significant achievements:

CMRP provides high-quality clinical trials/regulatory/pharmacovigilance/protocol navigation and development/program and project management in facilitating the conduct of more than 400 Phase I, II, and III domestic and international trials to investigate the prevention, diagnosis, and treatment of cancer, influenza, HIV, and other infectious diseases (such as HCV, TB, and malaria); heart, lung, and blood diseases and conditions; parasitic infections; and rheumatic and inflammatory diseases in support to NCI, NIAID, NHLBI, and NIAMS clinical research.

Molecular Imaging Program (MIP), NCI

The laboratory director submitted a paper for publication titled, "A Method for Statistical Image Quality Normalization." The paper was the culmination of a project involving the NIH Clinical Center and physicists from NIST and involved studying how patients could be scanned on different PET/CT scanners while attaining data of similar statistical image quality. This is important work needed to help harmonize data sets for multicenter clinical trials involving protocols requiring PET/CT scans of subjects under study.

One protocol of interest has started accruing patients; "Phase I Trial of Z-Endoxifen in Adults with Refractory Hormone Receptor-Positive Breast Cancer, Desmoid Tumors, Gynecologic Tumors, or Other Hormone Receptor-Positive Solid Tumors," uses F18-labeled Fluoroestradiol (F18 FES), which is fabricated at the SAIC-Frederick Radiopharmacy and was developed with the help of SAIC-Frederick radiochemists in a joint collaboration between the Applied/Developmental Research Directorate (ADRD) and CMRP-CIP staff. To date, three patients have been scanned with this new agent, between December 2011 and May 2012.

A PET physicist furthered work on multicenter imaging harmonization by guiding QA tests on the NCI/Molecular Imaging Clinic (MIC)/PET/CT scanner and one at the University of Wisconsin. This was motivated by a multicenter clinical trial in which the NCI/MIC is participating. The goal of the multicenter clinical trial is to use sodium fluoride (F18 NaF) as an agent to study metastatic prostate cancer across multiple cancer centers. This work follows on the heels of the image data harmonization work which involved the NIH Clinical Center and physicists from NIST. The project involved studying how patients could be scanned on different PET/CT scanners while attaining data of similar statistical image quality. An oral presentation of this work with University of Wisconsin will be presented at the RSNA meeting in November 2012.

Protocol Support Office (PSO), NCI

CMRP staff played key roles in processing clinical protocols for submission to various regulatory agencies, such as the IRB, the FDA, the Office of Biotechnology Activities, and the Institutional Biosafety Committee (IBC). The team assisted clinical investigators with the review of 20 new protocols and informed consent documents, 50 protocol amendments, and 10 OBA/IBC submissions, and was involved in 10 protocol navigation projects. Currently, the team provides support for approximately 40 active INDs, one active IDE, and one active drug master file (DMF). Seven new initial IND applications were submitted to the FDA during this reporting year. As part of the ongoing maintenance for these new and existing applications, staff developed and submitted approximately 80 IND, IDE, and DMF serial submissions to the FDA.

Clinical Core (Transplantation), NCI

The Experimental Transplant and Immunology Branch (ETIB) is dedicated to coordinating efforts for basic, preclinical, and clinical investigations in the area of transplantation science. CMRP staff members supporting ETIB serve as the associate investigators on 11 protocols, 7 of which are actively recruiting and performing transplants on 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.

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 the 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 this fiscal year, CMRP also facilitated, coordinated, and managed all unrelated donor product/research activity at NIH. CMRP staff assisted in the development of standards and processes to support this initiative, and continues to perform searches and advise on donor selection for all unrelated donor products and patients.

Developmental Therapeutics Clinic (DTC)/Phase 0, NCI

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), and a randomized phase II trial of Cediranib/Sunitinib, which are some of the most promising regimens in a rare form of sarcoma (alveolar soft-part sarcoma), and a multi-histology Phase II trial with R788.

Urologic Oncology Branch (UOB), NCI

During the reporting period, CMRP staff efficiently recruited and enrolled an additional 261 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.

Vaccine Branch, NCI

CMRP staff has 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 the IRB.

HIV/AIDS Malignancy Branch (HAMB), NCI

The CMRP patient care coordinator is responsible for providing administrative support to HAMB. This staff member currently assists three investigators and two research nurses with approximately 200 patients who are in enrolled on seven active protocols. In addition, the patient care coordinator works with the team on the recruitment process to increase patient referrals for new protocols.

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

During this fiscal year, both psychometricians participated in the collaborative development of research posters that were accepted for the 2012 Children's Tumor Foundation held in New Orleans, LA, and the 12th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer held in Williamsburg, VA. One of the psychometricians presented a poster at the POB Research Round Up.

Division of Cancer Epidemiology and Genetics (DCEG) – Tumor Heterogeneity, NCI

During the reporting period, the physician II published three peer-reviewed articles in scientific journals: (1) "Correlation of LINE-1 Methylation Levels in Patient-Matched Buffy Coat, Serum, Buccal Cell, and Bladder Tumor Tissue DNA Samples," published in *Cancer Epidemiology, Biomarkers and Prevention* July 2012; (2) "Von Hippel-Lindau (VHL) Inactivation in Sporadic Clear Cell Renal Cancer: Associations with Germline VHL Polymorphisms and Etiologic Risk Factors," published in *PLoS Genetics* October 2011; and (3) "Analysis of the Distribution and Temporal Trends of Grade and Stage in Urothelial Bladder Cancer in Northern New England from 1994 to 2004," published in *International Scholarly Research Network Pathology* in January 2012.

The Cancer Genome Atlas (TCGA), NCI

In support of TCGA's effort to actively augment their network of tissues source sites (TSS) to provide tumor specimens that are collected retrospectively and prospectively by August 2012, 31 proposals were received and evaluated, and 24 basic ordering agreements (BOAs) awarded, 15 with follow-on Task Orders that allow for specimens to be shipped (only after sites have met all other technical requirements required prior to shipment).

NCI Community Cancer Centers Program (NCCCP)

CMRP programmatic support to NCCCP included ongoing management of multiple sets of individual research subcontracts that comprise the NCCCP effort. Dedicated CMRP staff members manage the relationships between the awarded organizations, SAIC-Frederick, and NCI to support project objectives and activities. Through June 2012 of this reporting period, there were four sets of research subcontracts (total of 45 subcontracts), each with a defined scope of work and specific deliverables.

In support of the NCCCP period of performance extension, CMRP staff supported the acquisition and procurement activities for the limited competition among 24 subcontractors. The RFP was issued in February 2012, and 23 subcontractors competed for the additional funding. In July 2012, 18 subcontracts supporting 21 community hospitals were awarded. For the 24-month extension period (12 months covered by remaining ARRA funds and 12 months to be covered by new FY2013 appropriated funds), a smaller number of more strategic and focused deliverables are included in the research subcontracts. Starting in July 2012, CMRP staff managed two sets of subcontracts (total of 28 subcontracts).

During the reporting period, staff continued to assist with the formal evaluation of the NCCCP pilot network. This assistance included collaborating with the NCI contractor, RTI International, Inc., to finalize official report documents, including a cost study, patient surveys and focus groups, data outcomes, and clinical trials accrual analyses. CMRP staff worked with NCI advisers to review report drafts, provide editorial assistance, and ensure content accuracy. This involved coordinating feedback from the NCI Program Advisory Committee (NPAC), the Evaluation Oversight Committee, and the CMRP team through several rounds of reviews. CMRP consolidated comments and provided comprehensive revision requests to RTI International, Inc. Additionally, CMRP de-identified NCCCP site names in the final drafts of the integrated report, economic evaluation, and document appendices. Staff also assisted with the creation of summary documents to share with the NCCCP network and external stakeholders and partners.

CMRP directed, coordinated, and managed efficient data collection, advanced analytics, data storage, and data sharing across all programmatic components of NCCCP. This ensured the comprehensive collection and analysis of high-quality data. Staff developed new tools and question sets, reviewed and analyzed data to measure and document programmatic progress, prepared data presentations, and shared results with NCI and NCCCP stakeholders.

Coordinating Center for Clinical Trials (CCCT), NCI

Between 2008 and 2012, the Scientific Steering Committee (SSC) program increased from six SSCs and 140 consulting agreements to the current 16 SSCs and 468 vendor agreements. CMRP continued to monitor the effectiveness of the newly-implemented vendor agreement process. The efficiencies gained with the new process continue, with an average turnaround time of approximately three days. CMRP's support of the SSCs includes project management, program analysis, and management of the massive and growing vendor agreement effort. NCI anticipates adding an additional SSC (Rare Tumor Steering Committee) during this fiscal year.

New CCCT project management support this year has included an expanded role for the CCCT clinical project manager I, including: (1) Designing and facilitating (hosting) webinars within the CCCT for NCI Task Forces and Working Groups. This successful endeavor has seen widened utilization within the program and is being considered for monthly SSC meetings. The pilot SSC meeting webinar went very well; (2) Becoming the responsible person for all CCCT website updates, which includes updating information related to all 16 SSCs, postings of non-SSC related materials, Section 508 compliance issues for the website (reported at 95 percent compliance), and gaining full permission to update or remove data posted on the site without having to go through IT; (3) Creating two Clinical Trials Planning Meeting (CTPM) templates for CCCT, including a CTPM Proposal template and an Executive Summary template; (4) Joining the CTPM Administrative Team wherein project management support is provided in order to ensure effective CTPM and SSC face-to-face meetings. This has included the creation of timelines and effective communication processes with other teams (outside of CCCT).

Additional new CMRP support to the SSCs was provided by the clinical project manager II's facilitation of a mock protocol review and BIQSFP Evaluation for the NCI Patient Advocates Steering Committee workshop. The support included designing a complete mock protocol/study and application for CCCT mock reviewers to review and present at the workshop. CCCT staff was the "Steering Committee" and the "Reviewers." The review included a script to follow as the review process was presented to workshop participants; feedback and participation was excellent.

Biomarker, Imaging, and Quality-of-Life Studies Funding Program (BIQSFP)

Ten new research subcontracts have been completed this fiscal year for BIQSFP-funded studies, one of which is pending, with anticipated completion by the end of this fiscal year. SAIC-Frederick Research Subcontracts and CMRP have provided support to the management of three existing BIQSFP research subcontracts.

CMRP staff facilitated and supported the April 2012 revision of the BIQSFP announcement, including updating and clarifying the announcement and the requisite revisions to the official BIQSFP website, which has received approximately 5,000 visitors to date.

Cancer Imaging Program (CIP), NCI

More than 20 procurements (including research subcontracts and consulting agreements) have been executed to meet the needs of the CIP principals. Research subcontracts have been established with major medical institutions, experts in the field of cancer imaging, and commercial companies that are assisting in the analysis and development of CIP's portfolio of radiopharmaceuticals.

CIP's chemistry program primarily supports the goals of the Imaging Drug Group, providing development of new imaging agents and follow-up testing of currently administered agents. This groundbreaking work may lead to increased availability of types of agents for clinical trials. Maturation of this effort is documented by the fact that the original SAIC-Frederick space designated for this work was turned into a United States Pharmacopeia (USP)-level radiopharmacy capable of delivering clinical-grade human doses for use in preclinical and clinical evaluation efforts by a certified nuclear pharmacist. Currently, the SAIC-Frederick Radiopharmacy has supplied six doses of FES for administration to three subjects at the Clinical Center in Bethesda under CIP's IND.

CMRP personnel were involved with negotiations with the three major suppliers of cyclotron-produced isotopes and radiopharmaceuticals, for implementing fluoro-L-thymidine (FLT) tracer synthesis and applying for a drug master file (DMF) so the tracer could be supplied to NCI trials. The combined number of FLT sites available for supplying NCI clinical trials reached a maximum of 23 sites in 2012.

There are currently seven CIP-sponsored INDs and one NDA managed and supported by the Regulatory Affairs staff. Multiple protocols (the majority of them Phase II trials, but running the gamut from Phase 0 to III with differing regulatory requirements) are being conducted under each of the CIP-sponsored INDs. Twelve trials were active and enrolling patients during this period. Many of the trials have inherent regulatory complexities due to the involvement of multiple investigators, sites, local IRBs, and contract organizations located in the United States, Canada, and other foreign sites. CIP Regulatory has issued approximately 15 letters of authorization allowing independent researchers to cross-reference the materials in CIP INDs for their trials during this period.

CMRP staff completed modifications and evaluation of existing adverse events (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.

CMRP has developed state-of-the art image de-identification methodologies and tooling by partnering with standards organizations and professional societies. CMRP has tightly managed The Cancer Imaging Archive (TCIA) contracting team to develop detailed SOPs, 100+ pages of wiki documentation, and more than a terabyte of highly curated de-identified data.

TCIA was highlighted on the whitehouse.gov federal government fact sheet as one of two NCI programs leading "the big data revolution."

The TCIA initiative, with an extraordinarily low operational budget to NCI, has opened new opportunities to join radiology, genomics, and pathology. CMRP has provided IRB support to, and has contract agreements in place with, nine institutions to provide imaging data match with TCGA cases.

Leveraging TCIA, CMRP has helped all of the funded institutions within the NCI Quantitative Imaging Network (QIN) load de-identified data onto a common platform and developed new integration strategies to incorporate tooling in place at the institutions. CMRP has provided web-based technology support to facilitate management workflow and is an active participant in the QIN informatics working group.

Cancer Diagnosis Program (CDP), NCI

As of July 2012, 20 research subcontracts were awarded to 14 different institutions for a total award amount in excess of $2.1 million.

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

In support of intramural research efforts ranging from tobacco use and other behavioral risk factors (e.g., physical inactivity, poor dietary behaviors, and sun safety) to genetic susceptibility and breast cancer screening practices, and measurement and methods related to cancer prevention and control research, CMRP staff members have published and presented more than 90 papers and abstracts in peer-reviewed journals and leading scientific conferences.

In a leadership role, CMRP staff contributed scientific content to NCI's Division of Cancer Control and Population Sciences' Behavioral Research Program surveillance efforts to examine trends in cancer communication and cancer prevention behaviors, and to seek better understanding of the mechanisms and theories of behavior change. CMRP led the development of the Health Information National Trends Survey 4 (HINTS 4) and managed the HINTS Grid-Enabled Measures (GEM) website, which allows the extramural community to contribute and comment on HINTS 4 survey items.

CMRP provided a central leadership role in developing, maintaining, and evaluating several NCI websites, 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.

Health Behaviors Research Branch (HBRB), NCI

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's C.L.A.S.S. website, http://class.cancer.gov. This website 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, state policy profiles, data updates, development of policy briefs, fact sheet updates, and the inclusion of new policy areas on the website and database.

Basic Biobehavioral and Psychology Sciences Branch (BBPSB), NCI

CMRP staff supported and participated in a fourth Basic Biobehavioral and Psychology Sciences Research Branch (BBPSB) meeting, "Neural Mechanisms that Underlie Biobehavioral Pathways in Cancer," in Houston, Texas, in mid-October 2011. The medical affairs scientist, working with the BBPSB chief, strategically planned the pathway for future pilot studies and scientific programming proposals. The outcome of this meeting was the selection of two specific scientific projects to accomplish network objectives. During the reporting period, two research subcontracts were established, and the projects are ongoing.

Tobacco Control Research Branch (TCRB), NCI

The clinical project manager I continues to provide research and administrative support to research networks supported by the NCI/Tobacco Control Research Branch (TCRB), including the Tobacco-Research Network on Disparities (TReND) and the Tobacco Harm Reduction Network (THRN), and served as the technical lead and meeting liaison for the Global Smokeless Tobacco pre-conference workshop and hemi-plenary session at the World Conference on Tobacco or Health (WCTOH) in Singapore. The clinical project manager I coordinated the development of TReND's final special journal issue on Global Tobacco Inequalities and coordinated initial efforts on another special issue examining the role of smoking imagery found in movies and other entertainment media in tobacco-related health disparities worldwide. In addition, the clinical project manager I maintains the THRN website and serves as the primary communications liaison between NCI, CDC, and external collaborators from the academic and private sectors.

Health Communication and Informatics Research Branch (HCIRB), NCI

The behavioral scientist serves on an expert panel for the Behavioral Research Program 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. Since September 2011, the behavioral scientist has led an effort to identify, prioritize, and upload measures of health behavior theory constructs relevant to cancer behavior into the Grid-Enabled Measures (GEM) website. 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.

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

A major contribution of the behavioral scientist has been as project lead of the Science of Team Science Toolkit, an interactive website that supports information exchange and knowledge sharing to promote the growth and unification of the interdisciplinary field called the "Science of Team Science" (SciTS). In this capacity, the behavioral scientist works with a multidisciplinary team comprised of computer programmers, social and clinical psychologists, and experts in communications, education, and informatics, to develop the structure and content of the Toolkit, solicit public contributions to the Toolkit, and promote the Toolkit through internal NIH meetings of interested groups, national and international conferences, listservs, websites, and social media.

The behavioral scientist is co-lead on an important theory-development study to build the evidence based on how oncologists' psychological traits influence their decisions to refer patients to cancer clinical trials. This is a priority topic area for the Behavioral Research Program and NCI, as there continues to be severe shortages of patients participating in cancer clinical trials, which delays production of important research findings related to cancer therapeutics. Physician psychological traits are hypothesized to be one important contributor to these shortages.

During the reporting period, the behavioral scientist assembled a team of experts from multiple programs and divisions with NCI to serve as the research team for this study. In addition, the behavioral scientist has secured financial support for this work from NCI. Over the last year, with the leadership of the behavioral scientist, this team has developed a two-phase study design involving a national panel survey of oncologists, followed by a survey of oncologists participating in an NCI-supported program to enhance clinical trials referrals, and is currently developing the survey instruments and necessary internal partnerships at NCI to support the second phase of this research.

United States-Latin American Cancer Research Network (US-LA CRN), Center for Global Health (CGH), NCI

In addition to presenting the project's achievements at the third US-LA CRN Annual Meeting and leading the coordination of the scientific agenda for the first meeting of virtual Data Coordinating and Analysis Teams (vDCAT) in Buenos Aires, Argentina, and the Annual Meetings in Guadalajara, Mexico, and Buenos Aires, Argentina, the scientific program manager provided high-level support to the US-LA CRN committees, including the preparation of agendas, minutes, and meeting materials for the Steering Committee, the Basic Research and Advanced Technology Committee, Pathology Committee, Clinical Oncology and Breast Cancer Surgeons Committee, vDCAT Committee, and Epidemiology Committee. With the scientific program manager taking the lead, there were two additions to the list of US–LA CRN Committees: Data Monitoring Committee and Data Sharing and Publications Committee.

The scientific program manager coordinated the development of the first and second interim analysis, oversaw the activities, and assigned priorities to the clinical program manager for operations (clinical project manager II), the senior program coordinator, and the secretary III.

The CMRP scientific program manager and the clinical project manager for operations continued to provide expert support in the refinement of the study protocol, revision of an extensive epidemiology questionnaire, and development of the corresponding manual and other clinically relevant documents, as well as associated revisions of a detailed Study Monitoring Plan and accompanying Site Monitoring Guidelines. CMRP continues to contribute to the revision of the manual of procedures. Both managers provide extensive capacity-building support to sites and investigators.

An SAIC-Frederick biobanking expert and an on-site senior adviser conducted site visits to biobanks and hospitals in Argentina, Chile, Uruguay, Mexico, and Brazil to provide guidance on biospecimen collection, processing, transport, and storage, as well as to assess operations at the biorepositories.

CMRP staff was instrumental in the planning and coordinating of a major meeting in support of the NCI director and NCI Center for Global Health director. The NCI Center for Global Health Inaugural Meeting, Setting Priorities for Global Cancer Research, included approximately 200 researchers, who discussed research priorities to reduce the worldwide burden of disease that cancer imposes.

Regulatory Compliance and Human Subjects Protection Program (RCHSPP) Regulatory Affairs, NIAID

In December 2011 and January 2012, the regulatory affairs director and eCTD subject matter experts gave presentations to members of the regulatory teams in the Division of AIDS (DAIDS), NIAID, and the Cancer Therapy Evaluation Program, NCI, sharing information about the development of our eCTD program, lessons learned in the process, giving a demonstration of the eCTD software, and showing examples of finalized, FDA-accepted documents. In early March 2012, a meeting was hosted for the DAIDS regulatory group to provide them with additional, more directed eCTD training. Staff has also shared eCTD experiences and

information with members of the Cancer Imaging Program and the Surgery Branch of NCI. All of these presentations were well received and greatly appreciated. Staff also developed and presented a poster regarding our experience transitioning from paper INDs to an eCTD program at the FNL NCI Spring Research Festival on Fort Detrick.

RCHSPP Clinical Trials Management (CTM)

The CTM team is involved with the management and/or monitoring of approximately 165 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/IDE. During FY2012, the team conducted approximately 58 study initiation visits, 169 interim monitoring visits, two audit visits, and 29 study close-out visits. In addition, the team attended three other types of visits this year at clinical sites. 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 CTM team also conducted international site-initiation visits in Thailand, China, Argentina, Mexico City, Uganda, Cameroon, and Mali, and conducted seven study-site audits in hospitals in Korea.

RCHSPP Clinical Safety Office (CSO)

The medical monitors and clinical safety associates reviewed 118 clinical research protocols over the contract year, consisting of 23 principal investigator (PI) reviews, 82 amendment reviews, and 13 site-specific informed consent form (ICF) reviews, along with the associated ICDs. 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.

Standardized AE data reporting tables pulled from the Clinical Research Information Management System of NIAID (CRIMSON) database for use during DSMB reviews, were revised to improve the efficiency and accuracy of the data submitted to the DSMB for review. A total of 8 newly revised data table templates were developed and include: (1) Enrollment Summary and two supporting tables; (2) Frequency of Adverse Events by Cohort and Severity; (3) Frequency of Adverse Events by Cohort and Causality; (4) Frequency of Reactogenicity Adverse Events by Cohort and Severity; (5) Line Listing of Adverse Events by Cohort and Subject; and (6) Line Listing of Serious Adverse Events by Cohort and Subject. These tables were used by the DSMB in the July 2012 face-to-face meeting. The CSO staff was trained and given access to CRIMSON-generated data tables. These tables were beta tested during this reporting period. A new guidance document on the procedures to generate these tables has been provided to study coordinators and PIs. The implementation of these tables has enhanced the ability of reviewers (PIs, oversight committees, medical monitors) to analyze AE data that are entered into CRIMSON. These tables are also being reprogrammed, 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.

In April 2011, the Code of Federal Regulation Title 21, section 312, was revised to expand and clarify the responsibilities of an IND Sponsor for overseeing safety aspects of clinical research trials. These new oversight responsibilities took effect in September 2011, and in response, the Clinical Safety Office (CSO), in consultation with various internal and external stakeholders, developed a Safety Review Communications Plan (SRCP). The SRCP is an internal communications document between the PI and the IND sponsor CSO, which delineates the safety oversight responsibilities of the PI, the CSO, and other stakeholders. The purpose of the SRCP is to identify all safety-related responsibilities and communications pathways in a single document, and aims to ensure that these responsibilities are being conducted in a timely and thorough manner to protect research participants and comply with regulatory reporting requirements. In some instances, the PI will be responsible for conducting the periodic safety assessments under a Transfer of Regulatory Obligations (TORO) agreement, drafted by the CSO and signed by the RCHSPB branch chief and the PI.

The CSO has developed a comprehensive template for the safety section of IND protocols, which included changes required by new IND regulations and the need to identify and report UPs. Following initial introduction and approval in September 2011, the "Safety Template Language for INDs Held by RCHSPB V 7.0," for use in drafting and amending protocols was linked from the NIAID IRB website in February 2012 after extensive review and revision. This template includes all NIH and NIAID IRB required safety reporting language and is available to anyone drafting a protocol with access to the NIAID IRB site.

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

The Protocol Navigation/Protocol Development Program (PN/PDP) continues to spread the word on the utility of this program. A manuscript is in revision titled "Protocol Development Program: A Novel Approach to Overcoming Barriers to Clinical Research Trials," and once revised, will be submitted to *Contemporary Clinical Trials* before the end of this fiscal year. A poster abstract entitled "A Medical Writer's Role in the New Protocol Development Program at the National Institute of Allergy and Infectious Diseases" has been accepted for presentation at the 2012 AMWA Annual Conference. Two other abstracts for posters are pending approval: one

to the NIH Research Festival in October 2012, entitled "Customer Feedback Suggests Satisfaction with NIAID's New Protocol Development Program," and another entitled "New Program Shows Promise for Improving the Path to Clinical Research" to the Public Responsibility in Medicine and Research (PRIM&R) for the 2012 Advancing Ethical Research conference in December 2012.

PN/PDP received a request from the coordinator, *PhD Student Summer Program in Clinical and Translational Research Coordinator, Sabbatical in Clinical Research Management Office of Clinical Research Training and Medical Education, Clinical Center (CC) National Institutes of Health* to present interactive sessions on "Anatomy of IND and Natural History Protocols" and "Logistics in Protocol Implementation." This is an introductory program for postdoctoral students (selected by the NIH) with no prior experience in clinical research or human subjects protocols. This request provides an opportunity for the PN/PDP to advertise and demonstrate the resources available within NIAID to future PIs.

RCHSPP Learning and Professional Development (L&PD)

The CMRP L&PD Group collaborated with the IT Group to implement TrackWise® Training Manager, a program that will enhance CMRP training compliance efforts and will allow employees to monitor their own training record. This implementation included role-specific curriculum identification, back population of critical trainings and a 100 percent audit of back-populated information.

RCHSPP Document Control (DC)

During the reporting period, the project to improve the protocol review process by utilizing TrackWise® and Livelink® was completed. This new system allows for better control of the protocol review documents, as it offers an audit trail and other features that allow DC to control the read and write capabilities of individuals based on their roles. DC coordinated the development of specific training guides and coordinated the training for CTM, CSO, Regulatory, DC, and IT groups. DC also provided oversight of the migration of all archived reviews into the new system, and all three staff members of DC are administrators for the LiveLink® system. On March 15, 2012, the review process was officially launched, and all reviews are now processed through the new system.

RCHSPP Information Technology (IT)

The RCHSPP IT group, in conjunction with the Learning and Professional Development Group (L&PD), was able to successfully develop and deploy TrackWise® Training Manager. This significant component of TrackWise® tracks all training records for every program employee, from noncurricular group training to individualized curricular training. Following the release, several thousand training records were back-populated by the L&PD with assistance from designated administrative staff. As a quality control mechanism, members of the IT group reviewed the corresponding TrackWise® records for accuracy and provided the L&PD group with reports that could be used to further verify the data. More than 6,000 noncurricular and 1,000 curricular records have been entered and managed through the system.

The integration of the OpenText® Enterprise Content Management suite, also known as Livelink®, and TrackWise® to manage content for clinical protocols undergoing an initial or amendment review by the RCHSPP was completed. The system is being successfully used by program staff.

Rakai Project, NIAID

CMRP staff members 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 the 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.

Division of Intramural Research's International Centers for Excellence in Research (ICER) Core, NIAID

CMRP provided good laboratory practice (GLP) research support service to NIAID's International Centers for Excellence in Research (ICER) initiative in Mali. 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.

CMRP staff continued CAP accreditation of the Mali ICER Clinical Laboratory; supported the path to ISO 15189 accreditation for the SEREFO Laboratory at the Mali ICER; assisted with the development of the NIAID enterprise electronic biospecimen management system (BSI-II) to international and domestic DIR laboratories; and provided quality management of biorepositories.

IL-15 Project, NIAID

CMRP continued to provide support to NIAID's LIR for the recombinant human interleukin-15 (rhIL-15) project, working in collaboration with NCI's DCTD and CCR-Metabolism Branch. CMRP's Administrative Support Group continued to provide project management support in concert with the SAIC-Frederick Research Subcontracts Department and Clinical Services Program (CSP) to oversee coordination with a subcontractor

(Biological Consulting Group), and Avanza Laboratories (formerly Bridge Laboratories) to perform pharmacodynamic and pharmacokinetic studies. In September 2011, the CMRP assisted NIAID with the preparation and solicitation of a research subcontract awarded to Avanza to perform a second ARM study to examine the immunologic and virologic effects of rhIL-15 when administered via continuous IV infusion (CIV) to SIV-infected Rhesus monkeys. Based on the information received from these two studies, CMRP, Research Subcontracts, and CSP assisted with a request from NIAID to perform a third ARM study similar to the second ARM study to determine the effects of multiple cycles of treatment using IL-15 and antiretrovirals.

Southeast Asia Initiative, NIAID

Through a new Yellow Task, NIAID DCR asked SAIC-Frederick to create and release a request for proposal in December 2011 for a subcontractor to manage the Thailand and Vietnam protocols and sites in the Southeast Asia Clinical Research Network. This new research subcontract supports a new protocol to identify and enroll patients with sepsis and fevers of unidentified etiology as well as provide coordination for a redesigned Network Operations Center, and will initially support three sites in Thailand and three sites in Vietnam; additional sites will be added as directed by the expansion into additional protocols. In the past year, CMRP staff members spent several weeks in Southeast Asia supporting NIAID. Activities both abroad and domestically included: (1) developing, releasing, and awarding an RFP for research support; (2) assisting with transitioning and mentoring new network personnel; (3) developing tools and procedures for project oversight; and (4) providing expertise on establishing working partnerships in the region.

Phidisa Project, NIAID

A major focus for the Phidisa Project during 2012 was implementing the five-year strategic plan developed in 2011 collaboratively with the South African National Defense Force (SANDF), South African Military Health Service (SAMHS), U.S. DoD, and U.S. NIAID-DCR and SAIC-Frederick colleagues. The CMRP director and clinical trials director participated in a Phidisa Program Workshop held in December 2011. At the workshop, the CMRP director facilitated a session for the Laboratory Working Group (LWG) co-chairs to develop and refine operational plans for transitioning laboratory operations to the SAMHS. The director drafted the final presentation delivered to the Executive Committee and meeting participants by one of the laboratory working group co-chairs.

Office of Cyber Infrastructure and Computational Biology (OCICB), NIAID

CMRP supported the integration of the DataFax® clinical data system into several NIAID clinical research sites sponsored by the DIR, DCR, and the Office of Cyber Infrastructure and Computational Biology (OCICB) in Uganda, Tanzania, India, Mali, South Korea, Cambodia, China, Cameroon, and Thailand. The clinical project manager I traveled to NIH in Bethesda, MD, and completed training for NIAID and CMRP clinical trial personnel. The training covered issues pertinent to DataFax® case report form development and the use of the DataFax® system for monitoring DIR clinical protocols. The clinical project manager was instrumental in organizing the first monthly DataFax® users group meeting for NIH data management staff, CMRP/CTM study monitors, and the DataFax® project manager.

Office of Planning and Operations Support (OPOS)

During the current reporting period, the clinical project manager II spearheaded a collaboration with the Office of Cyber Infrastructure and Computational Biology (OCICB) Business Intelligence (BI) Group to enhance the integration of strategic planning within the DCR through automated reporting of operational metrics related to the strategic objectives of the Office of Planning and Operational Support (OPOS). Key accomplishments include: (1) formulation of the Project Oversight Team and Project Work Group; (2) draft of project charter; (3) identification of core functions, including a visual representation of key metrics, automated standardized operational reporting process, tools and templates for the input of data, and workflow procedure for data input and integration; and (4) development of a beta dashboard to view key metrics.

OPOS L&PD

The CMRP Learning and Professional Development (L&PD) group participated extensively in the development and review of Data Safety Monitoring Board (DSMB) Computer-Based Training (CBT), which is currently under review and revision. The clinical training manager has also contributed to a poster and article on this topic, both under development, and has been accepted to present a platform presentation on this topic.

The CMRP L&PD group is leading the team responsible for implementing a leadership culture within DCR. A leadership model, based on the Baldrige leadership competencies, is in progress, with a 360-degree feedback survey completed, aggregate data, as well as individual feedback data provided, and six leader-participants selected to work with leadership coaches to improve leadership areas of their choice. The second phase of this initiative, which includes DCR "emerging leaders," is under development.

Intramural Clinical Operations Branch (ICMOB), Laboratory of Immunoregulation (LIR)

During the reporting period, the Recruitment Office for the OP8 Clinic transitioned from its on-site NIH clinic location to an off-site office in Rhode Island. With the full support of the NIAID clinical director, the project began as a pilot program in order to retain the patient recruiter for the OP8 clinic. Working in collaboration with NIAID

clinic management, the patient recruiter was able to fulfill all aspects of the recruiting activities and has been able to provide enhanced recruitment activities. The attention to detail and outstanding coordination has led this pilot program to evolve into a permanent off-site program.

Influenza Support to the Division of Clinical Research, NIAID

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

- IRC 001: Anti-influenza Plasma Collection Study. A plasma collection study that enrolls healthy volunteers who have had the flu or received the flu vaccine and are found to have high levels of anti-influenza antibodies in their blood. This protocol was launched in September 2009. During the reporting period, six sites additional sites were activated (for a total of 12 sites), 336 subjects were enrolled (total to date, 714 subjects), and 651 units of human plasma with high-titer H1N1 antibody collected (total to date 1,141 units of plasma). In addition, five submissions have been made to FDA under an IND.
- IRC 001B: Anti-influenza Plasma Collection at a Community Blood Bank. In an effort to increase plasma collection, and to lower the costs of plasma units to the U.S. government, a pilot study has been established to collect plasma from a community blood bank. Collaborating with Mississippi Valley Community Blood Center (MVRBC) in Iowa, this study will test plasma units collected as part of the routine collection at MVRBC for high-titer anti-influenza antibodies. This study was established in June 2012.
- IRC 002: H1N1 Plasma Therapy Study. This 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. During the reporting period, seven sites were activated (for a total of 19 sites), and six subjects were enrolled (for a total of 13 subjects). There was also one DSMB meeting and five submissions to FDA under an IND.
- IRC 003: Combination Therapy Study. This 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. The IRC003 protocol was launched in January 2011 in the United States followed by Australia in August 2011, Mexico in February 2012, Thailand in June 2012, and Argentina in July 2012. There are currently 23 domestic sites and 19 international participating in the study. In the reporting period, 17 sites were activated (for a total of 34 sites), and 15 subjects were enrolled (for a total of 17). There were 10 submissions to FDA under an IND.
- IRC 004: Tamiflu (Oseltamivir) Versus Placebo. This study seeks to understand whether subjects on Tamiflu show decreases in the amount of virus detected in the nose or throat, and to understand whether 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. The IRC 004 protocol was launched in January 2012 in the United States followed by Thailand in June 2012, and Argentina in July 2012. There are currently 20 domestic sites and two international sites participating in the study. During this reporting period, 22 sites were activated, and 16 subjects were enrolled.

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 (ARIC) 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. Over 800 subjects are enrolled to date. During this contract period, manuscripts were developed for publication of the initial findings.

An additional symptoms scale study, the Influenza Patient Reported Outcome Questionnaire Development Project (FLU-PRO), is being conducted in the United States and Mexico to develop a single, standardized instrument of patient influenza symptoms for use in clinical studies involving adult and pediatric patients. Under a contract established with United BioSource Corporation (UBC) and a partnership between NIAID and the U.S. Department of Defense (DoD) Uniformed Services University, the FLU-PRO study began enrolling subjects in the U.S. during the 2010 flu season. A research subcontract was established with UBC to provide services for two phases of this protocol: (1) performance of one-on-one elicitation interviews with subjects; and (2) analysis of interviews to develop the draft FLU-PRO instrument, resulting in a detailed report of the findings formatted for submission to the FDA.

District of Columbia – Partnership for HIV/AIDS Progress (DC-PFAP)

In 2008, the Washington, D.C., Department of Health and NIH launched a new partnership to make Washington, D.C., a leader in the response to the

HIV/AIDS epidemic. 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. During the reporting period, there have been multiple advances in the program's development, moving from initial care implementation into the research phase. As part of this effort, CMRP supported the initiation of an innovative and paradigm-shifting interferon-free HCV therapeutic clinical trial at NIH. This is the first interferon-free, single, direct-acting antiviral (DAA) agent study to be approved for evaluation by the FDA with a DC-PFAP physician as the lead investigator with heavy recruitment from the DC-PFAP clinic population. In addition, the staff supported the initiation of a novel trial in the DC-PFAP clinics using new DAA agents with pegylated -interferon and ribavirin for HCV treatment in both HCV monoinfected and HIV/HCV coinfected individuals, with a DC-PFAP medical affairs scientist and a physician as the Lead Investigator and the Associate Investigator, respectively. Development of two additional clinical protocols as lead associate investigator or associate investigator by DC-PFAP physicians has occurred. The first protocol, the DC-PFAP Fibrosis study; "Liver Fibrosis Progression in African Americans with HIV-HCV Co-Infection: A Retrospective Study," has evaluated more than 150 patients. The second study, TLR7, is "A Double-Blind, Randomized, Placebo-Controlled, Single and Multiple-Dose Ranging Study Evaluating the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Antiviral Activity of GS-9620 in Treatment Naïve" and is a multicenter study.

CMRP staff continued clinical care of more than 450 new patients in the past three years for subspecialty hepatitis care and treatment within three integrated HIV community clinics in Washington, D.C., totaling over 1,600 patient visits.

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

CMRP staff support clinical research operations for NIAMS IND Phase I and Phase II clinical trials, including protocol writing, regulatory guidance and compliance, training, and clinical trials management, to include case report form review and monitoring activities; document creation, collection and compilation for regulatory filings (pre-IND, IND) with the FDA and other regulatory authorities; and technical review and report preparation. CMRP has created template monitoring language for the NIAMS support group to use when they prepare a new protocol that will require CMRP monitoring of the trial.

National Heart, Lung, and Blood Institute (NHLBI)

During this fiscal year, the clinical trials director and the CMRP director met with key NHLBI leadership to discuss approaches in developing an appropriate clinical trials management/regulatory program to support the NHLBI clinical research program. It was critical to assess the needs of the PIs and study teams prior to initiating the recruitment and hiring of staff to support this work effort. To fully assess PI needs, CMRP staff met with several PIs to discuss their clinical research needs. Numerous branch chiefs and PIs have taken advantage of talking with the team to discuss their unique research and regulatory requirements.

To meet the requirements of the NHLBI initiative, CMRP hired one clinical project manager I and two clinical research associate IIIs. During the reporting period, there have been four new hires, one clinical project manager II (July 2012), one clinical research associate II (November 2011), and two protocol navigators (January 2012).

CMRP Recognitions/ Awards/ Distinctions

- Thirty-one CMRP employees were mentioned in the FNL SAIC-Frederick *Coordinator's Report*: Beth Baseler, John Beigel, Melissa Borucki, Gabriella Diaz, Thomas DiMaggio, Lila Finney-Rutten, Taree Foltz, Silvina Frech, Debi Grossman, Lubna Hooda, Jen Imes, Sara Jones, Laurie Lambert, Yin Li, Daphne Mann, Sandra Maxwell, Maryellen McManus, Tracey Miller, Tamika Mitchell, Kim Montgomery-Recht, April Oh, Cynthia (CK) Osborne, Christen Osburn, Michelle Paulson, John Powers, Alice Rosenberg, Shelly Simpson, Kate Spates, Barbara van der Schalie, Julia Welch, and Kimberly Wesmiller.
- Seven CMRP teams were mentioned in the *Coordinator's Report*: Clinical Trials Monitoring Team, Protocol Navigator Team, NCCCP Team, NCI/CCR Team, NCI/CCR – Physician Extenders, NCI-OD CCCT Team and NCI/CIP Team.
- Two CMRP employees received the 2011 NIH Merit Award: April Oh and Amanda Vogel.
- Twenty CMRP employees received the 2011 NIAID Merit Award: Amy Adams, Nancy Aprill, Joy Beeler, Molly Buehn, Robert Eackles, Michelle Eby, Michael Galcik, Scott Garrand, Lisa Giebeig, Tom Harvey, Stacy Kopka, Joshua Lorenzo, Tracey Miller, Devon Moore, Thomas Platek, Val Sevastita, Shelly Simpson, Sara Stallings, Ilmiya Yarullina, and Kristin Young.
- Eleven CMRP employees received Project Recognition Awards: Melanie Baker, Lana Cross, Allison Eyler, Silvia France, Lisa Giebeig, Lynda Huber, Laurie McMahon, Merertu Tesso, Kim Wesmiller, Martin White, and Jeremy Wilhide.
- One CMRP employee received the Office of Cyber Infrastructure and Computational Biology (OCICB) chief information officer's award for excellent service in recognition of the accomplishments of staff supporting the OCICB mission: Kevin Newell.
- Fourteen CMRP employees received their SAIC-Frederick 5-Year Service Awards: James Albert, Rocco Caldararo, Thomas DiMaggio, Cathleen Frein, Wenjuan (Jesse) Gu, Lydia Lacuesta, Irene Mueller,

Sandra Paul, John Powers, Mary (Kathy) Simpson, Ismahan Ugas, Barbara van der Schalie, Jennifer Wilder, and Michael Young.

- Four CMRP employees received their SAIC-Frederick 10-Year Service Awards: Dr. Lamin Juwara, April Kennedy, Corina May, and Geoffrey Seidel.
- Two CMRP employees received their SAIC-Frederick 20-Year Service Award: Taree Foltz and Linda Ritchie.
- One CMRP employee received his SAIC-Frederick 25-Year Service Awards: Craig Gladden.
- One CMRP employee received a bachelor's degree in business administration and health care management: Melinda Hohnke.
- Three CMRP employees received their master's degree in business administration: Melissa Borucki, Jennifer Farrell, and Jennifer Hertsch.
- CMRP employees received their master's degree in science: Tom Harvey (bioscience regulatory affairs), Jennifer Hertsch (biology), and Lisa Hoopengardner (health sciences with a concentration in clinical research administration).
- One CMRP employee received a doctorate in nursing practice: Dr. Lamin Juwara.
- One CMRP employee became a certified clinical research professional: Devon Moore.
- One CMRP employee completed the Essential Skills certificate program for Excellences in Medical Communications from the American Medical Writers Association: Dr. Terry Mainprize.
- One CMRP employee completed the American Management Association's Supervisory Excellence certificate program: Dr. Barry Eagel.
- One CMRP employee completed Cornell University's certificate program in Executive Leadership: Ms. Beth Baseler.
- One CMRP employee completed the Kirkpatrick Four Levels of Evaluation certificate program: Ms. Beth Baseler.
- Twenty-four CMRP employees were recognized by their peers through the Recognizing Excellent Service Promotes Employee Commitment and Teamwork (RESPECT) employee recognition program: Angela Carrigan, Dan Cogswell, Luis Cordeiro, Tracy Dean, Maureen Dyer, Brenda Fevrier-Sullivan, Silvia France, Michael Galcik, Deborah Hill, Lisa Hoopengardner, Kathleen Igo, Stacy Kopka, Alyssa La Reginia, Laurie McMahon, Kevin Newell, Yvonne Rempel, Silvana Rivero (awarded twice), Maria Singarayan, Kelly Spore (awarded twice), Sara Stallings, Lisa Timmer, Ismahan Ugas, Jeremy Wilhide (awarded twice), and Kristin Young.

CMRP Products and Services

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

- Provides comprehensive clinical trials monitoring/management, regulatory, pharmacovigilance, protocol development and navigation, training, programmatic, and other operational support;
- Ensures the protection of human subjects by effective management and monitoring of clinical trial sites in accordance with the applicable regulations and International Conference on Harmonization/Good Clinical Practices (ICH/CGP);
- 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 Institutional Review Board (IRB) application/approval; initiates protocol monitoring to protect the well-being of human subjects; reports accurate trial data (e.g., safety/efficacy and adherence to clinical protocol); compliance with regulatory authorities (e.g., NIH/HHS and/or FDA) and with ICH/GCP; and meets with Principal Investigators (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;
- Maintains regulatory surveillance of clinical trials to ensure that trials are conducted in accordance with HHS/FDA/NIH regulations and ICH/GCP guidelines;
- Develops, assembles, maintains, and submits Investigational New Drug (IND)/ Investigational Device Exemption (IDE) applications to sponsors and interim/annual reports to the FDA; offers regulatory guidance (assists in determining whether an IND/IDE is needed; IND/IDE application document review for new protocols); offers consultation, preparation, and submission of IND/IDE applications (investigator's brochure; protocol review; informed consent form review; and pre-IND meetings with the FDA); provides IND/IDE maintenance (maintains IND/IDE, prepares IND/IDE amendments, annual reports, IND/IDE safety reports); and serves as a communication link with the FDA;
- Acts as a liaison for regulatory issues with the FDA, the pharmaceutical industry, and the Office for Human Research Protection while facilitating the initiation and conduct of clinical trials;
- Evaluates regulatory documents to ensure consistency and accuracy from a quality control perspective;
- Supports pharmacovigilance by providing medical monitoring and safety surveillance of clinical trials, and establishment and management of data safety monitoring boards and safety monitoring committees;

- 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 serious adverse events (SAEs); develops uniform SAE reporting forms;
- Develops training programs in the principles of GCPs and the regulations pertaining to the standards of clinical research for clinical research personnel;
- Conducts specialized technical training and professional development (e.g., clinical site, protocol, Good Clinical Practices (GCP), Good Laboratory Practices (GLP), and data management);
- 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 guidelines;
- Provides medical personnel (e.g., physicians, clinical research nurses, protocol nurse coordinators, physician assistants, clinical assistants) to support various NCI, NIAID, NHLBI, and NIAMS intramural clinics;
- Facilitates logistical aspects critical to the implementation of clinical protocols through protocol development and navigation expertise;
- Creates medical, scientific, and technical documents including clinical protocols, scientific papers, and materials;
- 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 research 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 (QA)/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 effective strategic support services, including:
  - Project management
  - Travel and logistical support
- Supports program expansion activities; and
- Coordinates a comprehensive approach to communication plans.

CMRP Personnel

CMRP personnel currently consist of 253 staff members, including 82 professionals, 109 technical, 45 administrative, nine information technology (IT), two courier/drivers, and seven staff members that are operating on full-time, approved telecommuting agreements. Those CMRP staff are located in Frederick, MD, and the surrounding greater Washington, D.C., area. The current CMRP staff (positions filled) located at Industry Lane and Building 363/Fort Detrick in Frederick, MD, consist of 98 staff members, including 30 professionals, 33 technical, 25 administrative, nine IT, and one shuttle bus driver. CMRP continues to receive new work requests and as such, the program has a need to continually recruit qualified personnel to fill professional, administrative, and technical positions to meet the needs of the NCI, NIAID, NHLBI, and NIAMS customers. During the reporting period, we have recruited and successfully hired 28 new staff members, as well as filled 19 open positions with internal transfer candidates. Included in CMRP, but working off-site, are 149 staff members who support the Bethesda, MD, Rockville, MD, and Washington, D.C., operations: 52 professionals, 76 technical, 20 administrative, and one shuttle bus driver. Several employees are approved for full-time telecommuting, including professional employees who reside in North Carolina, Minnesota, Alabama, Texas, Florida, and Rhode Island. One employee supports international operations in Africa and telecommutes from South Africa.

CMRP Initiatives

CMRP staff frequently take part in activities that promote and inform others about NCI and NIAID projects and share their diverse knowledge base, including volunteering in the Frederick National Laboratory-sponsored Take Your Child to Work Day (TYCTWD), volunteering in various Frederick County school classrooms on a routine basis, teaching both undergraduate and graduate classes at Hood College, Mount Saint Mary's University, and Frederick Community College, serving on professional journal editorial boards and participating in the bi-weekly New Employee Orientation program.

Moreover, CMRP staff members are highly committed to creating and maintaining an atmosphere with a strong sense of teamwork and high employee morale. A number of CMRP members were recognized by their peers through the RESPECT (Recognizing Excellent Service Promotes Employee Commitment and Teamwork) employee recognition program for their service to others. In addition, a number of staff members received NCI and NIAID Director Awards for outstanding contributions to a variety of high-level projects and initiatives.

CMRP staff and SAIC-Frederick completed the BEDSIDE-Focused SAIC-Frederick Slide Templates

Working Group effort by publishing the BEDSIDE-focused slide set templates on the SAIC-Frederick website. This is now available for clinical staff to utilize when presenting at conferences or meetings.

CMRP staff participated with the SAIC-Frederick Green Team to ensure collection and recycling for off-site SAIC-Frederick buildings; worked with the SAIC-Frederick Purchasing/User Group to identify purchasing concerns/issues and presented them to the committee and Purchasing Department representatives to develop solutions; worked with the newly-formed SAIC-Frederick Recreation and Welfare (R&W) Advisory Board to help establish the R&W at Frederick National Laboratory, and served on the CMRP Presentation Advisory Board for planning the annual CMRP Training Retreats.

Many CMRP team members were designated to participate in NCI, NIAID, and NHLBI projects within FY2012. 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, NIH, and professional society conferences.

During FY2012, the CMRP team continued to expand its technical and professional skill competencies. Team members completed coursework in clinical research, current Good Clinical Practice (cGCP), program evaluation strategies, and regulatory affairs. Some members of the CMRP administrative team participated in the design of the newly implemented SAIC-Frederick Administrative Professionals Certificate Program, while others taught and/or participated in the program.

The third annual CMRP Training Retreat was held in June 2012. This event was hosted in Building 549 in Frederick and included 16 sessions organized into four major categories: (1) professional skills; (2) clinical research; (3) medical/disease topics; and (4) business practices. This year, 136 staff members participated in the CMRP Training Retreat. In addition, a number of sessions were offered by webinar to allow participation by personnel unable to join the retreat in person. The event also featured the initial session of the HIPAA/HITECH training, which is required of all CMRP employees. There were 112 attendees for this session.

In December 2011, CMRP hosted their first Employee Learning Week celebration. This week-long event, offered in webinar format, provided staff members opportunities to expand their knowledge in diverse areas through daily Lunch and Learn sessions and daily training tips. The training sessions included presentations on topics such as individual learning style, the HHS Learning Management System, and active listening.

Finally, with an eye to the future, CMRP took the preliminary steps in preparing their first strategic plan. This plan will provide a blueprint for success, aligning the goals of CMRP to those of SAIC-Frederick, as well as our government clients.

New Initiatives

New work efforts have recently been requested and approved by the government for support under CMRP operations. The following paragraphs summarize the work requested and the support that CMRP is providing for each effort:

Influenza, Influenza-like Illness (ILI), and Emerging Infectious Diseases (EID)

At the end of the fiscal year, several new Yellow Tasks requests were received from the Division of Clinical Research (DCR), NIAID. In support of DCR's influenza, ILI, and EID initiative, NIAID has asked CMRP to facilitate the conduct of INSIGHT clinical research studies that enroll subjects with influenza, ILI, and/or other EID within southern hemisphere sites in Australia, South America, Asia, and Africa. The anticipated length of these studies will be two to five years. CMRP staff will work with SAIC-Frederick Contracts and Administration staff to establish a research subcontract with the University of Minnesota to provide for the recruiting and enrolling of patients to NIAID/DCR influenza, ILI, and/or EID protocols under the International Network for Strategic Initiatives in Global HIV Trials (INSIGHT) Network. For additional details, please see the section under "Support to NIAID, Influenza Efforts."

Office of Planning and Operations Support (OPOS) Performance Measure

At the end of the fiscal year, the Division of Clinical Research (DCR), NIAID, requested support to a DCR initiative to ascertain performance measures in order to provide data-driven progress reports for the individual branches within NIAID. The DCR currently tracks changes in health practices and policies, research capacity of domestic and international clinical research networks, development of new mathematical models to describe the biology of infectious diseases or immune responses, and applicable regulations to ensure GCP compliance during clinical trials. In such a situation, it is important to develop, for each type of work, the appropriate performance measures that contribute to the mission and goals of the Division, i.e., metrics that capture the complexity and nuances of the interwoven, multi-factorial, collaborative productivity that DCR's individual branches bring to the facilitation of clinical research in other entities. The anticipated length of this effort is one to two years.

CMRP staff will work with SAIC-Frederick Contracts and Administration staff to establish a research subcontract with a vendor who will be tasked with producing metrics that provide data-driven assessments of performance and productivity in DCR. The goals of the project are to: (1) develop key performance indicators (KPIs) that provide data-driven assessments of performance and productivity in DCR; (2) assess and refine existing KPIs; (3) develop appropriate goal-setting benchmarks; and (4) identify measures against which the performance of the program can be compared. It is envisioned that the statement of work will be developed

by the clinical project manager II by the end of September 2012. Additional details can be found within the OPOS section of the report.

Support to the Chinese Clinical Trials Network, Division of AIDS (DAIDS), NIAID

NIAID, the lead NIH Institute for tuberculosis (TB) research, is developing collaborations with Ministries of Health and other funding agencies in various countries to conduct high-quality clinical research in TB. An integrated, structured, and reproducible approach for building sustainable capacity across the following key disciplines is required: regulatory processes and standards; clinical management; laboratory and specimen management; research pharmacy and data management; and biostatistics. A framework for assessing capability, training to correct and fill capability gaps, establishing a clinical research management infrastructure, and periodically assessing performance through a quality assurance review is needed across all key disciplines. Additionally, training to apply sound administrative and information management practices is required.

With the second largest TB epidemic in the world and the largest number of patients with multidrug-resistant TB (MDR-TB), China is a major priority. NIAID is establishing a collaboration/partnership with the investigators currently funded by the Chinese Ministry of Health (MOH) to build a sustainable Chinese research network/consortium that will conduct multicenter clinical TB studies.

NIAID has designed a multiphase strategic plan for the establishment of this research network/consortium. The first phase focuses on capacity building and network/consortium development; the second phase is to conduct TB clinical research studies, including trials with approved drugs, and to more fully establish the network/consortium; and the third phase is to advance full TB clinical trial implementation with new, investigational drugs/combinations.

The Division of AIDS (DAIDS), NIAID, has asked SAIC-Frederick to assist the DAIDS staff to establish a clinical trials network working with multiple sites in China in order to perform studies on multidrug-resistant TB. DAIDS designed a multiphase strategic plan for the establishment of this research network/consortium. The first phase focuses on capacity building and network/consortium development; this phase is anticipated to last two to three years. The goal of Phase I is to strengthen/build the Chinese network/consortium working towards the goal of the Chinese investigators, eventually developing the expertise to independently run and manage the network/consortium. Direct support for this network/consortium from SAIC-Frederick staff, subcontractors and consultants is expected to decrease over the duration of Phase I.

SAIC-Frederick will support this initiative through the use of several mechanisms in order to collaborate with DAIDS staff to build capacity within this network/consortium. Technical expertise and oversight will be provided by a to-be-hired clinical project manager III. The clinical project manager III will oversee all aspects of SAIC-Frederick program planning and performance in support of this initiative. This includes, but is not limited to: SAIC-Frederick project planning and reporting, procurement management, communications, travel, and logistical support. Administrative support will be provided by a part-time, to-be-hired secretary III who will assist the clinical project manager III in administrative support activities. A number of SAIC-Frederick staff will serve as subject matter experts (e.g., biobanking; regulatory, safety, and clinical trials management services; training, etc.) in supporting this initiative, and their current staffing levels are sufficient to provide supplemental support. Additional subject matter experts may be required to provide support, and these may be acquired through consulting agreements/research subcontracts to provide expertise and support where either direct SAIC-Frederick personnel are not available or where specialized external experts are needed to support the initiative.

Esophageal Cancer Precursor Lesion Genomic Study – China

At the end of the fiscal year, the NCI Division of Cancer Epidemiology and Genetics requested support for an esophageal cancer precursor lesion genomic study to be conducted in China. Esophageal cancer is the sixth most common fatal human cancer in the world with over 406,000 deaths annually, and the fourth most common new cancer in China. Due to its large population and high rates, over half of all esophageal cancer deaths in the world occur in China. North central China has esophageal cancer rates that are among the highest in China, and nearly all of these cases are esophageal squamous cell carcinoma (ESCC). ESCC is an aggressive tumor that is typically diagnosed only after the onset of symptoms, when prognosis is very poor. The five-year survival rate of 19 percent is fourth worst among all cancer in the U.S. One promising strategy to reduce ESCC mortality is early detection, and a better understanding of molecular mechanisms underlying esophageal carcinogenesis and its molecular pathology will facilitate the development of biomarkers for early detection.

The overall objective of this project is to identify and test strategies to reduce mortality from esophageal and gastric cancer in high-risk populations in China, where rates of these cancers are the highest in the world. Building on collaborative research that has been ongoing between the Cancer Institute of the Chinese Academy of Medical Sciences (CICAMS) and NCI since 1982, this new initiative will conduct new studies in this high-risk population to further evaluate etiologic and early-detection hypotheses and advance disease prevention strategies. The specific purpose of the new study is to conduct a precursor lesion genomics study to determine DNA alterations in premalignant esophageal lesions.

The goal for this new study is to understand the molecular underpinnings of premalignant esophageal

lesions, so that researchers can incorporate testing of molecular lesions found in high-grade premalignant lesions as biomarkers in early-detection screening programs to reduce or prevent esophageal cancer mortality.

The proposed new study has two components, including both a field study part (to obtain data and biologic samples) and a genomic analysis part (to perform sequencing of the biologic samples and bioinformatics analysis of the sequencing data). As a practical matter, both components need to be conducted in China. The field study is only feasible in the high-risk regions of China, where both the rates of ESCC and the prevalence of ESCC precursor lesions are the highest in the world.

CMRP will support this initiative by working with SAIC-Frederick Contracts and Administration staff to establish a research subcontract with CICAMS to support an esophageal cancer precursor lesion genomics study in the northern Henan and southern Hebei provinces of China. CICAMS, located in Beijing, will manage this project locally, including performing a field study to collect specimens from 30 patients, as well as managing a subcontract for whole-genome sequencing and bioinformatics.

Respiratory Viruses

At the end of the fiscal year, DCR NIAID, requested support for the initiation and management of a clinical trial(s) for the treatment of non-influenza respiratory viruses. It is anticipated that the length of these studies will be two to five years. CMRP staff has worked with the NIAID Division of Clinical Research to begin the development of a clinical trials protocol for the treatment of a non-influenza respiratory virus. This protocol is expected to enroll 100 patients and be conducted in the United States and one additional country. CMRP will be providing support to this initiative in the form of technical leadership and oversight, project/procurement management and logistics, and subcontract administration, as well as regulatory, safety, and clinical trials monitoring services. Strategically, CMRP will use several mechanisms in order to provide rapid deployment of clinical trials management services for this time-sensitive initiative. A research subcontract with a qualified clinical research organization (CRO) will be established to provide protocol development; clinical trials management and support; implementation of the protocol and training to the staff at approximately 10 clinical sites in one country; kit and study agent management and distribution; data management; biostatistician support; and monthly progress reports. Multiple research subcontracts with qualified vendors will be established for the following services: (1) study agent acquisition, packaging, and labeling; (2) laboratory kit manufacturing, storage, and distribution; (3) central laboratory analysis; and (4) virology testing laboratory services. Regulatory, safety, and clinical trials management services will be provided by CMRP Regulatory Compliance and Human Subjects Protection Program (RCHSPP) personnel.

CMRP Program Management

Beth Baseler, M.S., Director
Taree Foltz, Program Manager II

CMRP continues to provide high-quality program management and administrative support to the regulatory, clinical, and programmatic efforts being provided to NCI, NIAID, Clinical Center, NHLBI, and NIAMS initiatives. The ability to provide rapid responses, high-quality solutions, and to recruit and retain diverse subject matter experts is evidence of CMRP's continued success. CMRP programmatic management support was launched to offer a complete approach to clinical support services. The CMRP Program Management Office contributes to the various institutes' clinical research activities by providing centralized administrative and management support services that facilitate high-quality clinical research through program guidance and support, strategic planning and direction, program/project management, technical direction, learning and professional development (coordination of training requirements), and general assistance to various government entities.

The Program Management group is actively involved and works closely with CMRP hiring managers and the SAIC-Frederick HR Recruitment Office to interview and select top candidates for the numerous medical, clinical trials management, regulatory, IT, program/project management, and administrative positions within CMRP. In addition, group members traveled to both local and national job fairs and conferences to conduct programmatic outreach to present and discuss CMRP job openings with potential candidates. The group serves as a valuable resource for existing and new employees, providing a new employee orientation and logistical support to CMRP new hires while communicating and coordinating critical information pertaining to their upcoming activities and responsibilities. During this reporting period, the Program Management group scheduled 125 interviews for 59 different positions, ranging from administrative support to high-level medical/clinical experts. From those 125 interviews, 47 positions have been successfully filled. The Program Management group is currently actively recruiting for 12 open positions.

Policy and procedure updates are provided to all CMRP staff in order for our program to operate under the most current guidelines and requirements, and to ensure that changes and revisions are clearly identified. The Program Management group also, under the direction of the CMRP director, works closely with the HR Compensation Department to coordinate the necessary performance management activities throughout the year. The Program Management group consists of a program manager II, a clinical program administrator, three senior program coordinators, an administrative coordinator, and a secretary III.

CMRP Project Management

Theresa Engel, M.F.S., Clinical Project Manager II
Nichole Cline, M.S., Clinical Project Manager I
Alyssa La Regina, Medical Writer I

The CMRP Project Management Office provides project management and operational support to all overarching CMRP initiatives, as well as several external high-profile projects. The Project Management Office is comprised of one level II clinical project manager, one level I clinical project manager, one senior special projects administrator, one level I medical writer, two level II documentation specialists, and two level III secretaries.

Working in conjunction with the Program Management Office team and other CMRP functional groups, the Project Management Office manages the Yellow Task system workflow, including development of task responses, facilitation of budget preparation and approval, and tracking of process metrics. Once Yellow Tasks are finalized, the staff works with the respective CMRP group to track the status of tasks (including the hiring of staff and establishment of research subcontracts) to completion. When budget revisions are requested, Project Management Office staff work with the appropriate CMRP personnel to revise the budget and submit it through the Yellow Task webmail system.

In addition, Project Management Office staff is 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. The Project Management Office collects information for the Contract Performance Status Report, which highlights significant work conducted in the previous six-month period. Additionally, Project Management Office staff coordinates the efforts of generating and submitting an annual report to the FNL Office of Scientific Operations outlining specific CMRP activities, the CMRP portion of the SAIC-Frederick Annual Report, and the CMRP International Efforts Report each fall.

During the reporting period, the Project Management Office played a key role in developing and overseeing a SharePoint site for the coordination and tracking of the 2012 CMRP Annual Report. Under the guidance of CMRP IT, SharePoint developers, and the Project Management Office, the new CMRP Program Management site used a workflow platform to automatically distribute, track, and manage all sections of the CMRP Annual Report. The site eliminated tasks that historically were performed manually, including e-mailing individual report sections to appropriate staff, tracking document version history, and tracking the status of documents to ensure timely movement through the workflow, which allowed staff involved in this year's reporting process to concentrate on their individual tasks of preparing and reviewing report sections, conducting technical reviews, and approving each section for inclusion in the final report.

The Project Management Office provides overall project management support for internal CMRP initiatives, as well as external high-profile projects including the HIV/AIDS collaboration between NIH and the Washington, D.C., Department of Health, and multiple projects supporting NIAID's influenza initiatives. A document specialist II also provides critical data and document management support to the NCCCP as well as document formatting services for several projects.

During FY2012, the Project Management Office, in collaboration with CMRP IT, launched a new CMRP intranet site in response to the need for a central location for resources, tools, and links that can be easily accessed by all CMRP employees to assist them in their daily activities. Aside from being a tool for enhancing employee productivity, the intranet site facilitates communication and internal collaborations between CMRP employees. This site will further enhance CMRP internal communications among staff members working at multiple Frederick and Bethesda/ Rockville MD, locations.

In collaboration with the CMRP director and other CMRP managers, the Project Management Office staff answered an expedited request from SAIC Corporate to review all program activities and provide a summary of activities that had the potential to contact personally identifiable information/protected health information (PII/PHI). Project Management Office staff also took the lead in developing and presenting training materials on compliance with the Health Information Portability and Accountability Act (HIPAA) and the Health Information Technology for Economic and Clinical Health (HITECH) Act. Staff created a compliance guide to accompany the training and developed a fillable protected health information/personally identifiable information incident reporting form. Between June and August 2012 five HIPAA/HITECH compliance trainings were presented by the CMRP Compliance Working Group; all CMRP staff attended the training by the end of the contract year.

The Project Management Office also provided background research for projects, and assisted with creating and editing presentations. In addition, Project Management Office staff began to develop the CMRP strategic plan. Supporting the CMRP director, the Project Management Office provides medical writing services to prepare presentations, edits statements of work (SOWs), reviews job requisitions, generates and distributes meeting minutes, and writes internal procedures.

During the reporting year, the Project Management Office also assisted multiple CMRP programs in the establishment of research subcontracts, including assisting in the preparation of SOWs, shepherding contract documents through the research subcontracts process, and performing a critical review of proposals and budgets. Project Management Office staff assumed responsibility

for uploading documents associated with multiple projects to the CMRP research subcontracts SharePoint site; staff also assisted in the review and further development of the document management system and created a SharePoint user's manual to assist CMRP staff.

Project Management Office staff compiled a database of 2011/2012 staff publications that can be accessed to provide report data; further refined and continued publication of a CMRP newsletter, *The CMRP Insider*; and worked with management to periodically review and update the new employee orientation presentation that provides an overview of CMRP support.

CMRP Document Control

Nichole Cline, M.S., Clinical Project Manager I
Alyssa La Regina, Medical Writer I
Tara Whipp, Documentation Specialist II

CMRP Document Control is comprised of one level II documentation specialist, who coordinates the process for compiling and tracking all program documents and maintains CMRP master documentation and archive, appropriately naming and banking files. Additionally, the documentation specialist provides administrative and clerical support related to CMRP program initiatives.

To simplify the process for collecting and storing data for tracking employee publications, CMRP began loading publication data into Manutrak II, a document management software system, in March 2011. The software is used and maintained by the documentation specialist to gather and summarize publication data to ensure program reports are in compliance with NIH requirements. Internal audits are performed by a medical writer I to ensure all CMRP publication data is entered and to affirm the software is correctly pulling reports from the entered data. Publication reporting results from Manutrak II were successfully used to prepare the 2012 CMRP Annual Report.

During the reporting period, CMRP electronic file data storage was reviewed monthly to ensure that new information was deposited appropriately, thus maintaining a simplified navigation of the folders and files held within the internal CMRP shared drive. The documentation specialist also assisted in the maintenance of a CMRP subcontracts database by uploading the appropriate documentation into a SharePoint library, tracking and loading financial updates into the SharePoint library, and maintaining a spreadsheet to track historical Yellow Task data.

CMRP Financial Management Group (FMG)

Craig Gladden, M.B.A., Program Manager II
Denise Motok, Financial Analyst II
Sherry Howard, Financial Analyst I
Gabriel White, Financial Analyst I

The CMRP FMG continues to expand its capabilities and take on new challenges in support of NCI, NIAID, NHLBI, NIAMS, and the Clinical Center. This group collaborates with other SAIC-Frederick directorates, managers, and inner departments, as well as with government officials, and manages the following 98 cost centers: 3 for CRD; 2 for the Office of the Clinical Directorate; 5 for the OD CSSI; 19 for the OD-Immediate Office of the Director; 1 for the NCI Division of Cancer Epidemiology and Genetics; 22 for the NCI Center for Clinical Research; 9 for the NCI's DCTD; 1 for the NCI DCCPS; 3 for the Clinical Center/Agency; 2 for other clinical centers/institutions; 13 for the NIAID DIR; and 18 for the NIAID DCR. Working in collaboration with technical support services, the FMG developed and implemented a central CMRP Financial Management SharePoint site to manage the preparation, documentation, review, and internal approval of all FY2013 annual budgets for submission based contract deadlines. This site provided quick access from one location to all source documents and financial information, allowing the program to increase efficiency, eliminate materials and supply costs associated with the printing and storage of hard copies by having a centralized electronic source. The implementation of the Financial Management SharePoint site allowed budget preparers to quickly access electronic files from various locations to prepare assumptions, include budgeted costs based on existing and new requirements, and submit to appropriate functional managers, financial analysts, and the director of the program using electronic approvals. This effort resulted in "going green" by eliminating the routing of files, paper documents, copying, and space for the storage of documents since all information is stored in this centralized SharePoint site. In addition, the inclusion of timelines in the system resulted in all CMRP budgets being submitted to the Financial Planning and Analysis Office by the established due dates to meet the NCI-stated deadline.

During the reporting period, the FMG 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 expenses for all budgets to ensure accuracy and accountability of all costs. In addition, as a result of excellent planning and documenting of static financial worksheets, the group responded to multiyear spending predictions, which was used to quickly generate the information needed as part of the submission of the FY2013 budgets to meet contractual deadlines.

CMRP Learning and Professional Development (L&PD) Group

Barbara van der Schalie, M.S., Clinical Training Manager
Nancy Becker, Clinical Training Specialist
Debra Gilchrist, M.A., M. Ed., Clinical Training Specialist
Sherri Lewelling, Secretary III

CMRP training support is provided by the L&PD group, which is composed of a clinical training manager, a training specialist/instructional designer, a training specialist and an administrative support staff member. The L&PD group supports CMRP, the Regulatory Compliance and Human Subjects Protection Program (RCHSPP), and the Office of Planning and Operations Support (OPOS). In supporting these various clients, L&PD participates in activities that fall into five categories: (1) identifying/developing training resources to address client-identified training needs; (2) providing training and professional development subject matter expertise; (3) providing administrative support for activities with training components; (4) ensuring compliance and continuous improvement of training processes and initiatives; and (5) conducting 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

The clinical training manager designed and delivered three new competency-based courses: (1) Managing Multiple Priorities; (2) Managing Up; and (3) Influencing without Authority for the SAIC-Frederick Administrative Professionals Certificate Program. The clinical training manager worked with the CMRP Administrative Leadership Team to introduce "StrengthFinder" as a professional development program for CMRP administrative professionals and continued to provide the Communication Style Preference Training to SAIC-Frederick new managers biannually as part of the Manager as Communicator initiative. In addition, the clinical training manager developed and delivered training on S.M.A.R.T. Goals to all CMRP managers and supervisors to ensure that they were prepared to write appropriate goals for their teams.

The L&PD group hosted an Administrative Professionals Recognition Event on Administrative Professional's Day® in April 2012; supported the implementation of a HIPAA/HITECH Act training presentation, which fulfilled a mandatory training requirement for all CMRP staff; and supported training for LiveLink®, the new document repository, by assisting in review of training presentations and training materials, and facilitating and documenting role-specific training sessions for all affected staff.

Provide Training and Professional Development Subject Matter Expertise

The clinical training manager served on the Scientific Publications, Graphics & Media Advisory Board, and the SAIC-Frederick Administrative Professionals Certificate Program Advisory Board, as well as providing courses in this program (see above).

The clinical training manager provided support for the introduction of strategic planning to the Senior Leadership Team as the first step in the development of a CMRP strategic plan.

The L&PD group began the process of investigating the granting of continuing education units (CEUs) through the International Association of Continuing Education and Training (IACET). This process involves a rigorous evaluation by IACET to demonstrate a well-documented, effective training program provided by qualified trainers. L&PD hopes to complete the evaluation program by the end of 2013, allowing us to grant CEUs to our clinical research professionals who require them for their on-going certifications.

Provide Administrative Support for Activities with Training Implications

The L&PD group facilitated a monthly seminar series (spanning five months) on topics of interest to CMRP staff. These seminars are available via webinar to all staff and cover diverse topics, such as specific diseases, compliance/regulations, and professional skills. Specific seminar topics offered included Statistics for the Non-statistician and Project Management 101, each provided by CMRP/SAIC-Frederick colleagues.

The L&PD group also facilitated 15 training sessions on various topics; each session included presentation evaluation and attendance documentation for each participant, including the Deputy Director of Management (DDM) webinar series.

In addition, the L&PD group facilitated 18 New Employee Orientation sessions for 28 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.

The L&PD 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

The L&PD group administered the 2012 résumé/curriculum vitae (CV) and signature log review project for all CMRP staff. This effort 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. This year's effort also included redacting personal information from existing résumés and ensuring that new résumés do not contain personal information.

This year, the L&PD group collaborated with IT to launch TrackWise® Training Manager as an enterprise-wide training tracking system. This software system provides visibility of the completion of all training requirements, as well as professional credentials. CMRP staff can now be accountable for completing all of their training requirements, and their compliance can be tracked in real time. All CMRP staff received a copy of their personal training record twice in the last six months to allow them to review their record critically and provide any documentation that is missing.

Conduct Professional Development Activities

The L&PD group provided extensive facilitation services for the 2012 CMRP Training Retreat, including venue and speaker identification, participant communication, retreat day logistics, and post-retreat evaluation and thank-you e-mails. The event involved sessions from over 25 presenters and 131 participants from all CMRP locations. Retreat sessions were also available by webinar to our geographically diverse workforce. This year's retreat also included a session of the HIPAA/HITECH training, which was available both in person and by webinar.

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 L&PD, 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.

During the reporting period, the L&PD group hosted the first annual Employee Learning Week for all CMRP staff at all locations. The week included a lunch and learn session each day, as well as a training tip of the day.

CMRP Information Technology (IT) Group

Michael Galcik, M.S., Information Technology Manager
Scott Schiffhauer, LAN/Network Specialist I

The CMRP 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 satisfying customer requirements and meeting the unique operational requirements for management of clinical trial, regulatory, and clinical safety data.

During the past year, the IT group was involved in several key technical initiatives for the program, as described below:

The IT Group participated in the FNL intrusion detection tests for the assessment of network host vulnerabilities and in post-remediation efforts to mitigate identified findings. This exercise was essential in providing a comprehensive review of potential threats to the program's IT assets based at the FNL campus and in identifying changes in existing business processes necessary to prevent future threats.

The group planned, facilitated, and executed the transfer of the IT infrastructure from a leased facility at Grove Road to an available building at Fort Detrick in 2011. In order to do so, a technical project team was assembled consisting of CMRP, Information Systems Program (ISP) staff, and non-SAIC-Frederick contract staff. Tasks were identified, timelines set, and responsibilities for the successful completion of each task allocated to a member of the team. The activities occurred within a narrow timeframe and were completed successfully, with minimal disruption to the business unit.

The IT Group established a CMRP IT infrastructure within the FNL Building 430 datacenter to better support CMRP operations and groups located throughout the NIH community. The project required drafting a Service Level Agreement (SLA) between the ISP and CMRP, in which specific information systems and system services were defined, as well as the levels of response, availability, and maintenance associated with the services, and the responsibilities of each group in providing assurance that all would function as expected. The technical framework required a collaborative effort with staff from the ISP and the CMRP IT group to identify the appropriate rack space, power supply, cooling, and cabling requirements to support the equipment that would be placed in the space. The SLA became fully authorized in 2012, and the operational environment is in effect, providing capabilities to program and technical staff to utilize multiple platforms, whether production or development, for testing and developing new software or system functionality enhancements, to store program materials, financial reports, and similar content, and to electronically manage business processes. Disaster recovery service and capabilities were integrated into the technical framework, with the release of a fully redundant, automated tape backup library system that utilizes fiber optic channel cards to collect data from the servers.

IT Group staff designed, developed, and released a CMRP intranet platform to provide a central location for program related resources, tools, shared documents, and common links occurred in the latter part of FY2012. The platform was custom developed and features an online phonebook, public and private team pages, and a repository for previous issues of the program's newsletter, *The CMRP Insider*. As a tool to improve employee productivity, the platform also promotes internal collaboration among members of the various areas within

the program, as team pages describing the roles and purposes of each group, fostering an environment in which staff can learn about others and reach out to them for assistance or to share information.

Staff provided technical support and facilitation of web-based videoconferencing for the inaugural meeting of the NCI Center for Global Health. This high-profile conference featured world leaders in cancer research, with the purpose of helping establish the NCI's scientific and public health priorities and building capacity for global cancer research. The CMRP IT group supported each presentation and coordinated several test windows of remote videoconferencing prior to the keynote delivery, which was given via Skype on day two of the conference.

Additionally, many ongoing and long-term initiatives continue to be led and/or facilitated by the IT group, as described below:

The IT Group developed and released two new SharePoint sites, one for the management of the many documents related to supporting the submission of the annual budget, and the other for collecting and managing the multiple sections that comprise the CMRP annual report. Both of these releases were custom implementations, with unique requirements and timelines. Workflow functionality was built in to supplement the sites, thereby allowing not only documents to be managed in the system, but the underlying business process for collection, review, and approval of the documents as well. E-mail notifications were included for ease of navigation for the end user. In addition, continuous quality improvement of the existing sites occurred, with several stakeholder-requested programmatic and operational enhancements developed and released during 2012. The CMRP IT group continues to serve a critical role in participating in a working group for this application and to support the change request process developed by the group to manage system changes, ensure proper communication channels are open, and 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 CMRP IT group also provides maintenance and technical support for a public-facing website, which highlights the diverse clinical research service offerings and support functions provided by CMRP. The site provides information about the many high-profile NIAID, NCI, Clinical Center, NHLBI, and NIAMS initiatives to investigators, clinicians, prospective job seekers, and the general public. Content management support, bug fixes, and similar activities continue to be provided.

This group provided continued support of the 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. Per applicable guidance, the ability to use smart cards as a form of dual factor authentication when utilizing remote access technologies such as Virtual Private Network was deployed. Monitoring of any additional requirements or mandates is ongoing.

An expansion of the document types with the ability to be electronically signed via the initiative introduced last year, in which HHS-verified Public Key Infrastructure software certificates embedded on individual personal identity verification (PIV) cards, were utilized to digitally sign program documents in lieu of paper-based, wet signatures for approvals. This effort continues to gain momentum and has been very beneficial to the program, as it has reduced the time it takes to get approvals and has a cost-benefit and environmental impact (less paper is being used).

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

CMRP ARRA Infrastructure Administrative Group

Joy Beveridge, M.S., Clinical Project Manager III
Lenny Smith, Clinical Project Manager II
Silvana Rivero, Senior Program Coordinator
Kathleen Igo, Medical Writer I
Yvonne Rempel, Document Specialist II

The CMRP ARRA Infrastructure Administrative Group provided project management, medical writing, documentation, and administrative support to the CMRP back-office, as well as to the NCCCP and TCGA ARRA initiatives during this contract year. Project management support provided to the TCGA and NCCCP initiatives included participating in project team meetings, coordinating monthly and quarterly ARRA reports, and supporting several research subcontracts to collect retrospective and prospective cancer tissue samples. Medical writing support was provided to the NCCCP for developing progress reports for the annual meeting, writing feature stories highlighting specific NCCCP activities, and reviewing several potential publications, abstracts, and presentations related to ARRA-funded activities occurring at network sites. The documentation specialist provided ongoing support for the NCCCP database, including creating templates, testing forms,

formatting documents, database testing, and data extraction, as well as supporting the development of the TCGA Microsoft Access database. Support was also provided for the development of timesheet authorization and notification memos, and filing of ARRA infrastructure-related financial and administrative documents. Administrative support services were provided by the senior project coordinator and consisted of coordinating and tracking recruitment efforts, assistance with new employee orientation, and tracking of research subcontracts. In addition, the back-office infrastructure team managed space requirements for CMRP back-office infrastructure, TCGA, 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.

CMRP ARRA Financial Management Group (FMG)

Craig Gladden, M.B.A., Program Manager II
Gabriel White, Financial Analyst I

The CMRP FMG continued to maintain budgets and staffing for a number of ARRA projects, including one CMRP infrastructure, one TCGA, and three NCCCP ARRA projects, as well as three Clinical Research Development–Clinical Assay Development Program ARRA projects.

The FMG, working in collaboration with technical support services, developed and implemented a central CMRP Financial Management SharePoint site to manage the preparation, documentation, review, and internal approval of all ARRA FY2013 annual budgets for submission-based contract deadlines.

Within the reporting period, the FMG continued to manage and develop cost estimates for ARRA 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 multiyear spending predictions, which were used to generate the needed information quickly as part of the submission of the FY2013 budgets.

CMRP ARRA IT

Michael Galcik, M.S., Information Technology Manager
Daniel Cogswell, Programmer Analyst III
Kris Ghimire, Systems Administrator II

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 reporting period, as outlined below:

This group designed and developed a custom application for the NCI Community Cancer Centers Program (NCCCP) to gather all quarterly survey responses from each participating center and aggregated the results into a single, normalized database, with tools provided for viewing and reporting. Inception of the project occurred quickly, as some critical time points needed to be met. Critical tasks performed to achieve the objectives of this project included: the finalization of the database design; development of programs to load individual results from XML files; creation of report programs to show results by table and/or item, with selection by center and/or reporting period; creation of reports to chart the data; development of a secure in-house web application to view individual centers' results; design of a system to automatically generate data-entry spreadsheets that are pre-filled with the prior quarter's survey results; provision of assistance to NCCCP staff in the creation of templates; verification that forms could be read back into our NCCCP database; addition of baseline reporting, which included creating the database structure, posting the reports from spreadsheets, and viewing the results; alteration of the structure of the question sets to allow additions/deletions/updates based on reporting type and period, thereby giving NCCCP staff a history of the various question sets; and working with staff to finalize new reports.

CMRP staff was instrumental in the installation, configuration, and management of backup and disaster recovery services for CMRP ARRA and NCI program IT infrastructure. To accommodate increasing amounts of data storage requirements, a new backup system was acquired and brought online. The system utilized a fiber channel card for data transfer and required that the corresponding server used to run the backup jobs be similarly outfitted. Software for the system was upgraded to the most current vendor release, and deployment of the new backup system was completed and is successfully operating.

The IT Group continued its 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.

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

Cancer Diagnostic Program (CDP) ARRA Initiatives

Rhona McVicker, CTEP Administrator

CMRP continues to provide ad hoc administrative and research subcontract management support to the Patient Characterization Center/Clinical Assay Development Program (CADP) research 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.

The Specimen Retrieval System (SRS) is a contract project of the CDP to find and gather archival pathology specimens, couple them with clinical annotations, and provide them to the CADP. These specimens, in turn, will constitute the material that members of the Clinical Assay Development Network will use to test and refine assays within the CADP.

The SRS has contracted with an institution of the NCI-funded Cancer Research Network (CRN), and will solicit in FY2013 for new institutions particularly interested in cancer research. These institutions will be chosen for the SRS because they are large health plans and have stable membership and relatively long periods of enrollment, highly automated data systems with comprehensive electronic medical records, and large numbers of archived pathology specimens dating back three to four decades. CMRP will initiate the subcontracting process to solicit and award Basic Ordering Agreements (BOAs) and subsequent specimen-specific task orders.

NCI Community Cancer Centers Program (NCCCP) ARRA Initiatives

Joy Beveridge, M.S., Clinical Project Manager III
Deborah Hill, M.S., Clinical Project Manager I

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. In July 2012, following a limited competition to receive continued support for an additional two years, the network was reduced to 21 community hospitals in 16 states. Dedicated CMRP staff continued to manage and support the comprehensive communications infrastructure of the expanded program, and the research subcontracts awarded to the NCCCP community hospitals and collaborating institutions. Additional information regarding the NCCCP can be found in the more detailed section describing NCCCP activities.

The Cancer Genome Atlas (TCGA) ARRA Initiatives

Joy Beveridge, M.S., Clinical Project Manager III
Sylvie Kwedi, Ph.D., Clinical Project Manager III

Support to The Cancer Genome Atlas program ARRA activities included increasing the network of Tissues Source Sites (TSS) to provide tumor specimens that are collected retrospectively, or prospectively. Beginning in November 2012, CMRP staff provided the competitive SOW that was incorporated into the Request for Proposal (RFP) solicited to vendors to collect up to 35 different tissue types. Staff continued to support the outreach efforts to potential vendors and to accept proposals, and to coordinate the review and evaluation of proposals. Management of the resulting ARRA subcontracts began in early 2012 and will continue until mid-September 2014. Additional information regarding TCGA can be found in the more detailed section describing TCGA support activities.

SUPPORT TO NCI

Support to the Molecular Imaging Program (MIP), NCI

Barry L. Gause, M.D., Clinical Director
Stephen Adler, Ph.D., Laboratory Director

The mission of the 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 positron emission tomography (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.

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. CMRP staff has met the rigorous credentialing requirements necessary to function as

authorized users of radiopharmaceuticals. This accomplishment provides support directly to the principal investigator (PI), as well as to the entire department.

The MRI/CT/radiology technologist 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 multicenter 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.

The director and the PET physicist were 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. After a detailed study of the preclinical instrument was performed, it was deemed to be inadequate for Dr. Choyke's program and was returned to the manufacturer. A new and different model preclinical PET/CT scanner was delivered, and another set of performance measurements and site qualification tests were made on the new scanner. The results of the tests proved the new scanner was working at or beyond the specifications required by Dr. Choyke's preclinical program. A poster was presented at the Society of Nuclear Medicine meeting this year detailing the results of the qualification tests. These results were also published in a peer-reviewed journal and presented at the World Molecular Imaging Congress in September 2011. An abstract was submitted to the Annual Meeting of the Radiological Society of North America (RSNA) held in Chicago in November 2011, which presented the results of data harmonization using both phantom and clinical data.

During the reporting period, the PET physicist furthered his work on multicenter imaging harmonization by guiding QA tests on the NCI/Molecular Imaging Clinic (MIC)/PET/CT scanner and one located at the University of Wisconsin. This was motivated by a multicenter clinical trial in which the NCI/MIC is participating. The goal of the multicenter clinical trial is to use sodium fluoride (F18 NaF) as an agent to study metastatic prostate cancer across multiple cancer centers. This work follows on the heels of the image data harmonization work, which involved 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. An oral presentation of this work with University of Wisconsin will be presented at the RSNA meeting in November 2012.

With respect to the ongoing clinical trials, one protocol of interest has started accruing patients. The clinical protocol titled, "Phase I Trial of Z-Endoxifen in Adults with Refractory Hormone Receptor-Positive Breast Cancer, Desmoid Tumors, Gynecologic Tumors, or Other Hormone Receptor-Positive Solid Tumors," uses F18-labeled Fluoroestradiol (F18 FES), which is fabricated at the SAIC-Frederick Radiopharmacy and was developed with the help of SAIC radiochemists in a joint collaboration between ADRP and CMRP-CIP staff. Between December 2011 and May 2012, three patients have been scanned with this new agent.

Ongoing projects for the remainder of the year include expanding a web-based database and interface to track all the patients participating in the many clinical trials run by the NCI/MIC. This will be used to track all the quantitative tumor information extracted from the imaging data acquired in all the trials, as well as to help the NCI physicians, scientists, and fellows analyze and publish the results of the clinical trials.

Support to the Metabolism Branch, NCI

Barry L. Gause, M.D., Clinical Director
Beth Baseler, M.S., Director
Lamin Juwara, Ph.D., 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 patient care coordinator II and a clinical research associate II to support these efforts.

The patient care coordinator II is responsible for various administrative tasks including: scheduling participants seeking treatment and coordinating their visits; scheduling follow-up appointments; coordinating team schedules; scheduling diagnostic tests; communicating with outside physicians; and creating databases and reports. The patient care coordinator is responsible for providing administrative support to 18 protocols.

The clinical research associate II performed many integral functions, including: developing several collaborative relationships with investigative sites and client personnel; performing and coordinating assigned aspects of the clinical monitoring process in accordance with Good Clinical Practices 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.

Due to a clinical trial closing and budget constraints, the clinical research associate II position was eliminated during this reporting period.

Support to the Protocol Support Office (PSO), NCI

Rashmika Patel, Protocol Nurse Coordinator II
Aisha Wellington, M.P.H., Protocol Nurse Coordinator I
Merertu Tesso, M.P.H., Protocol Nurse Coordinator I
Michele Richman, Medical Writer III

The Center for Cancer Research (CCR) re-engineered its processes related to the development, review, and initiation 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 Support Office (PSO) and a Protocol Review Office (PRO). The 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 and/ or changes to protocol amendments and other documents related to research studies. In addition, the team assists with training new staff. CMRP staff are required to attend the IRB and Scientific Review Committee meetings. In addition, staff members are in charge of contacting PIs for the review board, as needed.

In support of the PSO, CMRP hired three protocol coordinators to serve as liaisons between CMRP and CCR/NCI staff to initiate and complete tasks related to protocol support. The regulatory associate II prepares and reviews submissions to the FDA and ensures that all documents are in compliance with FDA regulations. The two medical writer IIIs 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.

Staff played key roles in processing clinical protocols for submission to various regulatory agencies, such as the IRB, the FDA, the Office of Biotechnology Activities, and the Institutional Biosafety Committee. The team assisted clinical investigators with the review of 20 new protocols and informed consent documents, 50 protocol amendments, 10 OBA/IBC submissions, and was involved in 10 protocol navigation projects. Currently, the team provides support for approximately 40 active INDs, one active IDE, and one active drug master file (DMF). Seven new initial IND applications were submitted to the FDA during this reporting year. As part of the ongoing maintenance for these new and existing applications, staff developed and submitted approximately 80 IND, IDE, and DMF serial submissions to the FDA.

Support to the Protocol Review Office (PRO), NCI

The PRO is under the direction of the CCR Clinical Director's Office, and provides administrative support for the NCI intramural Institutional Review Board (IRB). Currently, the IRB has approximately 400 protocols under its review. PRO staff provides review of protocol actions (e.g., expedited, full board, etc.) for completeness before submission of review and approval by the IRB chair and clinical director.

The protocol coordinator assists IRB staff with the review of documents submitted for IRB review by the PIs and/or study coordinators, and extracts relevant technical information to include in the IRB packets and database. The protocol coordinator is responsible for distributing correspondence and approved documents by the IRB chair and clinical director to the PIs and study contacts. Additional duties include: processing and distributing other protocol actions (e.g., deviations/violations, closure to accrual, short consent forms, and miscellaneous documents) to the IRB chair and/or clinical director using the iRIS database; assisting in preparing IRB meeting packets in a timely manner; receiving internal calls regarding protocol submissions using iRIS; monitoring the task box in iRIS; and routing issues to the appropriate analyst.

The protocol coordinator updates/maintains the CCR Wiki for the IRB Administrative Office; prepares documents to renew IRB members before term expires; prepares the agenda for 23 IRB meetings annually; and attends bi-weekly IRB meetings.

CMRP manages a research subcontract providing the chair for the NCI IRB. The position of IRB chair is of utmost importance and ensures the safety of clinical trial participants as well as the scientific validity of study findings. Support provided by the IRB chair includes leading twice-monthly IRB meetings; directing discussions; leading the review of and voting on research proposals; playing an active role in establishing and reviewing IRB policies and procedures; identifying issues within research proposals; and conducting expedited reviews of safety reports, recruitment materials, informed consents, and special exemptions.

Support to Clinical Core (Transplantation), NCI

Lamin Juwara, Ph.D., 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 is in the process of recruiting and hiring a second nurse practitioner or physician assistant.

CMRP staff members serve as the associate investigators on 11 protocols, 7 of which are actively recruiting and performing transplants on 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 the 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 this fiscal 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
Lamin Juwara, Ph.D., Senior Nurse Practitioner

The overarching mission of the 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-human 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) and a randomized phase II trial of Cediranib/Sunitinib, which are some 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 continue to perform protocol-required hair root extractions to facilitate the research process for the Phase I LMP776 protocol and continue to collaborate with other cancer centers in multiple trials, including a Phase I 5FdCyd +THU trial and a Phase II ABT-888 + Cytoxan trial. In addition, staff participated extensively in the Phase Ib Study of the Combination of Pazopanib, an

Oral VEGFR Inhibitor, and ARQ 197 (Tivantinib), an Oral MET Inhibitor, in Patients with Refractory Advanced Solid Tumors.

The clinical research nurse supporting DTC's early drug development team under the Medical Oncology Branch (MOB) is currently involved in coordinating six research protocols and capturing research data to assist the team in fulfilling its mission. The clinical research nurse is also actively involved in evaluating patients for protocol eligibility, recruiting patients, helping consent patients for trials, and following up with patients via e-mails/phone calls daily to ensure protocol integrity. In addition, the clinical research nurse prepares reports for the IRB, drug suppliers for CTEP, and the FDA for audits.

The clinical research nurse supports the MOB thoracic team, which reports to the MOB's branch chief. The team is involved in various research projects/protocols using targeted agents alone and in combination with conventional chemotherapeutic agents. The clinical research nurse supporting the MOB thoracic team is currently involved in coordinating five research protocols and capturing research data to assist the team in fulfilling its mission. The clinical research nurse is also actively involved in reporting protocol deviations and violations to the IRB and/or Sponsoring Company, and conducting offsite visits to multicenter trials, to ensure regulatory compliance by all participating sites, such as VA Medical Center for protocol 09-C-0103.

Support to the Surgery Branch, NCI

Adriana Byrnes, Ph.D., Clinical Project Manager I*
Tatiana Beresneva, M.H.S.H., Clinical Research Associate III
Yvonne Shutack, M.D., Clinical Research Associate II
**Adriana Byrnes transferred to another department on 7/28/2012.*

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 five team members, including a clinical project manager I, two clinical research associates (level II and level III), a clinical coordinator, and a protocol coordinator I.

Staff members currently support 12 clinical investigators, who conduct approximately 30 active clinical studies and have 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. In the past year, the clinical research associate III has trained and provided continuous assistance to seven external clinical research associates hired by the Sponsor to complete Phase III data monitoring at NCI, and has trained nine monitors in anticipation of an August 2012 FDA filing of a new drug application. The clinical research associate III has also been readily available to assist external data analysts, providing the Sponsor with comprehensive and accurate information.

The clinical research associate II currently supports four protocols that have accrued 200 patients, and is responsible for data entry and analysis for these trials. The clinical research associate II also assists the Protocol Support Office (PSO) with reports for IRB continuing reviews and plays a key role in assisting the clinical monitors with presentation of the data. On several occasions, the primary PI has expressed his gratitude for the high-quality and timely turnaround of all reports requested.

The protocol nurse coordinator II was tasked with the coordination of five trials for the Endocrine Oncology Section of the Surgery Branch in the past year. The clinical research nurse has been praised by the client, clinical fellows, and designated patients as a caring and highly competent individual. This position was terminated with the Surgery Branch and moved to the newly created Endocrine Oncology Branch in April 2012. The protocol nurse coordinator II has expertly managed this transfer, facilitating a clean and smooth transition of the team to the new branch.

The clinical coordinator position underwent a switch in both personnel and focus in the past year. The original coordinator position assisted the Hepatobiliary Section team, and the staff member holding that position was highly praised for her efforts. However, the position became temporarily vacant in January 2012. At the same time, the PI responsible for this team left the NCI, and internal priorities shifted. This position was filled in March 2012 and now supports primarily the Thoracic Oncology Section of the Surgery Branch, with secondary support provided to the Immunotherapy Section. The new clinical coordinator has integrated very well with both teams and has been highly praised for the quality of her work and for having learned all her assigned duties in record time, thereby allowing the teams to focus on other tasks.

While the number of active Surgery Branch protocols may have diminished in the past year, the number of patients accrued and the complexity of the new protocols has increased, which has led to an increase in the number of regulatory submissions. The protocol coordinator continues to play a key role in processing 30–40 protocols for submission and maintains databases to track all submissions to various regulatory agencies, such as the IRB, the FDA, the Office of Biotechnology Activities, and the Institutional Biosafety Committee. In addition, the protocol coordinator spearheaded the development and design of a new Access database for patient screening for all sections of the Surgery Branch. The database is currently being used to generate queries and reports for

meetings. The protocol coordinator also supervises the clinical coordinator I.

The clinical project manager I is responsible for providing regulatory and scientific support to the PSO. The clinical project manager I has been instrumental in the successful submission and approval of two protocols and maintenance of six separate clinical protocols for three PIs, including two gene therapy protocols. The clinical project manager I assists other PSO staff as needed with submission and maintenance of an additional 20 clinical protocols, and reviews and assists in the updates of up to 15 SOPs from two separate laboratory teams, submitting them to the regulatory agencies as needed. In addition, the clinical project manager I prepared four initial Investigational New Drug (IND) applications 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
Lamin Juwara, Ph.D., Senior Nurse Practitioner

The 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 recruit 261 new patients last year, leading to the expansion of their prostate program. Additionally, the clinical research nurse II manages more than 100 patients with low-volume and low-risk prostate cancer, who are interested in active surveillance. This surveillance program involves monitoring patients' outside PSA levels, scheduling all restaging visits, diagnostic studies, and tests, and coordinating and arranging MRI-guided biopsies.

During the reporting period, CMRP staff efficiently recruited and enrolled an additional 261 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 Molecular Imaging Program 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
Lamin Juwara, Ph.D., 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 the 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, including IND annual reports and amendments related to sponsor-investigator-held INDs.

Support to the Endocrine Oncology Branch (EOB), NCI

Krisana Gesuwan, M.S.N., Protocol Nurse Coordinator II

The ultimate goal of the EOB is to establish an integrated basic, translational, and clinical research program for the development of innovative diagnostic and prognostic approaches and treatments for endocrine cancers. This goal is consistent with the mission of the CCR to: (1) understand the cause and mechanism of cancer; (2) improve early detection and diagnosis of cancer; (3) understand the factors that influence cancer outcomes; and (4) develop effective and efficient treatments for patients with cancer.

The EOB was established in April 2012 by former members of the Surgery Branch, NCI. The protocol nurse coordinator II, who was originally assigned to work with the Endocrine Section of the Surgery Branch, accompanied PIs to the newly established EOB and has been instrumental in assisting with the establishment of the Branch by actively interacting with other clinical and

support teams to create new processes that better fit this group. The protocol nurse coordinator II has designed and implemented new tracking databases for patient management and is currently responsible for the five surgery protocols that have collectively accrued approximately 162 patients during this fiscal year, and has also assisted in coordinating for two newly inherited medical oncology protocols that belong to a new PI who has joined the EOB.

With the establishment of the new Branch, the protocol nurse coordinator II has become the senior support staff in the group and is responsible for training new team members. The protocol nurse coordinator II is working with new team members to establish and coordinate a formal endocrine surgery fellowship, to start in the coming weeks. The protocol nurse coordinator II is also working closely with the new branch chief to formalize interdisciplinary rounds and is planning conferences to fully utilize NCI resources in patient care.

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

Taree Foltz, Program Manager II
Kirsta Waldon, Patient Care Coordinator

The HIV/AIDS Malignancy Branch (HAMB) is instrumental in focusing on AIDS-related malignancies that are positive for Kaposi's sarcoma–associated herpesvirus (KSHV). Pathogenesis of KSHV, a causal agent of Kaposi's sarcoma, primary effusion lymphoma, and multicentric Castleman's disease research efforts are ongoing.

The CMRP patient care coordinator is responsible for providing administrative support to HAMB. This staff member currently assists three investigators and two research nurses with approximately 200 patients who are in enrolled on seven active protocols. In addition, the patient care coordinator works with the team on the recruitment process to increase patient referrals for new protocols.

The patient care coordinator implemented and currently monitors 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 journal articles written by the investigators.

Additionally, the patient care 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.

During this reporting period, the patient care coordinator has continued to support the team on the recruitment process to increase patient accrual, in addition to performing many new duties, including: preparing scientific research samples for transport to the repository; collecting and disseminating medical resource documents on new patients for fellow's review prior to initial assessment of the patient; and obtaining saliva from protocol recipients for scientific testing.

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

Barry L. Gause, M.D., Clinical Director
Mary Ann Tamula, M.A., 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) study 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; (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; and (3) investigate potential cognitive interventions that could help ameliorate some of the cognitive deficits and declines as a result of the disease and treatment. 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 work primarily with the neurobehavioral program to conduct 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 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 in completing data entry, administrative, and other research-related tasks.

During this fiscal year, both psychometricians participated in the collaborative development of research posters that were accepted for the 2012 Children's Tumor Foundation held in New Orleans, LA, and the 12th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer, held in Williamsburg, VA. One of the psychometricians presented a poster at the POB Research Round Up.

Support to NCI Division of Cancer Epidemiology and Genetics (DCEG) – Tumor Heterogeneity

Barry L. Gause, M.D., Clinical Director
Petra Lenz, Physician II

A physician II provides ongoing scientific and pathology support to the Occupational and Environmental Epidemiology Branch of the DCEG and the CCR, which work together to conduct studies in the United States and abroad to identify and evaluate environmental and workplace exposures that may be associated with cancer risk. The main focus of the research is to: identify occupational, environmental, and other factors affecting cancer risk; characterize exposure response relationships; identify biomarkers for disease detection, diagnosis, and prognosis that are associated with certain risk factors; identify susceptible populations and gene environment interactions; and improve research methods for occupational investigations. Projects involve sophisticated methods and intensive collaboration among epidemiologists, pathologists, industrial hygienists, and molecular biologists.

Several ongoing collaborations are also being conducted with the Applied Molecular Pathology (AMP) Laboratory to perform research using novel high-throughput techniques for studying tissues in large cancer investigations focusing mainly on handling, processing, and evaluating fixed tissues, with a particular emphasis on using tissue microarrays for immunohistochemical analysis with subsequent digital imaging and automated evaluation of stains.

Ongoing large studies involving these technologies include the investigation of cell cycle control proteins and methylation enzymes in urothelial carcinomas using tumor tissue from the "New England Bladder Cancer Study" to examine the possible effect of tobacco and arsenic exposure on protein expression profiles and methylation status. The United States and Eastern European Kidney Cancer Study focuses on the effects of von Hippel-Lindau (VHL) somatic mutation and promoter methylation in renal cancer.

Specifically, the physician II provides immunohistochemical staining of tissue arrays (assay development and review); image, digital image, and stain analysis (developing algorithms for specific staining patterns); pathology slide and report review; annotation of tumor tissue for RNA extraction; and manuscript preparation and review.

During the reporting period, the physician II published three peer-reviewed articles in scientific journals: (1) "Correlation of LINE-1 Methylation Levels in Patient-Matched Buffy Coat, Serum, Buccal Cell, and Bladder Tumor Tissue DNA Samples," published in *Cancer Epidemiology, Biomarkers and Prevention* in July 2012; (2) "Von Hippel-Lindau (VHL) Inactivation in Sporadic Clear Cell Renal Cancer: Associations with Germline VHL Polymorphisms and Etiologic Risk Factors," published in *PLoS Genetics* in October 2011; and (3) "Analysis of the Distribution and Temporal Trends of Grade and Stage in Urothelial Bladder Cancer in Northern New England from 1994 to 2004," published in *International Scholarly Research Network Pathology* in January 2012.

SUPPORT TO THE OFFICE OF THE NCI DIRECTOR

Support to The Cancer Genome Atlas (TCGA), NCI

Joy Beveridge, M.S., Clinical Project Manager III
Sylvie Kwedi, Ph.D., Clinical Project Manager III
Lenny Smith, M.S., Clinical Project Manager II

In 2005, NCI and the National Human Genome Research Institute (NHGRI) established 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 assisted with the oversight and management of 26 new or extended tissue source site (TSS) research 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 are 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 established research subcontracts with academic medical institutions to obtain actively and retrospectively collected biospecimens through the SAIC-Frederick prime contract. The project also selected, through research subcontracts with SAIC-Frederick, the services of two BCRs: International Genomics Consortium and Nationwide Children's Hospital.

During the reporting period, two CMRP positions (clinical project manager I and III) were filled in support of TCGA activities. The clinical project manager I position was filled in January 2012 and the clinical project manager III position in March 2012.

Legacy Research Subcontracts

CMRP is extending MD Anderson, Mayo Clinic, and Fox Chase research subcontracts with no cost extensions through March 2013, to collect all remaining data and complete any tissue subcontract requirements.

CMRP continues to manage a research subcontract that was awarded to the National Cancer Center of Korea (NCC of Korea), which offers NCI the opportunity to collect rare samples from non-U.S.-source sites, where the standard of care in the United States would preclude the use of samples in the TCGA program. The U.S. 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 specimens. To date, this site has provided 86 samples to TCGA's pipeline.

CMRP also continues to manage two research subcontracts awarded to NCI Community Cancer Centers Program (NCCCP) hospitals to collect prospective biospecimens for the expanded list of tumors. CMRP is supporting the modification of the subcontracts with Catholic Health Initiatives (CHI) and Christiana Health Care to complete their contractual obligations by providing additional tissue types from the current list of TCGA tumors for the program.

2012 Research Subcontracts

With support of ARRA funding, TCGA actively augmented its network of TSSs during this reporting period, to provide tumor specimens that are collected retrospectively (tissues that had already been collected and stored) or prospectively (tissues that will be collected in the future). CMRP staff provided the competitive SOW that was incorporated into the Request for Proposal (RFP). Up to 35 different tissue types need to be procured from the new TSS. The RFP release date was posted to the Fort Detrick Business Opportunities website on November 30, 2011. The RFP was also announced by e-mail to potential offerors belonging to the following groups: NCCCP awarded institutions 2007 and 2010 PIs/Leads; NCI and SAIC-Frederick past and present TSSs; NCI Cancer Centers Program (P30 awardees) – PIs and administrative personnel for NCI Cooperative Groups; College of American Pathologists; NCI Specialized Programs of Research Excellence awardees; vendors identified from past market research conducted for the Office of Biorepositories and Biospecimen Research (OBBR); NCI Center to Reduce Cancer Healthcare Disparities awardees, including Geographic Management Program Regional Coordinators; Early Detection Research Network awardees; and OBBR-BRN Symposium Members. Proposals are being accepted on a rolling basis, with no specific application deadline. As proposals are received, they are reviewed for responsiveness prior to sending to the Source Evaluation Group (SEG) for their technical review and scoring. A recurring, two-week cycle, rolling review and evaluation is being coordinated.

By August 2012, 32 proposals were received and evaluated, and 16 BOAs awarded—more than half with follow-on Task Orders that allow for specimens to be shipped (only after sites have met all other technical requirements required prior to shipment). The response rate to the request for proposal (RFP) has been slower than anticipated. As such, efforts are under way to be more aggressive in seeking potential offerors. Between March and April 2012, three bidders' conference calls were held to answer potential offerors' questions and to ensure a clear understanding of the published RFP. The questions and answers provided were formally documented and distributed in the form of amendments to the solicitation.

The strategy to increase the RFP response rate includes: (1) directed phone calls to potential offerors who indicated strong interest, but still have not submitted proposals; (2) one-on-one phone calls to potential offerors who have not yet acknowledged the RFP (approximately 1,200 contacts from more than 400 sites) to entice them to submit proposals by offering technical assistance; (3) discussion of ways to increase the RFPs' visibility by advertising in various venues, such as conferences, trade organizations' websites, and scientific journals; and (4) enhancing the Fort Detrick Business Development Office webpage where the RFP is advertised. In addition, in order to abbreviate the review/selection/award process for current contributors of high-quality specimens, sole-source research subcontracts are considered to alleviate the full SEG review process.

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

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

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. The official NCCCP began in 2007 as a three-year pilot program with 16 community cancer centers. In 2010, stimulus funding allowed program expansion by adding 14 sites to the network and creating additional work for the original 16 NCCCP community cancer centers. In July 2012, following a limited competition for an additional 24 months of funding, the network was reduced to 21 community cancer centers.

Through June 2012 of this reporting period, the NCCCP was a network of 30 community cancer centers located in rural, suburban, and inner-city communities in 22 states. These 30 sites saw approximately 62,000 new cancer patients per year and served a population of approximately 23 million Americans.

NCCCP hospitals are continuing to address 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 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 multiple program 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 website; (3) oversight of more than 30 NCI listservs; (4) management of the NCCCP wiki content; (5) coordination of the 2.5-day 2012 NCCCP Annual Meeting for nearly 300 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; (6) coordination/tracking of the review/approval of network presentations/publications from network authors (reviewed/edited more than 40 presentations/publications, including the comprehensive online monograph, published in FY2012 as a series of 13 articles in *Oncology Issues*, which highlighted the program's major focus areas to share lessons learned with other community cancer centers; (7) development of data collection tools; and (8) management and analysis of an increasing volume of subcontract data.

CMRP programmatic support to NCCCP also included ongoing management of the multiple sets of individual research subcontracts that comprise the NCCCP effort. Dedicated CMRP staff manages the relationships between the awarded organizations, SAIC-Frederick, and NCI, to support project objectives and activities. Through June 2012 of this reporting period, there were four sets of research subcontracts (a total of 45 subcontracts), each with a defined scope of work and specific deliverables, as follows:

- 10 original pilot awards that address the comprehensive and overarching NCCCP activities (July 2007–June 2012);
- 10 ARRA awards to the original pilot organizations to conduct 18 additional individual projects in support of the NCCCP mission (April 2010–June 2012);
- 11 ARRA awards to academic institutions to support the NCCCP sites with two specific projects; these awards represent a collaboration of NCCCP with two NCI programs: (1) the Community Networks Program; and (2) the CTEP Early Drug Development Program (April 2010–June 2012);
- 14 ARRA awards to additional organizations to address the comprehensive and overarching NCCCP activities (April 2010–June 2012).

In October 2011, the NCI director approved funding to extend the NCCCP's period of performance for an additional 24 months, through June 2014. CMRP staff supported the acquisition and procurement activities for the limited competition among the 24 subcontractors. The RFP was issued in February 2012, and 23 subcontractors competed for the additional funding. In July 2012, 18 subcontracts supporting 21 community hospitals were awarded. For the 24-month extension period (12 months covered by remaining ARRA funds and 12 months to be covered by new FY2013 appropriated funds), a smaller number of more strategic and focused deliverables are included in the research subcontracts. Starting in July 2012, CMRP staff managed two sets of subcontracts (a total of 28 subcontracts):

1. 18 ARRA awards (9 original pilot award subcontractors plus 9 sites that were added in 2010) that address the comprehensive and overarching NCCCP activities (July 2012–June 2014); and

2. 10 ARRA awards to the original pilot organizations to complete ARRA Project 9, a research study related to multidisciplinary care coordination (July 2012–June 2013).

During the reporting period, staff continued to assist with the formal evaluation of the NCCCP pilot network. This assistance included collaborating with NCI contractor, RTI International, Inc., to finalize official report documents, including a cost study, patient surveys and focus groups, data outcomes, and clinical trials accrual analyses. CMRP staff worked with NCI advisors to review report drafts, provide editorial assistance, and ensure content accuracy. This involved coordinating feedback from the NCI Program Advisory Committee (NPAC), the Evaluation Oversight Committee, and the CMRP team through several rounds of reviews. CMRP consolidated comments and provided comprehensive revision requests to RTI International, Inc. Additionally, CMRP de-identified NCCCP site names in the final drafts of the integrated report, economic evaluation, and document appendices. Staff also assisted with the creation of summary documents to share with the NCCCP network and external stakeholders and partners.

CMRP continued to provide data and planning support for the evaluation of the expanded program – Assessing Research Collaborations (ARC) Evaluation.

CMRP directed, coordinated, and managed efficient data collection, advanced analytics, data storage, and data sharing across all programmatic components of NCCCP to ensure the comprehensive collection and analysis of high-quality data. Staff developed new tools and question sets, reviewed and analyzed data to measure and document programmatic progress, prepared data presentations, and shared results with NCI and NCCCP stakeholders. One abstract using NCCCP data was accepted at the American Society of Clinical Oncology in 2012, and an additional six journal publications are currently being prepared.

Until January 2012, CMRP assisted an NCI contractor to provide an online data collection tool that provided a solution for storing, collecting, and reporting NCCCP data. Due to limitations in NCI funding, that contract was discontinued in January 2012, and it was decided that CMRP would manage the multiple data collection activities using comprehensive Microsoft® Excel spreadsheets that feed data into a custom-made SQL database. The CMRP solution meets the backend data storage, reporting, and retrieval needs, is more cost effective than the previous collection method, and allows more control of the data without timeline and contract limitations. Longer-term data collection and reporting needs are being coordinated by CMRP staff and include the expansion of the database functionalities. Upgrades include the ability to easily modify question sets, minimizing the burden on NCCCP sites by decreasing the volume of questions asked each quarter. A Quick Reports feature is also being developed to give NCCCP advisors more timely access to the data that will inform decisions about the program. The database can also expand its capabilities to collect data online if needed.

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 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 NCI leadership apprised of NCCCP activities.

The NCI director remains supportive of the NCCCP and all of the NCI community programs. In October 2011, the director tasked an internal Community Programs Alignment Working Group to review the programs and to determine where there are redundancies and synergies, in an attempt to better align NCI community programs. NCI leadership drew upon the findings from the formal pilot program evaluation, as well as input from NCI divisions. The process and initial recommendations of the leadership group were shared with CMRP in April 2012, demonstrating a significant strategic decision to create a single network that builds upon the strengths of multiple NCI community-based research networks.

The multiple programs will be united under the NCI Community Oncology Research Program. The funding mechanism for the new program will be via NCI awarded cooperative agreements; the role of SAIC-Frederick has not yet been determined. A new Yellow Task is anticipated in order to continue the NCCCP until those plans are formalized and the NCI award process is completed (anticipated by spring 2014). This Yellow Task would request that SAIC-Frederick provide support to extend the NCCCP research subcontracts (those selected for award via the limited competition process outlined above) from July 2013 through June 2014, and provide additional appropriated funds to cover research subcontract and staffing costs.

The CMRP NCCCP team continued to facilitate the learning collaborative of NCI and the network sites by managing the efficient network communications and facilitating exchange of information via the use of the private intranet and wiki resource, and highly coordinated meetings and webinars (outlined above).

Key activities and accomplishments at the community hospitals are summarized below. Collectively, they illustrate the progress made over the past year as the NCCCP sites focused on the program's objectives to enhance access to care, improve the quality of care, and expand research capacity in the community setting.

Enhancing Access

A cross-cutting theme of the program is to reduce healthcare disparities across the full cancer continuum. All NCCCP sites are focused on addressing disparities in each of the program components (i.e., clinical trials, quality of care, survivorship and palliative care, information technology, biospecimens, communications).

From increasing community outreach activities and screening events to tracking race and ethnicity data and promoting increased accrual of underserved populations in clinical trials, the network sites are working to enhance access to cancer care and cancer research for underserved populations. In the past year, a rural initiative was launched, and three webinars were developed by the sites to address challenges and successful strategies for these specific areas: frontier and remote access; patient education; and transportation and lodging.
Key areas of activity reported by the sites are:

- Building Community Partnerships: More than 2,400 community partnerships are in place, with many of them serving the following populations: African American (n=251); Hispanic (n=337); rural (n=216); uninsured (n=333); and the poor (n=384).
- Conducting Screening Events: Between April 2011 and March 2012, sites conducted more than 3,200 screening events, reaching over 147,000 community residents.

Improving Quality

To improve the quality of cancer care provided in the community setting, NCCCP sites are increasing the use of evidence-based guidelines, utilizing a multidisciplinary model of care, and participating in national quality reporting initiatives. By the spring of 2012, 25 NCCCP sites had affiliated oncology practices participating in the American Society of Clinical Oncology's (ASCO's) Quality Oncology Practice Initiative (QOPI®)— a program that collects data and reports on measures from evidence-based guidelines to help improve cancer care—on behalf of the NCCCP. Additionally, 11 sites achieved QOPI® certification, and 18 sites are participating in the American College of Surgeons Commission on Cancer (CoC) Rapid Quality Reporting System (RQRS)— a tool to monitor and assess adherence to National Quality Forum-endorsed measures for breast and colorectal cancers—with all other NCCCP sites working towards RQRS reporting.

Building network-level partnerships and projects helped to advance the NCCCP's goal of improving the quality of cancer care. Significant activities and accomplishments include:

- **Genetics Performance Improvement Project – 2010 Cohort:** These 14 sites participated in a project aimed at increasing the number of cases referred for genetics counseling services for breast or colorectal cancer. Collecting and reviewing data monthly, sites were able to identify areas for improvement in the referral process, share data with hospital executive management, and chart plans for future enhancements to genetics programs. For example, universal screening for Lynch syndrome is now being implemented at many of the sites, and several are focusing on patient education, particularly for colorectal cancer patients, to increase knowledge regarding genetic screening guidelines.
- **Multidisciplinary Care Study – 2007 Cohort:** The 16 original pilot sites are participating in an ARRA-funded quality research study to conduct a preliminary study of the relationship between specific multidisciplinary care assessment areas and selected processes and outcomes of cancer care. The study was open for enrollment through September 2012, with data collection continuing until December 2012.
- **American Cancer Society (ASC) RQRS Symptom Surveillance and Disparities Study – 2007 Cohort:** Sites are participating in the ACS's Patient-Reported Outcomes study. Working with ACS and the CoC, this project is piloting a cost-effective method for collecting patient-reported data on symptom experiences and investigating disparities in symptom burden and management. The data collection process is using a methodology that maximizes scalability and minimizes costs for providers by using resources from partnering organizations. The study's goal is to recruit 1,500 breast and colon cancer patients; more than 900 patients have completed surveys for this project to date.
- **Completion of the Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) Study:** Five NCCCP sites, along with four NCI-designated Cancer Centers, participated with Memorial Sloan Kettering in a validation study to test the PRO-CTCAE. The NCCCP sites accrued 536 patients to the study, 25 percent of them minorities, and all sites met their accrual goals.
- **Survivorship and Palliative Care Initiatives:** The NCCCP community cancer centers continue to expand survivorship and palliative care services through increased use of patient treatment summaries, implementation of survivorship care plans, integration of palliative care resources in the cancer programs, and incorporation of processes to deliver psychosocial screening, care and referrals.
Key activities reported by the sites include:
    - **Addressing CoC 2015 Program Standards:** All sites are incorporating the 2015 CoC requirements specific to survivorship and palliative care program standards;
    - **Collaborating with Research Studies:** NCCCP sites are providing extramural research partners with access to community-based clinicians and survivors treated in the community setting;
    - **Offering Palliative Care Programs:** In the past year, more than 6,000 patients have been served by palliative care programs at NCCCP cancer centers; and
    - **Improving Capacity to Deliver Psychosocial Care:** NCCCP sites developed and utilized a tool to assess components of their psychosocial care programs and are using the information to

develop processes to address gap areas and implement services, such as distress screening with a standardized tool.

Expanding Research

With the accelerated speed of scientific discoveries and rapidly changing advances in technology, the NCCCP cancer centers are continuing efforts to become research-ready organizations. The NCCCP has helped participating community hospitals enhance cancer research capacity within their cancer centers. Several organizations and investigators have reached out to NCCCP sites, developing partnerships for study recruitment and/or research contributions. Additionally, many sites have formed relationships with NCI Community Networks Program (CNP) Centers and are participating in research studies with the goal of reducing cancer health disparities through community-based participatory education, training, and research among racial/ethnic minorities and underserved populations.

Clinical Trials

Newly identified cancer molecular subtypes and new knowledge about cancer genetics are driving changes in the infrastructure required to conduct early-phase clinical trials. One of the NCCCP's goals has been to increase capacity for the community hospitals to participate in early-phase trials, thereby offering more treatment options to patients closer to their homes. Combined with the program's focus on disparities, NCCCP sites are also working on approaches to increase patient participation in clinical trials—particularly for patients from underserved populations—to provide a broader base for cancer research. Over the past year, the sites broadened their clinical trials portfolios and opened more early-phase trials. Also of note, the network sites:

- **Focused efforts on the clinical trials' underserved accrual working group:** Emerging from a special session on underserved accruals at the 2011 NCCCP Annual Meeting, this group established metrics and collected data to help sites measure progress in three specific areas: physician/community outreach related to clinical trials; navigator/clinical trials research team coordination; and translation strategies.
- **Increased racial minority accruals to clinical trials:** Along with an increased number of overall accruals to clinical trials, NCCCP sites have increased racial minority accruals to NCI-sponsored Division of Cancer Prevention and Cancer Therapy Evaluation Program treatment, prevention, and supportive care/quality of life trials. Utilizing the NCCCP-developed Minority/Rural Matrix helped sites track and assess accruals for these underserved populations.
- **Expanded capacity and increased enrollment on early-phase trials:** Collaborations with NCI-designated Cancer Centers, Cooperative Groups, and industry partners have helped sites activate Phase II trials and increase their access to more early-phase trials. With a higher number of open treatment trials, sites are contributing to higher accrual numbers in the community setting.
- **Developed a clinical trials best practice matrix:** This tool contains nine elements for sites to assess their clinical trials infrastructure. The sites completed the matrix in spring 2011 to establish a baseline assessment and then again in June 2012; an analysis of results is under way.

Information Technology (IT)

IT initiatives are addressing program goals by integrating IT activities across the NCCCP area of focus to speed the incorporation of NCCCP data collection needs within technology expansion plans at the sites. During the past year, the IT Subcommittee gave special attention to the technical work required to support the disparities and biospecimen pillars, and also focused resources on technology expansion to meet the national technology agenda and meaningful use timelines. Key projects to support research expansion included:

- **Enabling Race and Ethnicity Data Capture:** All sites successfully implemented mandatory system configurations that required the collection of race and ethnicity data according to OMB guidelines.
- **Enhancing Local Data Warehousing:** Sites worked collaboratively to define an initial list of community-based oncology outcomes data elements mapped to common systems, locally addressing common data integration issues. Four sites created local data warehouses.
- **Improving and Sharing System Documentation:** IT representatives worked to improve and share system documentation, adding code to NCI open source solutions to enhance the deployment experience nationally.

Biospecimens

Advancement towards complete implementation of *NCI Best Practices for Biospecimen Resources* improved capabilities and contributed to recognition of NCCCP sites as valuable research partners in accruing high-quality subjects and specimens. The community hospitals are able to participate in biospecimen initiatives that will advance the NCI research agenda. For example, seven sites are participating in tissue collection trials for Moffitt Total Cancer Care, and nine sites have agreements to serve as tissue source sites for The Cancer Genome Atlas. Other key research capability expansion efforts include:

- **Collaboration to Identify Technology Gaps:** Collaboration with the College of American Pathology (CAP) led to a network project to elucidate the national gap in Laboratory Information System's

(LIS) ability to adequately calculate formalin fixation and cold ischemia time for accurate reporting of results, quality initiatives, and molecular research.

- **Partnering with CAP:** NCCCP partnered with CAP to address issues with the vendor community in an effort to ensure that formalin fixation time and cold ischemia time are captured adequately within electronic Cancer Checklists and to ensure inclusion in the national Case Report Form harmonization effort being led by NCI.
- **Enhancing Tissue Management Infrastructures:** Sites are improving local standard operating procedures and enhancing infrastructures to extend capabilities, improve quality, and expand participation in national biospecimen initiatives and research efforts.

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

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

CMRP continued to provide a cost-effective and efficient support mechanism to reimburse the efforts of the clinical, scientific, and advocate experts serving on NCI's Scientific Steering Committees (SSCs) in support of the NCI Clinical Trials Working Group (CTWG) initiative. Additionally, CMRP staff supported the Biomarker, Imaging, and Quality-of-Life Studies Funding Program (BIQSFP). The Special Translational Research Acceleration Program (STRAP) Yellow Task remained unstaffed and with $0 budgeted, as NCI weighed its options of continuing the program or stopping with the two funded efforts.

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

Scientific Steering Committees (SSCs)

Between 2008 and 2012, the SSC program increased from 6 SSCs and 140 consulting agreements to the current 16 SSCs and 468 vendor agreements. CMRP continued to monitor the effectiveness of the newly implemented vendor agreement process. The efficiencies gained with the new process continue, with an average turnaround time of approximately three days. CMRP's support of the SSCs includes project management, program analysis, and management of the massive and growing vendor agreement effort. NCI anticipates adding an additional SSC (Rare Tumor Steering Committee) during this fiscal year.

CMRP support continues with the maintenance of the Clinical Trials Working Groups research subcontracts database, which contains conflict of interest and confidentiality disclosure agreement documents, as well as term dates for the SSC vendors. Clinical project manager I support also includes supporting weekly CCCT program director meetings and designing slide presentations for CCCT program directors.

New CCCT project management support this year has included an expanded role for the CCCT clinical project manager I, including: (1) designing and facilitating (hosting) webinars within the CCCT for NCI Task Forces and Working Groups. This successful endeavor has seen widened utilization within the program and is being considered for monthly SSC meetings. The pilot SSC meeting webinar went very well; (2) becoming the responsible person for all CCCT website updates, which includes updating information related to all 16 of SSC's, postings of non-SSC-related materials, Section 508 compliance issues for the website (reported at 95 percent compliance), and full permission to update or remove data posted on the site without having to go through IT; (3) creating two Clinical Trials Planning Meeting (CTPM) templates for CCCT, including a CTPM Proposal template and an Executive Summary template; (4) joining the CTPM Administrative Team wherein project management support is provided to ensure effective CTPM and SSC face-to-face meetings. This has included the creation of timelines and effective communication processes with other teams (outside of CCCT).

Additional new CMRP support to the SSCs was provided by the clinical project manager II's facilitation of a mock protocol review and BIQSFP Evaluation for the NCI Patient Advocates Steering Committee workshop. The support included designing a complete mock protocol/study and application for CCCT mock reviewers to review and present at the workshop. CCCT staff played the roles of "Steering Committee" and "Reviewers." The Review included a script to follow as the review PROCESS was presented to workshop participants; feedback and participation was excellent.

Biomarker, Imaging, and Quality-of-Life Studies Funding Program

During the reporting period, the BIQSFP program continued to grow in scope and effort, with twelve BIQSFP applications being submitted and reviewed. NCI approved two BIQSFP study applications, with five currently under evaluation. Support efforts have entailed collaborating with several NCI programs, including Cancer Therapy Evaluation Program (CTEP); the Division of Cancer Prevention (DCP); Cancer Imaging Program (CIP); Cancer Diagnostic Program (CDP); and the various SSCs, as appropriate. Support also included facilitating the identification and coordination of expert external reviewers.

CMRP's BIQSFP support has included assisting CCCT and the FNL in determination of severability/non-severability funding for FY2008 – FY2011 approved

BIQSFP studies. Once the determinations were made, CMRP and SAIC-Frederick Research Subcontracts began contract negotiations for the eleven approved studies. Ten new research subcontracts have been completed this fiscal year for BIQSFP-funded studies, one of which is pending, with anticipated completion by the end of this fiscal year. SAIC-Frederick Research Subcontracts and CMRP have provided support to manage three existing BIQSFP research subcontracts.

Effective this fiscal year, NCI chose to move from a subcontracting model via SAIC-Frederick to an NCI Administrative Supplement model, via NCI Administrative Contracting. As such, CMRP will continue to support the current 14 subcontracts until their expiration (approximately 5 years). In addition, CMRP staff will provide programmatic support for the new model.

Project management support was provided to CCCT, the CCCT AO, and FNL in order to reconcile CCCT funding/budget issues. The result of this effort was the creation of a new document by the NCI AO for the CCCT director that clearly tracks monthly SAIC-Frederick costs/spend-down, funding, and account balances.

CMRP staff facilitated and supported the April 2012 revision of the BIQSFP Announcement, including updating and clarifying the Announcement and the requisite revisions to the official BIQSFP website, which has received approximately 5,000 visitors to date. 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 website. CMRP staff presented a BIQSFP poster at the Office of Biorepositories and Biospecimen Research (OBBR) Biospecimen Research Network Symposium, Advancing Cancer Research through Biospecimen Science, February 2012, Bethesda, MD. In addition, staff presented at two "Meet-the-Expert" sessions.

Special Translational Research Acceleration Program

NCI anticipates continuing the STRAP program with the supplement model of funding currently in place. At this time, NCI does not anticipate the need for any additional STRAP program support. The plan for FY2013 is to close the STRAP Yellow Task.

SUPPORT TO DCTD

Support to the Cancer Imaging Program (CIP), NCI

Joy Beveridge, M.S., Clinical Project Manager III
G. Craig Hill, Ph.D., Medical Affairs Scientist I
John Freymann, B.A., IT Manager I
Marlene Schultz-DePalo, M.S., M.A., RAC, Sr. IND Manager

Overview

Since 2002, overarching support to CIP has included the oversight of chemistry and quality assurance support, medical imaging agent availability, regulatory affairs, and imaging informatics. Oversight of critical research subcontracts awarded to facilitate both preclinical and clinical research activities for imaging agents, as well as the specific chemistry management support provided to the radiopharmaceutical facility in Frederick, has also served to ensure wider availability of investigational agents for exploratory and Phase I–III clinical trials. Regulatory support has been focused on management of the life cycle of the CIP Investigational New Drugs (INDs), assisting the advanced development of the CIP- and non-CIP-sponsored investigational imaging agents, intramural and extramural clinical trials support, and on providing access to CIP imaging agents for additional researchers via several cross-reference mechanisms that have been implemented. Oversight of imaging informatics, including the teams' participation in numerous informatics communities and imaging networking endeavors, has also been a key contribution. These efforts, either through research subcontracts, regulatory affairs, medical affairs, and/or participation in the imaging informatics communities, have served to support the mission and goals of CIP for the NIH intramural and extramural research communities, and high-profile NCI programs, such as the NCI Experimental Therapeutics (NExT) Program.

The CMRP managers, in support of CIP, have collaborated not only with other NCI programs, but also with groups within NIH at the Clinical Center and in Frederick, MD, with networks such as the American College of Radiology Imaging Network (ACRIN), American College of Radiology (ACR), Society for Nuclear Medicine (SNM), and with other scientific and regulatory organizations, including the FDA. This year, interagency meetings were initiated between regulatory and medical counterparts in the FDA's Division of Medical Imaging Products (DMIP) and NCI's CIP. 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 for cancer patients.

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 has proven to be extremely important in NCI's development of an infrastructure that supports higher-level compatibility with the Center for Biomedical Informatics and Information Technology's 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 the needs of the image processing community by providing submission, digital curation, and hosting services. As a result, a new vision has come to fruition as The Cancer Imaging Archive.

Since May 2009, a Ph.D. chemist has provided oversight to the group, serving both a radiopharmaceutical-scientific and management role, as well as being a resource for the development of both the SAIC-Frederick Radiopharmacy and SAIC-Frederick Radiopharmaceutical Chemistry group to support NCI.

A new leader for FDA regulatory affairs joined the CIP support team in November 2009 and oversees the regulatory life cycle and compliance for CIP's imaging agent portfolio: seven INDs with multiple clinical trials ranging from Phase 0 to III, and one new drug application (NDA), the first NDA that the NIH has ever held.

A clinical research associate III with nursing experience was hired in June 2012 to support the Clinical Trials Branch and will be assisting the CIP Clinical Trials Branch chief in administering procedures covering modification to new and existing CIP protocols in order to appropriately address adverse event (AE) reporting for CIP imaging agents, and to provide oversight on quality assurance (QA) issues. The departure of the medical affairs scientist and two clinical research associates for internal SAIC-Frederick advancement opportunities during FY2012 coincided with a hiatus in the implemented site visit program.

Both the Regulatory and QA staff increased their respective oversight of all of the ACRIN QA, monitoring, and audit programs during the past year, directly participating in teleconferences, meetings, and revising and commenting on processes and procedures to ensure compliance at ACRIN, with Cooperative Groups, and at the clinical trial site level for NCI studies under way in CIP.

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.

More than 20 procurements (including research subcontracts and consulting agreements) have been executed to meet the needs of the CIP principals. Research subcontracts have been established with major medical institutions, experts in the field of cancer imaging, and commercial companies that are assisting in the analysis and development of CIP's portfolio of radiopharmaceuticals.

The NExT Program integrated the activities of several cross-institute imaging drug activities into two decision-making committees; as mentioned, CIP continues to be involved in NExT projects by providing support and guidance to the SAIC-Frederick Radiopharmaceutical Chemistry group and the SAIC-Frederick Radiopharmacy.

CMRP staff also serves in an advisory role with the Center for Cancer Research's (CCR's) Molecular Imaging Program (MIP), the Small Animal Imaging Program (SAIP), and the Nanotechnology Characterization Laboratory, resulting in additional on-site CMRP support to CIP.

CIP's chemistry program primarily supports the goals of the Imaging Drug Group, providing development of new imaging agents and follow-up testing of currently administered agents. This groundbreaking work may lead to increased availability of types of agents for clinical trials. Maturation of this effort is documented by the fact that the original SAIC-Frederick space designated for this work was turned into a United States Pharmacopeia (USP)-level radiopharmacy capable of delivering clinical-grade human doses for use in preclinical and clinical evaluation efforts by a certified nuclear pharmacist. Currently, the SAIC-Frederick Radiopharmacy has supplied six doses of FES for administration to three subjects at the Clinical Center in Bethesda under CIP's IND.

The radiopharmaceutical chemistry lab was set up in Frederick, MD (in Building 325 on the Fort Detrick campus), in April 2009 to develop PET/single-photon emission computer tomography (SPECT) tracers for NCI's CIP and the Small Animal Imaging Program. This lab became fully operational in August 2009. In early 2010, CIP implemented a plan to convert the Building 325 laboratory into a USP Radiopharmacy and to create a new tracer developmental laboratory in Building 376. The two rooms in 376 are mainly for the development of existing and new radiotracers for preclinical studies. The Radiochemistry Laboratory is now fully functional. Radiochemical projects and experiments using 18F, 89Zr, 111In, and 99mTc isotopes occur regularly. Many doses of PET and SPECT tracers have been provided to SAIP for mice studies, and future animal doses will continue to be produced in this space. All nonradioactive chemical manipulations (protein purifications, bioconjugation, and assay development) are performed in the cold chemistry laboratory.

When the 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 certified nuclear pharmacist and a technician were also 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 SAIC-Frederick Radiopharmacy was able to deliver product to the Clinical Center in Bethesda as of April 2011. Due to the scheduled destruction of Building 325 in 2013, the SAIC-Frederick Radiopharmacy will be relocated to Building 538. Planning meetings to this end are already ongoing, with the newly identified space being superior in layout and size than the previous space in 325. The nine members of the CMRP CIP support team provide comprehensive and critical scientific, regulatory, informatics, and administrative support to the program. Additional details of this support and are outlined below.

Chemistry and Imaging Agent Contract Support

Research subcontracts with extramural sites were coordinated to facilitate the formal clinical trials performed at the CIP Phase I and II NCI contract sites. In addition, 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 were involved with negotiations with the three major suppliers of cyclotron-produced isotopes and radiopharmaceuticals, for implementing fluoro-L-thymidine (FLT) tracer synthesis and applying for a drug master file (DMF) so the tracer could be supplied to NCI trials. Two manufacturers, Cardinal Health and PETNET are still currently under contract. Every six months, these same companies are queried about any new DMF sites brought on line and what their sites of expansion might be. These PET manufacturers 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 subcontractors to avoid commercial conflicts. The combined number of FLT sites available for supplying NCI clinical trials reached a maximum of 23 sites in 2012.

Additional tracers have been or are being investigated under SAIC-Frederick Research Subcontracts, whereby the vendor holds the IND or obtains Radioactive Drug Research Committee approval. These studies include: (1) a recently closed synthesis and exploratory clinical study of three PET tracers (1-(2 ′-deoxy-2 ′-fluoro-beta-D-arabinofuranosyl) uracil [FAU], five patients; 3 ′-deoxy-3 ′-18F-fluorothymidine, five patients; and 18F -1-(2 ′-deoxy-2 ′-fluoro-beta-d-arabinofuranosyl) thymine [FMAU], 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 recently closed pilot study of ^{11}C-SN-38 uptake and retention in patients who will be receiving irinotecan as part of their standard of care, six patients.

Regulatory Affairs Support

During the past year, comprehensive regulatory support was provided to CIP activities related to the IND and NDA development process for imaging agents. CIP facilitates the development of promising diagnostic agents. Many of these agents are PET drugs that fall under special FDA oversight and regulation, as their manufacturing often poses unique challenges, and they may not be able to undergo the same amount of standard preclinical testing or early-phase clinical testing as is required for more conventional drug development. A variety of regulatory mechanisms and strategies must therefore be kept in place at CIP as part of the life cycle of the CIP-sponsored imaging agents, and to enable others to cross-reference for their own research.

There are currently seven CIP-sponsored INDs and one NDA managed and supported by the regulatory affairs staff:

1. IND 71,260 ([^{18}F]-fluoro-L-thymidine), a proliferation agent;
2. IND 68,556 (ferumoxytol), a blood pool MR agent;
3. IND 70,900 (ferumoxtran-10), a lymph node MR agent;
4. IND 76,042 ([^{18}F]-fluoromisonidazole), an hypoxia agent;
5. IND 79,005 ([^{18}F]-fluoroestradiol), an estrogen receptor agent;
6. IND 100,429 [^{111}In]-Herceptin, a Her2 receptor agent;
7. IND 103,429 [^{18}F]-NaF, a bone scanning agent; and
8. NDA 22-494 sodium fluoride

Multiple protocols (the majority of them Phase II trials, but running the gamut from Phase 0 to III, with differing regulatory requirements) are being conducted under each of the CIP-sponsored INDs. Twelve trials were active and enrolling patients during this period. Many of the trials have inherent regulatory complexities due to the involvement of multiple investigators, sites, local IRBs, and contract organizations located in the United States, Canada, and other foreign sites. During this period, CIP Regulatory has issued approximately 15 letters of authorization allowing independent researchers to cross-reference the materials in CIP INDs for their trials.

During the past year, increasing CIP regulatory and chemistry support has been required to guide the

development process of several INDs and NDAs being developed by researchers within the larger NIH community. A new IND for Zirconium-89-labeled Panitumumab is also being developed in-house for sponsorship by CIP. Additionally, CMRP support personnel are working closely with federal staff to revise and update the hundreds of regulatory and production materials on the Cancer Tracer Synthesis Resources pages located on the CIP website.

The CMRP Regulatory Affairs group continues to provide, with CIP leadership, regulatory support for the subsequent requirements of the [^{18}F]-NaF NDA, which, due to its FDA status as a Reference Listed Drug, enables Abbreviated New Drug Applications to be submitted by drug manufacturers around the country.

Medical Affairs/Quality Assurance Support

The CIP support team works with the ACRIN program director, CIP medical officer, and CIP Clinical Trials Branch chief 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 Regulatory and QA support team. Audit tracking schedules are reviewed in advance and evaluated against actual audit performance. Preliminary audit reports are sent to the Regulatory QA team for review immediately post-audit, thus providing an early-warning opportunity to CIP. Should prompt action be necessary, the CMRP and Regulatory and QA team works hand-in-hand with CIP and ACRIN to define and implement a course of timely intervention to mitigate a suboptimal site issue. Items requiring immediate action are brought to the attention of the ACRIN program director at CIP and the branch chief. The Regulatory 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 toward this end. Federal staff and the CIP CMRP Regulatory and 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.

Imaging Informatics Support

The informatics component of CMRP support to CIP is comprised of an IT manager, bioinformatics analyst III, and consultant (half-time). The CMRP/CIP Informatics group manages The Cancer Imaging Archive (TCIA) research subcontract, facilitates imaging–genomics research projects, and supports data and tool sharing by CIP-funded grantee networks, namely the Quantitative Imaging Network (QIN).

The Cancer Imaging Archive

The NCI CIP asked CMRP to develop and manage TCIA (http://cancerimagingarchive.net/) to provide de-identification and curating services to overcome traditional radiological image data-sharing barriers. CMRP has developed state-of-the art image de-identification methodologies and tooling by partnering with standards organizations and professional societies. CMRP has tightly managed the TCIA contracting team to develop detailed SOPs, more than 100 pages of wiki documentation, and more than a terabyte of highly curated de-identified data.

TCIA was highlighted on the whitehouse.gov federal government fact sheet as one of two NCI programs leading “the big data revolution.” Over 7,000 unique web visitors from 104 countries have accessed TCIA. More than 1,000 bioinformatics and medical/clinical researchers have registered to use TCIA over the past year. Over 20 institutions have contributed image data to TCIA. At least 18 journal publications have been written based on data hosted in TCIA. By retrospectively accruing clinical images from patient participants in TCGA, TCIA has enabled newly formed cross-disciplinary teams to investigate the links between radiological images of patients and the matching genomic and pathology data from their tissues. This has led to the creation of volunteer-driven research teams centered on each of the cancer types in the same manner as the official TCGA project. As of June 2012, glioblastoma, breast, and renal cancer teams are at work, with prostate and lung teams to follow. The glioblastoma group has produced more than 24 accepted abstracts for posters and scientific presentations as well as multiple accepted journal publications. CMRP led high-visibility community development events to stimulate imaging–genomics research, including a workshop with the American College of Radiology and a special session of leaders in this field during the Radiological Society of North America 2012 annual meeting. TCIA is providing support to the NCI’s Quantitative Imaging Network by serving as a central, trusted broker of image data sharing between sites within the network to help them attain their goal of validating high-throughput, automated software tools that perform quantitative image analysis against varying data sets.

Imaging-Genomics Research

TCIA has been used by CMRP to acquire large numbers of case-matched images from The Cancer

Genome Atlas (TCGA) subjects for the community to analyze. Ad hoc multi-institutional, multidisciplinary research groups have been encouraged and facilitated around this data by providing outreach and substantial facilitation support. Extensive remote tooling systems have been developed to leverage innovative cloud-based solutions. Groups are not currently funded, but instead participate on a volunteer basis due to the high value of the data. This initiative, with an extraordinarily low operational budget to NCI, has opened new opportunities to join radiology, genomics and pathology. CMRP has provided IRB support to, and has contract agreements in place with nine institutions to provide imaging data match with TCGA cases.

Quantitative Imaging Network (QIN)

CMRP supports the informatics activities of the NCI QIN, a network or 14 U01 grantees that collaborate on data and tool sharing to advance algorithm development and validation. Leveraging TCIA, CMRP has helped all of the funded institutions load de-identified data onto a common platform and has developed new integration strategies to incorporate tooling in place at the institutions. CMRP has provided web-based technology support to facilitate management workflow and is an active participant in the QIN informatics working group.

Cancer Therapy Evaluation Program (CTEP), NCI

The NCI's CTEP funds correlative studies performed during the conduct of sponsored clinical trials of CTEP IND agents. This serves the extramural community by supporting critical correlative studies with material from, or examinations of patients participating in, NCI-sponsored clinical trials. The approved CRADA-supported correlative studies must be linked to the NCI-sponsored trials being conducted with CTEP-IND agents.

CMRP provided high-level administrative and subcontract management support to CTEP–CRADA-supported correlative science.

Four CRADA-supported research subcontracts were awarded to the following institutions, with a total value of $238,000:

- Johns Hopkins University (P8269): A Phase I Open-Label, Dose-Escalating Trial Evaluating the Safety and Tolerability of AZD6244 and IMC-A12 in Patients with Advanced Solid Malignancies
- Mayo Clinic (P8233): A Phase II Trial of CCI-779 and Bevacizumab in Patients with Endometrial, Ovarian, Hepatocellular, Carcinoid, or Islet Cell Cancer
- Mayo Clinic (P8810): A Phase I Study of the Combination of the VEGFR Inhibitor, AZD2171, and MEK Inhibitor, AZD6244, in the Treatment of Solid Malignancies
- Moffitt Cancer Center and Research Institute (P8631): A Phase II Study of AZD6244 in Patients with Relapsed or Relapsed/Refractory Multiple Myeloma

At the time of this report, discussions were being held for possible future support utilizing a previous established framework. This framework is serving as a model for potential additional CRADA-supported correlative science research subcontracts.

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) Phase II calibration of the BCR-ABL assay; (4) creation of a specimen retrieval system to collect cases for validation of NCI-supported clinical assays; and (5) implementation of a Clinical Assay Development Program focused on supporting the development and optimization of clinical-grade assays. As of July 2012, 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 University 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 research subcontract will end September 2012.

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

Beth Baseler, M.S., Director
Taree Foltz, Program Manager II
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

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 12 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); the Process of Care Research Branch (PCRB); the Office of the Associate Director and Science of Research and Technology Branch; the Basic Biobehavioral and Psychology Sciences Research Branch (BBPSB); and the Health Behaviors Research Branch (HBRB).

CMRP behavioral scientists and project managers 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. In addition, CMRP staff 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 behavioral risk factors (e.g., physical inactivity, poor dietary behaviors, and sun safety) to genetic susceptibility and breast cancer screening practices, and measurement and methods related to cancer prevention and control research, CMRP staff members have published and presented over 90 papers and abstracts in peer-reviewed journals and leading scientific conferences. 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 NCI's DCCPS BRP surveillance efforts to examine trends in cancer communication and cancer prevention behaviors, and to seek better understanding of the mechanisms and theories of behavior change. CMRP led the development of the Health Information National Trends Survey 4 (HINTS 4) and managed the HINTS Grid-Enabled Measures (GEM) website, 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 3 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 this fiscal year, CMRP staff have led the development of instruments for cycles 1 and 2 of data collection and overseen the implementation of the first round of data collection for the HINT initiative. CMRP staff also contributes to the conceptualization, management, and development of other BRP surveys, including a physician survey examining patient enrollment in clinical trials and the Family Life, Activity, Sun Safety, Health and Eating survey. CMRP staff has been integral in the identification of survey items, scientific review, and the support, development, and submission of related IRB and OMB protocols for cognitive testing.

During FY2012, staff also supported the dissemination of the Food, Attitude, and Behaviors survey, and the development of a website and related fact sheets and publications 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 websites, 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.) website. This website, http://class.cancer.gov, offers an online tool for evaluating state laws that target obesogenic behaviors, such as physical activity and diet in the school environment.

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 have also played key management roles and contributed to the scientific content of high-level BRP meetings, workshops, and conferences, including: The International Smokeless Tobacco Meeting, held in partnership with NCI and the Centers for Disease Control and Prevention (CDC); and the publication of an issue for a groundbreaking meeting sponsored by PCRB, "Multilevel Interventions in Health Care: Building the Foundation for Future Research Goals."

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 and consulting agreements; coordinating the planning and support for various conferences and seminars for the program; and serving as the point of contact on these efforts.

The medical affairs scientist continues to contribute to the development of a biobehavioral research network and assists in planning the pathways for future pilot projects and scientific programming proposals. The medical affairs scientist participated in the fourth network meeting in mid-October 2011and provided significant contributions in selecting specific scientific studies to accomplish network objectives.

Support to the Health Behaviors Research Branch (HBRB), NCI

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

The mission of the Health Behaviors Research Branch (HBRB) is to support research on cancer prevention behaviors and outcomes, which includes diet, physical activity, sedentary behavior, energy balance, obesity, sun safety and indoor tanning, genetic influences on behaviors, and virus exposure. Activities include providing leadership in developing methodologies for the measurement of health behaviors and psychosocial correlates of behaviors; focusing research on effective multi-level influences and 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. website, the Family Life, Activity, Sun-Safety, Health and Eating survey and the Transdisciplinary Research on Energetics and Cancer (TREC) centers. 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 HBRB's C.L.A.S.S. website, http://class.cancer.gov. This website 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, state policy profiles, data updates, development of policy briefs, fact sheet updates and the inclusion of new policy areas on the website and database. During this fiscal year, the senior behavioral scientist presented website demonstrations at several national and local conferences and meetings. In addition, a symposium focused on the website and related policies and practices was presented at the Weight of the Nation Conference in Washington, D.C. The senior behavioral scientist continues to support research analyses and papers. Scientists in HBRB are preparing for submission in peer-reviewed journals.

The Food, Attitude, and Behaviors survey examines national fruit and vegetable intake. The senior behavioral scientist has been integral in developing a new website to disseminate information about this survey, developing text for a new fact sheet and managing the Food, Attitude, and Behaviors survey data distribution.

The Family Life, Activity, Sun-Safety, Health and Eating survey seeks to examine psychosocial, generational, and environmental correlates of cancer preventive behaviors. The goal of this survey 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 CDC 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 supports the Transdisciplinary Research on Energetics and Cancer (TREC) centers by serving on three special interest groups and also serves as co-chair of the Training and Education special interest group and the Health Disparities Interest group. The senior behavioral scientist has written, presented, and submitted more than eight 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 BBPSB. In 2010, the BBPSB established the NCI Network on Biobehavioral Pathways in Cancer. The mission of the branch is to: accelerate the translation and communication of biobehavioral discoveries to advance clinical cancer care; foster research excellence through the integration and dissemination of relevant scientific discoveries; and identify, support, and communicate new research directions in the field of biobehavioral pathways in cancer. The strategic plan of the branch focuses on expanding the understanding of biological mechanisms connecting biobehavioral factors and the cancer continuum; fostering biobehavioral research in clinical cancer care; training and supporting young investigators; and encouraging transdisciplinary collaborative research efforts.

CMRP provides scientific, programmatic, and administrative support, meeting and travel coordination, and establishes consulting agreements and research subcontracts for the BBPSB. In particular, CMRP staff is part of the network steering committee and provides scientific contribution to the network initiatives and research projects.

The clinical program administrator, working with the BBPSB chief, was responsible for establishing and maintaining four consulting agreements and five subcontracts during this reporting period. The consultants are responsible for providing expertise in the area of biobehavioral research and attend meetings in person and via conference call, in support of the branch. Two of the five subcontracts provide literature reviews on MRI-based research on brain stem control of the sympathetic nervous system and its regulation by higher brain regions; behavioral probe paradigms; and empirical neural activity correlates of social support, attachment, affiliation, and related psychological constructs.

The branch has established a research subcontract with the University of California, Los Angeles, to test two hypotheses about how b-adrenergic signaling may influence all cancer progression by modulation of the SDF-1/CXCR4 chemokine system, and macrophage recruitment/activation. Defining the cellular and molecular mechanisms involved will allow potential development of novel therapeutic interventions, thus increasing chances for survival and lifelong health.

The branch has also established a research subcontract with the University of Wisconsin to investigate gene expression patterns of CD14+ cells as a potential pathway by which stress-related psychosocial factors may influence clinical outcomes following hematopoietic stem cell transplantation (HSCT).

A research subcontract with the University of Miami will provide data analysis on the examination of women in a Cognitive-Behavioral Stress Management (CBSM) program versus those in a psychoeducational control group on clinical disease endpoints, including recurrence-free survival, breast cancer–specific survival, and overall survival at 6–13 years follow-up. The study will determine whether women who showed more favorable biobehavioral changes and better psychological adaptation over the initial 12 months of the trial differ on clinical disease endpoints at 6–13 years follow-up.

A final research subcontract with Metabolon provided metabolic analysis of human ovarian cancer. The goal of the study was to characterize the metabolic profiles of tissue from various human ovarian tumors. The outcome of this study proved that the global metabolic analysis of ovarian tumor tissues in comparison with either normal ovarian tissue or fallopian tissue identified a number of metabolic changes consistent with the demands of hyperproliferative cancer cells. The analysis indicated significant inflammation and oxidative stress associated with ovarian tumors, a mark also observed in the fallopian tissue. The production of N-Acetylaspartate (NAA) and N-Acetylaspartylglutamate (NAAG) was higher in ovarian tumor tissue, than it was in both normal ovarian and fallopian tissues.

In addition, CMRP staff supported and participated in a fourth BBPSB meeting, "Neural Mechanisms that Underlie Biobehavioral Pathways in Cancer," in Houston, Texas, in mid-October 2011. The medical affairs scientist, working with the BBPSB chief, strategically planned the pathway for future pilot studies and scientific programming proposals. The outcome of this meeting was the selection of two specific scientific projects to accomplish network objectives. During the reporting period, two research subcontracts were established and the projects are ongoing.

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 include reviewing abstracts for scientific conferences; preparing presentations for national and local conferences and meetings; coordinating publication and dissemination of special journal issues and meeting reports; and authoring and co-authoring scholarly publications, including a chapter for the NCI Tobacco Control Monograph series on tobacco-related health disparities.

The clinical project manager I continues to provide research and administrative support to research networks supported by the NCI/TCRB, including the Tobacco-Research Network on Disparities (TReND) and the

Tobacco Harm Reduction Network (THRN), and served as the technical lead and meeting liaison for the Global Smokeless Tobacco pre-conference workshop and hemi-plenary session held at the World Conference on Tobacco or Health (WCTOH) in Singapore. The clinical project manager I coordinated the development of TReND's final special journal issue on Global Tobacco Inequalities and coordinated initial efforts on another special issue examining the role of smoking imagery in the movies and other entertainment media on tobacco-related health disparities worldwide. In addition, the clinical project manager I maintains the THRN website and serves as the primary communications liaison between NCI, CDC, and external collaborators from the academic and private sectors.

The clinical project manager I functions as scientific note-taker at high-priority meetings and drafts meeting reports to inform NCI staff of critical issues and action steps. As follow-up to one of these meetings, the clinical project manager I is now serving as the NCI point of contact for the federal government's North American Tobacco Regulatory Laboratory Technical working group. Additionally, in May/June 2012, the clinical project manager I worked closely with TCRB staff to draft a briefing document on the Indonesian tobacco epidemic. This document was submitted to the NCI director in preparation for his presentation to the Indonesian government in July 2012 and has been shared with other key stakeholders, including U.S. embassy staff in Indonesia and staff at the United States Agency for International Development (USAID), the World Lung Foundation, and Campaign for Tobacco-Free Kids.

Since 2008, CMRP staff has contributed to the development and promotion of NCI's nationally recognized smoking cessation websites, including smokefree.gov and women.smokefree.gov. The clinical project manager I continues to support these efforts on women.smokefree.gov by developing and reviewing new content to enhance the website with a more holistic focus on smoking cessation and physical activity, nutrition, sleep, stress management, and other mind-body practices such as mindful eating. New content for the site will go live in fall 2012 and will provide women with additional resources for smoking cessation and health living.

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 this fiscal year included: leading weekly planning meetings for the program; developing program publications; developing HINTS instruments; analyzing HINTS data; supporting HINTS data users and responding to their questions; updating and providing content to the HINTS website; 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. Since September 2011, the behavioral scientist has led the development of instruments for cycles 1 and 2 of data collection and overseen the implementation of the first round of data collection.

The behavioral scientist serves on the Steering Committee for the Center for Excellence in Cancer Communication Research (CECCR). CECCR duties include participating in monthly planning 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 Seattle, Washington, in April 2011. In addition, the behavioral scientist 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 2011, the behavioral scientist published nine manuscripts in peer-reviewed journals including the following: *Preventing Chronic Disease*, *Journal of Cancer Education*, *Journal of Medical Internet Research*, *Journal of Health Communication*, and *Journal of Cancer Epidemiology*.

The behavioral scientist actively participates in and presents work at national meetings. The behavioral scientist presented nine papers at the following meetings since September 2011: International Research Congress on Integrative Medicine and Health, Portland, Oregon, 2012; HMO Research Network Conference, Seattle, Washington, 2012; Society of Behavioral Medicine, New Orleans, Louisiana, 2012; Society of Personality and Social Psychology, San Diego, California, 2012; and the American Medical Informatics Association, Public Health Informatics section, Orlando, Florida, 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. Since September 2011, the behavioral scientist has led an effort

to identify, prioritize, and upload into GEM measures of health behavior theory constructs relevant to cancer behavior. 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. Since September 2011, the behavioral scientist has provided feedback on several iterations of the survey content and methodology.

The behavioral scientist has served as a reviewer for a number of journals since September 2011, including the following: *Journal of Cancer Education, Annals of Behavioral Medicine,* and *Journal of Health Communication, and Preventive Medicine.*

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

A major contribution of the behavioral scientist has been as project lead of the Science of Team Science Toolkit, an interactive website that supports information exchange and knowledge sharing to promote the growth and unification of the interdisciplinary field called the "Science of Team Science" (SciTS). In this capacity, the behavioral scientist works with a multidisciplinary team comprising computer programmers, social and clinical psychologists, and experts in communications, education, and informatics, to develop the structure and content of the Toolkit, solicit public contributions to the Toolkit, and promote the Toolkit through internal NIH meetings of interested groups, national and international conferences, listservs, websites, and social media.

With the leadership of the behavioral scientist, the Team Science Toolkit was radically redesigned after its debut in April 2011, and was re-launched with an entirely new, more accessible user interface in October 2011 at the annual conference of the American Public Health Association (APHA). The redesigned Toolkit was featured at the National Cancer Institute kiosk in the exhibitors' hall, and through two "Meet the Experts" sessions. The Toolkit was also highlighted through two interactive demonstration sessions at the Third Annual International Science of Team Science Conference, in Chicago, Illinois, in April 2012, the primary conference venue for stakeholders in team science practice and research.

During the reporting period, the behavioral scientist has co-authored three publications and four oral presentations.

The behavioral scientist continues to lead a study to identify lessons learned from the BRP Transdisciplinary Research in Energetics and Cancer (TREC) Initiative regarding key processes for successful team science, related challenges, strategies for success, and proximal and distal outcomes. The TREC Initiative is one of the largest and highest profile BRP grant initiatives, which represents a trend of large center grant initiatives that fund teams of collaborators within and across centers at different academic institutions to engage in cross-disciplinary research at the intersection of diverse fields. In the previous reporting period, the behavioral scientist interviewed over 40 individuals funded by TREC or involved in the TREC initiative's administration at NCI. During this reporting period, the behavioral scientist analyzed interview transcripts and has reported results through an oral presentation at the October 2011 annual conference of the American Public Health Association, a January 2012 meeting of TREC investigators, and two webinars involving past and current TREC investigators. The behavioral scientist is currently developing a manuscript featuring results of this study. The behavioral scientist also provides technical assistance as a member of the Collaboration and Outcomes Working Group of the TREC initiative. The behavioral scientist participates in the working group's monthly calls and, during the reporting period, has provided important technical assistance related to the development of goals and priorities for the working group, and related evaluation activities, including providing technical assistance to develop study designs, interview guides and protocols, and survey instruments that will be used in the next few months to assess collaborative processes and proximal outcomes of the TREC initiative.

In addition, the behavioral scientist is co-lead on an important theory development study to build the evidence base on how oncologists' psychological traits play into their decisions to refer patients to cancer clinical trials. This is a priority topic area for BRP and NCI, as there continue to be severe shortages of patients participating in cancer clinical trials, which delays production of important research findings related to cancer therapeutics. Physician psychological traits are hypothesized to be one important contributor to these shortages. During the reporting period, the behavioral scientist assembled a team of experts from multiple programs and divisions within NCI to serve as the research team for this study. In addition, the behavioral scientist has secured financial support for this work from the NCI. Over the last year, with the leadership of the behavioral scientist, this team has developed a two-phase study design involving a national panel survey of oncologists, followed by a survey of oncologists participating in an NCI-supported program to enhance clinical trials referrals, and is currently developing the survey instruments and necessary internal partnerships at NCI to support the second phase of this research.

The behavioral scientist supports the BRP through additional technical assistance on a wide range of projects. In particular, the behavioral scientist provides technical assistance as a member of the Evaluation Working Group of the Centers for Population Health and Health Disparities (CPHHD) Initiative. CPHHD is another of the largest and highest profile grant initiatives

supported by BRP. The behavioral scientist participates in the working group's monthly calls and during the past year has provided expert assistance to develop study designs, interview guides and protocols, and survey instruments that are being used to assess collaborative processes among CPHHD-supported investigators and community partners in research. This research is currently ongoing.

Support to the Process of Care Research Branch (PCRB), NCI

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

The PCRB 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 scientist provides scientific support to PCRB by providing data and portfolio analysis, preparing manuscripts and supporting other research-related projects. The behavioral scientist 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 scientist 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 leading meetings, serving as an internal editor for a project-related journal supplement, and managing aspects of the project's dissemination and promotion. The behavioral scientist conducts research, collaborates on proposals for new projects and funding, and works on the development of meetings with external researchers. During the reporting period, the behavioral scientist authored and co-authored manuscripts and a presentation delivered at the American Society of Preventive Oncology Annual Meeting in March 2012.

Support to the United States – Latin America Cancer Research Network (US–LA CRN), Center for Global Health (CGH), NCI

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

The United States–Latin America Cancer Research Network (US–LA CRN) is a partnership between NCI's newly formed Center for Global Health (CGH) and participating Latin American countries that was 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 US–LA CRN currently comprises six study sites in five countries (Mexico, Argentina, Brazil, Chile, and Uruguay). Each country has a formal agreement with 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." Twenty-five of the twenty-seven recruitment sites are activated and enrolling participants into the study. During the current reporting period, CMRP supported many administrative, scientific, and operational aspects of this US–LA CRN endeavor as it transitioned to NCI's new CGH.

The scientific program manager provided guidance to US–LA CRN partners in meeting the project's scientific objectives. In addition to presenting the project's achievements at the third US–LA CRN Annual Meeting, and leading the coordination of the scientific agenda for the first meeting of virtual Data Coordinating and Analysis Teams (vDCAT) in Buenos Aires, Argentina, and the Annual Meetings in Guadalajara, Mexico, and Buenos Aires, Argentina, the scientific program manager provided high-level support to the US–LA CRN committees, including the preparation of agendas, minutes, and meeting materials for the Steering Committee, the Basic Research and Advanced Technology Committee, Pathology Committee, Clinical Oncology and Breast Cancer Surgeons Committee, vDCAT Committee, and Epidemiology Committee. With the scientific program manager taking the lead, there were two new additions to the list of US–LA CRN

Committees: Data Monitoring Committee and Data Sharing & Publications Committee. During FY2012, the scientific program manager presented "Building Biorepositories for the United States–Latin America Cancer Research Network" at NCI's 2012 Biospecimen Research Network Symposium in Bethesda, MD. The scientific program manager also coordinated the development of the first and second interim analysis, and oversaw the activities of, and assigned priorities to, the clinical program manager for operations (clinical project manager II), the senior program coordinator, and the secretary III.

The clinical project manager for operations supported the day-to-day functions of the study, collaborating with NCI, SAIC-Frederick staff from relevant scientific disciplines, subcontractors, on-site research staff, and scientific advisors to address queries from the sites and develop additional guidance documents as necessary (e.g., training plan guidance documents). The clinical project manager for operations coordinated the revisions to the *Manual of Operations* (MOP) v3.0 with CCS Associates (CCSA) and subject matter experts, including the corresponding translations into Spanish and Portuguese. The MOP is comprised of SOPs, guidelines, workflows, checklists, and responsibility descriptions in the following areas: (1) clinical operations; (2) biospecimen management; (3) molecular biology; (4) pathology; (5) quality assurance and quality control; and (6) informatics data management. In addition, the clinical project manager for operations contributed to the refinement of study CRFs, reviewed and provided feedback on changes to be made to OpenClinica® databases, and coordinated the user testing of the OpenClinica® system v1.2 and v2.0/2.1 from the NCI/SAIC-Frederick side, to ensure that requested changes and newly established rules were implemented correctly. The clinical project manager for operations provided support to several of the US–LA CRN Committees, including the Biobanking Committee, by preparing agendas, minutes, and summaries with action items. The clinical project manager for operations also provided technical assistance with issues related to site training on a variety of topics and to the supply of DAKO kits, Brady labels and equipment, Agilent reagents, and instrumentation to study sites. The clinical project manager for operations presented on operational topics at the 2011 Annual Meeting in Guadalajara, Mexico, and the vDCAT meeting in Buenos Aires, Argentina, and contributed to the planning and development of the 2012 Annual Meeting.

The CMRP scientific program manager and the clinical project manager for operations continued to provide expert support in the refinement of the study protocol, revision of an extensive epidemiology questionnaire, and development of the corresponding manual, and other clinically relevant documents, as well as associated revisions, a detailed Study Monitoring Plan, and accompanying Site Monitoring Guidelines. CMRP continues to contribute to the revision of the MOP. Both managers provide extensive capacity-building support to sites and investigators.

In addition, the SAIC-Frederick biobanking expert and on-site senior adviser conducted site visits to biobanks and hospitals in Argentina, Chile, Uruguay, Mexico, and Brazil to provide guidance on biospecimen collection, processing, and transport and storage, as well as to assess operations at the biorepositories.

Two SAIC-Frederick subcontractors, CCSA and Information Management Systems, Inc. (IMS) continued to play an important role in the progress achieved during the current reporting period. CCSA provided database and systems development, management and revision; systems technical documentation and training; quality assurance (QA) and quality control (QC) procedures, and application of study informatics. CCSA developed a plan to merge/migrate data from previous versions of the OpenClinica® database into version 2.0/2.1 of the database as requested by CGH. CCSA designed, developed, implemented, and maintained a study Data Warehouse and developed the tools for extracting and analyzing microarray data for use in preparing the molecular analyses for the study. CCSA also developed an MPBC Study dashboard with contributions from IMS and feedback from the NCI and CMRP.

CCSA contributed to the translation of the US–LA CRN MOP into Spanish and Portuguese and the assembly of the MOP in three languages. CCSA staff also attended, presented, and coordinated breakout sessions at the US–LA CRN Annual Meeting in Guadalajara, Mexico, and the vDCAT meeting in Buenos Aires, Argentina, as requested by NCI CGH and CMRP.

CSSA continued to maintain OpenClinica®, a clinical trials software system for electronic data capture and clinical data management, and maintains the production instances of OpenClinica® for each study site. Case report forms were modified and incorporated into the system in English, Spanish, and Portuguese, based on feedback from sites, subject matter experts, and SAIC-Frederick. In-person and webinar OpenClinica® training sessions were offered as needed, often in conjunction with BSI-II training. Access to the production sites is 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 the production version of OpenClinica® and BSI-II), also supported by CCSA. OpenClinica® help desk support continues to be offered via e-mail and a customized electronic "Squish" system for addressing and documenting problems and their resolution. Regular reports on data entered into OpenClinica® were produced every two weeks for NCI.

IMS maintained the 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 study. Data entry, requisition, report templates, and workflow documents were developed and/or revised according to study SOPs. In addition, IMS assisted with the development of the dashboard as related

to BSI. IMS staff participated in meetings, conferences, and workshops as requested, including the 2012 OpenClinica® Conference in Boston. IMS offered BSI training to sites in conjunction with CCSA training sessions on OpenClinica® as well as on an ad-hoc basis; and provided help desk support via e-mail and a customized electronic "Squish" system.

CMRP maintained formal agreements between SAIC-Frederick and the six participating countries implementing the MPBC Study and two subcontractors providing data and project management support, and renewed the agreement with the consulting clinical pathologist. In addition, new agreements were established with an on-site senior clinical research adviser, a senior biostatistician and an assistant biostatistician, an epidemiologist and an assistant epidemiologist, a medical oncologist, a consultant molecular biologist and a molecular pathologist. These subject matter experts are members of the various US–LA CRN scientific committees and regularly attended teleconferences. They guided the respective working sessions at the US–LA CRN Annual Meeting in Guadalajara, Mexico, and contributed to the development of SOPs and guidance documents pertinent to the MPBC Study and the preparation of the first interim data analysis. The research subcontracts are interrelated in that they support the main objectives of the study, whether it is developing systems that collect, store, and analyze biological specimens; provide technical and scientific guidance; contribute to infrastructure support; manage, monitor, and analyze the clinical, molecular, and epidemiological data; or guide the use of advanced microarray technology for analyzing molecular profiles.

A senior program coordinator has supported US–LA CRN since fall 2010 and contributed to the ordering and monitoring of DAKO diagnostic reagents and instrumentation for the sites. The senior program coordinator updated project management tools for tracking materials and projecting budget needs, and provided study site research subcontract and budget support as well as scientific conference, seminar, workshop, and travel support.

During FY2012, CMRP successfully recruited a secretary III to provide dedicated administrative support to the US–LA CRN initiatives as the program plans for expansion in the upcoming year.

From an administrative standpoint, CMRP provided monitoring of the FY2012 budget and assistance with the FY2013 budget preparation. Together with NCI personnel, CMRP staff provided logistical assistance and/or travel coordination. This support included the preparation of more than 100 domestic and international nongovernment and CMRP employee travels for the third US–LA CRN Annual Meeting in Guadalajara, Mexico; the American Society for Hematology Cytogenetics Annual Meeting in San Diego, CA; the first and second combined bioinformatics and statistical analysis team meeting at NCI, Bethesda, MD; the first vDCAT meeting in Buenos Aires, Argentina; the CGH's inaugural meeting in Bethesda, MD; an NIH grants writing workshop in Bogota, Colombia; the American Society of Clinical Oncology International Clinical Trials Workshop in Sao Paolo, Brazil; and the American Association for Cancer Research Health Disparities Meeting in San Diego, CA.

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 and maintaining a regulatory environment that supports the research priorities of the NIAID Intramural Research Program. CMRP established and managed RCHSPP, which included development of the Regulatory Affairs Group, Clinical Trials Management Team, Clinical Safety Office (CSO), and Protocol Navigation/ Protocol Development Program (PN/PDP).

The primary objective driving the purpose of RCHSPP is the continued provision of 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; protocol logistics and development services; IRB support; IT systems maintenance; QA compliance; document management; and training program support. All of these efforts are to ensure that NIAID-sponsored 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 research subcontracts, logistical/project management, and operational support to a variety of clinical projects.

CMRP's mission is to provide regulatory support to the PIs in order 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 effectively supported, allowing PIs more opportunity to focus on the main objectives of their research 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. The PN/PDP has become well established and continues to experience success 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., staff also travel to remote sites, such as Mali, Kenya, India, Uganda, Cambodia, Peru, China, Indonesia, Thailand, Vietnam, Singapore, Korea, Mexico City, Australia, Argentina, and South Africa. CMRP staff also monitors domestic sites, including the 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), as well as HIV, general infectious diseases, and Acute Respiratory Infections Consortium clinical protocols, including H1N1.

RCHSPP maintains a position on the forefront of expanding to new and innovative regulatory technologies, as well as addressing new safety oversight requirements. The Regulatory Affairs Group successfully established and maintained a platform for submitting INDs in electronic common technical document (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. The CSO has launched an initiative to address the enhanced safety oversight responsibilities as required by 21 CFR 312. Current progress includes the development and implementation of various tools, processes, and strategies to track compliance.

RCHSPP has implemented strategic planning concepts and practices to ensure mission alignment with our government counterpart, RCHSPB. RCHSPP formulated strategic goals with four important organization components in mind: (1) Processes; (2) People; (3) Customers; and (4) Resources. These goals served as a platform for operational effectiveness. A strategic initiative was identified for each goal area, IRB Stipulations (Processes); Core Competencies (People); Protocol Review Services (Customers); and Resource Utilization (Resources). Through the implementation of an operational plan, the scope, timelines, and resources for each strategic initiative were identified and monitored. Goal committees were established to drive the success of each initiative. These groups defined key performance indicators to set expectations and serve as a guide to measure RCHSPP progress towards strategic goals and objectives. Progress was monitored and reported regularly. A new strategic planning cycle has been initiated to review the current strategy and identify priorities for the future.

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 (L&PD) Group, the Strategic Planning Working Group, the Protocol Navigation Working Group, and the steering committee for the Office of Planning and Operations Support (OPOS).

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. The Regulatory Affairs Group consists of one regulatory affairs director, one senior IND manager, six regulatory associates, and one regulatory submissions coordinator.

In collaboration with the RCHSPB IND clinical research oversight manager, the Regulatory Affairs Group 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: protocol amendments; information amendments; annual reports; safety reports; and 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 website.

Currently, the group provides support for 56 active IND applications, two active IDEs, and four active DMFs, several of which include protocols conducted at multiple sites including international locations. During the contract year, the group prepared and submitted 11 new IND applications. Additionally, there are approximately 17 INDs/IDEs in various stages of development. As part of the ongoing maintenance for these new and existing applications, staff developed and submitted approximately 225 IND, IDE, and DMF serial submissions, and five 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 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, HSV vaccine [Sanofi-Aventis], HPIV3cp45 IMPAACT study, and MedImmune pandemic influenza CRADA projects); and (2) providing cGMP guidance to RCHSPB about product storage, labeling, and manufacturing issues.

The Regulatory Affairs Group has fully implemented the electronic common technical document (eCTD) format and now prepares and submits all new IND applications in this format. Since obtaining and completing training on the required software and processes and submitting the first eCTD IND to FDA in April 2011, the staff has submitted nearly all new INDs in this format, with nine submitted during this reporting period. In addition, 60 serial submissions of various types (e.g., notices of intent to convert to eCTD, IND annual reports, and responses to FDA requests for information) were submitted during this period.

Of special significance is the Regulatory Affairs Group's effort to share this eCTD knowledge with staff in other NIH Divisions and Institutes. In December 2011 and January 2012 the regulatory affairs director and eCTD subject matter experts gave presentations to members of the regulatory teams in the Division of AIDS (DAIDS), NIAID, and the Cancer Therapy Evaluation Program, NCI, about the development of our eCTD program and lessons learned in the process, gave a demonstration of the eCTD software, and showed examples of finalized, FDA-accepted documents. In early March 2012, a meeting was hosted for the DAIDS regulatory group to provide them with additional, more directed, eCTD training. Staff has also shared eCTD experiences and information with members of the Cancer Imaging Program and the Surgery Branch of NCI. All of these presentations were well received and greatly appreciated. Staff also developed and presented a poster at the FNL and Fort Detrick Spring Research Festival regarding our experience transitioning from paper INDs to an eCTD program.

Another requirement for the new program was the development of Regulatory Affairs Group–specific SOPs and work instructions to define and educate current and new staff on the processes for developing eCTD documents. To address this requirement, staff drafted one broad-scope SOP encompassing the entire eCTD submission process. This document, entitled "Preparation and Submission of eCTD Applications and Submissions," was approved and went into effect on March 1, 2012. Three additional work instructions were also developed during this period: (1) for preparing MS Word and PDF documents for eCTD submission; (2) for creating and publishing the submission with eCTD software (OmniSUITE); and (3) for use of the FDA electronic submission gateway and distribution of archive copies. Staff also created instructions for extracting regulatory documents from an eCTD submission and for setting up a computer in preparation for eCTD production, and developed a map showing where traditional paper IND components should be located in an eCTD.

Staff continued to provide ongoing maintenance for three high-profile IND applications for influenza. The H1N1 hyperimmune plasma IND covers two protocols and involves a coordinated effort among study sites to collect high-titer anti-influenza H1N1 plasma from human volunteers for immunotherapy. The second IND uses treatment with collected investigational anti-H1N1 hyperimmune plasma as treatment for influenza. The third IND is evaluating combination antivirals to treat influenza. In addition to submitting more than 17 IND amendments for the general maintenance of these INDs, staff worked closely with the PI and RCHSPB to prepare responses to multiple FDA requests for information. This often required extensive review of previously submitted information and the development of a matrix to ensure that responses to FDA questions were adequately addressed. Staff provided regulatory review and input on an important substudy that will allow the purchase of H1N1 immune plasma from the Mississippi Valley Regional Blood Center; successful implementation of this substudy should eliminate the need for enrollment of additional subjects at existing clinical sites and result in a significant cost savings. Regulatory Affairs Group members participated in weekly study status teleconferences with DCR, NIH PIs, and other IRC study stakeholders, and submitted information on these protocols and the combined, active 60 clinical study sites to the clinicaltrials.gov website in accordance with the federal regulations. Staff also reviewed product labeling (in both English and Spanish) for domestic and

international distribution of drug kits to ensure FDA compliance, and coordinated with the manufacturer for the review of product quality data (i.e., stability) for the annual report and to support the shipment of drug kits to all study sites.

The senior IND manager continued to direct the ongoing processes related to the RCHSPP Inspection Readiness Program, which underwent a semiannual audit in May 2012. 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. The system was "tested" by a mock inspection in late November 2011, and, although many staff were out of the office on the day of the mock inspection, the process was effective. A follow-up debriefing and review meeting was held to define areas needing improvement, and the senior IND manager developed and implemented corrective and preventive action (CAPA) plans as appropriate and updated any inspection readiness documents (e.g., instructions, templates, etc.) that required changes.

The regulatory affairs director completed a thorough annual review of the "NIAID Division of Clinical Research Practices and Guidelines for the Management of Investigational New Drug Applications" and incorporated multiple changes to improve the utility and clarity of the document. The substantial edits reflected any changes during the previous year to FDA regulations/guidance, changes in RCHSPP/B practices and procedures, as well as new/modified hyperlinks and webpage addresses. In addition, the director worked with the IND clinical research oversight manager to develop a draft Transfer of Regulatory Obligations (TOROs) agreement to meet the IND sponsor requirement for selecting qualified investigators based on training, education, and/or experience. Implementation of these IND-specific TOROs is pending. The director also worked with the clinical research oversight manager to develop and submit to three FDA Centers a request that RCHSPB be granted a formal waiver from the requirements to collect financial disclosure documentation from non–National Institutes of Health (NIH) investigators conducting IND clinical studies. In a February 2012 teleconference with FDA to discuss this request, it was determined that, for studies conducted at NIH with industry-developed products, financial disclosure will need to be collected as there could be financial conflicts of interest in these circumstances.

After RCHSPB learned that a study subject inadvertently received an expired investigational product, the Regulatory Affairs Group worked with the IND, Safety clinical research oversight managers, and others to learn the details of the event and the resulting follow-up actions. The regulatory affairs director subsequently developed a CAPA for this incident and obtained RCHSPB review and approval for the document. The Regulatory Affairs Group and CTM then worked to design and implement necessary changes to the TrackWise® system and current processes so that appropriate staff will receive advance notice of product expiry/retest dates and thus prevent such occurrences in the future.

Aside from their regulatory duties and responsibilities, the Regulatory Affairs group contributed to the Learning and Professional Development group's third annual CMRP Training Retreat. In this effort, the Regulatory Affairs group recruited an outside subject matter expert in regulatory compliance as a speaker to share knowledge on compliance issues affecting the development of regulatory strategies for the CMRP.

Clinical Trials Management Team (CTM)

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

Currently, the CTM is involved with the management and/or monitoring of approximately 165 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/IDE. During FY2012, the team conducted approximately 58 study-initiation visits, 169 interim monitoring visits, 2 audit visits, and 29 study close-out visits. In addition the team attended three other types of visits this year at clinical sites. Trial monitoring was conducted at 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 CTM also conducted international site-initiation visits in Thailand, China, Argentina, Mexico City, Uganda, Cameroon, and Mali, and conducted seven study-site audits in hospitals in Korea.

CTM continues to provide sponsor-related clinical trials management for several newly established NIAID networks, including the IRC Network, INSIGHT (START), and the Mexico Flu networks. The team also initiated several new studies in the Washington, D.C., area that are part of the District of Columbia–Partnership for HIV/AIDS Progress (DC–PFAP) program and provided extensive training to the site staff involved with these studies. The training focused on IND studies, specifically, regulations/guidelines, monitoring and best practices.

CTM manages the sponsor's essential document files for the 38 domestic sites participating in one or more IRC studies and 19 international sites (including Mexico) participating in one or more studies 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 FY2012. CTM also expedited the initiation of two new multicenter influenza studies this fiscal year for IRC-003 and IRC-004 internationally, which also included the expansion of the IRC-003 study to five Argentina sites and four Thailand sites in the IRC Network. The kickoff meeting for Thailand occurred in May 2012. RCHSPP, and CTM activated the first site in Thailand during the summer of 2012.

The team reviewed clinical research protocols and informed consent forms, and provided commentary to NIAID, Infectious Diseases Clinical Research Program (IDCRP), and PIs at Johns Hopkins University The group also reviewed and revised IDCRP protocol study manuals, source documents, and case report forms on various new studies and studies that were previously activated. The clinical trials director and clinical project manager II assisted the IDCRP management with drafting review and implementation of their QA program. They received and commented on several IDCRP report templates for this group. The two teams (CTM and IDCRP) have excelled this year in their communication pathways. Last year, IDCRP management solicited the team's guidance on some of their new initiatives and included some of the CTM team members in their new study planning activities. Several team members also received invitations for an investigators meeting in England. These efforts allow CMRP to excel and enhance the level of efficiency for this group.

The CTM provided input for the updated RCHSPP Clinical Safety Office sponsor and NIAID unanticipated problem language, and assisted with the draft guidance documents they will provide to PIs regarding reporting SAE and unanticipated problem template language. In addition, the team helped to revise the NIAID CTM website page, updated several tools on the website, and created another version of 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 website. The team also completed 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. CTM conducted an internal review of the HHS Federal Register ANPRM, "Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay and Ambiguity for Investigators." Team designees provided comments to the FDA by the October 26, 2011, deadline. In addition, CTM conducted a review of FDA's new draft guidance, "Overview of Risk Based Monitoring," and provided comments by the November 28, 2011, deadline. The following DRAFT FDA guidance was also reviewed in FY2012 by the team: "FDA Guidance for IRBs, Clinical Investigators, and Sponsors: Consideration when Transferring Clinical Investigators Oversight to Another IRB."

A clinical project manager I and clinical trials director worked with the Branch to assess and develop three new study-initiation visit (SIV) slides extrapolating violation data by NIH lab. These three slides are to be presented by the CTM project management staffs that are present at each SIV moving forward. The draft slides were reviewed by the clinical trials director and the branch clinical research oversight manager in May 2012 and implemented in June 2012. This fiscal year, a clinical project manager I and clinical project manager II presented at the RCHSPB retreat for CTM summarizing data on monitoring trends, new initiatives within CTM, and findings uncovered during visits. Following the retreat, a clinical project manager I and clinical trials director developed slides and presented data to the branch chief and DCR director, along with others on monitoring trends and new monitoring approaches. At the request of the Branch, a clinical project manager II presented IND investigator responsibility training to the Laboratory of Host Defenses staff on June 11, 2012; the presentation was entitled "IND Studies: Regulations, Guidelines, Monitoring and Best Practices."

A clinical project manager I and clinical research associate II presented 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. For the NIH Fall poster Session in FY2013, team members are developing posters on the topics of strategies for overcoming challenges abroad, protocol reviews of IRB stipulations, and risk-based monitoring. The team continues to review all protocol amendments that affect the activated DoD/IDCRP general infectious diseases and HIV studies, and began to 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 Project Management Team, in addition to working with the group to enhance the protocol project life cycle and associated 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 continued to help 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.

All CTM team members completed the Gallup Poll survey in FY2011 and continue to discuss areas of enhancement and improvement for team processes and communications. CTM staff also completed the two-day training with an outside vendor, which gave the team an opportunity to brainstorm ideas to improve monitoring in the field. The team revised several tools and template letters to enhance monitoring. In addition, staff updated the CTM policies and procedures manual to include these revised tools, and updated TrackWise® fields that have been added to the system throughout the year. The clinical project managers also met to discuss ways to improve the report review process carried out within the team.

CTM continues to provide oversight of Pharmaceutical Product Development (PPD), Inc.® Thailand, China, and Korea, and Quintiles® Korea for monitoring functions that are carried out in Korea, China, and Southeast Asia. To date, one new study is planned for the Southeast Asia network; NIH PI staff added two new studies in Korea this year; and one PI added one new study in China, and extended a study to Thailand. The increase in protocol-related activities and the closure of other protocols has impacted the clinical research organization's efforts for the research subcontracts that are currently in place. The plan for FY2013 is for one new study to be opened in Thailand and one to be opened in Vietnam at several sites. CTM will continue to work with NIH staff and the PPD, Inc.® 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 Shanghai High Public Heath Clinical Center in Shanghai, China.

The team continued to review and provide extensive comments on several draft documents for RCHSPB, including monitoring guidelines, RCHSPP SOPs, draft outlines for TrackWise® trainings, the *Clinical Trials Management Policy and Procedures Manual* updates to version 5.0, and other Clinical Trials Management team CBTs. The CTD assisted the RCHSPB CROM with reviewing several drafts 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 and tools with which to assist the PIs this fiscal year, such as the "PI Responsibility Checklist," and the "Investigator Study Start-Up Guidance." The team is also continuing to review several other draft guidance documents. In addition, the CTM team continued to maintain 11 approved SOPs specific to major processes for clinical site monitoring and internal procedures, and has revised 9 of the 11 active SOPs. Two new SOPs are in development.

The clinical trials director participated in the review of several of the regulatory and training group's SOPs. Additionally, a clinical project manager I and II are preparing a talk to be given in the Fall of FY2013 at a vendor conference.

The CTM team performed a comprehensive review and finalized the IRC-004 monitoring plan in support of the IRC Network initiative. In addition, the clinical trials director and clinical research associate II 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 CTM team designees continued to perform comprehensive revisions of PPD, Inc.® monitoring reports produced by the clinical research organization that monitors the studies in Thailand, China, Korea, and those that are monitored by an independent clinical research associate in Mali.

The team created and updated lessons learned and items observed from monitoring visits for the IRC, DoD, and Johns Hopkins University (JHU) studies. The clinical research associates designated to work on JHU studies have continued to monitor many studies in Baltimore, Seattle, Rochester, and Vermont, and new studies have been added at all of the sites. Great strides have been made on several LID/JHU protocols as the JHU PI moves towards developing a vaccine for the Dengue virus.

One challenge this year for CTM has been related to study sites changing in Korea. The NIH PI transitioned some studies from one site to three others in Korea. CTM continues to work closely with them during this period of transition. The team is planning to start a new study in the near future at one of the newer sites.

The IRC Network is one of the larger projects the team is currently involved in since it consists of four study protocols globally. CTM currently has four clinical research associates responsible for monitoring all domestic sites as well as sites in Mexico. There is one in-house clinical research associate who handles all the regulatory document reviews, MDF file maintenance, and assists with other tasks as needed. Because many other external groups are involved with this program, processes have been implemented to ensure that all communications go out to the appropriate parties. Template e-mails were written and filed on our shared drive to aid in the notification process and ensure that the correct information is being sent. Examples of these types of communications are protocol Registration Approval, Site Activation Notification, as well as Study Agent Orders.

In order to have smooth and continuous communications within all the groups involved in the program, a communication plan was developed by the CTM clinical project manager and a senior site specialist from Social Scientific Solutions (SSS). One of the challenges is the sheer number of people involved with the operational aspects of this study, which is sometimes confusing for site staff when there are questions about the study:

knowing whom to ask, as well as knowing who on the operations team should weigh in/respond before a reply is provided to the site are aspects that must be clearly understood.

CTM has worked on communication flows for all studies as well as for all countries. Plans and documents have been developed by the group to aid in the flow of information based on the internal processes.

Study agent re-test dates had to be updated in March 2012 for the study agent for two IRC protocols that was out at the clinical sites. A clinical project manager II and clinical research associate III worked collaboratively with Fisher Clinical as well as SSS to devise a plan for rolling out the re-labeling effort to sites that had the study agent that needed to be re-labeled. Once CTM was notified that the labels were available to be shipped to the sites, the group had about two weeks to put together instructions and forms to send out to the sites. This was completed in a very short period of time, and the sites were given very little time to complete their part, but the effort was put forth, and all sites returned completed paperwork and completed the relabeling on schedule.

In an effort to provide an all-inclusive update to sites for all studies, the clinical project manager II suggested crafting a program newsletter, with articles from each of the various groups involved in the study such as Safety, Data Management, Operations, CTM, etc. A newsletter group was formed, a sample template of a newsletter was designed by the clinical project manager, and a format and plan for how articles would be solicited and approved was decided by the group. The first monthly newsletter was sent to participating sites in March 2012 and has been a monthly publication since then. Two CTM staff wrote the first article, related to re-labeling study agent, for the first issue in March. The clinical project manager II wrote an article regarding communications to be filed in the Site Study Binder for the April issue, and also wrote an article with the RCHSPB Safety CROM for the April issue related to important safety information. For the May issue, the clinical project manager II wrote an article about how sites report deviations in the database, and for the June issue, she and a clinical research associate II wrote an article about documentation of the Informed Consent Process. The clinical project manager II has been working with the clinical research associates to bring ideas to the group for upcoming articles for the monthly newsletter.

For the IRC001 study, one site was closed and another initiated. This effort is currently on enrollment pause, as the required number of plasma units may have been met. The protocol chair is researching the possibility of having one site to collect all the plasma needed to support the IRC002 study during the next flu season. Therefore, monitoring visits are ongoing for the study as needed, but enrollment is paused at this time.

For the IRC002 study, the final two sites were initiated and activated during this fiscal year. CTM staff participated in site calls to update site staff on protocol amendments and provided additional training, which occurred multiple times during the year. The lead clinical research associate II assisted the protocol team in researching and writing a plan for Plasma Unit Look-back. This task was initiated as a result of a site requesting information on how donors would be identified if a subject who received plasma on this protocol were to contract a disease through plasma donated in the IRC001 protocol. The clinical research associate II also wrote a contingency plan to be used if the protocol chair were not available to designate plasma units, should a request come through.

For the IRC003 study, CTM completed site visits for all domestic sites, in addition to conducting all SIVs in Mexico, which were completed in February 2012. The team, in collaboration with the PPD, Inc.® contractor, completed the SIVs in Thailand. The local clinical research associate (CTM team designee) completed the SIVs in Argentina.

The Mexico Investigator Meeting was held in December 2011 in Mexico City, Mexico. The clinical trials director and clinical project manager II were present via teleconference and gave presentations on Safety Reporting, Study Agent Request, Maintenance and Accountability, Monitoring, Investigator and Sponsor Responsibilities, and Randomization. The Mexico *Manual of Operations* (MOP) was reviewed and edited by the lead clinical research associate III and clinical project manager II for monitoring and country-specific safety reporting information. The clinical project manager II also aided in the coordination of study agent shipping and storage in Fisher Clinical Services, Mexico City depot, developed country specific forms, and worked directly with the staff at Fisher Clinical Services in Mexico to ensure a plan was in place for the study agent request and dispensing process. A bilingual clinical research associate II was hired in December 2011 to primarily monitor the four sites in Mexico. The clinical research associate II also attended all the SIVs conducted in January/February 2012, and has conducted one monitoring visit at one site in Mexico.

A clinical project manager I and clinical project manager II attended the Thailand Investigator Meeting (IM) in April 2012, in Bangkok, Thailand. The clinical project manager II collected most information for the presentations on safety reporting with respect to local regulations. Slide presentations for monitoring, study agent request, maintenance, and accountability, randomization, safety reporting, and investigator and sponsor responsibilities were compiled by the clinical project manager II, with special attention paid to the local regulatory requirements of Thailand. A PPD, Inc.® clinical research associate presented most of the material in Thai during the meeting, and a clinical project manager II participated in the meeting by presenting the auditing information for Thailand and answering many of the questions that arose during the meeting. The PPD, Inc.® clinical research associate carried out the SIVs, which were conducted during the same week as the IM, and both the clinical project manager II and clinical project manager I attended these visits. The Thailand MOP was

reviewed and edited for monitoring and country-specific safety information, as well as communications with in-country coordinating center. The clinical project manager II also aided in the coordination of study agent shipping and storage at the in-country repository, developed country-specific forms with the coordinating center, and worked directly with the pharmacist at the coordinating center via webinar during the IM and during the SIV, to ensure that an appropriate plan is in place for study agent dispensing to the Thailand sites.

The Argentina IM was held in May 2012 in Buenos Aires, Argentina. The lead clinical research associate II and clinical project manager II compiled slides to be presented by the RCHSPB/CROM during the IM for monitoring, study agent request, maintenance, and accountability, randomization, safety reporting, and investigator and sponsor responsibilities. The clinical project manager II also worked with Fisher Clinical Services to initiate the in-country repository set-up, designed the country-specific forms for study agent requests, and compiled a list of questions to be addressed at each SIV.

Team site calls to update site staff, provide additional training, and answer protocol-related questions for all the studies have occurred at various times throughout this fiscal year. CTM designees have participated in these calls and have conducted various sections of the presentations.

For the Australia sites, a team call was held with the clinical sites on June 18, 2012, to provide refresher training for the upcoming influenza season, as well as for Amendment 4 changes to be implemented in Australia once those sites obtain Ethics Committee approval. The lead clinical research associate III presented the Study Agent and Lessons Learned sections of the training.

Overall, CTM reviewed approximately 29 initial clinical research protocols/informed consent forms, 82 amendment reviews, and 13 site-specific informed consent forms. The clinical trials director and clinical project manager I worked with other management staff to update the RCHSPP Protocol Review and Amendment Review reference tool. In addition, the team was involved in reviewing the Livelink® document entitled, "Protocol Review Process – Reviewers & Compiler of Comments," and assisted with editing this document to mirror sections of the protocol review guidance. All staff members have been trained in Livelink® and reviewing protocols in this system since Spring FY2012.

The clinical trials director also supported the review efforts by making significant revisions to CTM's policy and procedure manual for the CTM team to reference. A disclaimer has been added to this document, which is used across all functional groups within RCHSPP. The clinical trials director also participated in scheduled calls to review/discuss the timelines associated with the protocols under the protocol navigation process that were implemented in FY2012.

Several of the international study PIs started to use a system called DataFax® this year, which has been a learning opportunity for CTM. Though it has been a challenge to learn the software for the CTM-designated staff members who have been helping create forms in FrameMaker® (which then have to be scanned into DataFax®), there have been many successes with this challenge. The FrameMaker®/DataFax® CRF creation has made great strides over the past year, with three sets completed and 13 others in progress. CTM was trained in the fall of 2012 on how to create CRFs in FrameMaker that are adoptable to this new database system. The development of this new service for CTM has also allowed the team leads to write a white paper on the DataFax® system that is currently in review, and the team expects to finalize it this fiscal year for posting on the RCHSPB website for PIs to access.

This year, the clinical project manager I helped to implement four new studies (and two older studies that needed to be updated) in the CRIMSON data collection system external to NIH; studies are currently conducted at Johns Hopkins University, the University of Vermont, Rocky Mountain Laboratories, and, the newest site added at the end of FY2011, Seattle Children's Hospital.

One of the challenges that CTM faces is helping to manage the data in CRIMSON for studies conducted at Johns Hopkins University that have since closed. A working group was established in May 2011 to develop a way to add this into the system, draft instructional documents and test this new part of the system. The working group established included several members of the CTM team, CRIMSON staff, and Johns Hopkins University staff, as well as the RCHSPB CROM. The development and testing of this system component is complete and instructional documents have been written. The system went live during the reporting period and is working well.

Designees from CTM are also working with the CRIMSON staff and RCHSPB CROM to develop CRIMSON to allow for electronic monitoring. To aid in this development, CTM created a monitoring visit procedure document for the CRIMSON staff to review. The document detailed each step of CTM 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. At this time, the members of CTM are meeting with the CRIMSON staff on a monthly basis to continue work on this project.

Other CRIMSON initiatives that the CTM team has been involved in are helping to review the new DSMB and FDA data tables that are now generated by CRIMSON. These will play an even larger role in the initiative to update and revise the adverse event tables that are also generated by the system.

A clinical research associate hired to monitor in Mali, Africa, also performed one GCP training session at the request of the site PIs in Mali. In addition, the clinical research associate traveled to Cameroon, Africa, and trained several new study staff members on the GCPs

there, as well as carried out a study-initiation visit for a new protocol at a new site in this country.

The clinical trials director and several CTM team designees continue to participate in a steering committee and working group to ensure we are prepared for an FDA inspection.

During the reporting period, the team worked internally to revise the customer-specific site-initiation visit templates for studies that now include the new NIH/FDA SAE reporting language. 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 templates for other non-IND studies that may be initiated domestically and internationally. Team members were also trained on each of the updated languages and new processes developed by the safety office that need to be in place before an IND study can be activated. A clinical research associate II took the lead on creating a letter to send to the PIs when a study is being closed and a final monitoring visit must be scheduled.

CTM continues to enhance the field training program for newly hired clinical research associates. A clinical research associate II presented the case report form training tool that enables new clinical research associates to review a set of fictitious source documents and compare them to the data on a case report form. In addition, the clinical research associates worked with management to help ensure that monitoring plans (MPs) are written and sent to PIs shortly after the activation of their studies. The team completed 50 percent of MPs within 30 days of SIVs between January and March 2012. CTM's risk-based monitoring approach CTM has had a great impact on enabling the PIs and CTM to make better assessments of resources and schedule timely monitoring visits.

A mini-group has been formed within CTM called the Clinical Trials Management Compliance Committee (CTMCC). This group has made great progress on conducting internal reviews of study files. Each clinical research associate has had at least one bucket review completed from one of their studies over the past year. The review of these documents has led to great discussions within the team and allowed for the implementation of new procedures aiming to improve consistency among all clinical research associates in filing for study documents.

The team updated several CTM template forms for further enhancement/function, made suggestions to Johns Hopkins University staff on revising some of their template forms, and participated in several calls with IDCRP key staff and RCHSPB staff to streamline Quality Assurance documents. The Quality Management/Quality Control documents that the clinical project manager II prepared were reviewed and presented at a meeting in England with IDCRP, which helped us promote quality enhancements and process improvements for the IDCRP study teams. Staff members assisted with providing training topics for the two-day, in-house training session, that was presented by an outside vendor to RCHSPP and NIAID staff in the spring of 2012.

The team updated and distributed a work distribution flow chart to CTM for reference, so all members will know who 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 team has worked with IDCRP on the development and review of several study manuals and CRF development as they have moved toward using an electronic system.

The clinical trials director and the clinical project manager I regularly review the newly created monitoring plan tracker data in the TW system, and have made minor edits to 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 TrackWise® support designee to streamline CTM process entry screens, and helped to create and test reports that are generated out of TW. This effort also helped again this year to update the Program Management Team, the DCR clinical director, the RCHSPB CROM, 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 CTM, and have been essential in developing other reports for CTM. The RCHSPB CROM requested and implemented several new reports that are distributed to the RCHSPB CROM at quarterly intervals to help with assessing targets for their strategic plan goals. These reports include some of the activities the team performs for NIH PIs as well as summary tables for easy tracking and trending of data. In addition, in FY2012 the clinical project manager I designated to be the super user for TrackWise® worked on the submission of 22 TrackWise® requests for implementation, and a working group was developed for collecting IND product expiration dates. The TrackWise® requests have been submitted, and a demo of this field should be forthcoming. CTM also initiated the addition of a new Data Management Field to TrackWise®, which will allow the clinical research associates to identify what data systems are being used for all the RCHSPP protocols. The clinical project manager I has also been reviewing TrackWise® fields to assess some areas that can be enhanced for the clinical research associates. Therefore, TrackWise® fields are now deemed "required" in the system, to enhance the data entry process for the clinical research associates.

The clinical trials director and the clinical project manager II continue to work with the RCHSPB CROM to identify ways for PIs to inform the group in a timely manner about upcoming projects. This information helps in the clinical trials director's assessment of new projects in the pipeline to ensure that proper resources are in place within the RCHSPP CTM.

CTM 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 CTM mini-group continue to meet quarterly to review the timelines, completed protocol reviews, and IRB stipulations.

CTM staff consists of one clinical trials director, four clinical project managers, thirteen clinical research associates, and one 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.

Members of CTM participate in calls involving the IRC Network, including team calls related to the Argentina and Australia sites. The monthly IRC team calls include those to a coordinating center for the other countries and to RCHSPB members for updates on the networks. Members also participate in quarterly program-related calls with RCHSPB and IDCRP staff. In addition, CTM 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 CTM team members have continued to initiate or collaborate on include assisting with strategic planning activities and IRB stipulation monthly protocol enhancement meetings. To date, the group and RCHSPP staff have met and reviewed eight protocols/IRB stipulations that have been IRB reviewed. From these reviews, the key leads have worked to develop a lessons learned document for RCHSPP staff to refer to as they perform protocol reviews for PIs. The team continues to assist in the development and beta testing of computer-based training, covering TrackWise® database fundamentals and proficiency; participating in the protocol development project; implementing CRIMSON at clinical sites external to the NIH; and writing approval documents related to CRIMSON.

The team continues to work with the RCHSPB and other NIH customers to provide quality improvement on clinical trials and enhancement to streamline study documentation.

Clinical Safety Office (CSO)

The CSO provides primary professional support to the Regulatory Compliance and Human Subjects Protection Branch (RCHSPB) in three distinct functional areas: (1) scientific and clinical support; (2) data and safety oversight committee support; and (3) medical writing support.

The CSO also provides surveillance, monitoring, and regulatory reporting of serious adverse events (SAEs) occurring on NIAID intramural clinical trials, including all trials where RCHSPB is the investigational new drug (IND) sponsor. The CSO ensures compliance with the Code of Federal Regulations, National Institutes of Health (NIH) policies, International Conference on Harmonization (ICH)/Good Clinical Practice (GCP) guidelines for protocols, informed consent documents (ICDs), and case report forms (CRFs).

The CSO staff consists of one director/medical monitor; one newly hired medical monitor; one medical writer; one clinical safety associate who serves as the Safety Monitoring Committee executive secretary; one clinical safety associate who is the NIAID Data Safety Monitoring Board (DSMB) executive secretary; and one secretary III.

Program Activities

During the contract year, 42 SAEs were processed and completed with 23 updates of continuing correspondence with the reporting investigators. The CSO filed one 15-Day IND Safety Report to the FDA. Adverse event (AE) tables were reviewed for SAE reconciliation and standard (MedDRA) AE terminology in preparation for 21 IND annual reports to the FDA.

The medical monitors and clinical safety associates reviewed 118 clinical research protocols over the contract year, consisting of 23 principal investigator (PI) reviews, 82 amendment reviews, 13 site-specific informed consent form (ICF) reviews, along with the associated ICDs. 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. At the completion of the review, a “No Regulatory Concerns” e-mail is sent to the PI. The template language for this e-mail has been updated during this reporting period. Nearly universally, the PIs have commended these reviews as being useful in addressing concerns prior to IRB submission.

The CSO staff participated in the Protocol Navigation/ Protocol Development Program (PN/PDP), providing medical monitoring and clinical safety support to assist in the development of nine protocols. This task includes weekly meetings and close cooperation between the MM and protocol navigators.

The 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 15 teleconferences involving 15 PIs for 16 protocols. The DSMB executive secretary also

arranged and facilitated two face-to-face meetings in which 29 protocols were presented by 15 PIs. Following each meeting, the DSMB executive secretary prepared summaries of the reviewed protocol discussions and recommendations, and distributed them to the PIs, DSMB members, RCHSPB, and select RCHSPP management.

Standardized AE data reporting tables pulled from the Clinical Research Information Management System of the NIAID (CRIMSON) database for use during DSMB reviews were revised to improve the efficiency and accuracy of the data submitted to the DSMB for review. A total of eight newly revised data table templates were developed and include: (1) Enrollment Summary and two supporting tables; (2) Frequency of Adverse Events by Cohort and Severity; (3) Frequency of Adverse Events by Cohort and Causality; (4) Frequency of Reactogenicity Adverse Events by Cohort and Severity; (5) Line Listing of Adverse Events by Cohort and Subject; and (6) Line Listing of Serious Adverse Events by Cohort and Subject. These tables were used by the DSMB in the July 2012 face-to-face meeting. The CSO staff was trained and given access to CRIMSON-generated data tables. These tables were beta tested during this reporting period. A new Guidance Document on the procedures to generate these tables has been provided to Study Coordinators and principal investigators (PIs). The implementation of these tables has enhanced the ability of reviewers (PIs, oversight committees, medical monitors) to analyze AE data that are entered into CRIMSON. These tables are also being reprogrammed, 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.

The CSO staff is collaborating in the development of the *CSO Procedure Manual*. Project tasks and milestones have been established for the completion of the manual, and a project tracker has been developed to monitor the completion of the individual procedures. A total of 14 procedures are in the process of being drafted.

The CSO is responsible for oversight, support, and facilitation of five protocol-specific Safety Monitoring Committees (SMCs) and five Independent Safety Monitors (ISMs). A clinical safety associate serves as the SMC executive secretary and 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. In the past contract year, the SMC executive secretary arranged and facilitated 19 ISMs and six SMC teleconferences. The confidential correspondence of the SMCs and ISMs are now maintained in a separate SMC/ISM mailbox that was newly established during this reporting period.

The CSO also collaborates with the Regulatory Affairs group and the Clinical Trials Management team (CTM), providing guidance, instruction, and expertise to the staff. The CSO reviewed Monitoring Visit Reports (MVRs) and collaborated with the clinical research associates to resolve any safety discrepancies found during these reviews. A review of one of these MVRs resulted in an expedited IND safety report to the FDA.

The CSO medical writer provided grammatical, formatting, and content review for 23 PI review protocols, and associated ICDs. The medical writer drafts original documents, edits, and reviews documents generated by or received from CMRP sources. As a whole, the CSO also developed documents for both internal and external use. Examples of key documents include the Transfer of Regulatory Obligations (TORO) and Safety Review and Communications Plan (SRCP) Template; TORO/SRCP Training Slide Presentation; NIAID intramural DSMB Data Tables; IND Protocol Safety Template Language; Guidance Document for Unanticipated Problems (UPs); and the *CSO Procedure Manual*.

Consistent with the RCHSPP operational plan for 2010–2012 to improve the review of protocols, a CSO staff member has presented a monthly review of the IRB stipulations from nine individual protocols to representatives of the RCHSPP functional groups (CSO, Regulatory Affairs, and CTM). Summary tables of lessons learned and IRB-suggested language have been created. A database of 1,885 IRB stipulations for all initial protocol reviews (70 protocols) during 2010–2012 is updated monthly. A total of 400 new stipulations were added during this reporting period. Databases of stipulations and lessons learned have been provided to the RCHSPP functional groups. A separate line listing of 141 stipulations related to safety has been identified and compiled from the stipulation database. During this reporting period, 24 new safety stipulations were identified. A subset of safety stipulations for select topics (e.g., withdrawal, halting, pausing, and stopping) has also been used in refining safety IND template language.

The LiveLink® system was released into production on March 16, 2012, for the review and storage of all new protocol reviews and amendments. All CSO staff members were trained and have successfully used the new system. During the development of the training materials for LiveLink®, the medical writer reviewed and edited three training guides (*Medical Writers Guide*, *Document Control Guide*, and *Reviewers and Compiler of Comments Guide*). The medical writer's review comments, suggestions, and edits were generated and incorporated for each of the multiple versions of the three guides.

Program Accomplishments

In April 2011, the Code of Federal Regulation Title 21, section 312 was revised to expand and clarify the responsibilities of an IND Sponsor for overseeing safety aspects of clinical research trials. These new oversight responsibilities went into effect September 2011, and in response, the CSO, in consultation with various internal and external stakeholders, developed a Safety Review Communications Plan (SRCP). The SRCP is an internal communications document between the Principal Investigator (PI) and the IND sponsor CSO, which

delineates the safety oversight responsibilities of the PI, the CSO, and other stakeholders.

The purpose of the SRCP is to identify all safety-related responsibilities and communications pathways in a single document, and aims to ensure that these responsibilities are being conducted in a timely and thorough manner to protect research participants and comply with regulatory reporting requirements. In some instances, the PI will be responsible for conducting the periodic safety assessments under a Transfer of Regulatory Obligations (TORO) agreement drafted by the CSO and signed by the RCHSPB Branch Chief and the PI. The PI conducts the reviews and then provides documentation to the CSO, which disseminates this information to CTM and Regulatory Affairs group.

In developing this overall program, multiple components have been implemented, including drafting SRCP/TORO and SRCP-only agreement templates, template correspondence language, and conference checklists; developing and routinely updating tracking systems; and developing standardized processes for periodic safety assessment review, verification documentation, and compliance. A physician within the CSO is assigned as the Sponsor MM on all IND protocols.

Since the beginning of FY2012, there have been six SRCP/TORO agreements drafted or finalized, and three SRCP-only agreements.

The CSO has developed a standard SAE narrative template to be used for all SAEs. This template enables reviewers 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. The template has been used for all SAE reports during this reporting period and was used for the filing of a 15-Day IND Safety Report filed with the FDA.

The CSO has developed a comprehensive template for the safety section of IND protocols that included changes required by new IND Regulations and the need to identify and report UPs. Following initial introduction and approval in September 2011, the "Safety Template Language for INDs Held by RCHSPB V 7.0," for use in drafting and amending protocols was linked from the NIAID IRB website in February 2012 after extensive review and revision. This template includes all NIH and NIAID IRB required safety reporting language and is available for use by anyone drafting a protocol with access to the NIAID IRB site.

The CSO revised and further updated the SAE Report Form, which is now the Combined Serious Adverse Event (SAE) and UP Report Form, to accommodate the need to report UPs to the NIAID IRB in compliance with OHRP guidance. The combined event form instructions were extensively revised and simplified. Upon final approval by the branch, the updated instructions will be made available via the NIAID IRB website.

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 position requirements. The CSO director continues to serve on the Editorial Board of the cancer.gov website and is an active member of the Academy of Physicians in Clinical Research (APCR). The medical writer is an active member of the American Medical Writers Association (AMWA) and is the Frederick Regional Coordinator for the Mid-Atlantic Chapter.

To more fully provide support to RCHSPB, the CSO has expanded its documentation of events reported to the Sponsor. The DSMB Record was expanded to include all safety oversight committees including ISM and SMC committees and is now referred to as the Safety Oversight Committee Record (SOCR), and the Event Record was an expansion of the SAE Record to now document other events reported to the CSO including SAEs, UPs, Unanticipated Adverse Device Effects (UADEs), SAE/UPs, Protocol-Specific Events (PSEs), and pregnancies.

CSO staff members have collaborated with other RCHSPP staff on the implementation of 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. Further, a CSO staff member provided TrackWise® event record training to the CSO staff, the Regulatory Affairs Group, and CTM.

CSO staff finalized the revisions to standard operating procedure (SOP) CS-0101. As the CSO updates its procedures, it has also obsoleted seven SOPs (CS-102; CS-103; CS-104; CS-105; CS-106; CS-107; and CS-112). The CSO currently has three active SOPs (CS-0100; CS-0101; and CS-0111), and training has been completed on the three SOPs by all CSO staff members.

The CSO participates in training and develops educational and procedural programs for both internal and external groups. Over the course of the contract year, 28 New Employee Orientation (NEO) presentations were given by three members of the team; both the CSO and the medical writer provide presentations. Additionally, the CSO staff has given and participated in multiple presentations during this reporting period including: (1) CSO director presentation of the SRCP process to CTM on April 19, 2012; (2) CSO director and CROM presentation of the SRCP process to Regulatory staff on April 27, 2012; (3) the CSO director presentation of "What's In a Name? Making Sense of Clinical Research Study Types" April 27, 2012; (4) the CSO staff participation at the presentation of the SRCP process and CRIMSON Data Tables to the PIs at the NIAID Grand Rounds May 4, 2012; (5) the CSO director presentation of the SRCP process to the RCHSPP management staff May 22, 2012; (6) the CSO director presentation of Making Sense of Clinical Trial Designs at the CMRP retreat June 14, 2012; (7) the CSO director presentation of a Webinar on IRC-004 Safety Start-up and Safety Section of the Protocol on December 13, 2011; (8) the CSO director presentation of a Webinar on IRC-003 Safety on June 14, 2012; and (9) the CSO MM delivered 2 lectures, an

Overview of Protocol Design and Developing an Informed Consent Document, at the PhD Student Summer Course in Clinical and Translational Research NIH Clinical Center (CC) 2012 Pilot.

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

The 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, which requested support from CMRP. There are two aspects of this program: (1) 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; and (2) the Protocol Development Program (PDP) aspect is critical to study start-up activities.

Current staff includes a PN/PDP manager, two protocol navigators, and three medical writers. The PDP continues to add significant value to the protocol development process by providing protocol services, both in protocol and consent drafting and logistics management, assisting both new and experienced clinical investigators. Logistics management includes the support the PDP provides to NIAID Intramural Principal Investigators and study teams with developing, writing, and tracking clinical protocols through the protocol life cycle (concept stage through protocol development, review, approval, and initiation). These investigators continue to express support for the services the protocol navigation team provides, citing that it keeps them on track with the protocol logistics ensuring that protocols include consistent and applicable language for IRB submission.

During the reporting period, the PN/PDP team was involved with the development of 21 initial protocols (10 were carried over from the previous year, of which 4 have received IRB approval; 11 were new requests). Of the 11 new requests, 6 were with repeat customers, 3 were new customers, and 2 involved first-time PIs, 1 of which was for an international study. 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, Laboratory of Infectious Diseases, the Laboratory of Molecular Immunology, and the Collaborative Clinical Research Branch. During this past year, additional labs have requested PN/PDP services, including the Laboratory of Host Defenses and Laboratory of Zoonotic Pathogens (LZP) at Rocky Mountain Labs (RML). LZP has not conducted clinical research and is attempting to implement a serosurvey study in remote villages in Mali. The logistical challenges involved in international research are complex, and PN/PDP involvement is very helpful to keep investigators and collaborators engaged in the often lengthy study start-up process. The PN/PDP team has also provided support to two initiatives, one for the newly formed Center for Infectious Disease Imaging (CIDI), and the other for a collaboration among several institutes seeking to conduct Neuro-HIV/ID studies. Additionally, CMRP support staff has assisted in amendments for nine other protocols.

The PN/PDP team provides advice ad hoc to other investigators and coordinators. To ensure provision of current information, the staff engages in webinars, videocasts, conferences, and trainings on scientific and human subjects protection issues offered by both internal NIH and SAIC-Frederick staff, as well as outside professional organizations. Program staff reviews IRB stipulations, both from navigation and non-navigation protocols, and updates 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.

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 monthly 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.

The program continues to collect metric data, which includes tracking milestones dates and categorizing stipulations from IRB reviews to identify areas needing quality improvement. The navigation program appears most beneficial in keeping the investigator engaged and expediting the time between scientific review to IRB submission. The PN/PDP is currently creating a workflow in the TrackWise® system to facilitate project management and capture details on milestones. This project is on target to be completed by September 30, 2012. The cycle time metrics have been evaluated by statisticians and at this point, since the sample size is small, additional data are needed to further analyze a significant difference in completion times between PN/PDP protocols and those that do not use this service.

The PN/PDP continues to spread the word on the utility of this program. A manuscript is in revision titled "Protocol Development Program: A Novel Approach to Overcoming Barriers to Clinical Research Trials," and once revised, will be submitted to *Contemporary Clinical Trials* before the end of this fiscal year. A poster abstract entitled "A Medical Writer's Role in the New Protocol Development Program at the National Institute of Allergy and Infectious Diseases" has been accepted for presentation

at the 2012 AMWA Annual Conference. Two other abstracts for posters are pending approval: one, for the NIH Research Festival in October 2012, is entitled "Customer Feedback Suggests Satisfaction with NIAID's New Protocol Development Program"; the other, for the Public Responsibility in Medicine and Research (PRIM&R) 2012 Advancing Ethical Research conference in December 2012, is entitled "New Program Shows Promise for Improving the Path to Clinical Research."

The program also provides the senior leadership at NIAID with slides and information for other presentations such as: IOM Forum Envisioning a Transformed Clinical Trials Enterprise in the U.S., branch chiefs meetings, town hall meetings, retreats, and performance, operational, and strategic plans for management. PN/PDP management took an active role in collaborating with NIAID on strategic planning and provides data to management on the status of the goals identified for the branch.

The PN/PDP received a request from the coordinator of the PhD Student Summer Program in Clinical and Translational Research, Sabbatical in Clinical Research Management Office of Clinical Research Training and Medical Education, Clinical Center (CC), National Institutes of Health, to present interactive sessions entitled Anatomy of IND and Natural History Protocols and Logistics in Protocol Implementation. This is an introductory program for Ph.D. graduate students (selected by the NIH) with no prior experience in clinical research or human subjects protocols. This request provides an opportunity for the PN/PDP to advertise and demonstrate the resources that are available within NIAID to future Principal Investigators. There will be a didactic session and an interactive session. The medical writers will review the sections of a protocol needed for IRB submission, such as background, rationale, objectives, endpoints, study design, eligibility, procedures, study drug, risk/benefits, human subjects protections, safety and data management. The protocol navigators will review the logistics of protocol implementation. This activity was held during July 2012.

A feedback tool to gauge customer satisfaction is distributed to investigators participating in the program on an ongoing basis. The program continues to receive the highest rating possible 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. All respondents indicated they would use the service again and would recommend this service to other investigators.

Project Management Team (PMT)

RCHSPP's PMT provides strategic planning, project management, operational planning; program planning and reporting; and program management and logistical support services to enhance the capacity of RCHSPB in conducting its mission and maintaining the infrastructure needed for RHCSPP to fulfill program management and contractual requirements. PMT considers each one of these services as core capabilities that are critical to the efficient and effective response to and execution of RCHSPP's internal and external stakeholders' needs. PMT works in collaboration with all program support team members and functional groups to align organizational strategy and operational and program activities with the tactical goals and objectives required to achieve overall success within RCHSPP.

PMT achieved several significant accomplishments and key milestones during FY2012. The team focused efforts on refining the 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, resource utilization reports were developed, which served as a tool for periodic planning and identification of resources needed to support RCHSPP's current portfolio of clinical research protocols. PMT presented the ISPMF to the NIAID clinical director and RCHSPB/OPOS senior management.

Through resource utilization reports, which were based on financial and labor utilization data, the team was able to demonstrate how the ISPMF model, which combines standard project management methodology and protocol life-cycle methodology, can be used to streamline research support processes and align budget and labor resources across all functional groups and protocols involving both domestic and international clinical research. PMT presented the resource utilization reports to RCHSPP/B senior managers; using the ISPMF at the program level, PMT demonstrated the alignment of budget and labor resources with protocol development and regulatory projects. The established alignment of budget and labor resources provided a platform to enhance existing clinical research support processes such as monitoring, tracking, and reporting progress. Using the ISPMF, PMT configured and streamlined the overall program management process to adequately retrieve, analyze, review, monitor, track, and report progress on key performance indicators at each major milestone and/or protocol life-cycle stage.

PMT continues to collaborate with RCHSPP senior management and functional group leaders to implement flexible, customizable, repeatable, and expandable service offering models to fit RCHPSB's strategic/project needs. These models have been accepted by the RCHSPB. PMT is working with the functional groups to pilot the models for a selected set of clinical protocols. During the implementation phase, PMT identified several areas for improvement and is proactively working with RCHSPB/P to streamline processes, address data entry errors, reconcile inconsistencies, and add/refine/realign lab codes to the budget flow for each protocol that RCHSPP supports. Currently, PMT has completed resource utilization reports using the ISPMF that integrates and

aligns technologies (TrackWise®, Unanet®, and SmartStream), workforce labor hours, and processes.

PMT continues to grow the list of pilot protocols to better understand the complexity of the protocols including all possible variables in the service-offering models. The resource utilization reports based on the larger set of protocols will enable senior managers to better plan, execute, monitor, track, control, and report progress on protocol projects in a timely manner. This will also allow RCHSPB/P to establish a program baseline for four major service-offering models and generate meaningful program-specific and functional group–specific utilization reports that enable senior management to make informed decisions for addressing the growing program management requirements related to budget and labor resources, and promptly respond to RCHSPB inquiries.

PMT is working with senior management to review and identify unique characteristics of clinical studies at various phases of the Protocol Project Management Life Cycle. Understanding how these factors influence resource utilization is essential to program sustainability and capacity building. Using the ISPMF, PMT's next effort is to analyze program budget and labor resource utilization reports to develop insight into the protocol complexities of each service-offering model. Resource utilization reports allow for visibility into the service-offering models and provide data to inform the decision making process. The PMT plans to: (1) assess the status of each protocol using defined milestones; (2) identify protocol type at an early stage of the life cycle, if available; and (3) define processes for capturing enrollment rates from various database sources. By using resource utilization reports of the past fiscal years, PMT is developing a process to assist senior managers in the areas of program planning, budget preparation, and resource forecasting.

Working in collaboration with the functional group leaders and senior managers, PMT developed an operational plan for implementing RCHSPP's strategic plan. The operational plan is being used to track and monitor progress against the strategic goals and objectives. PMT facilitated the implementation of the RCHSPP's strategic plan using PM tools and templates for monitoring, tracking, and reporting progress associated with defined key performance indicators. The team has presented the overall status of the strategic goals and objectives to RCHSPP managers and staff. PMT, in collaboration with RCHSPP's Learning and Professional Development (L&PD) Group, have initiated a process for developing the next strategic plan. Future planning activities will include: a focus on increasing employee engagement in the strategic plan development and implementation; enhancing communications related to overall progress; and maintaining effective, objective teams to drive operational success.

PMT submitted a poster presentation for sharing outcomes of the project management implementation within RCHSPB/P. The poster was presented at the NIH Fall Research Festival in October 2011. PMT has also submitted two additional abstracts describing the ISPMF, one abstract for a poster at the NIH Fall Research Festival to be held in October 2012, and another for consideration at the Association for Clinical Research Professionals (ACRP) Conference to be held in April 2013.

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 reporting period, 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 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 (10 minutes shells were completed); prepared 25 sets of IRB Meeting packets, which included generating quorum sheets, printing labels, and reviewing the collated packets for correctness; attending 12 IRB meetings in person throughout the year; and writing Serious Adverse Event 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, which included eight action-specific instruction sheets on how to correctly review and process these actions.

RCHSPP Learning and Professional Development (L&PD) Group

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

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

During FY2012, the instructional designer identified and developed training resources in support of RCHSPP, including the following trainings: TrackWise® CTM Protocol Review, TrackWise® 8 All Users, TrackWise® Protocol Review for Managers and Reviewers, TrackWise® CTM Site Record, TrackWise® CTM Site Visit Record; CTM Site Monitoring Visits and TrackWise® Regulatory Affairs IND/IMF Records for Managers. The Instructional Designer also converted the Travel Guidance and SOP RA-0715 trainings to the Adobe Captivate platform to allow enhanced interaction.

Provide Training and Professional Development Subject Matter Expertise

The L&PD group provided extensive support to RCHSPP functional teams, as well as the new RCHSPP Strategic Plan, as a member of the Steering Committee and as a team lead for the People Goal; facilitated the identification of core competencies for all RCHSPP technical staff, as well as group-specific core competencies; provided extensive support for the FDA Inspection Readiness initiative, serving on the Steering Committee, guiding the development of role-specific trainings, as well as co-presenting those trainings; and facilitated the development of position descriptions for RCHSPP senior management to initiate human capital planning for this team.

Provide Administrative Support for Activities with Training Implications

The L&PD group 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: Ethical Requirements and the Development of Guidelines for Pediatric Studies; FDA's Bioresearch Monitoring Program; Human Subjects Protection Programs – Analyzing the New Proposed Regulations; and Risk-Based Site Monitoring.

Ensure Compliance and Continuous Improvement of Training Processes and Initiatives

L&PD implemented 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.

L&PD collaborated with the IT Group to implement TW Training Manager, a program that will enhance CMRP training compliance efforts and will allow employees to monitor their own training records. This implementation included role-specific curriculum identification, back-population of critical trainings, and 100 percent audit of back-populated information.

L&PD continued to maintain a spreadsheet identifying FDA Warning Letters citing GCP issues, which is utilized extensively by clinical research professionals in ensuring compliance.

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

The L&PD group facilitated a two-day seminar for 80 staff members on "Building Quality into Clinical Research."

In addition, L&PD group members participated in several training events to include: The Art of Listening; Budget and Financial Management; Digital Signature Training; Effectively Using Effects in Adobe Captivate; Good Documentation Practices; Managing Multiple Priorities; and Yours, Mine and Ours: Copyright and Creative Commons in Education and Training.

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 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) RCHSPP Standard Operating Procedures; (3) paper and electronic file storage and maintenance of various documents; (4) creation of CDs, various databases, and logs; (5) document scanning and archiving; and (6) 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 205 active protocols, 73 active IND/IDE/MF, approximately 1,600 SAEs, and various other regulatory documents RCHSPP is required to maintain. DC is also responsible for assigning project codes and has assigned 45 new project codes this year (nine project codes requested [no review associated], 14 Navigational Protocols, 22 project codes assigned w/PI Review). To date, DC has processed approximately 127 protocol reviews (23 PI Reviews, 82 Amendment Reviews, 13 Site-Specific Reviews, 1 Other Review, 4 Navigational Pre-IRB Reviews, and 4 Navigational Pre-SRB Reviews).

During the reporting period, the project to improve the protocol review process by utilizing TrackWise® and Livelink® was completed. This new system allows for better control of the protocol review documents, as it offers an audit trail and other features that allow DC to control the read and write capabilities of individuals based

on their roles. DC coordinated the development of specific training guides and coordinated the training for CTM, CSO, Regulatory, DC, and IT groups. DC also provided oversight of the migration of all archived reviews into the new system, and all three staff members of DC are administrators for the LiveLink® system. On March 15, 2012, the review process was officially launched, and all reviews are now processed through the new system.

On May 10, 2012, DC and IT met with LiveLink® administrators to kick off the SOP project. The goal of this project is to transform several existing manual SOP processes into a single LiveLink® document management repository/system, leveraging LiveLink® workflows, functionality, and digital signatures capabilities. This will improve organizational efficiency and enhance reporting and compliance mechanisms, as all actions are audit trailed. A project team has been formed to develop system functional requirements and outline a timeline for implementation.

DC assisted the L&PD group in facilitating the routing of several new L&PD SOPs and forms through the RCHSPP SOP review and approval process. This was a complicated process, as a package of materials, containing the SOPs and all related forms, had to be compiled and circulated individually to each of the RCHSPP groups to review and approve, while still maintaining a balance of managing the normal DC SOP workload. Additionally, some forms were referenced in other SOPs, thereby requiring that reference copies be made for all reviewers, and following the approval of documents, DC was responsible for the generation and distribution of training copies to all members of RCHSPP.

In addition to the performance of daily document management responsibilities for the RCHSPP, the DC staff serves on the following groups/teams/committees: Site-Wide Event Planning Team; CMRP Training Work Group; TYCTWD; LiveLink®; Inspection Readiness; TrackWise® Working Group; and Strategic Planning Committee, as well as numerous other committees in support 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 one IT manager, three programmer analysts, one systems administrator, one network specialist, and one secretary. In the past year, the IT group was involved in several key technical initiatives for the program.

The RCHSPP IT group, in conjunction with the L&PD group, was able to successfully develop and deploy TrackWise® Training Manager. This significant component of TrackWise® tracks all training records for every program employee, from noncurricular group training to individualized curricular training. To expedite the development and release of the project, the vendor was brought on-site for a short period to assist in the effort, which included the prototyping, review, and approval by the project stakeholders, development of custom reports, reconstruction of approved development model in production environment, performance of user acceptance testing; and release of the system into production. Following the release, several thousand training records had to be back-populated by the L&PD, with assistance by designated administrative staff. As a quality control mechanism, members of the IT group reviewed the corresponding TrackWise® records for accuracy and provided the L&PD group with reports that could be used to further verify the data. As of the date this report went to print, more than 6,000 noncurricular and 1,000 curricular records had been entered and managed through the system.

Additionally, two new TrackWise® projects were released: the event record, to expand the capability of the system to manage additional types of requests received by the Clinical Safety Office, and the system service request record, to manage the routing and electronic approval of changes to the TrackWise® system.

The integration of the OpenText® Enterprise Content Management suite, also known as Livelink®, and TrackWise® to manage content for clinical protocols undergoing an initial or amendment review by the RCHSPP was completed. A restructuring of the project plan occurred midstream because it was determined that the application programming interface packaged with the TrackWise® system contained limitations that would prevent a successful production release. The move required many changes, such as creating new TrackWise® field types and transferring document workflow and permissions engine responsibilities to the Livelink® document repository rather than the TrackWise® 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 OpenText® Enterprise Content Management team were integral in both developing and delivering training to the program staff, and the system is being successfully used by program staff.

The IT group was active in evaluating and offering program staff the capability to utilize newly approved communication technologies, including Microsoft® Lync and Skype™. These applications enhance the office environment for the exchange of information, both while in domestic and international locations. Further benefits include a potential cost savings, as domestic and international phone calls can be replaced by lower-priced Skype™ or Lync calls.

A long-awaited bandwidth boost was completed in late 2011, as a dedicated 1 GB fiber optic Wide Area Network (WAN) connection to the NIH was implemented. In conjunction with the Operations and Engineering Branch (OEB) of NIAID's Office of Cyber Infrastructure and Computational Biology (OCICB), the primary WAN connection at the Industry Lane facility was transitioned

from a copper-based backbone to a high-speed, fiber optic–based solution. This project increased the WAN transmission speeds/bandwidth available within the Industry Lane facility from a maximum of 45 Mbps to 200+ Mbps. The increased capacity and throughput of the connection allows for improved collaboration with external researchers, better support to bandwidth-intensive applications such as IP-based videoteleconferencing, and sufficient scalability to support new technologies. As an additional cost savings measure, the existing 45 Mbps backup circuit was decommissioned and replaced with a more cost-effective 1.544 T1 circuit to provide fault-tolerant capabilities in the event the primary fiber connection is damaged.

The electronic common technical document (eCTD) system, deployed in early 2011, is being used by the RCHSPP Regulatory Affairs group to submit regulatory documents to FDA via the FDA's electronic submission gateway. Prior to the release, the IT group, along with project stakeholders from the Regulatory Affairs group and the OCICB, 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 determine 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 compiled 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. Ongoing support of the eCTD publishing system continues and includes the installation of several product service releases as well as responding to support inquiries from the RCHSPP Regulatory Affairs group for the Omnicia eCTD publishing system and Verisign digital ID certificate used for submissions to the FDA via the electronic gateway.

The IT group played a critical role in a cost-savings measure for the program, transitioning all BlackBerry devices to a common service provider. The effort required that existing BlackBerry devices' phone numbers be ported over from T-Mobile to AT&T, and that new AT&T-branded devices be issued to the users. The timeline for completion of these activities was short, and the location in which the devices were distributed was diverse, so careful organization, planning, and communication were necessary.

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 conduct 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 TrackWise®, 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 TrackWise®; (8) participation in RCHSPP strategic planning sessions, Section 508 compliance, TrackWise®, 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) provision of 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., Technology Review and Advisory Committee, Microsoft® Active Directory Working Group, and HIPAA/HITECH committee; (14) provision of videoconferencing and video collaboration support services for both near and remote locations; and (15) ensuring of 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.

Support to the Rakai Project, NIAID

Beth Baseler, M.S., Director
Jennifer Imes, Program Manager
Kevin Newell, M.Ed., M.P.H., Clinical Project Manager I
Irene Mueller, M.P.H., Clinical Project Manager I
Melissa Borucki, M.S., M.B.A., 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 the 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 the 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 the 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 11 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.

Under the BOA established with the Rakai Health Sciences Program to support clinical research protocols, Task Order 2 was issued to support a clinical protocol titled "Malaria Surveillance in Rakai." This one-year study is to determine the epidemiology of malaria infection in children and adolescents/adults by conducting surveillance in approximately 320 households selected from two of the ten 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. This study is ongoing and is expected to conclude in early FY2013.

The Rakai Project provides dedicated personnel, both on-site in Africa and off-site in Frederick, MD, to coordinate regulatory activities and provide data analysis support for clinical research, 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, the clinical project manager located in Noordhoek, South Africa, made two site visits to Uganda to assist the Ugandan research teams in implementing quality control procedures/processes required for human subjects research and to ensure GCPs and regulatory compliance for existing and new protocols. The clinical project manager assisted the research teams with data analyses and the preparation of manuscripts for peer-reviewed journal publications. Articles were published in the *Lancet*, *Journal of Acquired Immune Deficiency Syndrome*, and *AIDS Research and Human Retroviruses*. In addition, data analysis support was provided for two oral abstracts presented at the 2012 Conference on Retroviruses and Opportunistic Infections.

The clinical project manager continues to provide regulatory support to the scientific director. This responsibility includes managing NIAID Intramural IRB submissions for seven active protocols. Additionally, the clinical project manager oversees the local regulatory requirements in Uganda for these protocols, and provides direct supervision to a Ugandan regulatory coordinator in the NIH-Uganda office.

The clinical project manager continues to mentor the data teams at Rakai Health Sciences Program and the Infectious Diseases Institute, as well as provide direction to clinical research data management operations through the application of the DataFax® system. The Infectious Diseases Institute currently has ten clinical studies using DataFax®, with four additional studies to be included in the near future. Discussions are taking place to increase collaboration between the Infectious Diseases Institute and the NIH on the expanded use of DataFax® technology in clinical research.

During the reporting period, support was provided for logistical and administrative tasks related to daily international operations; budget preparation and monitoring; travel preparation for training and collaboration visits; and procurement of capital equipment and miscellaneous laboratory items, resulting in the coordination and tracking of five ambient and three perishable shipments.

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 and has conducted well-defined pilot projects. NIAID has now moved to facilitating multiple trials conducted by both intramural and extramural investigators.

The India/Mali effort provides dedicated personnel off-site in Frederick, MD, and through a research 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. The SAIC-Frederick research subcontract provides for a scientific director located in Chennai, India, who oversees the research projects conducted at the Laboratory of Parasitic Diseases at the Tuberculosis Research Center. The collaborative program has recently:

- Initiated 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 pulmonary and extra-pulmonary manifestations of TB are characterized by differences in multifunctional T cells elicited in response to TB antigens;
- Demonstrated diabetic individuals with active TB disease mount significantly enhanced immune responses to TB antigens compared to non-diabetic individuals with TB;
- Characterized the presence of multifunctional T and natural killer (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
- Validated a polymerase chain reaction (PCR) technique using stool DNA to identify eight different intestinal pathogens and compared the efficacy of PCR to stool microscopy.

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 capital equipment and more than 500 pieces of miscellaneous laboratory items; continued support of service agreements for equipment located in India and Mali and the coordination and tracking of five perishable and six bulk shipments.

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

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

The Laboratory of Virology within DIR initiated a collaborative research program with the National Institute for Communicable Diseases (NICD) in Johannesburg, South Africa, to study hemorrhagic fever viruses and other emerging infectious disease viruses. The collaborative research initiative involves ecological field studies of hemorrhagic fever viruses, pathogen discovery and sequencing of viral isolates collected in the field, as well as studies on potential animal intermediate hosts and vectors of these viruses, including African fruit bats. The studies include establishing field research sites in the Democratic Republic of the Congo, Kruger National Park in South Africa, and other sites to be determined. Investigators from the Laboratory of Virology work closely with their counterparts at the NICD in the training and execution of the research objectives.

In support of the NIAID–NICD collaborative research initiative, CMRP worked with Contracts and Administration to issue NICD a fixed price purchase order to perform full-genome sequencing of 102 Rift Valley Fever Virus isolates and 21 Arenavirus isolates. This procurement is one of the first steps in the collaboration between NIAID and NICD investigators. It provided a training opportunity for the investigators to utilize samples collected by NICD to validate the research processes and procedures. In addition, CMRP provided

assistance in researching the procurement and shipment of laboratory and field research equipment being sent to Kruger National Park in support of this effort.

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

Beth Baseler, M.S., Director
Joseph Shott, Quality Assurance Specialist for International Research*
Jennifer Imes, Program Manager
Irene Mueller, M.P.H., Clinical Project Manager I
**Joseph Shott resigned from SAIC-Frederick 2/24/2012.*

CMRP provided good laboratory practice (GLP) research support service to NIAID's ICER initiative in Mali. 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 quality assurance (QA) specialist provided continuing review of several research activities at the Mali site with respect to 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; supporting the path to ISO 15189 accreditation for the SEREFO Laboratory at the Mali ICER; development of the NIAID enterprise electronic biospecimen management system (BSI-II) for 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 the Mali site by providing a range of administrative, QA, and logistical services, including the establishment of research subcontracts for clinical study implementation, regulatory support for clinical trials, study monitoring to ensure GCP, and comprehensive travel support for personnel.

CMRP support to this ICER initiative concluded this year, as all activity in the program transitioned under the direction of the DIR.

Support to the NIAID–Mali HIV Research Initiative, NIAID

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

The NIAID–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 approximately 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 ensures that the reported study dates are accurate, complete, and verifiable from source documents; ensures the study conduct is in compliance with the protocol, ICH/GCP guidelines, and applicable regulations and standards; and detects, reports, and resolves discrepancies that occur during the conduct of the study. Since March 2012, a travel warning through the U.S. Department of State has been in place for Mali due to political instability in the country. This warning is still current and has resulted in the advisement against all travel to Mali per the U.S. Embassy and in coordination with NIAID. All on-site monitoring activities in Mali have been suspended until further notice.

During the reporting period, CMRP provided logistical and administrative support for daily international operations; budget preparation and monitoring; procurement of more than 1,000 pieces of miscellaneous laboratory items, including maintaining service agreements for equipment located in Bamako; coordination and tracking of 13 perishable, 12 bulk, and 8 dangerous goods from CMRP; coordination and tracking of two hazardous sample shipments from Mali to Frederick, MD, for testing; continuation of contracts to provide transportation service for the CMRP employees temporarily detailed to Bamako; and maintenance of the agreement with Johns Hopkins School of Public Health to provide training and mentoring to the Malian investigators. The political instability in Mali also briefly caused interruptions of shipments. However, the situation was closely monitored, and shipments resumed with minimal delays.

Support to the Recombinant Human Interleukin-15 (IL-15) Project, NIAID

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

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 and CCR-Metabolism Branch. CMRP's Administrative Support Group continues to provide project management support in concert with the SAIC-Frederick Research Subcontracts Department and Clinical Services Program (CSP) to oversee coordination with a subcontractor (Biological Consulting Group), and Avanza Laboratories (formerly Bridge Laboratories) to perform pharmacodynamic and pharmacokinetic studies. Since September 2011, CMRP staff has successfully completed the following activities in support of this effort:

In September 2011, CMRP assisted NIAID with the preparation and solicitation of a research subcontract awarded to Avanza to perform a second ARM study to examine the immunologic and virologic effects of recombinant human IL-15 (rhIL-15) when administered via continuous IV infusion (CIV) to SIV-infected Rhesus monkeys. The study consisted of Rhesus monkeys in a chronic phase of SIV infection that were treated with rhIL-15. Since the primates' SIV viral load was determined to be causing a negative 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 during the treatment phase with IL-15. The first portion of the study was completed in January 2012. The research subcontract was modified to procure additional antiretrovirals in order for the animals to continue receipt of the three antiretroviral drugs while data were being reviewed and plans for the second cycle were made. The second cycle was initiated in late January 2012 and completed in March 2012.

Upon the conclusion of this second ARM study, antiretroviral drug delivery to the non-human primates (NHP) was stopped for two weeks after the IL-15 dosing period ended, serial plasma viral loads were performed, and the NHPs were placed back on the three antiretroviral drugs. Cells from these studies were banked at NIAID to determine if the NHPs mounted an immune response to SIV. In addition, upon NIAID's request, CMRP assisted with modification of the research subcontract to send tissue blocks from one of the animals who had expired in an earlier study to the SAIC-Frederick AIDS and Cancer Virus Program for further evaluation. Based on the information received from these two studies, CMRP, Research Subcontracts, and CSP assisted with a request from NIAID to perform a third ARM study similar to the second ARM study, to determine the effects of multiple cycles of treatment using IL-15 and antiretrovirals. In addition, lymph node biopsies and endoscopies were performed.

The endoscopic information was required based on results from previous autopsies on two deceased animals. The third ARM study started on May 7, 2012, and was completed in August 2012. Once the study was completed, antiretrovirals were continued until the viral loads were suppressed to a normal level. Endoscopies were performed in July and August 2012. In order to perform the endoscopies, the CMRP administrative group prepared the request for the solicitation and procurement of a gastroscope and applicable accessories to be used by Avanza since this vendor did not have the appropriate equipment for performing the procedures. The CMRP administrative group facilitated the acquisition and set-up of the necessary endoscopic equipment at Avanza within a two-week period, resulting in continuation of the study with no delays to the protocol schedule.

In addition, CMRP staff, in collaboration with NIAID, CSP, and Research Subcontracts prepared a solicitation that was awarded to Avanza to perform a GLP-phase study that will mimic the second and third ARM studies. The research subcontract was awarded in January 2012; however, the GLP study was placed on hold until all of the data were received and reviewed, and a final report was completed from the previous ARM 2 and 3 non-GLP studies. The GLP-phase study is planned to begin in late August 2012.

Support to the Biostatistics Research Branch (BRB), 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 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 to support this effort, one biostatistician I, and two biostatistician IIs.

The CMRP biostatisticians provide statistical support as well as data management, programming, and statistical data analysis to many intramural clinical research protocols. They are also involved in analyzing novel, high-dimensional immune assay data collected through the Phase I vaccine studies conducted at NIAID's Vaccine Research Center (VRC), including HIV, H1N1 flu and BrdU labeling studies. During the reporting period, the biostatisticians were involved in a wide variety of projects, from the analysis plan development stage to performing complex statistical analyses, writing reports, and co-authoring manuscripts. Some of the projects included studies on H1N1 flu, Malaria, Lyme disease, and influenza-like illness. The biostatisticians also conducted various statistical tests and generated descriptive statistics and graphs for several VRC studies (VRC 307, 308, and 309) and Phidisa projects. In addition, CMRP

biostatisticians are helping develop novel statistical methods for researchers, assisting in safety evaluations, and preparing DSMB reports.

A biostatistician II provides statistical and mathematical programming support and aids in analyzing a broad range of clinical and laboratory studies, while directly involved in performing research experiments, data collection, processing, and assisting with the experimental imaging of SIV/SHIV in rhesus macaques. During FY2012, the biostatistician II has been involved in a variety of projects, including noninvasive in vivo single-photon emission computed tomography imaging of SIV/SHIV-infected non-human primates; estimating the multiphase HIV DNA and RNA viral load decay rates in patients who started Highly Active Antiretroviral Therapy (HAART); and developing mathematical models to estimate the effective efficacy of HAART treatment drugs.

Support to the Southeast Asia Initiative, NIAID

Beth Baseler, M.S., Director
Laurie Lambert, Clinical Project Manager III
*Julia Welch, M.S., Clinical Project Manager II**
Cynthia Osborne, Clinical Project Manager II
Julia Welch resigned from SAIC-Frederick 8/16/2012

The clinical project manager II, 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 seventh 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 under way. 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 of 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 research subcontracts. These research 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.

Through a new Yellow Task, NIAID DCR requested that SAIC-Frederick create and release a request for proposal in December 2011 for a subcontractor to manage the Thailand and Vietnam protocols and sites in the Southeast Asia Clinical Research Network. This new research subcontract supports a new protocol to identify and enroll patients with sepsis and fevers of unidentified etiology as well as provide coordination for a redesigned Network Operations Center, and will initially support three sites in Thailand and three sites in Vietnam; additional sites will be added as directed by the expansion into additional protocols. In the past year, CMRP staff members spent several weeks in Southeast Asia supporting NIAID. Activities both abroad and domestically included: (1) developing, releasing, and awarding an RFP for research support; (2) assisting with transitioning and mentoring new network personnel; (3) developing tools and procedures for project oversight; and (4) providing expertise in establishing working partnerships in the region.

CMRP provides 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., M.B.A., 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 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 the Phidisa Project, 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 2012 was implementing the five-year strategic plan developed in 2011 collaboratively with SANDF, South African Military Health Service (SAMHS), U.S. DoD, and U.S. NIAID-DCR and SAIC-Frederick colleagues. Significant progress was made in implementing the three major strategic goals and associated operational plans. The three major goals of the project are to: (1) integrate Phidisa

more effectively 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 Phidisa Program Workshop in December 2011. At the workshop, the CMRP director facilitated a session for the Laboratory Working Group (LWG) co-chairs to develop and refine operational plans for transitioning laboratory operations to the SAMHS. The director drafted the final presentation that was delivered to the Executive Committee and meeting participants by one of the LWG co-chairs.

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 Data Safety Monitoring Board, 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 continues to work with the group on a possible follow-up publication to the benchmark paper written in 2008, which would involve input from PIs and data management teams. Additional activities include periodically reviewing site reconsent tables, participating in discussions on satellite closure and strategies for subjects' follow-up visits at the lead site, and a continuing review of monitoring visit reports. Recently, internal discussions have occurred with regards to sending "Dear Participant" letters to subjects participating in the study and the timing and human subjects protection–related activities associated with a "Dear Participant" letter that relates to satellite sites closing.

The CMRP director continues to be an active participant of the Phidisa Laboratory Working Group (LWG) and serves as the COTR for the clinical monitoring (laboratory) research subcontract. Bioanalytical Research Corporation (BARC) Task Order 4, under the auspices of the BOA executed, April 1, 2008, continued supporting the Phidisa IA protocol for laboratory, shipping, sample storage, and courier services and other associated activities. A Phidisa Protocol Amendment was approved by the South African IRB in early February 2012, with implementation effective May 15, 2012. In support of this amendment, BARC revised the technical and laboratory manuals as well as provided edits to the *Manual of Operations* in order to prepare the sites for the changes. In addition, BARC prepared revised kits that shipped to all sites prior to the implementation date and arranged for the return of unused kits from the previous protocol. Just prior to the implementation of the protocol modification, the Roche platform for CT/NG PCR was discontinued by the company. BARC initiated and completed the validation of a new Abbott collection system. BARC staff then completed the implementation process for the new system, both in house and at the sites to be in effect with the modification.

The P1A modification also included genetic sample collection from Phidisa subjects to be stored at BARC in the Phidisa Repository. BARC worked with the LWG and Data Team to develop the CRF for tracking consent and collection of genetic samples. BARC developed a database to track what samples have been collected; since these genetic samples are de-identified, BARC also developed a database that links the BARC visit code with the blinded code. This database is only for BARC to identify samples from particular participants and will not be shared with the Phidisa staff, nor can the samples be linked to a participant by Phidisa.

BARC is an active participant in the research committee and in facilitating concepts. For TB, BARC, with the help of LWG and Data is developing a database to track results on clinical samples. BARC has been an active participant in the development of several concepts that have been approved for implementation or are in review by the Phidisa Executive Committee. The first concept is GeneXpert, a point-of-care assay to accelerate time to diagnosis. This assay allows for diagnosis of RIF resistance, which is associated with MDR, within a few hours of sputum collection. The second concept is TB epidemiology, or the evaluation of the molecular epidemiology of mycobacterial isolates from Phidisa TB epidemiology will be used to identify factors associated with tuberculosis transmission in South Africa. For STDs, a retrospective protocol looks at predictors and effects of sexually transmitted infection acquisition in HIV-infected participants. Due to this TB concept, BARC is implementing the use of microbanking for the storage of TB cultures for long term.

Support to the Clinical Consulting and Support (CCS) Group, NIAID

Beth Baseler, M.S., Director
Taree Foltz, Program Manager II
Jennifer Imes, Program Manager II
Melissa Borucki, M.S., M.B.A., Senior Special Projects Administrator
Tracy Dean, Program Manager I

The Clinical Consulting and Support (CCS) Group was established in the fall of 2004 to support NIAID's special initiatives and projects. The CMRP support group provides specialized management, logistics, administrative, and programmatic support for various NIAID, DCR, and DIR initiatives, including establishing and maintaining research subcontracts; travel, conference and meeting coordination; building management and overall administrative support. This support group consists of 15 staff members.

During the reporting period, this group has provided the following support: assisted in recruiting and hiring 21 positions; participated in two SAIC-Frederick/CMRP recruitment booth exhibits at national conferences; established and maintained 67 research subcontracts,

consulting, and professional service agreements; prepared 43 international and 166 domestic travel packages; coordinated arrangements for five conferences, seminars, retreats, and training sessions; prepared 14 nonemployee travel packages to attend conferences, seminars, and training sessions; completed 520 courier runs; and provided acquisitions support, including purchasing and property.

CCS Group support includes the following:

Research Subcontracts Management

The support group administers and oversees the establishment of research subcontracts in support of specific international and domestic NIAID research efforts. Activities include: preparing statements of work (SOWs); overseeing subcontractor progress; monitoring budgets; and collaborating with NIAID project officers to ensure the SOW goals are met in a timely and efficient manner. Throughout 2012, the CCS group:

- Actively prepared and managed research subcontracts with United BioSource Corporation and the University of Minnesota/INSIGHT to support domestic and international influenza initiatives;
- Prepared and managed a research subcontract with PPD, Inc.® to support continuing clinical monitoring efforts in Southeast Asia;
- Managed a research subcontract with the University of Pittsburgh to provide an additional clinical research site to conduct a clinical research protocol for NIAID;
- Managed BARC task order four to support the Phidisa clinical research protocol and substudies in South Africa;
- Managed research subcontracts with Ellen Cull and Quantum Performance Group to provide support for leadership and organizational development for NIAID OPOS;
- Managed research subcontracts with The Maine Group and Turner Consulting Group in support of the IRF;
- Managed research subcontracts with HCM Strategists and Martin Michael in support of the Barriers to Clinical Research project; and
- Managed a research subcontract with the HIV Resistance Response Database Initiative for modeling various antiretroviral therapy responses.

Travel, Conference, and Meeting Coordination

The CCS Group provides travel coordination for nongovernment and CMRP employees involved in major initiatives within NIAID. The support group coordinates international and domestic meetings, conferences, and training for nongovernment 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.

Building Management

The CCS Group provides support to a leased building located in Frederick, MD. This facility houses CMRP employees in support of the NIAID, DCR. CCS staff services include guidance and coordination for all areas of facilities maintenance, facility renovation and design, coordination of staff relocations, troubleshooting of issues, oversight of preventative maintenance schedules, and coordination with outside vendors.

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 one secretary III, one administrative assistant, and one senior program coordinator, all of whom support the Regulatory Compliance and Human Subjects Protection Branch (RCHSPB), the Collaborative Clinical Research Branch (CCRB), the Office of Planning and Operations Support (OPOS), and the Office of the Director (OD).

The CCS Group's 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 (OCICB), NIAID

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

The OCICB manages technologies that support NIAID intramural and extramural biomedical research programs and provides a wide range of project management, technologies development, applications/software

engineering, bioinformatics support, and professional development services for a global network of biomedical researchers.

CMRP supported the integration of the DataFax® clinical data system into several NIAID clinical research sites sponsored by the DIR, DCR, and the OCICB in Uganda, Tanzania, India, Mali, South Korea, Cambodia, China, Cameroon, and Thailand.

The clinical project manager I currently supporting the Rakai ICER initiative provided direction and training to the OCICB data management staff in the operation and configuration of DataFax®, with the goal of integrating the technology into other international protocols being developed by DIR. Consultation, training, and support for implementing clinical protocols on the DataFax® server infrastructure at DIR sites in Uganda, Mali, Tanzania, Cambodia, and South Korea was provided to a number of clinical site personnel.

The clinical project manager I traveled to NIH in Bethesda, MD, to complete training for NIAID and CMRP clinical trial personnel. The training covered issues pertinent to DataFax® case report form development and the use of the DataFax® system for monitoring DIR clinical protocols. The clinical project manager was instrumental in organizing the first monthly DataFax® users group meeting for NIH data management staff, CMRP/CTM study monitors, and the DataFax® project manager.

The clinical project manager I has worked with the CMRP CCS group and the RCHSPP CTM to ensure successful support and integration of the new system.

Support to the Office of Planning and Operational Support (OPOS), NIAID

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

During FY2012, 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 and assist with facilitating NIAID Clinical Research Subcommittee initiatives through the approval process. This year, the clinical program administrator continued to directly support four 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; (3) addressing barriers to international research caused by requirements of the European Union Clinical Trials Directive; and (4) creating a web-based information resource titled International Clinical Research Regulatory Matrix (ICRRM) to provide access to country-specific regulations for use by NIAID divisions when making decisions about performing clinical trials in the EU and other countries. In addition, the clinical program administrator is involved in planning and coordinating high-level, complex, division-wide meetings and collaborative forums. 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 continues to be 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. In addition, the clinical program administrator will be providing support to other SharePoint initiatives, such as the International Clinical Research Regulatory Matrix, and is also responsible for maintaining the Clinical Research Working Group SOPs and preparing quarterly progress report updates in conjunction with the 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 has implemented plans for 11 DCR branches/offices/projects: Office of Planning and Operations Support (OPOS); Program Planning and Analysis Branch (PPAB); Regulatory Compliance and Human Subjects Protection Branch (RCHSPB); Intramural Clinical Operations Branch (ICMOB); Biostatistical Research Branch (BRB); Collaborative Clinical Research Branch (CCRB); Integrated Research Facility (IRF); Infectious Disease Clinical Research Program (IDCRP); La Red Network; Phidisa; and National Interagency Confederation for Biological Research (NICBR). In 2012, PPAB and RCHSPB implemented new strategic plans.

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 BRB to support its new strategic plan, and three operational plans were revised to ensure meaningful alignment to the strategy: PPAB, RCHSPB, and La Red. Operational plans for OPOS and ICMOB

remain deployed and monitored. 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, IDCRP, and the Indonesia Research Partnership on Infectious Disease.

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 were prepared for OPOS, RCHSPB, PPAB, and ICMOB. Strategy reviews for operational plans were completed for PPAB, RCHSPB, OPOS, and ICMOB. During this review, objectives and key performance indicators were assessed 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 and subcontracting. During the current reporting period, the clinical project manager II spearheaded a collaboration with the Office of Cyber Infrastructure and Computational Biology (OCICB) Business Intelligence (BI) Group to enhance the integration of strategic planning within the DCR through automated reporting of operational metrics related to OPOS' strategic objectives. Key accomplishments include: (1) formulation of Project Oversight Team and Project Work Group; (2) drafting of project charter; (3) identification of core functions, including a visual representation of key metrics, automated standardized operational reporting process, tools and templates for the input of data, and workflow procedure for data input and integration; and (4) development of a beta dashboard to view key metrics. In addition, the clinical project manager II is the contracting officer's technical representative (COTR) on the Performance Measures Evaluation subcontract. During this reporting period, the clinical project manager II drafted the statement of work for a request for proposal to develop and assess DCR program performance measures. The goals of the project are to: (1) develop key performance indicators (KPIs) that provide data-driven assessments of performance and productivity in DCR; (2) assess and refine existing KPIs; (3) develop appropriate goal-setting benchmarks; and (4) identify comparison measures against which the performance of the program can be compared.

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. During the reporting period, the clinical project manager II assisted 20 DCR staff members with workforce alignment strategies.

OPOS Management Support

In November 2011, a second time-to-task analysis was performed to assess administrative support resources to ensure appropriate allocation of time and effort on specified projects and tasks. A new administrative support plan was presented to DCR; however, due to staff turnover and attrition, the new plan was not implemented. Organizational tools, such as an organizational chart, roles and responsibility matrix, and functional job descriptions, have been updated and redeployed. Efforts continue to be directed to develop standards for job performance and service excellence.

OPOS Learning and Professional Development (L&PD) Support

A clinical training manager and a clinical training specialist provide training support for OPOS by serving as members of the Learning and Professional Development (L&PD) group. L&PD provides training support to OPOS in three areas: (1) identifying/developing training resources to address client-identified training needs; (2) providing training and professional development subject matter expertise; and (3) participating in professional development to ensure that staff members maintain their subject matter expertise.

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

During the reporting period, most training requests within OPOS were initiated by DCR's ICMOB, PPAB, and OPOS. This year, the clinical training manager has provided training on active listening, setting standards to avoid micromanagement, giving and receiving constructive feedback, strengths-based leadership, and professional standards and principles for evaluation practice. L&PD has also provided extensive organizational development support for PPAB as they focused on roles and responsibilities, in addition to facilitating a strengths-based leadership initiative with ICMOB. OPOS has also requested this training initiative.

The clinical training manager analyzed and presented customer satisfaction survey data in multiple facilitated sessions at the PPAB retreat, in addition to preparing individual survey data reports for each member of PPAB.

Provide Training and Professional Development Subject Matter Expertise

ICMOB, OPOS, and PPAB requested assistance in human capital allocation, using succession planning tools supplied by L&PD. This project, which includes job analyses, alignment of roles and responsibilities to their strategic plans, competency identification, and internal training resource identification, has been completed for ICMOB, and is still in progress with PPAB and OPOS.

L&PD participated extensively in the development and review of DSMB Computer-Based Training (CBT), which is currently under review and revision. The clinical training manager has also contributed to a poster and article on this

topic, both under development, as well as being accepted to give a platform presentation on this topic.

The L&PD group is leading the team responsible for implementing a leadership culture within DCR. A leadership model, based on the Baldrige leadership competencies, is in progress, with a 360-degree feedback survey completed, aggregate data, as well as individual feedback data, provided, and six leader-participants selected to work with leadership coaches to improve leadership areas of their choice. The second phase of this initiative, which includes DCR "emerging leaders," is under development.

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

This year, the clinical training manager gave two presentations at national conferences: To Test or Not to Test? And If So, How? (Barnett Clinical Training Forum in Cambridge, Massachusetts, October 2011); and The Care and Feeding of Subject Matter Experts (SMEs), which was presented at the SoCRA Annual Conference in Las Vegas, Nevada, September 2012.

The clinical training manager attended a course on evaluation provided by The Evaluator's Institute of George Washington University's Graduate School. The training specialist attended the following trainings to increase professional development: The Human Element; the AMA Train the Trainer course; Adobe Captivate 5 (to develop CBTs); and the ASTD annual conference. Both the clinical training manager and the training specialist attended the organizational development series provided by an outside consultant.

OPOS Technical Solutions Group (TSG)

Jeannie Tower, Special Projects Administrator

The special projects administrator provides support to the Technical Solutions Group (TSG) within the Office of Planning and Operations Support (OPOS). TSG is responsible for the identification, description, development, deployment, and evaluation of technical solutions for DCR. TSG manages the numerous technical, information and data challenges encountered in a clinical research environment. TSG works closely with the OCICB, CIT, and other partners to provide high-quality, special and enterprise solutions to DCR workgroups.

During this reporting period, the special projects administrator supported the eighth and ninth CRIMSON Contract Award Fee reviews. These bi-annual reviews assess contract performance against the metrics outlined in the SOW. Throughout each six-month review period, the special projects administrator extracted data from the CRIMSON project manager's monthly status reports into Microsoft® Excel spreadsheets that are used for comparative purposes, in addition to creating dashboards for the review documentation packet. The special projects administrator writes a summary for the current review period, assembles it along with the dashboards and scoring form into a review packet that is disseminated to panel members prior to the scheduled scoring/rating meetings. The special projects administrator maintains scores, spreadsheets, meeting comments, and documentation packets for all reviews conducted since 2008. In addition, the special projects administrator finalizes the Award memo for the contracting officer.

The special projects administrator successfully managed the transition of 80 DCR Mobile Telecommunication Devices (MTDs) to the centralized ordering and management system, iSYS. This transition required promptly responding to several data calls about equipment, level of service, and carriers for each user in DCR. Following the transition, the special projects administrator reviewed all information in iSYS for accuracy, submitted corrections, and resolved all outstanding issues.

The special projects administrator participated in the OPOS Strategic Planning Dashboard team, providing input on the reporting metrics tool, the design, and the presentation of the dashboard prototype for the director's review.

Serving as the central point of contact for ordering all technical equipment upgrades and replacements (laptops, desktops, and Blackberrries/iPhones), the special projects administrator determines hardware and software specifications/requirements, coordinates any specialty software purchases, provides IT support, and follows through to user satisfaction. During the reporting period, the special projects administrator coordinated the replacement of 60 computers for DCR staff and submitted 210 IT tickets on behalf of different users, following up with each one to user satisfaction. The special projects administrator also creates and manages the Central Computer annual budget and reconciles with the DCR Funding Report issued by OCICB on a monthly basis.

Annually, the special projects administrator plays an integral role in the Acquisition Management and Operations Branch (AMOB) inventory of equipment. This year's inventory was conducted in March 2012. This effort required the special projects administrator to collaborate with the inventory team to reconcile property records and research the locations of missing and/or at-home equipment to resolution. More than 450 pieces of equipment were inventoried. The special projects administrator also maintained 106 NIAID Property Checklists, updating each time equipment is added and/or removed, and issued more than 50 Long-Term Property Passes for telework and mobile equipment. In addition to the AMOB inventory, the special projects administrator supports the SAIC-Frederick annual equipment inventory.

Support to NIAID Clinical Teams

Taree Foltz, Program Manager II
Michelle Paulson, Physician II*
Daphne Mann, Nurse Case Manager III
Maryellen McManus, Protocol Nurse Coordinator III
Katherine Spates, Protocol Nurse Coordinator III
**Michelle Paulson resigned from SAIC-Frederick 7/13/2012.*

Support to the Intramural Clinical Management Operations Branch (ICMOB)

ICMOB oversees the logistical management of clinical research and related clinical operations for the NIAID intramural laboratories (Laboratory of Immunoregulation [LIR]; Laboratory of Host Diseases [LHD]; Laboratory of Clinical Infectious Diseases [LCID]; Laboratory of Parasitic Diseases [LPD]; and Laboratory of Allergic Diseases [LAD]), with a major emphasis on patient-oriented research. ICMOB manages one inpatient unit and two outpatient clinics in concert with the Clinical Center. In addition, the team is responsible for clinical protocol review and approval, assurance of scientific quality and human subject protection, quality of care delivered to NIAID patients, and the quality of professional performance of the health care providers. Our program provides direct clinical and research support to NIAID.

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, for which 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.

Our group has six nurse practitioners who function as clinicians, managing acute and chronic diseases that are studied on NIAID protocols in both an inpatient and outpatient setting. Five protocol nurse coordinators provide direct protocol management, ranging from recruitment and patient consent, to collection and recording of research-driven data, to handling of regulatory reviews. One case manager coordinates and schedules patient visits. One clinical research nurse gathers clinical information for prospective and current patients, in addition to helping with case management. One physician serves as lead associate investigator on a protocol and provides outreach to a community clinic. Collectively, the group provides support to more than sixty protocols.

During the reporting period, one nurse practitioner was hired to assist the customer with increasing patient care needs. One nurse practitioner and two protocol nurse coordinators have contributed as co-authors on posters at national conferences. One protocol nurse coordinator was the first author on an abstract accepted at a national meeting. One physician has been a co-author on one manuscript accepted for publication and another case report accepted for publication, in addition to being co-author on two posters presented at national meetings.

Support to the Laboratory of Immunoregulation (LIR)

CMRP provides study coordination, case management, patient recruitment, laboratory, clinical, and research support to the LIR. During the reporting period, a new protocol nurse coordinator II was hired to provide regulatory support and clinical study management for new community-based clinical trials and ongoing studies in the Outpatient 8 Clinic (OP8). In addition, two case management positions, one part-time and one full time, were filled; these positions address much-needed patient care needs within OP8. The part-time position has also been utilized by the Laboratory of Parasitic Diseases to supplement clinical activities and stabilize staffing while a staff member is on a leave of absence. A third case management position is in the recruitment phase and is anticipated to be filled during the current fiscal year.

During the reporting period, the Recruitment Office for the OP8 Clinic transitioned from its on-site NIH clinic location to an off-site office in Rhode Island. With the full support of the NIAID clinical director, the project began as a pilot program in order to retain the patient recruiter for the OP8 clinic. Working in collaboration with NIAID clinic management, the patient recruiter was able to fulfill all aspects of the recruiting activities and has been able to provide enhanced recruitment activities. The attention to detail and outstanding coordination has led this pilot program to evolve into a permanent off-site program.

CMRP staff supporting the LIR is also encouraged to author abstracts and presentations. The protocol nurse coordinator III was an author on two pharmacokinetic abstracts presented at the Conference on Retroviruses and Opportunistic Infections (CROI) in March. The clinical research associate I was the first author on an abstract regarding immunologic nonresponders and presented the work while attending CROI. In addition, the clinical research associate I is the author of a number of other abstracts and manuscripts currently in review.

Support to the Laboratory of Host Diseases (LHD)

CMRP provides protocol nurse coordinator, case manager, and clinical research nurse support to the LHD. The LHD's major areas of research include the study of gene therapy, granulomatous disease, allogeneic transplantation using hematopoietic stem cell grafts, and acute and chronic graft-versus-host disease.

The protocol nurse coordinator supports LHD by reviewing activities related to screening and enrolling new subjects, in addition to performing continuing protocol reviews and protocol amendments. A protocol nurse coordinator currently oversees three protocols and has taken an active part in the development of a protocol by assisting the Principal Investigator and protocol navigator in writing the protocol. The protocol nurse coordinator has assisted with the close-out visit for the Osiris study (collaborations with Osiris Therapeutics, Inc., a pharmaceutical company), and during FY2012, accomplishments include data abstraction for a manuscript. The protocol nurse coordinator has also undergone training for the U.S. Immunodeficiency Network

(USIDNET) and participated in a seminar for Clinical Trial Management and in the Ethical and Regulatory Aspects of Clinical Research course offered at NIH.

Another protocol nurse coordinator currently oversees nine protocols and recently achieved CCRP certification. In addition, the protocol nurse coordinator has been asked to present at an upcoming Society of Clinical Research Associates (SoCRA) conference. Additional support has been provided by increasing the daily workload to LHD for a period of time during changes in staffing within the clinic.

In the coming months, the clinical research nurse II will assist with implementing a new gene therapy protocol. The clinical research nurse II will be directly involved with training the staff about the protocol, as well as serving as the liaison for the investigators, and will play a pivotal role in collecting data for the study. The clinical research nurse II is expected to be listed as a co-author on an abstract for an upcoming submission to the *Journal of Allergy and Clinical Immunology*.

Support to the Laboratory of Clinical Infectious Diseases (LCID)

NIAID's LCID conducts clinical and basic studies of important human infectious and immunologic diseases, including studies focusing on mycobacterial, bacterial, viral, and fungal infections, as well as the acquired and congenital immune disorders associated with infection susceptibility and resistance. The team is involved in a wide spectrum of diseases, including primary immunodeficiencies, hyper IgE syndrome, mycobacterial, viral, and tick-borne infections, and autoimmune lymphoproliferative syndrome. CMRP staffs five nurse practitioners to provide direct patient care to patients enrolled in LCID protocols. Selected clinical protocols include:

- Natural history and therapies of bacterial, mycobacterial, fungal, or viral infections
- Natural history and therapies of immune defects
- Immune responses to infections and vaccines
- Identification of novel bacteria, mycobacteria, viruses, fungi
- Lyme disease

A physician II supports 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 using CRIS and CRIMSON, safety data monitoring, as well as FDA correspondence for Single Patient Exceptions (SPEs). One of the protocol nurse coordinators co-authored an article titled "Additional Diverse Findings Expand the Clinical Presentation of DOCK8 Deficiency," published in the *Journal of Clinical Immunology* in August 2012.

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.

One of our protocol nurse coordinators has been actively involved in the coordination and scheduling of numerous "LCID Science Symposiums," which are held weekly and attended by their clinical nursing team to stay abreast on hot topics. Several members of the team are part of the iRIS documentation committee, which is a development team working on improvements to and implementation of the system.

Support to the Laboratory of Parasitic Diseases (LPD)

CMRP provides nurse case management support and study coordination services to the LPD. The protocol nurse coordinator II supports LPD by screening and enrolling subjects, and also serves as an associate investigator on the active protocols within LPD. During the reporting period, the protocol nurse coordinator II assisted the investigators in collecting retrospective data for the subjects with eosinophilia, resulting in acceptance of several manuscripts in international journals. In addition, the protocol nurse coordinator II was involved in the creation of a poster that was presented at the annual Society of Clinical Trials meeting, and attended two courses in the fall of 2011, Ethical and Regulatory Aspects of Clinical Research and Building Quality into the Clinical Research System. During a temporary absence of the main supervisor (protocol nurse coordinator III), clinical and supervisory responsibilities were covered by other qualified personnel. The protocol nurse coordinator II received an annual performance award for FY2013. It is expected that the protocol nurse coordinator II will be directly involved in the implementation of a new IND protocol in the coming months.

Support to the Laboratory of Allergic Diseases (LAD)

CMRP provides nurse case management support to the LAD, supporting 14 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. In addition, the nurse case manager II provides procedure support through skin punch biopsies, antigen skin testing, and pulmonary function testing.

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

Beth Baseler, M.S., Director
John Beigel, M.D., Medical Affairs Scientist II
Theresa Engel, M.F.S., Clinical Project Manager II
Laurie Lambert, Clinical Project Manager III
Hemaxi Patel, B.S.N., Clinical Research Nurse I
John Powers, M.D., Senior Medical Scientist

CMRP continues to provide support to the NIAID DCR influenza initiative. Influenza causes significant worldwide morbidity/mortality, and 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 several task orders, including three multi-million dollar research subcontracts; (9) general logistical and administrative services, such as conference planning, specimen shipping, invoice tracking and processing, travel, meeting planning and organization, and financial analyses; (10) protocol development and review; (11) website development and maintenance; (12) personnel; and (13) biostatistics support. Currently CMRP supports multiple efforts for the DCR influenza platform: the NIAID Influenza Research Collaboration, the Mexican Emerging Infectious Disease Clinical Research Network (La Red), and the Symptoms Scale initiatives, as well as inpatient and outpatient influenza observational studies being performed through the International Network for Strategic Initiatives in Global HIV Trials (INSIGHT) Network.

Support to NIAID Influenza Research Collaboration

The NIAID Influenza Research Collaboration (NIRC) is an 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-Frederick:

- IRC 001 – Anti-influenza Plasma Collection Study. A plasma collection study that enrolls healthy volunteers who have had the flu or received the flu vaccine and are found to have high levels of anti-influenza antibodies in their blood. This protocol was launched in September 2009. In the reporting period, six additional sites (for a total of 12 sites) have been activated, 336 subjects were enrolled (total to date 714 subjects), and 651 units of human plasma with high-titer H1N1 antibody have been collected (total to date 1,141 units of plasma). In addition, five submissions have been made to FDA under an IND.
- IRC001B – Anti-influenza Plasma Collection at a Community Blood Bank. In an effort to increase plasma collection and to lower the costs of plasma units to the U.S. government, a pilot study has been established to collect plasma from a community blood bank. Collaborating with Mississippi Valley Community Blood Center (MVRBC) in Iowa, this study will obtain plasma units collected as part of the routine collection at MVRBC and test them for high-titer anti-influenza antibodies. This study was established in June 2012.
- IRC 002 – H1N1 Plasma Therapy Study. This research 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. During the reporting period, seven sites were activated (for a total of 19 sites), and six subjects were enrolled (for a total of 13 subjects). There was also one DSMB meeting and five submissions to FDA under an IND.
- IRC 003 – Combination Therapy Study. This 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. The IRC 003 protocol was launched in January 2011 in the United States followed by Australia in August 2011, Mexico in February 2012, Thailand in June 2012, and Argentina in July 2012. There are currently 23 domestic and 19 international sites participating in the study. In the reporting period, 17 sites were activated (for a total of 34 sites), and 15 subjects were enrolled (for a total of 17). There were 10 submissions to FDA under an IND.
- IRC 004 – Tamiflu (Oseltamivir) Versus Placebo Study. This research seeks to understand whether subjects on Tamiflu show decreases in the amount of virus detected in the nose or throat, and to understand whether 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. The IRC 004 protocol was launched in January 2012 in the United States, followed by Thailand in June 2012, and Argentina in July 2012. There are currently 20 domestic and two international sites participating in the study. In the reporting period, 22 sites were activated, and 16 subjects were enrolled.

Prior to the onset of flu season in each respective country, investigator meetings were held in Argentina, Mexico, and Thailand to train the PIs and clinical site

staff on the protocol. The medical affairs scientist provided ongoing technical leadership to the projects, including meeting with principal investigators, revising protocols, serving as the Contracting Officer's Technical Representative (COTR) on several research subcontracts, and providing scientific guidance related to study procedures, subject enrollment/inclusion/exclusion criteria, and global influenza status.

During the reporting period, CMRP project management and administrative staff streamlined international biospecimen shipping by uniting all countries under one international shipping account. Under this account, SAIC-Frederick staff was able to set up notification strings for each type of shipment such that the team (shipper, recipient, repository, laboratory, and protocol team) is aware of shipment orders, pick-ups, deliveries, and delays due to customs, or other issues. This new procedure allows the staff to track and manage the shipment proactively, distribute study-specific shipping forms and permits to each site, ensure that customs issues are resolved as quickly as possible, and monitor the temperature of the shipments are during any shipping delay. Updates to the Centers for Disease Control and Prevention (CDC) import permits are supplied to all sites via the NIAID Influenza Research Collaboration (NIRC) study web portal and provided to World Courier for inclusion in their clinical trials database. Additionally, the new procedure allows the staff to monitor costs and forecast expenditures in a more efficient manner.

The secretary III was hired in December 2011 and has played an integral part in the success of the influenza program. The secretary III has taken over responsibilities pertaining to arranging staff travel, generating meeting minutes, processing vendor invoices, managing and updating clinical site lists for international shipping and CDC import permits, tracking biospecimen shipments and notification lists, organizing and maintaining electronic study files, and navigating newly implemented conference and meeting planning requirements.

The clinical project manager was heavily involved in the day-to-day administrative management of several subcontracts, routinely reviewing and approving monthly reports and invoices, subcontractor travel requests, and trip reports as well as monitoring budgets, budget modifications, expenditures, and end-of-year forecasting. Additionally, the clinical project manager was a catalyst for the development of pro forma invoices and extensive study-specific documentation packages for the international shipments of study agent to Thailand and Argentina, successfully navigating the rigorous and ever-changing landscape of the customs authorities in both countries.

During the reporting period, CMRP staff also worked diligently to assign several research subcontracts/ purchasing agreements from one of the subcontractors directly to SAIC-Frederick. As a result, direct agreements were executed with multiple laboratory supply companies, one kit manufacturing and distribution company, one study agent storage and distribution facility, and two central laboratories in Australia (located in Sydney and Melbourne). Managing these efforts internally allows CMRP to have greater direct oversight of their activities and to realize significant cost savings for the client.

Support to the Mexican Emerging Infectious Disease Clinical Research Network – La Red

In March 2009, a new influenza A virus, novel H1N1 (commonly referred to as "swine flu"), caused an increase in reports of influenza-like illness in North America. In late April 2009, the Mexican Ministry of Health responded to the public health threat by implementing a series of non-pharmaceutical interventions, which has been widely credited with halting the first wave of the outbreak in this country.

Conducting clinical research protocols at multiple sites requires coordinated oversight to ensure that implementation is standardized across the sites, and that interpretation of intent and procedures within the protocol are as identical as possible in each location, in order to maximize the validity of study data. To fulfill this need, NIAID and the Mexican Ministry of Health partnered to create La Red, an entity that will provide overarching scientific guidance and management support to clinical initiatives in Mexico.

Currently, La Red is overseeing the conduct of three clinical studies in Mexico: (1) IRC 003; (2) FLU-PRO; and (3) ILI 002, which is supported by NIAID through a separate contract mechanism.

A network coordinating center (NCC) has been developed to assist La Red in conducting the highest-quality research in support of multiple protocols through different funding sources. To accomplish this goal, the NCC will establish standard research procedures as directed by the network steering committee (NSC), provide training on these procedures, and ensure the clinical research sites are in accord with these shared procedures, as well as support all other operational and administrative functions to maintain the network.

During the reporting period, CMRP staff administered research subcontracts for the oversight and management of the NCC, including the acquisition of staff, which currently comprises an office manager, a data/IT manager, and a network director. The La Red Annual Meeting was held in October 2011, followed by the La Red scientific retreat in March 2012. Throughout the year, the NCC staff assisted clinical study sites with acquisition of materials and supplies, specimen courier services, travel, data management, technical support, meeting coordination, annual reports, invoice processing, and equipment ordering. The La Red data manager traveled to Buffalo, NY, for a two-day, intensive training on the e-Data and Laboratory Data Management System (LDMS) applications, so that he can function as a first-line resource to data managers at the clinical sites in Mexico. The medical affairs scientist provided ongoing technical leadership to the projects, including serving as project lead for NIAID, meeting with principal investigators, revising protocols, serving as the

Contracting Officer's Technical Representative (COTR) on several subcontracts, and providing scientific guidance related to study procedures and subject enrollment/inclusion/exclusion criteria.

Influenza Support to NIAID Symptoms Scale

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 (ARIC) 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. More than 800 subjects are enrolled to date. During this contract period, manuscripts were developed for publication of the initial findings.

An additional symptoms-scale study, the Influenza Patient Reported Outcome Questionnaire Development Project (FLU-PRO), is being conducted in the United States and Mexico to develop a single, standardized instrument of patient influenza symptoms for use in clinical studies involving adult and pediatric patients. Under a contract established with United BioSource Corporation (UBC) and a partnership between NIAID and the U.S. Department of Defense (DoD) Uniformed Services University, the FLU-PRO study began enrolling subjects in the U.S. during the 2010 flu season. A research subcontract was established with UBC to provide services for two phases of this protocol: (1) performance of one-on-one elicitation interviews with subjects; and (2) analysis of interviews to develop the draft FLU-PRO instrument, resulting in a detailed report of the findings formatted for submission to the FDA. During the past contract year, a research subcontract was established with the Instituto Nacional de Ciencias Medicas Y Nutricion Salvador Zubiran (Nutricion) in Mexico, one of the participating La Red clinical sites, to provide a Mexico call center and perform one-on-one elicitation interviews in Spanish during the 2011 flu season. UBC's research subcontract was modified to include training of the Mexico call center staff and analysis of the data collected in the elicitation interviews performed there. UBC will also provide a "translatability assessment" of the draft instrument and provide feedback regarding any words or phrases that are structurally or culturally problematic when being translated from English into another language. By the end of the 2011 influenza season, more than 60 adult subjects were enrolled in the U.S. and Mexico, completing stage 1 of the protocol in adult subjects.

The analysis phase of this project is currently in the beginning stages for the adult population. Meetings were held with investigators to discuss continuing enrollment of children and adolescents for stage 1 of the protocol and plans to begin stage 2 of the protocol in adults in the upcoming influenza season. Meetings were held with DoD officers to expand the protocol to family practice sites within the military in order to increase enrollment in children and adolescents. During the upcoming year, investigator meetings will be held to discuss analysis of subject data collected to date and publication of the initial findings.

Support to FLU002 and FLU003 Protocols – INSIGHT Network

During the reporting period, CMRP staff has provided administrative support and contractual oversight services for the on-going, multi-million dollar research subcontract established with the University of Minnesota. The University of Minnesota, utilizing the established INSIGHT network, is acting as a global coordinating center for two influenza studies in support of these initiatives:

- FLU 002: An International Observational Study to Characterize Adults with Influenza A-Pandemic H1N1 opened in September 2009 and seeks to enroll 5,000 patients with H1N1in geographically diverse locations and follow them for 14 days. Specific objectives are to estimate the percentage of patients who go on to develop severe disease or complications that require hospitalizations, to obtain information on risk factors for disease severity, and to establish a central repository of specimens for use in virus characterization. More than 2,200 subjects have been enrolled to date.
- FLU 003: An International Observational Study to Characterize Adults Who Are Hospitalized with Complications of Influenza A-Pandemic H1N1 opened in September 2009 and seeks to enroll 1,000 patients hospitalized with severe and/or complicated influenza A in geographically diverse locations and follow them for 60 days. Specific objectives are to estimate the percentage of patients who die, to obtain information on risk factors for mortality, and to establish a central repository of specimens for use in virus characterization. More than 700 subjects have been enrolled to date.

Biodefense Initiative, NIAID

Taree Foltz, Program Manager II
Lana Cross, Senior Program Coordinator
Silvana Rivero, Senior Program Coordinator

CMRP provides administrative and programmatic support services for the facilitation and coordination of scientific workshops and conferences. In the past, CMRP has facilitated the logistics and planned the provisions for several workshops and conferences both locally and nationwide, including arranging international travel and coordinating with large conference facilities. These workshops and conferences bring together experts from various areas of scientific and clinical research as well as multidisciplined research professionals to share and

disseminate information and research outcomes. These activities directly align to the Division of Clinical Research strategic GOAL 2: "Facilitate the generation of new knowledge and insight from research." In the spring of 2012, CMRP staff assisted with a brainstorming session called Imaging of SIV-Infected Cells through HSC Modified NHPs. This session allowed the group to develop a consensus on the use of in vivo imaging to accelerate research in HIV reservoirs, a very challenging goal. Those in attendance were basic scientists, imaging specialists, and infectious disease clinicians.

CMRP is currently planning two meetings to foster knowledge sharing and promote the dissemination of new research findings to the clinical community. These meetings include an Imaging Workshop and a pre-meeting for the Triage and Management of Accidental laboratory Exposure to Bio-Safety Level III and IV Agents. Future activities include the coordination of the Concept Incubator meeting which is instrumental for the review and prioritization of research efforts for the Integrated Research Facility at Fort Detrick. In addition, the Triage and Management of Accidental Laboratory Exposure to Bio-Safety Level III and IV Agents will be planned for a larger audience.

Office of Chief Scientist, Integrated Research Facility (OCSIRF)

Laurie Lambert, Clinical Project Manager III
Melissa Borucki, M.S., M.B.A., Senior Special Projects Administrator

The OCSIRF is part of the Office of the Chief Scientist for the Division of Clinical Research in the NIAID Office of the Director. The mission of OCSIRF is to manage, coordinate, and facilitate the conduct of emerging infectious disease and biodefense research to develop vaccines, countermeasures, and improved medical outcomes for patients.

The NIAID OCSIRF was created to carry out biodefense research needed to understand the clinical disease processes that correlate with the severity of microbial-induced disease. Central to the core mission of the NIAID OCSIRF is the use of hospital tools, such as endoscopy, cardiac telemetry monitors, and CT, MRI, SPECT, and PET imaging, to systematically evaluate the pathogenic processes and clinical course of disease in animal models exposed to microbes.

CMRP provides programmatic support and management oversight for research subcontracts to support initiatives of the Biodefense Clinical Research Branch, OCSIRF.

CMRP established a research subcontract with Turner Consulting Group (TCG) to gather, codify, and present the functional requirements and features of an Information Technology and Telecommunications technology infrastructure from the network cabling to the desktop and mobile solutions for the IRF. Through the subcontract, TCG provides project management and oversight of the wireless and RMS deliverables.

During the reporting period, TCG has delivered RMS (Digital Infuzion) recommendations and support, including STARLIMS and LabWare demos, project charter and acquisition strategy, and transition support to OCICB for procurement of scientific systems and a scientific system integrator; reviewed, edited, and delivered the Pragmatics WLAN implementation report; completed B-Block wireless design, scanning, and inputting APs into the Wireless Control System; and, identified additional enclosures, antennae, or software upgrades necessary to complete installation tasks.

CMRP also established a research subcontract with The Maine Group (TMG) for program coordination in support of the IRF, including program analysis and reporting program status to leadership, to include schedules, risks, and status of issues. TMG provides infrastructure coordination with NIAID IRF Leadership and NIH Office of Research Facilities Construction and Activation leadership related to critical path construction and activation issues. TMG incorporates construction activities and milestones into NIAID occupancy and systems integrations projects and schedules.

Throughout 2012, TMG has facilitated Endurance Period planning among NIH stakeholders, including determining document requirements and activities and has provided oversight and coordination of Endurance activities. TMG also facilitated and coordinated the NIAID program validation of high-containment Air Pressure Resistant (APR) doors utilizing scripted and documented daily exercising of doors, and delivery of documented observations as related to the IRF. TMG collaborated with the NIAID/IRF and NIH Police to develop roles and responsibilities for the IRF program as well as develop a draft program integration and communication model. TMG also provided support to the Telemetry initiative by: (1) performing a systems gap analysis regarding current capabilities and requirements, developing a statement of requirements documenting reduced needs and cost models; (2) facilitating the development of systems workflows and staffing requirements; and (3) developed a draft Telemetry statement of work and cost analysis.

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 continue, with four long-term, follow-up patients completing their visits over two years. The final monitoring visit with CMRP RCHSPP's Clinical Trials Management team took place in July 2011. Currently protocol results have been analyzed, documented, and submitted for publication. All aspects of this procedure are supported by CMRP staff.

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 liver 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 has been completed there.

Currently, CMRP staff members have brought two new projects to Washington Hospital Center, and active recruitment for these projects is ongoing. One study is RASF-B, a blood collection study from patients who are viremic above 10,000 copies. This blood is then shipped back to the NIAID Director's lab to continue the study of the pathogenesis of HIV. The second study, PUMA, requires that a nurse be present to collect specimens obtained at bronchoscopies done to diagnose infection disease of the lungs. These samples are shipped back to NIH to be tested in the new TessArray scanner to determine exact cause of pulmonary infection. NIAID hopes to rent permanent office/exam space at Washington Hospital Center for NIH staff to use when seeing patients at this site. Since CMRP has established a very positive collaboration with Washington Hospital Center, several extended projects are being proposed for the site.

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

John Powers, M.D., Physician III
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 physician III 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 support the program by completing an amendment to the existing Inter-agency Agreement to provide additional funding for the HIV Natural History study (RV168) within IDCRP. CMRP staff also continued to facilitate the development of research capacity by aiding IDCRP staff in developing and implementing protocols for infectious diseases of military relevance, and assisted in prioritizing research protocols within the network, developing seven research areas of prime importance to the network.

Currently, 66 protocols are in various stages of development within IDCRP. 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 holds regular weekly meetings regarding function and vision of the IDCRP program and keeps NIAID staff up-to-date on the progress of the program. CMRP's physician III serves on the Scientific Review Board, ensuring the scientific validity of protocols before sending them to IRB. The physician III has also lectured to groups of PIs and mentors individual PIs to enhance their scientific understanding, and has worked closely with IDCRP staff to reorganize the data collection and analysis branch.

CMRP staff aided DoD staff in developing an infectious disease–specific IRB. In addition, RCHSPP staff provides protocol pre-review for regulatory compliance and, when appropriate, 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 a study in Europe, Africa, and the Middle East to evaluate various interventions in the treatment of diarrhea in military members.

RCHSPP staff has helped IDCRP develop an informed, independent staff for regulatory and monitoring functions. Under this mentorship, IDCRP staff now monitors some of its own protocols and has developed a QA/QC standard for the network.

SUPPORT TO CLINICAL CENTER

Support to the District of Columbia Partnership for HIV/AIDS Progress (DC-PFAP), Clinical Center

John Powers, M.D., Physician III
Dawn Fishbein, M.D., M.S., Medical Director, Medical Affairs Scientist II*
Rachel Silk, R.N., MPH, Clinical Nurse Administrator
Anu Osinusi, M.D., MPH, Physician II
Colleen Kotb, R.N., Clinical Nurse Coordinator
Chloe Gross, Clinical Research Nurse II
Erica Eaton, Clinical Program Administrator*
Michelle Espinosa, Secretary II
Alice Rosenberg, R.N., Clinical Research Nurse III (Outreach)
**Dawn Fishbein resigned from SAIC-Frederick 6/14/2012.*
**Erica Eaton resigned from SAIC-Frederick 11/7/2011.*

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 partnership is being referred to as DC-PFAP. For the first time, the nation's capital and leading health research institution have 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, from initial and subsequent staffing to acquisition of D.C. administrative office space and, currently, in maintaining operational contracts and staffing.

During the reporting period, there have been multiple advances in the program's development, moving from initial care implementation into the research phase. Achievements during FY2012 include the following:

- Initiation of an innovative and paradigm-shifting, interferon-free HCV therapeutic clinical trial at the NIH. This is the first interferon-free single DAA agent study to be approved for evaluation by the FDA. A DC-PFAP physician is the Lead Investigator, and subjects were heavily recruited from the DC-PFAP clinic population. The protocol title is "A Randomized Controlled Study to Assess Safety, Tolerability, and Efficacy of PSI-7977 Alone or in Combination with RBV in HCV Genotype 1, Monoinfected Treatment-Naïve Participants," also known as the SPARE study. This study has fully enrolled all 60 subjects to date and is following the subjects through end of study.
- Initiation of a novel trial in the D.C. clinics using a new, direct-acting antiviral (DAA) agent with pegylated -interferon and ribavirin for HCV treatment in both HCV-monoinfected and HIV/HCV-coinfected individuals, with a DC-PFAP medical affairs scientist and a physician as the Lead Investigator and the Associate Investigator, respectively. The protocol, titled "An Open-Label, On-Treatment Study to Assess the Effect of HIV-1 Coinfection on Therapeutic Response to Boceprevir, Peg-interferon alfa-2b and Ribavirin in HCV genotype 1, IFN Treatment-Naïve Subjects With or Without HIV-1 (BRIGHT)" has three subjects enrolled; staff are actively screening in the DC clinics.
- Development of two additional clinical protocols by DC-PFAP physicians as lead associate investigator or associate investigator. The first protocol, DC-PFAP Fibrosis study; "Liver Fibrosis Progression in African Americans with HIV-HCV Co-Infection: A Retrospective Study," has evaluated more than 150 patients. The second study, TLR7, is "A Double-Blind, Randomized, Placebo-Controlled, Single and Multiple-Dose Ranging Study Evaluating the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Antiviral Activity of GS-9620 in Treatment Naïve." This is a multicenter study for which two subjects have been screened and are awaiting eligibility. The DC-PFAP physician is an associate investigator on four on-going protocols conducted at the NIH focusing on the natural history of hepatitis C, fibrosis, and treatment.
- Expansion of the Natural History of Hepatitis study to the Washington VA Hospital, where enrollment continues on-site. Recruitment and enrollment of subjects from the VA have been rapid. To date, 65 patients have been enrolled into this study from the VA and 43 from the DC clinics.
- Presentations: Four oral and poster presentations by DC-PFAP physicians at various international conferences on hepatitis C.
- Publications: Six publications by DC-PFAP physician in peer-reviewed journals and a book chapter in *Emergency Medicine*. Two articles published in the *Journal of Medical Virology* focus on the genetic factors in the treatment of patients for hepatitis C, which continues to be a critical and much-needed area of research.
- Continued clinical care of more than 450 new patients in the past three years for subspecialty hepatitis care and treatment within three integrated HIV community clinics in DC, totaling over 1,600 patient visits.

- Arranged educational webinars, research network meetings, and conference calls involving the DC hepatitis treatment providers, with the goal of promoting clinical and research collaboration among academic institutions and young investigators in DC and restoration of NIH cross-institutional hepatitis research meetings. The CMRP medical affairs scientist II and physician II developed and presented two webinars to the DC hepatitis treatment providers on the research highlights presented at three international research meetings held during this reporting period. These education sessions provided an opportunity for community providers unable to attend these meetings to have access to the latest research in their field. Additionally, the medical affairs scientist II coordinated regular conference calls with key hepatitis treatment providers in DC to discuss hepatitis clinical care and share research being conducted within the greater DC community. These calls afforded providers a chance to discuss difficult cases with other providers and learn about research opportunities for their patients.
- Hiring of a nurse case manager to become a research coordinator in the DC community-integrated hepatitis clinics, as well as obtaining approval for an additional case manager position.
- Hiring of a secretarial/administrative assistant position.

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, DC.

Support to Radiology and Imaging Sciences, NCI Cardiac Imaging and Interventional Radiology (David Bluemke), Clinical Center

Barry L. Gause, M.D., Clinical Director
Lamin Juwara, Ph. D., Senior Nurse Practitioner
Julia Selah, C.R.N.P., Nurse Practitioner
*Sunni Kim, M.B.A., Clinical Research Nurse II**
**Sunni Kim resigned from SAIC-Frederick 7/10/2012.*

The Radiology and Imaging Sciences Branch provides resources for translational research and training, and performs basic and clinical research sponsored by NIH and the Clinical Center. Radiology and Imaging Sciences supports its training mission through sponsorship of the Imaging Sciences Training Program. This program provides the opportunity for interdisciplinary imaging research in radiology, molecular imaging, nuclear medicine, and other specialties in conjunction with institute researchers in cancer, cardiovascular disease, infectious disease, musculoskeletal imaging, and other areas. Specialized research in imaging sciences includes diagnostic radiology research, conducted in the Laboratory of Diagnostic Radiology Research, interventional radiology research, conducted in the Experimental Neuroimaging Laboratory and the Molecular Imaging Laboratory, and the computer-aided detection MEDx operations supporting Institute-wide initiatives in biomedical imaging.

CMRP staffs a nurse practitioner and clinical research nurse II to support these efforts. The clinical research nurse II recruits and evaluates participants for protocol eligibility, provides protocol coordination, and captures and documents AEs. The nurse practitioner reviews patient eligibility, performs history and physicals, schedules appointments for participants seeking treatment, and provides clinical trial education to participants. The nurse practitioner also participates in developing SOPs for the team.

Notably, the CMRP staff supporting the cardiac imaging services developed the key infrastructure in preparation for recruitment and follow-up of 200–300 study patients for Carotid Plaque Regression Protocol 10-CC-0214. Staff set up the implementation of the system needed for interdepartmental drug safety management and documentation to assure patient safety and accurate records, ordered charts for in-office filing of key patient documents, and began developing a system for managing a large volume of charts. Staff coordinated and helped to develop PowerPoint presentations for the community education outreach project on "Cardiovascular Risk Factor Reduction to Ensure a Healthier Future." Additionally, staff is instrumental in the orientation and training of new postbaccalaureate trainees to be able to fully participate in the research efforts of the team. CMRP staff initiated and networked with a national women's heart support group outside of NIH in order to facilitate the team's patient recruitment efforts.

In addition to the above protocols, staff has been instrumental in obtaining the imaging and radiology services for the Drug Eluting Bead with Irinotecan protocol (an investigator-held IDE with the FDA) through the submission of protocols and continuing reviews to the IRB for the chief information officer. Additionally, staff coordinates and maintains databases for trials as well as FDA audits.

Support to Interventional Radiology Research Team (Brad Wood), Clinical Center

Barry L. Gause, M.D., Clinical Director
Beth Baseler, M.S., Director
Lamin Juwara, Ph.D., Sr. Nurse Practitioner
*Stacey Gates, Clinical Research Nurse II**
**Stacey Gates resigned from SAIC-Frederick 3/7/2012.*

The mission of the Center for Interventional Oncology (CIO) at the NIH Clinical Center (CC) is to develop and translate image-guided technologies for localized cancer treatments. The CIO is a collaboration involving the CC, NCI, and the National Heart, Lung, and Blood Institute

(NHLBI). The CIO draws on the strengths of each institute to investigate how imaging technologies and advanced devices can diagnose and treat localized cancers in ways that are precisely targeted and minimally invasive or non-invasive. It also helps to bridge the gap between diagnosis and therapy, and between emerging technology and procedural medicine.

For a portion of this reporting period, CMRP provided a clinical research nurse II to support the Interventional Radiology Research team; however, that employee resigned in March 2012. The team is involved in research dealing with targeted agents singly and in using ultrasound techniques for tumor ablation. With support provided by CMRP staff, the team recently completed a Phase I Hifu trial, which is a pilot study of MRI-guided high intensity focused ultrasound ablation of uterine fibroids. Currently, the clinical research nurse II position is vacant, and CMRP is working to quickly fill this vacancy with a qualified candidate.

Support to National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

Overview

The mission of the NIAMS is to support research that will lead to the promotion of knowledge and understanding of the causes, treatment, and prevention of arthritis, musculoskeletal, and skin diseases. In that effort, the NIAMS Intramural Research Program conducts studies in natural history and treatment as well as basic investigations of the etiology and/or pathophysiology of rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, vasculitis, scleroderma, myositis, osteoarthritis, and 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.

CMRP provides protocol review services, and regulatory and clinical trials management support to allow NIAMS to streamline protocol development time, provide flexibility for emerging/fluctuating needs, eliminate costly time delays, and ensure the success of the their clinical mission. CMRP staff support clinical research operations for NIAMS IND Phase I and Phase II clinical trials, including protocol writing, regulatory guidance and compliance, training, and clinical trials management, including case report form review and monitoring activities; document creation, collection, and compilation for regulatory filings (pre-IND, IND) with the FDA and other regulatory authorities; and technical review and report preparation. CMRP has created template language for the NIAMS support group to use when they prepare a new protocol that will require CMRP monitoring of the trial.

In addition to the above, CTM designees provided NIAMS staff with information on how to best document a subject's ICF process in the clinic charts and guidance on training opportunities within NIH and outside groups that are related to investigators' responsibilities in overseeing an FDA-regulated IND clinical trial. In addition, a flow document was developed to outline the process the study teams can follow when submitting protocol deviations and violations to the NIAMS IRB. At the request of the NIAMS clinical director, CTM will also be providing training to the study teams on how to ensure proper source documentation practices for an IND study. During this fiscal year, CTM created and received approval on the NIAMS monitoring guidelines. The NIAMS clinical director approved these guidelines in May 2012 and informed the NIAMS PIs that they are available for reference.

In addition to the regulatory and monitoring support, the CMRP also provides clinical nursing and administrative support. CMRP is actively recruiting for a protocol nurse coordinator II to provide direct nursing support related to the clinical studies investigating the causes, treatment, and prevention of arthritis, and musculoskeletal and skin diseases. The protocol nurse coordinator II will work closely with the NIAMS clinical team to coordinate patient schedules, data collection, and assist physicians with skilled procedures. In addition, the protocol nurse coordinator II will consult with other health care professionals to meet patient medical, psychological, and/or social needs. The CMRP patient care coordinator II position has recently been filled to assist with scheduling appointments for the patients' routine clinical visits and act as liaison between physicians, nursing staff, and other departments. Identification and demographic data are maintained for each patient, as well as other pertinent information prior to an appointment or admission.

Highlights of CMRP work for NIAMS during this reporting period include the following:

- **Protocol number 03-AR-0298, Anakinra in Patients with NOMID.** Regulatory Affairs prepared an IND Annual Report (IND 11138), which included updated information for NIAMS protocols 03-AR-0298 and 11-AR-0241.
- **11-AR-0241, Ankinra in Behcet's Disease.** The IRB approval and finalized protocol/IC documents were submitted to FDA along with the IND annual report in December 2011. This was the first NIAMS study activated by CTM. Study activation occurred on October 31, 2011, and the first monitoring visit occurred in June 2012. CTM designees also received eCRF system training for this study from the NIH designees.
- **05-AR-0014, IL-1 Trap in Adults with Autoinflammatory Disease.** This protocol was closed with the IRB and FDA in late 2010; however, the IND remains active for the submission of the new DIRA protocol. The regulatory team prepared the annual report for this IND 100567 and delivered it to

FDA on May 24, 2012. CTM completed a monitoring visit for this study in October 2011; however, the study team has not yet decided on a date for CTM to complete a study close-out visit.

- **Study of Rilonacept in DIRA.** After developing and forwarding a draft protocol and associated documents to NIAMS in July 2011, the regulatory team learned in mid-February that the protocol and informed consent documents were being completed by a new NIAMS PI and that the manufacturer, Regeneron, remained interested in supporting this study. Regulatory Affairs and CTM conducted a regulatory review of the protocol and informed consents (IC) and returned their comments to the PI on May 30, 2012. Once finalized, the regulatory team will submit the protocol/IC documents to FDA under the existing IND 100567. Once SAIC-Frederick hears more from the NIAMS study team, CTM team will schedule this protocol for a study initiation visit.
- **03-AR-0173, Natural History and Pathogenesis of NOMID.** CTMis waiting to be contacted by the PI about whether they will monitor this study.
- **Study of Omalizumab in Lupus (STOP LUPUS).** A teleconference was held on November 1, 2011, between the NIAMS study team and CMRP to discuss this new protocol and plan for a regulatory review of the documents. The draft protocol was received by CMRP, and the Regulatory/CTM team completed the regulatory review and returned comments to NIAMS on November 9, 2011. NIAMS forwarded an informed consent template to CMRP in mid-November, and the regulatory team wrote and returned the draft informed consent document to the NIAMS study team in December 2011. The regulatory team subsequently obtained necessary cross-reference authorization, product package insert, and scientific publications in support of the planned IND. The draft IND sections were forwarded to the NIAMS Investigators for review and input in mid-January, and the regulatory team met with the study team on February 14, 2012, to discuss finalization of the protocol documents and completion of the IND. The regulatory team and NIAMS worked together over the next few months to complete the study documents, and the Regulatory/CTM team provided final regulatory review comments to the study team on May 22, 2012. NIAMS returned finalized versions of the protocol/IC to CMRP on May 31, 2012. The regulatory team then completed the IND application, obtained approval and signature, and submitted this new NIAMS IND to FDA on June 14, 2012. CTM designees reviewed draft forms for this study and will continue to work with the NIAMS staff as they design eCRFs for the study. A site visit (SIV) is anticipated in the third quarter of 2012.
- **MitoQ in TRAPS.** Members of CMRP's Regulatory and CTM teams met with the NIAMS PI in January 2012 to discuss plans for development of this new protocol, the IND, and monitoring plan. A pre-IND meeting was agreed upon, and NIAMS will develop a protocol outline to include with the meeting request. A template for pre-IND meeting information was forwarded to NIAMS in late January, and the regulatory team then obtained necessary cross-reference authorization and scientific publications in support of the planned IND. This project is currently on hold because questions remain as to whether NIAMS or the National Human Genome Research Institute (NHGRI) will take the lead on the study. If NIAMS sponsors the study, the regulatory team will develop a pre-IND package and schedule a meeting with FDA, and CTM will plan to conduct the SIV once the IND has been submitted to the FDA.

CTM designees have begun to work with the NIAMS Clinical Trials Database Developers to include a feature in the system that indicates which data fields have been verified as being monitored by a CRA; they have also provided advice on report templates that can be generated to help assess what data have been completed and verified. In addition, Regulatory Affairs has offered assistance with organizing and compiling complete files of existing NIAMS regulatory applications.

SUPPORT TO THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI)

Overview

During the reporting period, the services CMRP has provided to support the NHLBI have resulted in the rapid deployment of clinical services for time-sensitive, critical clinical research. Acquiring these services through CMRP has helped to 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 CRFs development, NHLBI support included data/document collection and compilation for regulatory filing (pre-IND, IND, IDE) with FDA and other regulatory authorities as needed; technical review and report preparation; clinical site monitoring activities; tracking of investigational products; data management support; administrative coordination and general logistical support for regulatory activities; training; and other services as required.

In addition, NHLBI requested that 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) general QA for data acquisition; (5) ad hoc review formulation and management; (6) scientific pre-reviews on protocols prior to IRB submission; and (7) interfacing between investigator and monitors.

During this fiscal year, the clinical trials director and the CMRP director have met with key NHLBI leadership to discuss approaches in developing an appropriate clinical trials management/regulatory program to support the NHLBI clinical research program. It was critical to assess the needs of the PIs and study teams prior to initiating the recruitment and hiring of staff to support this work effort. To fully assess PI needs, CMRP staff met with several PIs to discuss their clinical research needs. Numerous branch chiefs and PIs have taken advantage of talking with the team to discuss their unique research and regulatory requirements.

To meet the requirements for this initiative, CMRP hired one clinical project manager I and two clinical research associate IIIs. During the reporting period, there have been four new hires, one clinical project manager II (July 2012), one clinical research associate II (November 2011) and two protocol navigators (January 2012). NHLBI has multiple protocols that have been active for years but have never been monitored. The additional clinical research associate hired in November has assumed the duties on these studies to help CTM achieve the goal of having all currently active IND/IDE study protocols monitored. As of January 2012, CTM has provided protocol navigation as a new service in support of NHLBI's clinical research activities. In addition to the employees hired above to support the NHLBI SOW, a request was made to employ a research nurse. This position was filled in April 2012.

To date, CTM has been instrumental in providing comments to the staff of the NHLBI Office of the Clinical Director (OCD) on the following: NHLBI Intramural Clinical Protocol Monitoring Guidelines; DIR Clinical Research Quality Assurance and Quality Control Policy; Study Files and Regulatory Binder SOP; Roles and Responsibilities SOP; and a Delegation of Roles SOP.

CTM is in periodic communication with OCD staff and continues to report discrepancies/issues noted during monitoring visits and protocol navigation processes to improve the quality of work, such as omission of appropriate and relevant wording or procedures within the study protocol, lack of documentation pertaining to AEs in source documents, inclusion/clarification of reporting requirements for AEs, use of incorrect regulatory forms for initial applications and amendments to INDs/IDEs, and inconsistencies with documentation of consent process. The group is continuing to work with staff to ensure protocols are consistent and monitoring processes are streamlined across all NHBLI studies.

The clinical project manager I and clinical research associates have been involved in reviewing nine new study protocols that were developed by NHBLI PIs prior to the submissions to the IRB. The clinical research associates have completed study initiation visits and activated eight new study protocols. The clinical project manager I and clinical research associates have held four Meet & Greet sessions with study teams in preparation of the first monitoring visit for six study protocols.

The clinical research associates and clinical project manager I have conducted 23 monitoring visits this year, and, for each new protocol monitored, the staff has written and implemented nine monitoring plans that will be followed during the CTM monitoring visits of the assigned studies. The clinical research associates have also conducted two study close-out visits for NHBLI to date. During this reporting period, the clinical research associates have created five CRF packages and worked with study PIs to review and/or revise five CRF packages.

The NHBLI will have their first FDA inspection/audit for one IND study in the fall of 2012. The CTD and designated clinical research associate and clinical project manager I assisted the study team with preparations for the audit. Tools were provided for the study team to use as they reviewed their charts; a debriefing meeting was conducted with the study team, and guidance was provided on how to address some of the questions from the auditor. The clinical research associate completed an ad hoc monitoring visit in preparation for the FDA audit.

During the reporting period, the following regulatory (FDA) submissions were handled for NHLBI PIs: one initial IND to the FDA on behalf of NHLBI investigators, and 14 amendment submissions for active INDs. Protocol navigators have been supporting at least 49 study protocols, including IRB submissions, attending initiation visits and performing other study-related activities.

During the reporting period, protocol navigators have been involved in and/or submitted the following: (1) IRB Submissions: 3 initial/new protocols, 12 IRB Continuing Reviews, 18 protocol amendments, 6 SAE reports, 10 protocol deviations/violations, and 3 other types (advertisement, unanticipated problems, and a patient exemption); (2) 6 DMSB reports; (3) 4 NIH special exemptions; and (4) 6 Material Transfer Agreements.

CTM provided the following presentations/trainings to NHLBI staff: two regulatory presentations pertaining to the need and requirements of INDs/IDEs (November 2011 and January 2012); one presentation on how investigators should prepare for monitoring visits (February 2012); one presentation at the IRB Retreat (November 2011); and one training on source documentation and CRFs provided to an investigator's study team (November 2011).

CTM has met with several PIs and their protocol navigators to review draft CRF tools that will be used by the team while monitoring NHLBI studies. The tools include CRFs specific to certain types of studies and SOPs designed by Clinic staff. Staff members continue to create monitoring and regulatory guidance documents/ tools for NHLBI PIs. The team has also received an overview of the group's IRB tracking system and has engaged in discussions about the use of other tools.

CTM also met with a lead PI, who is the medical director of the Cell Processing Section (CPS) in the Department of Transfusion Medicine. The PI provided an

overview of processes that occur for each clinical study in CPS and the type of study data collected. Based on this overview, CTM is currently looking into the data being collected and plans to draft a CRF that can be used by CPS to centralize data collected that is pertinent to investigational product accountability.

In June 2012, the NHLBI requested that SAIC-Frederick recruit and hire a full-time clinical project manager. The position was filled on July 28, 2012. Overall support includes: (1) providing direction and regulatory information on protocol-related issues and logistics; (2) writing IND/IDE submissions, as well as providing information and guidance on the process; (3) coordinating clinical trials agreements with the staff and the Office of Technology Development; and (4) conducting meetings with the staff to disseminate information and provide a venue for staff feedback on protocol navigator tasks, processes, and issues.

Publications

Babu S, Anuradha R, Kumar NP, George PJ, Kumaraswami V, Nutman TB: Filarial lymphatic pathology reflects augmented toll-like receptor-mediated, mitogen-activated protein kinase-mediated proinflammatory cytokine production. Infect Immun, 79(11): 4600-4608, 2011. doi: 10.1128/IAI.05419-11 PMID: 21875961

Beigel JH, Luke TC: A study in scarlet-convalescent plasma for severe influenza. Crit Care Med, 40(3): 1027-1028, 2012. doi: 10.1097/CCM.0b013e31823d77c3 PMID: 22343871

Bemmel DV, **Lenz P**, Liao LM, Baris D, Sternberg LR, Warner A, Johnson A, Jones M, Kida M, Schwenn M, Schned AR, Silverman DT, Rothman N, Moore LE: Correlation of LINE-1 methylation levels in patient-matched buffy coat, serum, buccal cell, and bladder tumor tissue DNA samples, 21(7): 1143-1148. DOI: 10.1158/1055-9965.EPI-11-1030. PMID: 22539607. PMCID: PMC3397796

Cuellar-Rodriguez J, Gea-Banacloche J, Freeman AF, Hsu AP, Zerbe CS, Calvo KR, **Wilder J**, Kurlander R, Olivier KN, Holland SM, Hickstein DD: Successful allogeneic hematopoietic stem cell transplantation for GATA2 deficiency. Blood, 118(13): 3715-3720, 2011. doi: 10.1182/blood-2011-06-365049 PMID: 21816832

Edwards HM, Taplin SH, Chollette V, Clauser SB, Kaluzny AD: Summary of the multilevel interventions in health care conference. J Natl Cancer Inst Monogr, 44: 123-126, 2012. doi: 10.1093/jncimonographs/lgs018. PMID: 22623605

Erinosho TO, Moser RP, **Oh A**, Nebeling LC, Yaroch AL: Awareness of the fruits and veggies-more matters campaign, knowledge of the fruit and vegetable recommendation, and fruit and vegetable intake of adults in the 2007 food attitudes and behaviors (FAB) survey. Appetite, 59(1): 155-160, 2012. doi: 10.1016/j.appet.2012.04.010 PMID: 22524998

Erinosho TO, **Oh A**, Moser RP, Davis KL, Nebeling LC, Yaroch AL: Association between perceived food environment and self-efficacy for fruit and vegetable consumption among US adults, 2007. Prev Chronic Dis, 9: E10, 2012. doi: http://dx.doi.org/10.5888/pcd9.100291 PMID: 22172177

Finney Rutten LJ, Blake K, Hesse BW, Ackerson LK: Isolated and skeptical: social engagement and trust in information sources among smokers. J Cancer Educ, 26(3): 465-473, 2011. doi: 10.1007/s13187-011-0201-7 PMID: 21340632

Finney Rutten LJ, Blake KD, Hesse BW, Augustson EM, Evans S: Illness representations of lung cancer, lung cancer worry, and perceptions of risk by smoking status. J Cancer Educ, 26(4): 747-753, 2011. doi: 10.1007/s13187-011-0247-6 PMID: 21688184

Freymann JB, **Kirby JS**, Perry JH, Clunie DA, Jaffee CC: Image data sharing for biomedical research: meeting HIPAA requirements for de-identification. J Digit Imaging, 25(1): 14-24, 2012. doi: 10.1007/s10278-011-9422-x PMID: 22038512

Guindo MA, **Shott JP**, Saye R, Diakité ML, Sanogo S, Dembele MB, Keita S, Nagel MC, Ellis RD, Aebig JA, Diallo DA, Doumbo OK: Promoting good clinical laboratory practices and laboratory accreditation to support clinical trials in Sub-Saharan Africa. Am J Trop Med Hyg, 86(4): 573-579, 2012. doi: 10.4269/ajtmh.2012.11-0691 PMID: 22492138

Kitano M, Millo C, Rahbari R, Herscovitch P, **Gesuwan K,** Webb RC, Venkatesan AM, Phan GQ, Hughes MS, Libutti SK, Nilubol N, Linehan WM, Kebebew E: Comparison of 6-(18)F-Fluoro-L-DOPA, (18)F-2-deoxy-D-glucose, CT, and MRI in patients with pancreatic neuroendocrine neoplasms with von Hippel-Lindau disease. Surgery, 150(6): 1122-1128, 2011. doi: 10.1016/j.surg.2011.09.048 PMID: 22136831

Komarow HD, Skinner J, **Young M**, Gaskins D, Nelson C, Gergen PJ, Metcalfe DD: A study of the use of impulse oscillometry in the evaluation of children with asthma: analysis of lung parameters, order effect, and utility compared with spirometry. Pediatr Pulmonol, 47(1): 18-26, 2012. doi: 10.1002/ppul.21507 PMID: 22170806

Kumar NP, Anuradha R, Suresh R, Ganesh R, Shankar J, Kumaraswami V, Nutman TB, **Babu S**: Suppressed type 1, type 2, and type 17 cytokine responses in active tuberculosis in children. Clin Vaccine Immunol, 18(11): 1856-1864, 2011. doi: 10.1128/CVI.05366-11 PMID: 21955625

Mena E, Turkbey B, Mani H, **Adler S**, Valera VA, Bernardo M, Shah V, Pohida T, McKinney Y, **Kwarteng G**, **Daar D**, Lindenberg ML, **Eclarinal P**, **Wade R**, Linehan WM, Merino MJ, Pinto PA, Choyke PL, Kurdziel KA: 11C-Acetate PET/CT in localized prostate cancer: a study with MRI and histopathologic correlation.

J Nucl Med, 53(4): 538-545, 2012. doi: 10.2967/jnumed.111.096032 PMID: 22343504

Moore LE, Nickerson ML, Brennan P, Toro JR, Jaeger E, Rinsky J, Han SS, Zaridze D, Matveev V, Janout V, Kollarova H, Bencko V, Navratilova M, Szeszenia-Dabrowska N, Mates D, Schmidt LS, **Lenz P**, Karami S, Linehan WM, Merino M, Chanock S, Boffetta P, Chow WH, Waldman FM, Rothman N: Von hippel-lindau (VHL) inactivation in sporadic clear cell renal cancer: associations with germline VHL polymorphisms and etiologic risk factors. PLoS Genet, 7(10): e1002312, 2011. doi: 10.1371/journal.pgen.1002312 PMID: 22022277

Naggie S, **Osinusi A**, Katsounas A, Lempicki R, Hermann E, Thompson AJ, Clark PJ, Patel K, Muir AJ, McHutchison JG, Schlaak JF, Trippler M, Shivakumar B, Masur H, Polis MA, Kottilil S: Dysregulation of innate immunity in hepatitis C virus genotype 1 IL28B-unfavorable genotype patients: impaired viral kinetics and therapeutic response, 56(2): 444-454. DOI: 10.1002/hep.25647. PMID: 22331604. PMCID: PMC3361636

Osinusi A, Naggie S, Poonia S, Trippler M, Hu Z, Funk E, Schlaak J, **Fishbein D**, Masur H, Polis M, Kottilil S: ITPA gene polymorphisms significantly affect hemoglobin decline and treatment outcomes in patients co-infected with HIV and HCV. J Med Virol, 84(7): 1106-1114, 2012. doi: 10.1002/jmv.23302 PMID: 22585729

Paulson M, Olivier KN, Holland SM: Pulmonary non-tuberculous mycobacterial infection in congenital contractural arachnodactyly, 16(4): 561-563. DOI: 10.5588/ijtld.11.0301. PMID: 22325249

Pinto PA, Chung PH, Rastinehad AR, Baccala AA Jr, Kruecker J, Benjamin CJ, Xu S, Yan P, Kadoury S, **Chua C**, Locklin JK, Turkbey B, Shih JH, **Gates SP**, Buckner C, Bratslavsky G, Linehan WM, Glossop ND, Choyke PL, Wood BJ: Magnetic resonance imaging/ultrasound fusion guided prostate biopsy improves cancer detection following transrectal ultrasound biopsy and correlates with multiparametric magnetic resonance imaging. J Urol, 186(4): 1281-1285, 2011. doi: 10.1016/j.juro.2011.05.078 PMID: 21849184

Powers JH: Editorial commentary: asking the right questions: morbidity, mortality, and measuring what's important in unbiased evaluations of antimicrobials. Clin Infect Dis, 54(12): 1710-1713, 2012. doi: 10.1093/cid/cis274 PMID: 22467671

Rasimas JJ, Katsounas A, Raza H, Murphy AA, Yang J, Lempicki RA, **Osinusi A**, Masur H, Polis MA, Kottilil S, Rosenstein DL: Gene expression profiles predict emergence Of psychiatric adverse events in HIV/HCV coinfected patients on interferon-based HCV therapy, 60(3): 273-281, 2012. doi: 10.1097/QAI.0b013e31824c17c4. PMID: 22728749

Reynolds SJ, Makumbi F, **Newell K**, Kiwanuka N, Ssebbowa P, Mondo G, Boaz I, Wawer MJ, Gray RH, Serwadda D, Quinn TC: Effect of daily aciclovir on HIV disease progression in individuals in Rakai, Uganda, co-infected with HIV-1 and herpes simplex virus type 2: a randomized, double-blind placebo-controlled trial. Lancet Infect Dis, 12(6): 441-448, 2012. doi: 10.1016/S1473-3099(12)70037-3 PMID: 22433279

Rose A, Fagan P, Lawrence D, Hart A Jr, Shavers VL, Gibson JT: The role of worksite and home smoking bans in smoking cessation among U.S. employed adult female smokers. Am J Health Promot, 26(1): 26-36, 2011. doi: 10.4278/ajhp.091214-QUAN-391 PMID: 21879940

Sampaio EP, Bax HI, Hsu AP, Kristosturyan E, Pechacek J, Chandrasekaran P, **Paulson M**, Dias DL, Spalding C, Uzel G, Ding L, McFarland E, Holland SM: A novel STAT1 mutation associated with disseminated mycobacterial disease, 32(4): 681-689, 2012. DOI: 10.1007/s10875-012-9659-2. PMID: 22437822

Sanal O, Jing H, Ozgur T, Ayvaz D, Strauss-Albee DM, Ersoy-Evans S, Tezcan I, Turkkani G, **Matthews HF**, Haliloglu G, Yuce A, Yalcin B, Gokoz O, Oguz KK, Su HC: Additional diverse findings expand the clinical presentation of DOCK8 deficiency, 32(4): 698-708. DOI: 10.1007/s10875-012-9664-5. PMID: 22476911

Schned AR, **Lenz P**, Moore LE, Johnson A, Jones M, Kida M, Silverman DT, Schwenn M, Kelsey KT, Andrew AS, Baris D, Karagas MR: Analysis of the distribution and temporal trends of grade and stage in urothelial bladder cancer in northern New England from 1994 to 2004. ISRN Pathology. doi: 10.5402/2012/283670. NIHMS# 383216

Shott JP, Galiwango RM, Reynolds SJ: A quality management approach to implementing point-of-care technologies for HIV diagnosis and monitoring in Sub-Saharan Africa. J Trop Med, 2012: 651927, 2012. doi: 10.1155/2012/651927 PMID: 22287974

Surendar J, Mohan V, Pavankumar N, **Babu S**, Aravindhan V: Increased levels of serum granulocyte-macrophage colony-stimulating factor is associated with activated peripheral dendritic cells in type 2 diabetes subjects (CURES-99). Diabetes Technol Ther, 14(4): 344-349, 2012. doi: 10.1089/dia.2011.0182 PMID: 22149626

Taplin SH, **Price RA**, **Edwards HM**, Foster MK, Breslau ES, Chollette V, Prabhu Das I, Clauser SB, Fennell ML, Zapka J. Introduction: understanding and influencing multilevel factors across the cancer care continuum. J Natl Cancer Inst Monogr. 2012; 2012(44):2-10. doi: 10.1093/jncimonographs/lgs008 PMID: 22623590

Wanyama JN, Castelnuovo B, Robertson G, **Newell K**, Sempa JB, Kambugu A, Manabe YC, Colebunders R: A randomized controlled trial to evaluate the effectiveness of a board game on patients' knowledge uptake of HIV and sexually transmitted diseases at the infectious diseases institute, Kampala, Uganda. J Acquir Immune

Defic Syndr, 59(3): 253-258, 2012. doi: 10.1097/QAI.0b013e31824373d5 PMID: 22156910

Weisbrod AB, Kitano M, **Gesuwan K**, Millo C, Herscovitch P, Nilubol N, Linehan WM, Kebebew E: Clinical utility of functional imaging with 18F-FDOPA in von Hippel-Lindau syndrome. J Clin Endocrinol Metab, 97(4): E613-617, 2012. doi: 10.1210/jc.2011-2626 PMID: 22259055

Wood BJ, Poon RT, Locklin JK, Dreher MR, Ng KK, Eugeni M, **Seidel G**, Dromi S, Neeman Z, Kolf M, Black CD, Prabhakar R, Libutti SK: Phase I study of heat-deployed liposomal doxorubicin during radiofrequency ablation for hepatic malignancies. J Vasc Interv Radiol, 23(2): 248-255, 2012. doi: 10.1016/j.jvir.2011.10.018 PMID: 22178041

Xie Z, Ghosh CC, Patel R, Iwaki S, Gaskins D, Nelson C, **Jones N**, Greipp PR, Parikh SM, Druey KM: Vascular endothelial hyperpermeability induces the clinical symptoms of clarkson disease (the systemic capillary leak syndrome). Blood, 119(18): 4321-4332, 2012. doi: 10.1182/blood-2011-08-375816 PMID: 22411873

Abstracts

Cosentino M, **Frech S**, Gomez J, Brown T: Building biorepositories for the United States: Latin America Cancer Research Network. Biospecimen Research Network Symposium. Bethesda, Maryland, 10(3):301-302, 2012.

Go R, Zaren H, Nair S, Lanier K, Thompson M, Enos R, Zhao J, Fleming D, Leighton J, Gribbin T, Bryant D, **Carrigan A**, Corpening J, Csapo K, Dimond E, Ellison C, Gonzalez M, Harr J, Wilkinson K, Denifcoff A: Early-phase clinical trials in the community: results from the NCCCP early-phase working group baseline assessment study. J Clin Oncol 30: e16561, 2012.

Matharu K, Zarember KA, Ma SS, Kuhns DB, Marciano BE, Spalding C, Garofalo M, **Dimaggio T**, McDermott AB, Fleisher TA, Holland SM, Malech HL, Gallin JI: B-cell activating factor (BAFF/BLYS) in chronic granulomatous disease. J Clin Immunol, 2 (32):392, 2012.

Meyer J, Gorbach AM, Liu WM, Medic N, Nelson C, Arceo S, **Young M**, Desai A, Metcalfe DD, Komarow HD: Real-time imaging assessment of blood flow, temperature and skin color on patients with cold induced urticaria: correlation with histamine and tryptase release, 129(2): AB141-NaN, 2012.

Sevastita VS, **Miller T**, Chaitt DG, Pierson JF: A medical writer's role in the new protocol development program at the National Institute of Allergy and Infectious Diseases. AMWA Journal 27(3), 2012.

Book Chapter

Osinusi A, Joshi M: Principles of antimicrobial use in critical care. In: Critical Care Emergency Medicine 2012, Anne M. Sydor and Christie Naglieri, 359-370, McGraw-Hill Companies, Inc.

Posters/Presentations

Adams A, **Baseler B**, **Hoopengardner L**, Pierson J, **Simpson S**, Vogel S: Value added in using monitoring and training to improve the quality of clinical data from a clinical trial. NIH Research Festival. Bethesda, Maryland, October 2011.

Adams A, **Baseler B**, **Hoopengardner L**, Pierson J, **Simpson S**, Vogel S: Value added in using monitoring training to improve the quality of clinical data from a clinical trial. Frederick National Laboratory for Cancer Research Spring Research Festival. Frederick, Maryland, May 2012.

Adler S: Image visualization object model. Institute of Electrical and Electronics Engineers Nuclear Science Symposium and Medical Imaging Annual Conference. Valencia, Spain, October 2011.

Adler S, Seidel J, Green M, Choyke PP: NEMA and non-NEMA performance evaluation of the bioscan bioPET/CT pre-clinical small animal scanner. Society of Nuclear Medicine Annual Meeting. Miami Beach, Florida, June 2012.

Adler S, Seidel J, Green MV, Choyke PP: Compton backscatter background signature and effects in the bioscan bioPET/CT small animal pre-clinical scanner. Society of Nuclear Medicine Annual Meeting. Miami Beach, Florida, June 2012.

Baseler B, **Beveridge J**, **Foltz T**: Collaborative strategic support to clinical research. 2012 NCI Intramural Scientific Investigators Retreat. Bethesda, Maryland, January 2012.

Beckjord EB, **Finney Rutten LJ,** Moser RP, Hesse BW, Blake K: Advancing behavioral science through data sharing, measures harmonization, and participatory science: the National Cancer Institute's grid-enabled measures database. American Medical Informatics Association. Washington, District of Columbia, October 2011.

Bhattacharyya S, Wei L, Riffle L, **Hill CG**, Jacobs P, Tatum J, Doroshow J, Kalen J: Preclinical evaluation of 89Zr-labeled panitumumab as a potential PET probe for HER1-expressing carcinomas. 2012 Society for Nuclear Medicine. Miami, Florida, June 2012.

Boyd S, Hadigan C, Pau A, Kovacs JA, Alfaro R, Chairez C, **McManus M, Calderon M**, Penzak S: Darunavir/ Ritonavir does not significantly increase plasma concentrations of orally inhaled beclomethasone in

healthy volunteers. 19th Conference on Retroviruses and Opportunistic Infections. Seattle, Washington, March 2012.

Boyd S, Penzak S, Nieman L, Pau A, Kovacs J, Chairez C, **McManus M**, Hadigan C: Combined use of beclomethasone oral inhalation and HIV protease inhibitors did not significantly alter adrenal function in HIV-negative healthy volunteers. 19th Conference on Retroviruses and Opportunistic Infections. Seattle, Washington, March 2012.

Calderon M: Take control of your HIV by understanding your medications. La Clinica del Pueblo. Washington, District of Columbia, December 2011.

Cline N, Galcik M, Lambert L, Simpson S: HIPAA and the HITECH Act. Training, Frederick and Bethesda, Maryland, June and August 2012.

Cosentino M, **Gonzalez del Riego, M**: Deviations/violations, monitoring and reporting. Virtual Data Coordination and Analysis Team Meeting of the United States – Latin America Cancer Research Network. Buenos Aires, Argentina, April 2012.

Djordjevic MV, **Rose A**: Novel smokeless tobacco products in the U.S. chemical and toxicological characteristics. World Conference on Tobacco or Health. Singapore, March 2012.

Eagel BA: Genitourinary complications of cancer. National Cancer Institute PDQ Supportive and Palliative Care Editorial Board. Rockville, Maryland, April 2012.

Eby M: Working globally, working virtually: a survival guide for medical writers. American Medical Writers Association Annual Meeting. Jacksonville, Florida, October 2011.

Finney Rutten LJ, Beckjord EB, **Courtney PK**, Moser RP, Hesse BW: Science 2.0 solutions for developing national surveillance tools. American Medical Informatics Association. Orlando, Florida, October 2011.

Finney Rutten LJ, Dearing J, Mazor K, Arora N. Hesse B: Patient centered communication and the cancer control framework: research from the patient-centered communication special interest group of the National Cancer Institute's cancer research network. HMO Research Network Conference. Seattle, Washington, April 2012.

Finney Rutten LJ, Hesse BW, Moser RP, Beckjord E: Age differences in cancer survivors use of and trust in information resources. Society for Behavioral Medicine. New Orleans, Louisiana, April 2012.

Finney Rutten LJ, Patrick H, Klein W, Rothman A: Scientific advances at the interface of social/personality psychology and NIH: data resources. Society of Personality and Social Psychology. San Diego, California, January 2012.

Finney Rutten LJ, Stevenson S: Health information seeking, trust in information sources and use of complementary and alternative medicine conference. Integrative Medicine and Health. Portland, Oregon, May 2012.

Fishbein D: NASTAD presentation hepatitis coordinators DC Partnership for HIV/AIDS Progress subspecialty clinics. National Viral Hepatitis Technical Assistance Meeting. Washington, District of Columbia, October 2011.

Fishbein D: HCV therapy: a paradigm shift in treatment. Washington Hospital Center Medicine Grand Rounds. Washington, District of Columbia, January 2012.

Fishbein D: HCV therapy: a paradigm shift in treatment. GWIDS Spring Symposium. Bethesda, Maryland, March 2012.

Fishbein D: HCV therapy: a paradigm shift in treatment. Greater Washington Association of Nurses in AIDS Care. Bethesda, Maryland, April 2012.

Frech S: Building biorepositories for the United States – Latin America Cancer Research Network. National Cancer Institute 5th Annual Biospecimen Research Network (BRN) Symposium. Bethesda, Maryland, February 2012.

Frech S: Meeting objectives and study monitoring plan overview. Virtual Data Coordination and Analysis Team Meeting of the United States – Latin America Cancer Research Network. Buenos Aires, Argentina, April 2012.

Frech S, **Gonzalez del Riego M**: Molecular profiling of stage II and III breast cancer in Latin American women receiving standard of care treatment. United States - Latin America Cancer Research Network. Guadalajara, Mexico, November 2011.

Galcik M, La Regina A, Cline N: Digital signatures. Training. Frederick, Maryland, September 2011.

Galcik M, La Regina A: Digital signatures. Training. Frederick, Maryland, October 2011 and February 2012.

Giambarresi L, **Garrand S**, **Chakrabarti M**, **Eccard V**, **Gonzalez A**, **Harvey T**, **Hertsch J**, **Lacuesta L**, **Buehn M**: The electronic common technical document: one organization's experience. Frederick National Laboratory for Cancer Research Spring Research Festival, May 2012.

Gilchrist D: The HHS learning management system (LMS). Training. Frederick, Maryland, December 2011.

Gilchrist D: Learning style inventory. Training. Frederick, Maryland, December 2011.

Giri J, Lambert L, Osborne C, Tierney J, Pierson J, **Baseler B**: Mapping clinical study lifecycle with standard project management methodology for achieving program success in clinical research setting. NIH Research Festival. Bethesda, Maryland, October 2011.

Gormley N, **Wilder J**, Khuu H, Pantin J, Donohue T, Kurlander R, Sawa I, Battiwalla M, Barrett AJ, Grasmeder S, Cook L, Ramos C, Prince P, Stroncek D, Flegel W, Berg M, Reger R, Bolan C, Adams S, Childs R: Co-infusion of allogeneic cord blood with haploidentical CD34+ cells, improved transplant outcome for patients

with severe aplastic anemia undergoing cord blood transplantation. American Society of Hematology Annual Meeting and Exposition. San Diego, California, December 2011.

Hall K, **Vogel A**: Advancing science using transdisciplinary approaches: challenges and strategies for success. Transdisciplinary Research on Energetics and Cancer Scientific Meeting. Philadelphia, Pennsylvania, January 2012.

Hall KL, **Vogel AL,** Stipelman B, Stokols D, Okamoto J: Understanding and supporting team science. Elsevier Research Connect. Boston, Massachusetts, November 2011.

Henkel AG, **Paulson M**, Claypool RJ, Prevots DR, Holland SM, Olivier KN: Safety, toxicity and efficacy of clofazimine for the treatment of pulmonary nontuberculous mycobacterial infections. American Thoracic Society 2012 Conference. San Francisco, California, May 2012.

Kobetz-Kerman E, Kish J, Sussman D, Kornfeld J, **Finney Rutten LJ**, Vanderpool R, Leone P, Ball D: Differences in colorectal cancer screening rates of Haitian immigrants and other US blacks: a call to action. Society of Behavioral Medicine. New Orleans, Louisiana, April 2012

Kopka S: Protocol development and logistics of implementation: anatomy of a natural history protocol. PhD Student Summer Course in Clinical and Translational Research NIH Clinical Center. Bethesda, Maryland, July 2012.

Krishnan S, Rono E, Tian J, Agan B, Sawe F, Shaffer D, Sereti I: Characteristics of immunologic nonresponders in an ARV-naive, advanced HIV cohort in Kenya. Conference on Retroviruses and Opportunistic Infections. Seattle, Washington, March 2012.

Kurdziel KA, Kalen J, Bhattacharyya S, Riffle L, Wei L, **Hill CG** , Doroshow J, Jacobs P, Tatum J: Murine biodistribution and human dosimetry estimates of 111In DTPA- and 89Zr DFO-panitumumab. Society for Nuclear Medicine. Miami, Florida, June 2012.

Kushner LA, Wendelboe AM, Chary A, Winters MA, **Osinusi A**, Kottilil S, Polis MA, Holodniy M: Immune marker differences and changes in HCV monoinfected and HIV co-infected patients. Infectious Disease Society of America Annual Meeting. Boston, Massachusetts, October 2011.

La Regina A: Digital signatures. Training. Frederick, Maryland, February, March, and May 2012.

Makumbi F, Kiwanuka N, **Newell K**, Ssebbowa P, Ssempijja V, Bbosa F, Gray R, Wawer M, Quinn TC, Serwadda D, Reynolds SJ: Impact of HSV-2 suppressive therapy with daily acyclovir on HIV-1 disease progression among pregnant women: a randomized placebo-controlled trial in Rakai, Uganda. Conference on Retroviruses and Opportunistic Infections. Seattle, Washington, March 2012.

Martin S, Wolters P, Baldwin A, Roderick MC, **Tamula MA**, Gillespie A, Widemann B: Attitudes about internet support groups among adolescents and young adults with NF-1 and their parents. The Children's Tumor Foundation - Neurofibromatosis Type-1. New Orleans, Louisiana, June 2012.

Matharu K, Zarember KA, Ma SS, Kuhns DB, Marciano BE, Spalding C, Garofalo M, **Dimaggio T**, McDermott AB, Fleisher TA, Holland SM, Malech HL, Gallin JI: B-cell activating factor (BAFF/BLYS) in chronic granulomatous disease (CGD). Clinical Immunology Society Annual Meeting. Chicago, Illinois, May 2012.

McSpadden K, **Oh A**, Nebeling L, Yaroch A: Motivation as a correlate of fruit & vegetable intake among US adult participants in the NCI food attitudes and behaviors survey. Society of Behavioral Medicine. New Orleans, Louisiana, April 2012.

Moak Z, Silver D, **Osinusi A**, **Silk R**, **Kotb C**, **Rosenberg A**, Stabinski L, Jenkins V, Teferi G, Masur H, Kottilil S, **Fishbein D**: Community engagement in a unique federal-local partnership: a model for hepatitis care and research. AIDS Conference. Washington, District of Columbia, July 2012.

Moak Z, Silver D, **Osinusi A**, **Silk R**, **Kotb C**, **Rosenberg A**, Stabinski L, Jenkins V, Teferi G, Masur H, Kottilil S, **Fishbein D**: District of Columbia Partnership for HIV/AIDS Progress (DC PFAP) subspecialty clinics: a model for hepatitis C care and research in community clinics serving a predominantly HIV-infected population. AIDS Conference. Washington, District of Columbia, July 2012.

Oh A, Erinosha T, Dunton G, Nebeling L: Understanding eating episodes: predominant activities reported by US adults when eating or drinking in the American time use survey. American Public Health Association Annual Meeting. Washington, District of Columbia, November 2011.

Oh A, Hennessy E, Perna F, Agurs-Collins T, Chriqui J, Masse LC: State laws for time spent in physical education and its relationship with adolescent weight status. American Public Health Association Annual Meeting. Washington, District of Columbia, October 2011.

Osinusi A, Chary A, Winters MA, Naggie S, Masur H, Polis MA, Kottilil S, Holodniy M: IL28B polymorphism is not associated with HCV protease diversity in HIV/HCV-coinfected patients treated with an interferon-based regimen. American Association for the Study of Liver Diseases Annual Meeting. San Francisco, California, November 2011.

Osinusi A, Naggie S, Poonia S, Trippler M, Hu ZH, Funk E, Schlaak JF, **Fishbein D**, Masur H, Polis MA, Kottilil S: ITPA gene polymorphisms significantly affect hemoglobin decline and treatment outcomes in HIV/HCV co-infected patients. American Association for the Study

of Liver Diseases Annual Meeting. San Francisco, California, November 2011.

Osinusi A, Odigie M, Zhang X, Masur H, Polis MA, Kottilil S: IL23 promotes IFN responsiveness in HIV/HCV co-infected patients treated with pegylated interferon and ribavirin. American Association for the Study of Liver Diseases Annual Meeting. San Francisco, California, November 2011.

Osinusi A, Shivakumar B, Lee Y, Heytens L, Meissner E, Polis M, Masur H, Symonds B, Berry M, Kottilil S: HCV viral dynamics of interferon free treatment using PSI-7977 with ribavirin in difficult to treat patients. Conference on Retroviruses and Opportunistic Infections. Seattle, Washington, March 2012.

Osinusi A, Wang C, Zhang X, Shivabesan G, Shivakumar B, **Silk R**, Doonquah L, Henn S, Teferi G, Masur H, Kottilil S, **Fishbein D**: Augmentation of interferon signaling pathway by nitazoxanide: a therapeutic strategy for HIV/HCV coinfected relapsers to peg-interferon and ribavirin therapy. 2012 Conference on Retroviruses and Opportunistic Infections. Seattle, Washington, March 2012.

Paulson M: Maryland TB today course - presentation training for nurses involved in TB management. New Jersey Global TB Institute. Marriottsville, Maryland, April 2012.

Paulson, M: Extrapulmonary tuberculosis case presentation. TB Webinar for New Jersey Global TB Institute. Bethesda, Maryland, March 2012.

Pechacek JJ, Hsu AP, Bax H, Dias DL, **Paulson M**, Ding L, Uzel G, Rosen LB, Browne SK, Datta S, Milner J, Chandrasekaran P, Zerbe CS, Wiley H, Greenberg DE, Hoover S, Rosenzweig SD, Galgiani JN, Holland SM, Sampaio EP: Dominant STAT1 mutations leading to disseminated fungal infections. Clinical Immunology Society Annual Meeting: Primary Immune Deficiency Disease Conference. Chicago, Illinois, May 2012.

Pinard C, **Finney Rutten LJ**, Nebeling L, Yaroch A: Exploration of grocery shopping behaviors and sociodemographic factors associated with venue of meal consumption: results from the National Cancer Institute's food attitudes and behaviors (FAB) survey. Society of Behavioral Medicine. New Orleans, Louisiana, April 2012.

Ramirez AS, **Finney Rutten LJ**, Vanderpool R, Moser RP, Hesse BW: Physical activity, obesity, and cancer risk: sociodemographic, behavioral, and geographic patterns in the knowledge of risk and behaviors. Annual Meeting of the Society of Behavioral Medicine. New Orleans, Louisiana, March 2012.

Redmond G, Nordstrom R, **Fevrier-Sullivan B**, Farahani K, Tandon P, Zhang H, Clarke L: How to be a SharePoint "power user" for the quantitative imaging network (QIN). Bethesda, Maryland, March 2012.

Reynolds SJ, Laeyendecker O, Nakigozi G, Huang W, Boaz I, **Newell K**, Serwadda D, Gray RH, Wawer MJ, Eshleman SH: Antiretroviral drug susceptibility among HIV-infected adults failing antiretroviral therapy in Rakai, Uganda. Conference on Retroviruses and Opportunistic Infections. Seattle, Washington, February 2012.

Rono E, **Krishnan S**, Tian J, Shikuku KP, Agan B, Ngeno H, Kirui F, Khamadi S, Sawe F, Sereti I: Longitudinal analysis of T cell activation prior to and after anti-retroviral therapy (ART) initiation in an advanced HIV cohort in Kenya. AIDS Conference. Washington, District of Columbia, July 2012.

Salit RB, Bishop MR, Pavletic SZ, Hakim F, Steinberg S, Odom J, Bryant K, Schuver B, **Wilder J**, Avila DN, Gress RE, Fowler DH: Concurrent fludarabine and cyclophosphamide conditioning regimen prior to reduced intensity allogeneic hematopoietic stem cell transplantation ablates host T-cells and results in rapid full donor chimerism. American Society of Hematology. San Diego, California, December 2011.

Seidel GD, Petryshyn RA: NCI funding of biomarker, imaging, quality-of-life, and cost effectiveness analysis studies. OBBR's Biospecimen Research Network Symposium: Advancing Cancer Research through Biospecimen Science. Bethesda, Maryland, February 2012.

Sevastita V: Protocol development and logistics of implementation: anatomy of an IND protocol. PhD Student Summer Course in Clinical and Translational Research NIH Clinical Center. Bethesda, Maryland, July 2012.

Sheikh V, **Krishnan S**, Roby G, Adelsberger J, Higgins J, Rehm C, Sereti I: Older age, higher HIV viral load, higher CD4 T cell activation and lower CD8 T cell activation are associated with poor CD4+ T cell recovery following initiation of ART in advanced HIV infection. Keystone Symposia Frontiers in HIV Pathogenesis Therapy and Education. Whistler, British Columbia, March 2012.

Shott JP: Laboratory quality management in the international research setting. Training and Diversity Program, National Institute of Allergy and Infectious Diseases, National Institutes of Health Invited Talk. Bethesda, Maryland, December 2011.

Shott JP, Guindo MA, Keita S, Sanogo S, Dicko A, Sagara I, Fay MP, Duffy PE, Ellis RD: Performance of stabilization tubes for extending time to analysis of complete blood counts from trial participants at a rural field site in Mali. Annual Meeting of the American Society of Tropical Medicine and Hygiene. Philadelphia, Pennsylvania, December 2011.

Shott JP, Moyer BK, Lamine DM, Hersi JK, Galiwango J, Bwanika JB, Whalen CJ, Tatrakovsky M: Establishing FDA-compliant electronic biospecimen management and environmental monitoring systems to support biomedical research in Uganda and Mali. Annual Biospecimen

Research Network Symposium. Bethesda, Maryland, February 2012.

Silver D, Karnik G, **Osinusi A**, **Silk R**, Stabinski L, Doonquah L, Henn S, Teferi G, Masur H, Kotillil S, **Fishbein D**: Liver fibrosis in African Americans: comparing HCV mono-infection with HIV-HCV co-infection. American Association for the Study of Liver Diseases Annual Meeting. San Francisco, California, November 2011.

Simpson S, **Baseler B**: Clinical trials and regulatory management. Leadership Week, Virginia, April 2012.

Sowerwine KJ, **Boris L**, Davis J, Hsu A, **Welch P**, Holland SM, Freeman, AF: Clinical and immunologic findings in young children with early diagnosis of STAT3 deficient hyper IGE syndrome (STAT3 HIES). CIS Annual Meeting: Primary Immune Deficiency Disease North American Conference. Chicago, Illinois, May 2012.

Spates KE, **Holland NC**, Pabon AG, Ware JM, Nutman TB: Eosinophilia as a potential surrogate for definitive diagnosis of Strongyloidiasis in an immigrant population at a community clinic. Society for Clinical Trials 33rd Annual Meeting Poster Session. Miami, Florida, May 2012.

Stallings S, **Miller T**: Protocol development and logistics of implementation: logistics in implementation. PhD Student Summer Course in Clinical and Translational Research NIH Clinical Center. Bethesda, Maryland, July 2012.

Teitelbaum M: Protocol development and logistics of implementation: overview of protocol design. PhD Student Summer Course in Clinical and Translational Research NIH Clinical Center. Bethesda, Maryland, July 2012.

Teitelbaum M: Protocol development and logistics of implementation: developing an informed consent document. PhD Student Summer Course in Clinical and Translational Research NIH Clinical Center. Bethesda, Maryland, July 2012.

van der Schalie B: Inspection readiness (interviewers). Training. Frederick, Maryland, September 2011.

van der Schalie B: Manager as communicator. Training. Frederick, Maryland, September 2011.

van der Schalie B: To test or not to test? And if so, how? CHI Clinical Training Forum. Boston, Massachusetts, October 2011.

van der Schalie B: Setting standards: avoiding micromanagement. Training. Bethesda, Maryland, October 2011.

van der Schalie B: Active listening. Training. Bethesda, Maryland, October and November 2011.

van der Schalie B: Communication: Assertive? Aggressive? Which are we? And when?

Training. Frederick, Maryland, October 2011 and June 2012.

van der Schalie B: Inspection readiness (recorder). Training. Frederick, Maryland, October 2011.

van der Schalie B: Inspection readiness (CIC). Training. Frederick, Maryland, October 2011.

van der Schalie B: Inspection readiness (staging room). Training. Frederick, Maryland, October 2011.

van der Schalie B: Inspection readiness (front desk/reception). Training. Frederick, Maryland, November 2011.

van der Schalie B: Giving and receiving constructive feedback. Training. Bethesda, Maryland, November and December 2011.

van der Schalie B: Inspection readiness (runners). Training. Frederick, Maryland, November 2011.

van der Schalie B: The HHS Learning Management System (LMS). Training. Frederick, Maryland, December 2011.

van der Schalie B: Learning style inventory. Training. Frederick, Maryland, December 2011.

van der Schalie B: DCR branch chiefs briefing: leadership culture. Training. Bethesda, Maryland, January 2012.

van der Schalie B: DCR leadership culture initiative briefing. Training. Bethesda, Maryland, January 2012.

van der Schalie B: Strength based leadership session 1: introduction to strengths-based leadership. Training. Bethesda, Maryland, January 2012.

van der Schalie B: Professional standards and principles for evaluation practice: guiding principles. Training. Bethesda, Maryland, January 2012.

van der Schalie B, Cline N: CMRP goal setting training – setting S.M.A.R.T.(E.R.) goals. Training. Frederick, Maryland, January and February 2012.

van der Schalie B: Strength based leadership session 2: team prioritization. Training. Bethesda, Maryland, February 2012.

van der Schalie B: SOP training TR-0806 and TR-0807. Training. Frederick, Maryland, February and March 2012.

van der Schalie B: Strengths based leadership presentation: presentation of aggregate self-assessment data. Training. Bethesda, Maryland, March 2012.

van der Schalie B: Understanding your managerial style. Training. Bethesda, Maryland, March 2012.

van der Schalie B: Strengths based leadership presentation: discussion of value of strengths in ICMOB workplace. Training. Bethesda, Maryland, April 2012.

van der Schalie B: PPAB retreat: customer satisfaction survey data. Training. Bethesda, Maryland, April 2012.

van der Schalie B: Professional standards and principles for evaluation practice: professional standards. Training. Bethesda, Maryland, May 2012.

van der Schalie B: Managing multiple priorities. Training. Frederick, Maryland, May 2012.

van der Schalie B: Requesting and receiving constructive feedback. Training. Bethesda, Maryland, June 2012.

van der Schalie B: Influencing without authority. Training. Frederick, Maryland, July 2012.

van der Schalie B: Managing up. Training. Frederick, Maryland, September 2012.

van der Schalie B: The care and feeding of subject matter experts (SME). 2012 SoCRA Conference, Las Vegas, Nevada, September 2012.

Vogel AL, Hall KL: The National Cancer Institute's team science toolkit: advancing team-based research and practice. Annual Meeting and Exposition of the American Public Health Association. Washington, District of Columbia, October 2011.

Vogel AL, Stipelman BA, **Feng A**, Stokols D, Hall KL, Nebeling L: Strategies for facilitating and supporting cross-disciplinary team science on cancer: lessons from the National Cancer Institute's TREC initiative. Annual Meeting and Exposition of the American Public Health Association. Washington, District of Columbia, October 2011.

Welch J: Building site capacity for research - a real life example: developing site capacity in Southeast Asia. DIA 2012 Annual Meeting. Philadelphia, Pennsylvania, June 2012.

Wolters P, Martin S, **Tamula MA**, Bent R, Warren K: Early changes in specific neuropsychological functions and quality of life in children with CNS tumors: preliminary results up to 24 months post-radiation. 12th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer. Williamsburg, Virginia, June 2012.

Zapka J, **Edwards HM**, Chollette V, Taplin S: Research addressing follow-up for abnormal cancer screening tests: NCI portfolio analyses. American Society for Preventive Oncology. Washington, District of Columbia, March 2012.

Media

Young M, Support to NIAID/Laboratory of Allergic Diseases: Getting chilly for science. YouTube video, 2:15, uploaded by NIAID, September 28, 2011, http://www.youtube.com/watch?v=TVBLfrODKO4.