Annual Report

of the

Clinical Research Program

FY 2004

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I. Program Overview

The Clinical Research Program (CRP) is a scientific, interdisciplinary research program that provides methodologic assistance and expertise to investigators on the design, conduct, and analysis of clinical research studies and an infrastructure for the data coordination of extramurally sponsored studies.

The mission of the Clinical Research Program is to enhance the quality of clinical research at Children’s Hospital through scientific leadership in clinical research methodology (including biostatistics, epidemiology, and informatics); collaboration or consultation in the design, conduct, and analysis of clinical research studies; and educational activities targeting the clinical research community including residents, fellows, faculty, and study coordinators.

Various types of support are provided to investigators at all stages of protocol development and study implementation. The CRP also works closely with the General Clinical Research Center (GCRC), funded by the National Institutes of Health, to optimize the infrastructure for the conduct of effective clinical research at Children's Hospital.

Since its inception in 1998, the Program has sustained significant growth in staff and resources and increased visibility among the clinical research community. The CRP staff has grown to 29 full- or part-time staff from various disciplines, including epidemiologists, biostatisticians, application developers, research associates, data coordinators, and data entry staff. The Program occupies nearly 4000 square feet of space located in 333 Longwood Avenue.

Key accomplishments over the past year include:

- Participation on and/or leadership of major clinical research enterprise initiatives and committees including the CHB Clinical Research Task Force, Clinical Research Space Committee, Clinical Research Billing Working Group and the CHB Research Internet
- Completion of administrative standard operating procedures and guidelines for good clinical research practices, which also provide web accessible educational tools for the investigators
- Development of the Clinical Research Study Protocol Management Software
- Successful implementation of three multi-site clinical research protocols for the Glaser Pediatric Research Network
- Efforts to support Staff and Faculty Professional Development
- Successful Staff Hiring and Expansion
II. Overview of FY04 Activities and Accomplishments

This section highlights the major activities and accomplishments of the CRP staff, which serve to support and enhance the clinical research enterprise, support the investigator community, and improve Program operations.

1. Clinical Research Task Force

In October 2003, Dr. James Mandell established the Clinical Research Task Force, chaired by Dr. Richard Grand and mandated to evaluate the current state of clinical research at CHB and develop recommendations on organizational structure, resources and infrastructure that will grow and enhance the Clinical Research Enterprise. Dr. Osganian and Ms. Rogers were key members of the Task Force who worked to conduct the current state analysis from which recommendations were then developed. The Preliminary Report was successfully completed and presented to the hospital leadership in May 2004. As a result of this major effort, Dr. Mandell established the Clinical Research Executive Committee, as advisory to the President and Chief Operating Officer and charged with overseeing the allocation of institutional resources for clinical research and strategic planning for clinical research at CHB. The CREC is chaired by Dr. Jane Newburger and its members include Dr. Richard Grand, Dr. Ellis Neufeld, Dr. Tina Young Poussaint, Dr. Bart Cilento, Dr. Tom Jaksic, Dr. Voula Osganian, Dr. Deborah Waber, and Dr. Jean Emans. Ex-officio members include Sandra Fenwick, Dr. Carleen Brunelli, Patrick Taylor, and Brian Lobao. One of its key agenda items for FY05 will be to build upon the work of the Task Force and develop a 10-year strategic plan for Clinical Research.

2. Space Planning for Clinical Research

During FY04, Dr. Osganian provided leadership on a major planning effort to allocate space for Clinical Research at 1 Autumn Street. As part of this effort, Dr. Mandell established the Clinical Research Space Committee, charged with making recommendations on the assignment of clinical research space for the institution. The Committee is co-chaired by Dr. Osganian and Ms. Quan and its members include Dr. James Lock, Dr. Alan Retik, Dr. Gary Fleisher, Dr. Carleen Brunelli, and Brian Lobao. During FY04 the Committee established interim guidelines for the allocation of clinical research space and completed the review and assignment of nearly 12,000 net square feet of office space to clinical research at 1 Autumn Street. In addition, it developed improved procedures for requesting space that are now web-accessible through Research Operations. The Committee continues to actively review all space requests for clinical research and make recommendations on the assignment of space.
3. Clinical Research Billing

During FY04, Dr. Osganian chaired the Clinical Research Billing Working Group whose goal was to evaluate the current issues with the clinical research billing process and propose a plan for implementing improvements to address these issues. Based on its findings, the Working Group concluded that the clinical research billing process required a new system and integration with the current patient billing system. The hospital has since directed resources towards planning for the design a new system under the leadership of Dr. Carleen Brunelli and David Kirchner. Dr. Osganian continues to participate on the Steering Committee that oversees the progress of this multi-year initiative.

4. CHB Research Internet

Ms. Rogers actively participated as a member of the Research Internet Advisory Committee that developed the initial content and design of the CHB Research Site for the internet. CRP staff took the lead in writing section for Clinical Research, as well as in populating the content for the Clinical Research Program home page.

5. Patient Safety and Quality

Under the direction of Dr. Leslie Kalish, the CRP has provided significant research support for the hospital’s efforts to control an increased incidence of colonization with *Burkholderia dolosa* (*B. dolosa*), which has been observed in the hospital’s Cystic Fibrosis (CF) patient population over the past few years. CRP staff have collaborated on the design and analysis of two epidemiologic studies, a case-control study investigating possible exposures associated with the acquisition of *B. dolosa* and a cohort study in which changes in lung function among these patients were compared with two control groups of CF patients without *B. dolosa*. In addition, the CRP has designed a monitoring procedure to help interpret any future trends in incidence so that infection-control efforts can be evaluated quantitatively. The CRP will work collaboratively with the Program on Patient Safety and Quality, directed by Dr. Kathy Jenkins to provide continued data management and statistical support.

6. CRP Standard Operating Procedures (SOPs) and Guidelines for Good Clinical Research Practices.

The CRP leadership and staff identified several SOP’s that would improve the daily operations of the Program and quality and consistency of our work with investigators. During FY04, the CRP staff completed 23 administrative and research SOP’s related to program operations and staff assistance on clinical research projects. In addition, the research-related SOP’s were written so as to provide educational tools and guidelines for good clinical research practices in areas such as case report form and survey design, adverse event documentation and tracking, the development of study manuals and protocols and data collection and management practices. These guidelines have also been placed on the CRP intranet site for accessibility to the larger research community.

In response to a demand for solutions to data management, the CRP applications
development staff developed a software framework, named SciRIS (Scientific Research
Information System), designed to rapidly implement Web-based data management
systems for clinical research. This system is most useful for complex clinical trials or
longitudinal studies with multiple study visits and provides valuable protocol monitoring
features that can assist study coordinators in monitoring the implementation of the study
protocol. A detailed description of this system is featured in Section VI of this year's
Program Report.

8. Successful implementation of three multi-site clinical research protocols for the Glaser
Pediatric Research Network (GPRN)

As Data Coordinating Center for the GPRN, the CRP faculty and professional staff have
successfully implemented three multi-site studies in the Glaser Pediatric Research
Network. These studies include a clinical trial of Rituximab in patients with chronic ITP, a
trial of Metformin in obese adolescents, and a registry designed to better understand the
outcomes of Necrotizing Enterocolitis in infants. Highlights from our work on the GPRN
are presented in Section VI.

9. CRP staff and faculty professional development

The Program Leadership has recognized the importance of staff and faculty professional
development activities. As part of this effort, the CRP has developed written guidelines
for time spent on individual staff professional development and provided funds to support
some of these activities including relevant seminars and professional memberships. The
CRP has also sponsored two staff-wide training sessions on customer service and
effective meeting management. Additionally, the Program continues to hold annual staff
retreats to identify issues and establish common goals and objectives.

10. Staff Hiring and Expansion

Successful growth in staff has enhanced our capabilities and broadened our reach to
internal clinical research investigators. New hires included four full-time positions: a lead
biostatistician, Carl de Moor, Ph.D.; a Masters-level biostatistician, Dan Kinnamon, M.S.;
and two research data coordinators, Rajna Filip-Dhima, B.S., and Kerwin Tang, M.A.
III. Program Organizational Structure

The Program includes 26 full-time and three part-time staff organized into four major functional groups or Cores: Clinical Studies Operations, Applications Development, Biostatistics, and Administration and Finance.

A. Organizational Chart
B. Staff Roles and Biographies

Staff Publications can be found in Appendix B.

PROGRAM DIRECTOR

Stavroula Osganian, M.D., Sc.D., M.P.H./Program Director
Dr. Osganian is a physician-epidemiologist with over ten years of experience in the conduct of epidemiologic and clinical research. She joined the CRP as Associate Director in December 2001 and now serves as Director of the Program. She is also Associate Director of the NIH-funded General Clinical Research Center at Children’s Hospital and holds an appointment as Assistant Professor of Pediatrics at the Harvard Medical School.

Dr. Osganian’s research interests and activities have focused on studies of youth health promotion and chronic disease prevention. She has had a leadership role in one of the largest, nationally recognized NIH-funded school-based studies of cardiovascular health promotion in the United States, The Child and Adolescent Trial for Cardiovascular Health (CATCH). The work of the CATCH collaborative group has led to significant contributions to the design, conduct, and institutionalization of school health promotion programs and the study of cardiovascular risk factors in youth.

CLINICAL RESEARCH FACULTY

Christopher Duggan, M.D., M.P.H./Clinical Research Faculty
Dr. Duggan is a pediatric gastroenterologist and nutrition physician whose research interests include the nutritional management of acute and persistent diarrhea, clinical trials of micronutrient supplementation, and general aspects of nutritional support in catabolism. In studies in developing and industrialized countries, he is applying state of the art nutritional assessment techniques to patients with diarrhea, HIV/AIDS, inflammatory bowel disease, short bowel syndrome and cancer.

Dr. Duggan has been a member of several large multi-center clinical trial groups, including the Glaser Pediatric Research Network, a multicenter research network for cutting edge pediatric studies based at Children’s Hospital, Boston as well as Stanford, UCSF, UCLA and Baylor. He is an Assistant Professor of Pediatrics at Harvard Medical School, an Assistant Professor of Nutrition at the Harvard School of Public Health, and Director of the Clinical Nutrition Service at Children’s Hospital Boston.

BIOSTATISTICS

David Wypij, Ph.D./Director of Biostatistics
Dr. Wypij joined the CRP in July 1999. He has considerable experience in the leadership of biostatistical and data coordinating center efforts for single- and multi-center studies, with special expertise in pediatric cardiology, child growth and development, ICU management and surgical follow-up, and malaria in children. He is also an Associate Professor of Pediatrics at Harvard Medical School and Associate Professor of Biostatistics at Harvard School of Public Health.
Dr. Wypij’s methodologic research interests lie in the areas of longitudinal data analysis, spline and smoothing methods, the analysis of discrete data, and models for vaccine efficacy. He has collaborated on cardiac surgery clinical trials and follow-up studies at Children’s Hospital since 1989, including the Boston Circulatory Arrest Study, the Boston pH Study, and the Boston Hematocrit Study. He also collaborates with many other Children’s Hospital clinical investigators on their projects and supervises the data management and biostatistical activities of the Glaser Pediatric Research Network. Since 1997, he has been the Director of Biostatistics for the NIH-funded Severe Malaria in African Children clinical research network, which is conducting observational studies and clinical trials in five African countries. Dr. Wypij is an award-winning lecturer who has taught biostatistics at Harvard School of Public Health since 1989, as well as short courses in Brazil, Gabon, Greece, Italy, and Portugal.

Carlo de Moor, Ph.D./Lead Biostatistician
Dr. de Moor joined the CRP and the Department of Psychiatry in September 2004. Dr. de Moor’s statistical research interests focus on methods for analyzing longitudinal data, group randomized trials, and optimal methods of assigning participants to treatment conditions. Dr. de Moor has participated in numerous projects in behavioral science including studies in smoking prevention, smoking cessation, cancer screening, fruit and vegetable consumption, quality of life, alcohol consumption, and stress and immune functioning.

Prior to joining the CRP, Dr. de Moor was an Associate Professor of Biostatistics at the University of Texas, Houston School of Public Health (UTHSPH). At UTHSPH, he also served as Associate Director of Design and Analysis at the Center for Health Promotion and Prevention Research. Prior to this position, Dr. de Moor was Associate Professor at the University of Texas MD Anderson Cancer Center in the Department of Behavioral Sciences and the Department of Biostatistics and Section Chief, Behavioral Statistics, in the Department of Behavioral Science.

Henry A. Feldman, Ph.D./Lead Biostatistician
Dr. Feldman joined the CRP in September 2001, bringing long-held interests and extensive experience in medicine, public health, and biological science. He is actively consulting with fellows and faculty, collaborating as co-investigator on a variety of research proposals, and contributing to research training for fellows and residents. His research publications include clinical and community trials, epidemiological surveys, experiments in human and animal physiology, studies in cellular and biochemical kinetics, and methods for experimental design, data analysis, and mathematical modeling.

Dr. Feldman taught biostatistics full-time at Harvard School of Public Health from 1979-89 and, as Principal Research Scientist at New England Research Institutes from 1990-2001, served as lead analyst and Co-PI for the multi-site Child and Adolescent Trial for Cardiovascular Health (CATCH). He is a Fellow of the American Heart Association Council on Epidemiology and Prevention and a faculty member of the Council’s annual postdoctoral training course, the Ten-Day Seminar on Epidemiology and Prevention of Cardiovascular Disease.
Leslie A. Kalish, Sc.D./Lead Biostatistician and GCRC Director of Biostatistics
Dr. Kalish joined the CRP in April 2003. The focus of Dr. Kalish's professional career has been the design, coordination, and analysis of clinical trials and epidemiologic cohort studies. His statistical research has applied optimal statistical design methodology to treatment allocation procedures for clinical trials and to the selection of control groups in observational epidemiologic studies. Translating this work into practice, he has collaborated on clinical research in many areas, including HIV and other infectious diseases, transfusion medicine, alternative medicine, and oncology. Currently he serves as the Director of Biostatistics for the General Clinical Research Center.

Before coming to Children’s Hospital, Dr. Kalish held leadership positions in the coordinating centers of several multi-center studies at the New England Research Institutes and the Dana Farber Cancer Institute and taught in the Department of Biostatistics at Harvard School of Public Health.

Alex Kartashov, Ph.D./Senior Biostatistician
Dr. Kartashov holds a doctorate in biology. He is currently working on a doctoral thesis in Biostatistics at Boston University. He has experience in the design, conduct, and analysis of observational and interventional studies, including clinical trials, cohort studies, cross-sectional analyses of large national databases, and small-scale controlled physiological studies.

Dr. Kartashov consults with investigators in the design of studies, data analysis and interpretation of study results, and preparation of manuscripts and presentations. For the last two years, he worked with investigators in the Division of Endocrinology on the analysis of a large cohort study (CARDIA). He also serves as a biostatistician with the General Clinical Research Center, assisting with protocol review and data analysis.

Mei-Chiung Shih, Ph.D./Senior Biostatistician
Dr. Shih joined the CRP in September 2001. Dr. Shih's statistical research interests focus on statistical methods for genetic epidemiology studies of complex diseases, gene by environment interactions, design and analysis of group sequential clinical trials, and statistical methods for analyzing longitudinal data. She has participated in numerous projects including single- and multi-center clinical trials, genetic association studies of prostate cancer and ovarian cancer, and studies of quality of life in pediatric patients receiving hematopoietic stem cell transplantation and in brain tumor patients. Dr. Shih is also an Assistant Professor of Biostatistics at Harvard School of Public Health.

Prior to joining the CRP, Dr. Shih worked as a Research Statistician at Schering-Plough Research Institute from 1995-1998 and as a Postdoctoral Fellow at Stanford University School of Medicine from 1999 to 2001.

Peter Forbes, M.A./Biostatistician
Mr. Forbes joined the CRP as a biostatistician in October 2000. His responsibilities include data cleaning and data set creation, SAS programming, data reporting, data analysis, statistical graphics, and participation in the writing of grants and papers. Before joining the CRP, Mr. Forbes worked at Children's Hospital in the Department of Psychiatry's Learning Disabilities Research Center. His areas of interest include statistical software and programming, data analysis, sample design, and survey research methods.
Daniel Kinnamon, M.S./Biostatistician
Mr. Kinnamon joined the CRP in April 2004. He earned a Master’s degree in Statistics and a Bachelor’s degree in Economics and Latin American Studies from Stanford University. Over summers, he worked in research positions at Strong Capital Management, the World Bank’s Mexico City Office, and Criterion Economics, LLC. He also completed the first semester of the PhD program in economics at the Massachusetts Institute of Technology before deciding to pursue his strong and growing interest in biostatistics by joining the CRP.

His responsibilities include data cleaning and data set creation, statistical programming and data analysis, statistical graphics, and participation in the writing of grants and research papers.

Clarissa Valim, M.D., Sc.D., M.Sc., S. M./Biostatistician
Dr. Valim has a multidisciplinary background, with graduate studies in medicine, epidemiology, and biostatistics. She joined the CRP in June 2003, working in supporting and collaborating with other investigators in clinical research in protocol development and data analysis. In addition, Dr. Valim works on her methodological research in the estimation of vaccine efficacy and on the team of the NIH-funded Severe Malaria in African Children clinical research network.

Before joining Children’s Hospital, Dr. Valim worked in research and teaching in Brazil until coming to Harvard for her doctoral studies. Dr. Valim’s research interests and activities have focused in epidemiological, methodological, and clinical research in infectious diseases and health services research.

Xi Deng, B.S./Biostatistics Research Assistant
Ms. Deng is a doctoral student in Biostatistics at Harvard University. She joined the CRP in July 2004. Before joining the CRP, Ms. Deng was a student at Tsinghua University in China.

Samuel McDaniel, M.Phil./Biostatistics Research Assistant
Mr. McDaniel is a doctoral student in Biostatistics at Harvard University. He joined the CRP in August 2003. Before joining the CRP, Mr. McDaniel worked at the University of the West Indies, Jamaica, as a Lecturer in Applied Mathematics.

Armando Teixeira-Pinto, M.S./Biostatistics Research Assistant
Mr. Teixeira-Pinto is a doctoral student in Biostatistics at Harvard University. He joined the CRP in July 2002. Before joining the CRP, Mr. Teixeira-Pinto worked as an Assistant Lecturer at the Oporto Medical School in Portugal.

APPLICATIONS DEVELOPMENT

Jason Rightmyer, M.S./Applications Development Team Leader
Mr. Rightmyer joined the CRP in March 2003, and brings extensive experience in clinical research informatics. As the team leader of applications development, he is responsible for directing all software development activities, including setting standards for data management system design and promoting informatics in clinical research. Mr. Rightmyer holds a graduate degree in Health Informatics from the University of Minnesota.
Before joining Children’s Hospital, Mr. Rightmyer served as Project Director and Systems Programmer at New England Research Institutes. There he worked primarily on the co-design and development of a proprietary Web-based data management system for clinical and epidemiological research. He has co-authored several NIH Small Business Innovation Research grant proposals and directed a number of additional projects including the development of a computer application for scientific randomization, an evidence-based smoking cessation program, and an expert system for clinical specialists.

Andrew Nelson, M.S./Senior Applications Developer

Mr. Nelson joined the CRP in March 2002. He has a Master’s in Engineering and many years of experience as a programmer and applications developer. He has extensive skills and knowledge using a number of database, Web, and application technologies, including Microsoft .NET, Java, and Oracle. He has previously worked for a number of technical companies and healthcare institutions, including the Research and Development Department at Partners Healthcare System.

Joseph Rezuke, B.S./Lead Applications Developer and GCRC Informatics Manager

Mr. Rezuke joined the CRP in August 2002. As a Lead Applications Developer, he has designed several systems for clinical studies, including a laboratory inventory and specimen tracking system for the Pulmonary Medicine Tissue Bank project. Mr. Rezuke also serves as the Informatics Manager for the General Clinical Research Center (GCRC). His current project entails designing and developing a new comprehensive administration system for the GCRC.

Roumen Stoyanov, B.S./Senior Applications Developer

Mr. Stoyanov has a Bachelor’s degree in Computer Science and is a Microsoft Certified Solutions Developer. Before joining the CRP in July 2003, he worked as a consultant at New England Research Institutes. During his tenure there, he worked on the Teledoc system and developed randomization software for clinical research. Teledoc was a three-tiered software system that used telephony and speech recognition technology to clinically evaluate the working memory of geriatric patients. Currently, Mr. Stoyanov is developing a clinical trials data management system for the Glaser Pediatric Research Network using open data standards and Microsoft .NET technologies.

Alan Tam, B.S./Applications Developer

Mr. Tam has a Bachelor of Science in Systems Engineering and over nine years of programming and applications development experience. He has extensive expertise in C/C++, Microsoft, and other Web technologies. He joined the CRP in January 2003. He works closely with CRP staff members and investigators building applications for clinical research data storage and management.
CLINICAL STUDY OPERATIONS

Sion Kim Harris, Ph.D./Epidemiologist and Survey Design Specialist
Dr. Harris has over ten years of experience in survey/questionnaire design, implementation, and data analysis and provides consultation to investigators throughout Children’s Hospital in the design and implementation of surveys. Dr. Harris also has extensive experience in public health epidemiology, psychometric analysis methods, adolescent health research and program evaluation, and qualitative research methods. She has collaborated in the development and psychometric testing of a comprehensive adolescent health status questionnaire called the Child Health and Illness Profile (CHIP-AE), a brief screen for adolescent alcohol and drug abuse used in primary care settings (the CRAFFT), and a member survey for teen pregnancy prevention coalitions to assess functioning and capacity for action.

Dr. Harris received her doctorate from the Johns Hopkins Bloomberg School of Public Health in 1996, after which she worked for the Mass. Department of Public Health as the Project Manager of Adolescent and School Health for the Office of Statistics and Evaluation in the Bureau of Family and Community Health. She provided oversight and leadership in research and program evaluation projects related to teen births, teen pregnancy prevention, school health and school-based health centers, and youth risk behaviors. She continues to provide consultation to them on a number of survey and program evaluation projects.

Maureen Clark, M.S./Senior Clinical Research Specialist
Ms. Clark joined the CRP in June 2003. Her responsibilities include collaborating with investigators to develop and document clinical research protocols, advising investigators regarding data management systems and data collection tools for their research projects, in addition to developing study-specific data management and quality assurance procedures.

Ms. Clark has a Master’s Degree in Clinical Physiology. She has eleven years of experience in clinical trials management. Before joining Children’s Hospital, Ms. Clark worked as Manager of Clinical Trials at Massachusetts General Hospital in Pediatric Psychopharmacology and as a Project Manager in the Cardiovascular Division at Brigham and Women’s Hospital.

Maggie McCarthy, M.S., M.P.H./Senior Clinical Research Specialist
Ms. McCarthy has an MPH from Harvard School of Public Health and a Master of Clinical Immunology degree from Hahnemann University in Philadelphia. She has been working in the CRP since April 2002 and has been working on a number of multi-center studies funded by federal and foundation sponsors. In the past year, she has been instrumental as the Project Manager on three multi-center studies funded by the Glaser Pediatric Research Network assisting in protocol development, developing CRFs and a manual of operations, and assisting programmers in the development of specifications for data management systems.

Ms. McCarthy has many years of experience in the clinical arena working as a Laboratory Manager and Senior Research Technician. More recently, she had worked for five years as a Clinical Research Associate/Research Scientist at the New England Research Institutes, where she was the Project Director for a number of NIH-funded multi-site studies.
Amy Kroeplin, B.A., M.P.H./Clinical Research Specialist
Amy Kroeplin has four years experience in the management of clinical research studies. She has a Bachelor’s degree in Biology and Anthropology and a Master’s degree in Epidemiology and Biostatistics from Boston University. Ms. Kroeplin is certified in Coordinating Clinical Trials and a member of the Society of Clinical Research Associates (SOCRA) and American Public Health Association (APHA).

Ms. Kroeplin collaborates with principal investigators to develop data collection forms and study manuals of operation, and to train research staff in the conduct of the research protocol. Ms. Kroeplin works closely with the Applications Development group and is responsible for developing detailed specifications of the data management system functionality such as range and logic checks, inter and intra-form dependency and protocol tracking. Ms. Kroeplin is also committed to developing quality control procedures, data coordination for research studies and managing the flow of data received from study staff. She is responsible for training data entry staff, both internal to the Clinical Research Program and personnel hired by the principal investigator to ensure accurate data entry.

Sharon Wong, B.S./Research Data Coordinator
Ms. Wong joined the CRP in September 2001. Her responsibilities include testing CRP-developed databases, coordinating the data for single and multi-center clinical research studies, data entry, training and monitoring data entry clerks, data cleaning, performing quality assurance checks on entered data, and following up on any missing and conflicting data. She also assists the clinical research specialists in the editing of case report forms, and generates reports for studies and CRP courses.

Most recently, Ms. Wong has been programming databases using SPSS Data Builder. Using this program, Ms. Wong creates databases, assists in the building of databases through tutorials and supervision, installs the databases, and trains data entry clerks.

Raina Filip-Dhima, B.S./Research Data Coordinator
Ms. Filip-Dhima joined the CRP in March 2004. She has a Bachelor of Science degree in Psychology and a minor in Philosophy from Northeastern University. While completing her undergraduate studies, Rajna participated in the cooperative education program and worked as a research assistant at MGH, Boston City Hall, and the Laboratory of Social Psychology and Personality at Northeastern University, which further developed her interest and enthusiasm in clinical research. One of her major projects was a cross-cultural research study she conducted in Albania, where she collected data from 200 participants. She has used this data to study cultural differences in emotional and personality styles between the Albanian and American cultures.

Her current responsibilities include testing study-specific databases, coordinating data sent for both single- and multi-center CRP coordinated studies, data-entry and error resolution, data cleaning, performing quality assurance checks on entered data, and following up on any missing and/or conflicting data with clinical center staff.

Kerwin Tang, M.A./Research Data Coordinator
Mr. Tang joined the CRP in August 2004 after graduating from Boston University with a Master’s degree in Medical Sciences. His research experience includes working as a research assistant in the Infectious Diseases department at Boston Medical Center and in the Hematology and Oncology Department at Boston University School of Medicine.
Mr. Tang’s role as a data coordinator at the CRP is to coordinate data flow for the Glaser Pediatric Research Network sponsored pediatric research studies. His current responsibilities include providing administrative support to the development and implementation of the studies, performing data entry of case reports, communicating with clinical center sites on data queries, and maintaining study data files to ensure organization and confidentiality as required by institutional and federal regulations.

**Michael Wake, B.A./Glaser Data Coordinator**
Mr. Wake joined the CRP in October 2003. He has a degree in Brain and Cognitive Sciences from the University of Rochester. His current responsibilities include testing CRP-developed web-based databases for Glaser research studies, coordinating data for Glaser studies, data entry and error resolution, data cleaning, performing quality assurance checks on entered data, and following up on any missing and conflicting data. He also assists the clinical research specialists in the editing of case report forms.

**ADMINISTRATION & FINANCE**

**Terrie Rogers, M.S., M.B.A./Program Administrator**
Ms. Rogers has a M.S. in Immunology and an M.B.A., both from the University of Michigan. She has over twenty years of diversified global management experience in the healthcare, CRO, pharmaceutical, biotechnology, and genomics industries. Ms. Rogers has broad expertise and a proven record of accomplishment in healthcare service sales, marketing, project management, and strategic planning. She joined the CRP in November 2003.

Ms. Rogers’ role in the CRP is to oversee the daily operations of the department on matters of billing, budgets, purchasing, and administrative procedures and personnel. In conjunction with the CRP Director, she is also involved in strategic planning for the CRP.

**Cheryl Sweeney, B.S./Clinical Research Financial Analyst**
Ms. Sweeney has a degree in Medical Sociology and came to Children’s Hospital in 1986. She has held numerous positions, most recently as the Administrative Manager in the GCRC before joining the CRP in September 2000.

Her role in the CRP is to provide financial and budget support to CRP staff and to clinical investigators working on CRP-supported studies. She works closely with investigators, other CRP staff, and ancillary programs to ensure that budgets comply with external sponsors and Children’s Hospital policies. In addition, she provides financial data for CRP reports and projects.

**Laura Haley/Senior Administrative Associate**
Ms. Haley has worked in the administrative field for over twenty years. She joined the CRP in July 2003. Her duties include direct administrative support to the Director, coordinating the logistics and administration of CRP-sponsored courses, general administrative support to CRP staff, and common Program responsibilities such as requisitioning items and services.

Ms. Haley is the frontline individual for investigators requesting resources from the CRP, often scheduling initial meetings, and following each new project request to ensure that it has been triaged to the appropriate Program staff. Most recently, she has been involved in the establishment of formalized Standard Operating Procedures for the CRP.
**Patricia Hopkins, B.A./Administrative Associate**

Ms. Hopkins has a degree in Psychology and Philosophy from Boston University and previous experience in research from working on a study as a Data Coder at the Channing Laboratory, Brigham and Women's Hospital. She joined the CRP in July 2002. Her current responsibilities include providing direct administrative support to the Director of Biostatistics, payroll responsibilities, coordinating aspects of CRP-sponsored courses, general administrative support to CRP staff, and other Program activities. She has been involved in the data entry for a large multi-center clinical trial. Most recently, she organized the CRP biostatistics library.
IV. Utilization of Services

The Clinical Research Program (CRP) provides a range of services to assist investigators in the design, conduct, and analysis of their clinical research studies. Limited free support has been provided for consultative services to unfunded studies while more support is provided for collaborative relationships with funding. Services include:

- Protocol/Grant Proposal Development
- Study Design
- Sample Size and Power Calculations
- Biostatistical Analysis Methods
- Randomization
- Case Report Form / Survey Design
- Data Management Systems Design
- Data Analysis and Interpretation
- Education and Training
- Mentoring

Summary

During FY04, the CRP worked on 317 clinical research projects (Table IV-1). The majority of these projects (n=268) did not provide funding for CRP staff. Forty-nine (15%) of these projects funded the CRP staff for a total of $996,664 (see Table 1).

<table>
<thead>
<tr>
<th>Funding status</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No CRP funds received in FY04</td>
<td>268</td>
</tr>
<tr>
<td>Any CRP funds received in FY04</td>
<td>49</td>
</tr>
<tr>
<td># projects</td>
<td>317</td>
</tr>
<tr>
<td>Total CRP FY04 costs</td>
<td>$996,664</td>
</tr>
</tbody>
</table>

*Includes funding from CHB investigators and extramural funding from CRP faculty
Funded Projects

Table IV-2 presents the distribution of CRP services funded by the 49 projects during FY04 and the amount of support provided to each area. Data Management Services includes the combined service areas of Clinical Study Operations, Database Programming, and Data Entry.

### Table IV-2. Direct costs by service area for 49 projects funding CPR in FY04.

<table>
<thead>
<tr>
<th>Service areas</th>
<th># Projects requiring funded services*</th>
<th>FY04 CRP Funding (% of total dollars)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI</td>
<td>7</td>
<td>$98,319 (9%)</td>
</tr>
<tr>
<td>Biostatistics</td>
<td>38</td>
<td>$364,827 (37%)</td>
</tr>
<tr>
<td>Clinical Study Operations</td>
<td>25</td>
<td>$221,052 (22%)</td>
</tr>
<tr>
<td>Database Programming</td>
<td>16</td>
<td>$173,659 (17%)</td>
</tr>
<tr>
<td>Data entry</td>
<td>14</td>
<td>$104,879 (11%)</td>
</tr>
<tr>
<td>Other/Supplies</td>
<td>11</td>
<td>$33,929 (3%)</td>
</tr>
<tr>
<td>Total</td>
<td>49</td>
<td>$996,664 (100%)</td>
</tr>
</tbody>
</table>

*A single project often funds several service areas.

Figure IV-1
Table IV-3 presents the distribution of funding sources for the 49 projects providing financial support to the CPR. NIH and Foundations were the primary sources of funding for these projects (45% and 48%, respectively). Furthermore, among the 24 NIH funded projects, 13 were funded by R01 mechanisms, 2 were R03, 2 were R21, and 6 were other funding mechanisms (K23, R37, M01, P50, etc.).

More than half (n=26) of the 49 funded projects were from collaborations with researchers from the Department of Medicine. The remainder was from various departments in the Hospital including Cardiology, Radiology, Patient Care Operations and Surgery, Laboratory Medicine, Nursing, Otolaryngology, Neurology, Psychiatry, Anesthesia, the Brafelton Institute, and Urology. The Clinical Research Program faculty were PI's on six of the 49 projects. The rank of the PI for the funded projects was also variable: Professor (n=7), Associate Professor (n=8), Assistant Professor (n=13), Fellow (n=1), Instructor (n=15), Nurse (2), and Other (2).

Table IV-3. Funding sources for 49 projects funding CPR in FY04

<table>
<thead>
<tr>
<th>Source</th>
<th># Projects</th>
<th>FY04 CRP Funding (% of total dollars)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIH</td>
<td>24</td>
<td>$445,679 (45%)</td>
</tr>
<tr>
<td>Other Federal</td>
<td>4</td>
<td>$51,506 (5%)</td>
</tr>
<tr>
<td>Foundation</td>
<td>15</td>
<td>$473,744 (48%)</td>
</tr>
<tr>
<td>Industry</td>
<td>2</td>
<td>$4,295 (&gt;1%)</td>
</tr>
<tr>
<td>Departmental</td>
<td>1</td>
<td>$375 (&gt;1%)</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>$21,065 (2%)</td>
</tr>
<tr>
<td>Total</td>
<td>49</td>
<td>$996,664 (100%)</td>
</tr>
</tbody>
</table>

Figure IV-2

![Diagram showing sources of funding]

- NIH: $445,679 (45\%)
- Foundation: $473,744 (48\%)
- Other Federal: $51,506 (5\%)
- Industry: $4,295 (>1\%)
- Department: $375 (<1\%)
- Other: $21,065 (2\%)
New Requests for Assistance in FY04

During FY04, the CRP received 285 new requests for assistance from 189 Children’s Hospital faculty or staff. The distribution of requests according to hospital department is shown in Figure IV-3. The majority of requests were from investigators with appointments in Medicine (n=177) and within the Divisions of Emergency Medicine (n=24), Endocrinology (n=27), Adolescent Medicine (n=17), Hematology/Oncology (n=18), GI/Nutrition (n=14), General Pediatrics (n=18), Infectious Diseases (n=12), and Pulmonary (n=20).

Figure IV-3. FY04 CRP Requests for Assistance (N=285 Requests)
As shown in Figure IV-4, investigators requesting assistance were somewhat more likely to be at the rank of Fellow (n=36), Instructor (n=43), or Assistant Professor (n=36) as compared to Associate Professor (n=19) or Professor (n=10).

**Figure IV-4. Rank of Investigators Requesting CRP Assistance (N=189 Investigators)**
As shown in Figure IV-5, the majority of requests were for consultation on design and analysis including estimation of sample size and power (n=102), development of a statistical analysis plan (n=127), development of a grant proposal or study protocol (n=111), and/or analyses of data or data interpretation (n=99). Approximately 64 requests were related to study implementation, including case report form or survey design and/or database assistance.

Figure IV-5. Services Requested (N=285 Requests)

About one third (n=100) of the 285 new requests for CRP resources had funding to support the project and almost one-third (n=84) were applying for funding. Among the 100 funded projects, foundations (n=23) and NIH (n=24) were the primary funding sources. Among those investigators submitting grant proposals for funding, the majority (n=66) were first submissions, whereas the remainder were mainly resubmissions (n=12) or non-competing renewals (n=2).

Among the 84 new requests applying for funding, 46 are applying to NIH, 20 to foundations, six to other federal, six to department funds, and six to other. For those applying to NIH, the mechanisms for funding were 20 for R01s, 3 for R03s, 6 for R21s, 10 for various K awards, and 7 for other mechanisms.
V. Education and Training

The Clinical Research Program (CRP) provides education and training to the clinical research community at Children's Hospital through several courses and seminars offered each year. These include Introduction to Clinical Research, Coordinating Clinical Research, and Career Development Block; which are described below. Course syllabi are located in Appendix C. In addition, in the past year we have begun a Biostatistics Seminar Series that is open to members of the clinical research community at Children's Hospital. Speakers in this series are listed in the Biostatistics Seminar Series section.

A. Introduction to Clinical Research Course

1. Description

The Introduction to Clinical Research course is a 3 full-day course designed to introduce participants to the following key clinical research concepts:

- Study Design
- Clinical Trials
- Biostatistics
- Research Ethics
- Data Management
- Grant Writing

The target audience includes Junior Faculty, Fellows, Nurse Investigators, and others who will develop and write their own research protocols or grant proposal applications. The overall goal of the course is to provide participants with a knowledge base so that they may be better prepared to develop a study protocol and conduct their research. The course is sponsored by the CRP and General Clinical Research Center (GCRC) and is presently offered January and July of each year. Registration is limited to 50 participants and has reached maximum enrollment at each session.

2. Evaluation

The following table summarizes participants’ overall evaluation of the speakers and topics for the course that was offered in January and July of 2004:

<table>
<thead>
<tr>
<th>Session Date</th>
<th>Clarity of Presentations</th>
<th>Useful Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>January 2004</td>
<td>3.6</td>
<td>3.5</td>
</tr>
<tr>
<td>July 2004</td>
<td>3.4</td>
<td>3.4</td>
</tr>
</tbody>
</table>

* Score Range: 1-Poor to 4-Excellent
A summary of the participants’ ratings for each of the course objectives is shown below.

<table>
<thead>
<tr>
<th>Session Objective</th>
<th>January 2004</th>
<th>July 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>How to select a study design that makes it possible to answer the proposed study hypotheses</td>
<td>3.3</td>
<td>3.3</td>
</tr>
<tr>
<td>Potential biases associated with the various study designs</td>
<td>3.3</td>
<td>3.0</td>
</tr>
<tr>
<td>How to propose a plan for data analysis and/or provide information to a biostatistician so that study quality may be maximized</td>
<td>3.4</td>
<td>3.1</td>
</tr>
<tr>
<td>How to develop high quality data collection forms and effective approaches to data management</td>
<td>3.4</td>
<td>3.4</td>
</tr>
<tr>
<td>How to protect human subjects and ethical issues in pediatric research</td>
<td>3.7</td>
<td>3.5</td>
</tr>
<tr>
<td>Content of a NIH grant proposal and the application process</td>
<td>3.4</td>
<td>3.5</td>
</tr>
<tr>
<td>Resources available for the conduct of clinical research at Children’s Hospital</td>
<td>3.6</td>
<td>3.7</td>
</tr>
<tr>
<td>Approaches to improve the quality of scientific writing and presentations</td>
<td>3.6</td>
<td>3.6</td>
</tr>
</tbody>
</table>

* Score Range: 1-Poor to 4-Excellent

B. Coordinating Clinical Research

1. Description

The Coordinating Clinical Research course consists of three half-day sessions designed to provide participants with a knowledge base so that they may be better prepared to coordinate clinical research projects. The target audience includes Research Nurses and Study Coordinators who will be responsible for coordinating or managing a research study. The course, sponsored by the CRP, Committee on Clinical Investigation (CCI), and GCRC, is offered during the fall and spring of each year. Registration is limited to 20 participants and has reached the maximum enrollment for each session.

2. Evaluation

The following table summarizes participants' overall evaluation of the speakers and topics for the course that was offered in November 2003 and March 2004.

<table>
<thead>
<tr>
<th>Session Date</th>
<th>Clarity of Presentations</th>
<th>Useful Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>November 2003</td>
<td>3.5</td>
<td>3.5</td>
</tr>
<tr>
<td>March 2004</td>
<td>3.7</td>
<td>3.7</td>
</tr>
</tbody>
</table>

* Score Range: 1-Poor to 4-Excellent
A summary of the participants' ratings for each of the course objectives is shown below.

<table>
<thead>
<tr>
<th>Session Objective</th>
<th>November 2003</th>
<th>March 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistics of conducting a clinical research study</td>
<td>3.3</td>
<td>3.6</td>
</tr>
<tr>
<td>Approaches to reduce errors or bias in a study</td>
<td>3.5</td>
<td>3.7</td>
</tr>
<tr>
<td>Human subject protection responsibilities for conducting clinical research</td>
<td>3.7</td>
<td>3.8</td>
</tr>
<tr>
<td>The unique issues and process of obtaining informed consent in pediatric research</td>
<td>3.7</td>
<td>3.7</td>
</tr>
<tr>
<td>How to develop quality case report forms for effective data collection</td>
<td>3.6</td>
<td>3.7</td>
</tr>
<tr>
<td>How to develop manuals of operation for effective data collection</td>
<td>3.5</td>
<td>3.6</td>
</tr>
<tr>
<td>Approaches for effective data management</td>
<td>3.4</td>
<td>3.6</td>
</tr>
<tr>
<td>Approaches to monitoring the quality of data collection</td>
<td>3.5</td>
<td>3.6</td>
</tr>
<tr>
<td>Requirements for study audits and close-out activities</td>
<td>3.4</td>
<td>3.5</td>
</tr>
<tr>
<td>How to manage the budget, bill for services or make payments</td>
<td>3.1</td>
<td>3.3</td>
</tr>
</tbody>
</table>

* Score Range: 1-Poor to 4-Excellent

C. Career Development Block: Creating and Applying New Knowledge

1. Description

The Career Development Block is an innovative, 3-month component of training for all senior residents in the Boston Combined Residency Program in Pediatrics. Faculty and residents designed the rotation jointly to enhance residents' skills in five areas: (1) knowledge and skills that are fundamental to academic and clinical pediatric careers; (2) ability to participate in creating new knowledge through pediatric research; (3) understanding and ability to apply new developments in molecular medicine to research and clinical practice; (4) ability to identify policy issues and participate effectively in advocacy for children; (5) ability to participate in improving quality of health care at individual, process, and organizational levels. The rotation includes seminars taught by investigators, methodologists, clinicians, and ethicists two mornings a week and individual house officer projects in research, education, or clinical practice mentored by faculty throughout the Harvard and Boston University academic communities.

During FY04, the CRP and CCI lead the session entitled Creating and Applying New Knowledge. At the end of the 4 sessions, the objectives for the participants were to gain a better understanding of each of the following:

- Major study designs used in clinical research, their strengths and limitations, and the interpretation of their corresponding measures of occurrence and association
- How to estimate the sample size required for a study and the underlying statistical principles (type I error, type II error, power and effect size)
• Basic methods of data analyses and interpretation of study results
• The skills necessary to critically evaluate clinical research reports and apply findings to clinical practice
• The role of a DSMB
• Human subjects requirements and ethical considerations of conducting research with children

D. Biostatistics Seminar Series

1. Description

The Biostatistics Seminar Series offers an opportunity for the presentation of novel biostatistical methods and data analysis applications for the Children’s Hospital research community. The target audience includes biostatisticians and clinical investigators with an interest in statistical methods and data analysts. Attendees should have knowledge regarding basic biostatistical methods, including regression. A half-hour presentation is followed by a half-hour of discussion.

2. Presentations

Henry Feldman, PhD, “Agreement Statistics”, January 26, 2004

Leslie Kalish, ScD, “Sample Size for the Two-Sample Wilcoxon Test”, February 23, 2004

Alex Kartashov, PhD, “Statistical Problems in the Longitudinal Cohort Study: Interval-Censored Data and Covariate Measurement Error”, April 26, 2004

Clarissa Valim, MD, PhD, “Smoothing and Semi-parametric Regression”, May 24, 2004
VI. Clinical Research Program Spotlights

A. CRP Data Management System Technology

Introduction
The Clinical Research Program (CRP) provides a variety of informatics services to the clinical research community at Children’s Hospital, Boston. These services range from creating and supporting small databases to implementing complex software applications and Web-based systems. In response to a growing demand for more complex solutions, the CRP has developed a reusable software framework, named SciRIS (Scientific Research Information System), to rapidly implement Web-based data management systems for clinical research.

Technology
The SciRIS framework was designed by the CRP applications development team using best practice methodologies and as a result provides a scalable enterprise level architecture based on industry standards. The framework was developed using Microsoft technologies including ASP.NET, Web Services, Serviced Components (COM+), and SQL Server. The application utilizes the CDISC (Clinical Data Interchange Standards Consortium) object data model (ODM) to govern system operations and employs XML technologies to facilitate exchanging and transforming data between the client, server, and data repository.

System Features
The CRP applications development team employs the SciRIS framework for all moderate and large-scale collaborative research projects (Figure VI-1). With this framework, each data management system can support a variety of features including Web-based data capture, lab data management, and protocol tracking. The system provides a hierarchical view of each study participant, which allows study staff to manage study visits and case report forms as defined by the clinical protocol (Figure VI-2).

The data entry component validates user responses based on specified range checks, executes skip patterns, and resolves outlier responses through an integrated annotation dialog (Figure VI-3). The system supports double data entry, and a complete audit trail of transactions is maintained to ensure data integrity and regulatory compliance. Furthermore, the system provides staff with a variety of reports to assist project management and study data may be readily exported for use with Microsoft Excel, SPSS, or SAS.

All system users are required to enter a username and password to access study data. The system tracks when users enter the site and staff members are assigned security roles that are strictly enforced throughout the Web application. Currently, all SciRIS data management systems are available on the private hospital network only.

Current Assessment
As stated previously, the SciRIS framework is implemented on all moderate and large-scale clinical research projects supported by the CRP data management core. Since fall 2003, the applications development team has deployed 12 systems to the field, including several that support the multi-site clinical operations of the Glaser Pediatric Research Network.
The SciRIS software application has proven to be an invaluable resource and the CRP has benefited tremendously from its design. SciRIS has contributed to the success of the informatics core by reducing dramatically the time required to implement data management systems. In the past, development of clinical data management systems required several months of dedicated programming effort. However, using the SciRIS framework, the CRP can implement systems in less time with fewer defects and additional standard features.

The framework has benefited project management and biostatistics activities as well. The comprehensive data model and technical features facilitates data management by expediting start-up activities and assisting in protocol monitoring. Missing visits, forms and data are identified earlier and minimal cleaning is required prior to analysis. In consideration, the SciRIS framework has demonstrated significant benefit over traditional research tools such as SPSS Data Entry or Microsoft Access, and its features are comparable to more advanced and cost prohibitive systems such as Oracle Clinical or Phaseforward Clinicals.

Future Improvements
Although substantial progress has been made with the SciRIS framework, it requires additional development and continued financial support for staff and new servers. The CRP applications development team would like to add several study management features such as scheduling, document sharing, and specimen tracking. Furthermore, to support the growing demand for clinical registries and translational research initiatives, the development team would like to incorporate ad hoc query functionality, and genomic and related bioinformatics components into the system.

Figure VI-1
B. Glaser Pediatric Research Network

Since September 2002, CRP has held a contractual agreement with the Glaser Pediatric Research Network (GPRN) to serve as Design, Analysis, and Coordinating center for the network's program of pediatric research and training, with Dr. Wypij as Principal Investigator. Based at Stanford University, GPRN is a component of the Elizabeth Glaser Pediatric AIDS Foundation, a privately funded organization created in 1988. The Foundation has an international reach and a broad agenda including prevention, advocacy, and research in AIDS. The research network was launched in 2000 with the mission of conducting collaborative research on other serious pediatric illnesses, drawing from the diverse patient populations and deep pool of investigators available at five major pediatric research institutions. An important adjunct mission is to draw young investigators into collaborative research careers through a sponsored Fellowship. The organization of GPRN is detailed in Table VI-1. Dr. Christopher Duggan, faculty of the CRP and Boston site director for GPRN, was instrumental in introducing the GPRN leadership to CRP and facilitating the agreement.

<table>
<thead>
<tr>
<th>Scientific Director</th>
<th>Stanford University</th>
</tr>
</thead>
<tbody>
<tr>
<td>Charles Prober, MD</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Site Directors</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darrell Wilson, MD</td>
<td>Lucile Salter Packard Children's Hospital, Stanford University Medical Center</td>
</tr>
<tr>
<td>Lisa Bomgaars, MD</td>
<td>Texas Children's Hospital, Baylor College of Medicine</td>
</tr>
<tr>
<td>Christopher Duggan, MD</td>
<td>Children's Hospital Boston, Harvard Medical School</td>
</tr>
<tr>
<td>Ted Moore, MD</td>
<td>Mattel Children's Hospital, University of California, Los Angeles</td>
</tr>
<tr>
<td>Emily von Scheven, MD</td>
<td>Children's Medical Center, University of California, San Francisco</td>
</tr>
</tbody>
</table>

In 2003-2004, GPRN recruited new leaders at the Baylor and UCLA sites and significantly advanced its research activities. Enrollment was completed for two multi-site clinical trials; two other multi-site studies entered the operational stage, one of which reached 50% of its enrollment target; and one additional single-site study was initiated (Table VI-2). Drs. Wypij, Feldman, and Osganian each acted as coordinating-center PI for one GPRN multi-site study, and Maggie McCarthy, Senior Research Specialist at CRP, devoted the bulk of her time to directing operations for these studies. The combined budget of GPRN efforts at CRP in FY 2004 was $403,000.

CRP functions in several ways in the operations of the Glaser research network. First, it serves a Core resource, lending expertise in the design and conduct of clinical research to help the network develop and foster its programs. CRP Core investigators, including Drs. Wypij, Osganian, Feldman, and Kalish, participate in the evaluation of new research proposals and attend periodic meetings of the GPRN leadership at which progress of current projects is reviewed. CRP is also consulted ad hoc by the Glaser scientific director as issues arise in the conduct of ongoing studies (including those predating the CRP agreement, in which CRP has no direct role), particularly where statistical or design questions are concerned.
A second Core function of CRP is to act as a training resource. For first-year GPRN Fellows, Dr. Feldman organizes a monthly Work-in-Progress seminar via telephone, at which the new Fellows present and jointly critique each other’s protocols. In 2004-05, Dr. Kalish will participate with Dr. Charles Prober, GPRN Scientific Director, in a similar series of Work-in-Progress conference calls for second-year Fellows focused on developing K-series training award applications. CRP reserves places for the GPRN Fellows at the summer session of its three-day course, *Introduction to Clinical Research*; providing an opportunity for intensive methodological orientation at the start of their first Fellowship year.

In July 2004, immediately following the summer course, *Introduction to Clinical Research*, CRP collaborated with GPRN and Johnson & Johnson to sponsor a one-day symposium in Boston titled *Building a Career in Pediatric Clinical Research: Views from Academia, Government, and Industry*. Besides the GPRN Fellows, the symposium was attended by 75 Children’s Hospital junior faculty and fellows. The eminent national panel of presenters, included Drs. Philip Pizzo, formerly Chair of Medicine at CHB and now Dean at Stanford University School of Medicine; Stephen Spielberg, Dean of Dartmouth Medical School; Dianne Murphy, Director of the Office of Pediatric Drug Development at the Food and Drug Administration; Yvonne Maddox, Deputy Director of the National Institute of Child Health and Human Development; and James Ware, Academic Dean of Harvard School of Public Health and a statistical editor of the New England Journal of Medicine. Dr. Feldman organized and coordinated the event on behalf of CRP. The Agenda can be found in Appendix C.

Finally and most substantially, CRP has served the Glaser network since 2002 as data coordinating center for its multi-site studies, each via separate contract. As of fall 2004, agreements were in effect for two clinical trials and one registry project, listed in Table 2. CRP staff are assigned to the full variety of clinical research tasks for these studies, including statistical planning, design of case report forms, database programming, randomization, data management, preparation of data and safety monitoring reports, and presentation and authorship of final results.

<table>
<thead>
<tr>
<th>Table VI-2. Active GPRN Studies, Sep. 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title</strong></td>
</tr>
<tr>
<td>Multi-center trial of Metformin for treatment of obesity in adolescents</td>
</tr>
<tr>
<td>Multi-center neonatal surgical database: necrotizing enterocolitis</td>
</tr>
<tr>
<td>Multi-center open-label Phase I/II trial of rituximab for chronic, severe, idiopathic thrombocytopenic purpura in children and adolescents</td>
</tr>
<tr>
<td>Multi-center randomized trial of alendronate treatment for children receiving high doses of steroids</td>
</tr>
<tr>
<td>Pharmacokinetics of doxorubicin</td>
</tr>
</tbody>
</table>
C. The Severe Malaria in African Children Clinical Research Network

The Severe Malaria in African Children (SMAC) Clinical Research Network was established to conduct mortality-based trials in severe pediatric malaria. Dr. David Wypij, Director of Biostatistics in the CRP, has been involved with SMAC activities since its inception, starting with an NIH planning grant. The main objective of the network is to reduce the mortality of severe malaria in African children by supporting definitive clinical trials across the continent. Although malaria kills over a million African children each year, the disease is widely distributed across the continent and no single center can recruit sufficient number of patients for large scale clinical trial capable of detecting 20-30% reductions in case fatality rates. For these reasons, multi-center studies are required to identify interventions that reduce mortality or severe disease.

The SMAC Network is a truly international effort, funded under a cooperative agreement awarded by the National Institute of Allergy and Infectious Diseases. The Principal Investigator of the Network, Dr. Terrie Taylor, is from Michigan State University and she also works for half of each year at Queen Elizabeth Central Hospital, in Blantyre, Malawi. Dr. Taylor first met Dr. Wypij when she was on sabbatical visiting the Harvard School of Public Health in the mid 1990's. She attended his course on logistic regression and survival analysis and invited him to participate in the SMAC Network. SMAC comprises six participating hospitals in Banjul (The Gambia), Blantyre (Malawi), Kumasi (Ghana), Kilifi (Kenya), and Lambaréné and Libreville (both in Gabon). African, European, and American researchers coordinate the malaria clinical studies. The CRP at Children's Hospital serves as the biostatistical core, supervising data management activities and performing data analyses for all research in the Network. Dr. Wypij is the Principal Investigator for the biostatistical core subcontract, and he works closely with Dr. Clarissa Valim on SMAC data analysis activities.

The SMAC Network has standardized laboratory and clinical diagnosis procedures across centers, established high quality data collection and management systems, and developed a core database including over 20,000 malaria patient hospital admissions. Clinical presentation of severe malaria patients varies across hospital sites and includes cerebral malaria, severe anemia, and lactic acidosis. Several studies have been conducted in SMAC, with some manuscripts already submitted to scientific journals and others currently in preparation.

As part of SMAC activities, Dr. Michel Missinou et al. recently published a paper on a study comparing the accuracy of data entry based on paper-based case report forms with double-data entry with that using a personal digital assistant (PDA). This paper was published in the American Journal of Tropical Medicine and Hygiene. Two more papers have been recently submitted for publication. One paper provides a detailed description of SMAC methods for our surveillance study of malaria patient hospital admissions. Information regarding the heterogeneity of clinical presentation at admission across the six hospital sites is also included. Another paper focuses on the prognostic value of measures of acid/base balance in children with severe malaria. In particular, this research focused on determining whether the more expensive and technically demanding measurement of base excess and lactate added significantly to the prognostic value of using a combination of simple clinical observations and blood glucose concentrations in predicting mortality. Dr. Wypij and/or Dr. Valim have been coauthors of these investigations.
We are currently preparing several new papers related to SMAC activities. One paper will explore the heterogeneity of the clinical presentation of severe malaria across sites based on characteristics of the transmission of malaria in each site and the profile of the specific health services unit. A second paper will assess the prognostic value of the presence and amount of intraleukocytic and intraerythrocytic malaria pigment in predicting mortality among children with severe malaria. Future work will focus on identifying and assessing alternative prediction criteria for malaria mortality based on clinical and laboratory indicators through more complex statistical analysis methods including classification and regression trees and generalized additive models. These efforts will be primarily statistical and methodologic in nature, but we expect they will be helpful to clinicians in the field to decide on risks of mortality for their patients. We are also finishing a paper on predictors of acidosis among malaria patients.

Educational and training efforts have been an integral part of SMAC’s mission to support malaria clinical research. SMAC has promoted courses to strengthen expertise in Africa to conduct clinical research. As part of these efforts, Dr. Wypij supervises the data management activities at all sites. In addition, Dr. Wypij has led a short course on clinical trials and cohort studies for SMAC investigators, and Dr. Valim has taught a short course on introductory biostatistics, both in Gabon. Training of data management staff has also been carried out through courses in Africa. Mr. Christopher Olola, the Data Coordinator for the SMAC Network who is headquartered in Kenya, has visited the CRP at Children’s Hospital three times for training and supervision in biostatistics and data management methods.

Activities in the SMAC Network continue. Currently we are running a Phase I/II clinical trial of pentoxifylline to reduce mortality in severely ill malaria patients in Kenya. We are also looking to start a new project in 2005 to study the accuracy of fundoscopic exams in diagnosing cerebral malaria. We are hoping to implement a larger, multi-center clinical trial within the next few years. The SMAC Network has also established a goal of creating expertise in biostatistics in Malawi. As part of this effort, the Network hopes to sponsor Master’s degree programs to train African biostatisticians. Drs. Wypij and Valim will play an important role as collaborators in all of these new activities and initiatives of the SMAC Network.
VII. Collaborative Projects

The Clinical Research Program works collaboratively with numerous Children’s Hospital Boston investigators from a wide variety of disciplines. The program presently provides such support to the following funded studies (all dollar figures represent Annual Direct Cost).

A. Federal Awards

R01 HD045763 (Austin) 07/01/04-04/30/08
NIH/NIMH $58,000
Sexual Orientation and Health Disparities in Adolescence
This project is a prospective epidemiological study of the distribution and determinants of sexual orientation group disparities in health in the Growing Up Today Study, a national longitudinal cohort of over 16,000 adolescents.

R21 DA14929 (Boyer/CHB Subcontract: Shannon) 09/30/01-08/31/04
NIH/NIDA $22,852
The Relationship between the Internet and Illicit Drug Use
This is a cross-sectional study of individuals presenting to two emergency departments (one adult and one pediatric) using an interviewer-administered questionnaire. The specific aims are to determine proportion of individuals using the Internet to obtain information about the use of club and other drugs; to assess the association of knowledge, attitudes, and behavior toward drugs in which the Internet is used; and to determine the characteristics of individuals whose self-reported drug-using behavior has been altered by information obtained from the Internet.

5 U01 CA81457 (Boyett/CHB subcontract: Poussaint) 04/01/04-03/31/09
NIH/NCI $182,983
Pediatric Brain Tumor Consortium (PBTC)
The primary goal of this project is the establishment of a Neuroimaging Center for the Consortium. The center will develop and coordinate imaging protocols of PBTC trials, collect images, analyze data sets and establish a database of imaging results.

5 U01 CA81457 (Boyett/CHB subcontract: Poussaint) 01/01/03-03/31/04
NIH/NCI $260,141
Pediatric Brain Tumor Consortium (PBTC)
The primary goal of this project is the establishment of a Neuroimaging Center for the Consortium. The center will develop and coordinate imaging protocols of PBTC trials, collect images, analyze data sets and establish a database of imaging results.

R01 DK062363 (Castillo) 09/30/02-6/30/07
NIH/NIDDK $391,304
Metabolism of Endothelial Dysfunction in Renal Disease
The major goals of this project are to conduct a randomized, controlled, mechanistic study of the in vivo regulatory mechanisms of the metabolic pathways involved in endothelial dysfunction, in end stage renal disease and chronic renal disease patients and in healthy controls.
Effect of Prone Positioning in Pediatric Acute Lung Injury
The major goals of this project are to conduct a multi-center, randomized, non-crossover, controlled clinical trial comparing early, repeated, and prolonged prone positioning with supine positioning in children with acute lung injury or acute respiratory distress syndrome.

Sedation Management in Pediatric Patients supported on Mechanical Ventilation for Acute Respiratory Failure
The purpose of this two-year project (randomized controlled clinical trial of two matched pediatric intensive care units in two different hospitals) is to pilot test an intervention to change sedation management in pediatric patients supported on mechanical ventilation for acute respiratory failure in the pediatric intensive care unit (PICU). The hypothesis is that pediatric patients managed per sedation protocol will experience fewer days of mechanical ventilation than patients receiving usual care will.

Weight Control and Weight Change among Adolescents
The aim of this study is to assess the behavioral predictors of weight gain and the development of overweight and obesity in adolescence and early adulthood in the National Longitudinal Study of Adolescent Health (Add Health).

30 Year Follow-up of Mental Health Outcomes Following Childhood Malnutrition
The goal of this project is to assess the long-term cognitive and mental health consequences of infant malnutrition in adulthood. Individuals who were followed from infancy through late adolescence will now be re-evaluated as adults in order to determine whether and how effects that persisted through adolescence may be evident among adults, and if so, what their consequences are for those individuals regarding mental health and adaptation.

Adrenal and Gonadal Hormone Replacement in Anorexia Nervosa
A randomized, controlled trial in young women with anorexia nervosa, designed to measure the effects of an 18-month course of adrenal and gonadal steroid replacement on bone mass, markers of bone turnover, serum levels of IGF-I, and bone strength as assessed through cross-sectional geometric analysis of DXA data.

Protein Metabolism in Critically Ill Surgical Neonates
The project is designed to determine if the application of a hyperinsulinemic euglycemic clamp in parenterally fed neonates on Extracorporeal Life Support (ECLS) will result in an improvement in protein balance, and to elucidate the mechanisms by which the change occurs.
R01 DC05248 (Kenna) 8/16/02-07/31/06
NIH/NIDCD $225,000
Genetics and Pediatric Nonsyndromic Hearing Loss
A prospective cohort study to describe the phenotypic pattern of temporal bone abnormalities, progression of hearing loss, and cognitive development in infants and children with Cx26 mutations in relation to other children with nonsyndromic sensorineural hearing loss.

R01 DA018848 (Knight) 09/30/04-08/31/09
NIH/NIDA $429,442
Screening and Brief Advice to Reduce Teen Substance Abuse
The overall goal of this project is to augment the screening/brief advice intervention with educational materials, and then to assess the efficacy of this approach within a network of primary care practices.

R01 DA014553 (Knight) 06/01/04-03/31/09
NIH/NIDA $250,000
A Medical Office Intervention for Adolescent Drug Use
A randomized trial of a brief intervention, developmentally appropriate for adolescents and practical for use in busy clinic settings, designed to test its effect on drug use, engagement in treatment, and other substance-related outcomes. Factors that moderate or mediate the effect of intervention will be identified and measured.

R37 AI24643 (Lagakos / subcontract) 4/1/87-1/31/06
NIH/NIAID $21,919(salary only)
Statistical Methods in AIDS Research
The major goals of this project are to conduct biostatistical research in problems arising in HIV/AIDS research.

R01 MH59532 (Laird / subcontract) 9/30/98-11/30/05
NIH/NIMH $21,919(salary only)
Family Based Tests of Association for Complex Diseases
The major goal of this project is to enable the discovery of genes underlying complex traits using family-based association tests that detect linkage disequilibrium while protecting against spurious evidence of association due to population admixture.

R01 EB01998 (Levine / CHB subcontract: Estroff) 07/01/03-05/31/08
NIH/BIDMC $165,436
MRI of Fetal Ventriculomegaly: Morphology and Outcome
Comparison of Magnetic Resonance Imaging to Ultrasound for prenatal diagnosis, pregnancy management, and prediction of newborn cognitive, motor, and psychosocial development in cases of ventriculomegaly.

R01 DK63554 (Ludwig) 09/30/02-09/29/04
NIH/NIDDK $150,000
Sugar-Sweetened Beverages and Weight Gain
A randomized trial to determine the contribution of sweetened beverage consumption to obesity in adolescents.
R01 DK59240 (Ludwig) 4/01/02-3/31/05
NIH/NIDDK $285,001
Glycemic Index, Obesity, Insulin Resistance, and CVD Risk
Two related studies in obese adolescents: (1) a randomized controlled trial of a low-glycemic-index diet for treatment of obesity and prevention of related complications; (2) a crossover feeding study investigating the effects of weight-maintaining diets differing in glycemic index on insulin resistance and cardiovascular risk factors.

R01 DK59240-S1 (Ludwig/Botero) 4/01/02-2/28/06
NIH/NIDDK $103,189
Glycemic Index, Obesity, Insulin Resistance, and CVD Risk
(Research Supplement for Underrepresented Minorities)
Two related studies in obese adolescents: (1) a randomized controlled trial of a low-glycemic-index diet for treatment of obesity and prevention of related complications; (2) a crossover feeding study investigating the effects of weight-maintaining diets differing in glycemic index on insulin resistance and cardiovascular risk factors.

S07 RR013150 (Mandell) 09/01/02-08/31/04
NIH/NCRR $150,000
Human Subjects Research Enhancements Program
The goal is to develop recommendations to strengthen the informed consent process for clinical research at Children’s Hospital Boston. In addition one or more sustainable educational initiatives designed to enhance and strengthen the process of obtaining informed consent in pediatric research will be developed.

M01 RR02172 (Mandell) 04/01/04-03/31/09
NIH/NCRR $1,965,575
General Clinical Research Center
The major goals of this project are to provide the clinical research infrastructure for medical scientists who conduct patient-oriented research.

200-2003-01601 (Mandl) 09/12/03-11/30/04
DHHS/CDC $136,263
Pediatric Hospital Based Sentinel Surveillance Network for Vaccine Preventable Diseases
The purpose of this project is to determine the feasibility of conducting surveillance for vaccine preventable diseases.

U01 HL63411 (Newburger) 07/05/00-06/30/05
NIH/NHLBI $442,856
Clinical Trial of Hematocrit Strategy in Heart Surgery
The major goals of this project are to compare neurodevelopmental outcome and early postoperative course after two strategies of hemodilution during hypothermic cardiopulmonary bypass in infants undergoing reparative open-heart surgery.
P50 HL074734 (Newburger) 02/15/04-1/31/09
NIH/NHLBI $2,971,830 (Core A: $246,165)

SSCOR in Pediatric Heart Development and Disease
The goal of the SSCOR is to improve the prevention, detection, treatment, and outcomes of tetralogy of Fallot (TOF). There are 3 clinical and 3 basic projects that represent the diverse, but intersecting approaches to this central objective. In addition, there are 4 Core units to support the projects. Core A will provide data management, biostatistical analysis, and administrative support for all projects part of the SSCOR.

R01 HL077681 (Newburger) 07/15/04-06/30/09
NIH/NHLBI $377,205

Outcomes in Adolescence after Repair of d-TGA
The goal of this project is to characterize more fully any late effects of the arterial switch operation of the d-transposition of the great arteries (d-TGA). This study will utilize the same group of 160 children whom have been followed in a previous prospective single-center study during the perioperative period, and at ages 1, 4, and 8 years (for neurologic, developmental, speech and MRI studies).

R01 HL68922 (Platt) 09/30/01-07/31/06
NIH/NHLBI $653,056

Genetic Modifiers of Severity in Sickle Cell Anemia
This study proposes to identify the genes that influence baseline white blood count (WBC) in sickle cell anemia (SS) by studying a large series of nuclear and extended families with an SS proband.

R01 HS014947 (Porter) 09/30/04-09/29/06
DHHS/AHRQ $219,174

ParentLink: Better and Safer Emergency Care for Children
The goal of this proposal is to determine whether implementation of a patient-centered health information technology – ParentLink – can address system-level deficiencies and the unique “just-in-time” information needs of Emergency Department physicians and the parents of ill children. The proposed project would deliver an innovative product – an electronic interface linked to a pediatric knowledge base that integrates parent-derived data with best practices for safe and effective emergency care across five common pediatric disease conditions: occult bacteremia, otitis media, urinary tract infections, asthma, and head trauma.

FD-R-002202 (Rufo) 09/30/02-09/29/05
FDA $149,988

Clotrimazole Enemas for Pouchitis in Children and Adults
This study is a Phase II/II double-blinded, placebo controlled, dose escalating trial that will test the efficacy of topical CLT therapy (delivered as a retention enema) in two cohorts of pediatric and adult patients with pouchitis.
U19 AI45955 (Taylor/CHB subcontract: Wypij) 09/30/99-07/31/05
NIH/NIARID $34,504

Severe Malaria in African Children: A Clinical Network
The major goals of this project are to develop a clinical trials network for severe malaria in African children, which will provide a new structure for the rapid and efficient evaluation of novel treatments for this killing disease. The network will also provide a framework for collecting the data necessary to validate clinical observations made in individual sites and to evaluate pathogenetic hypotheses, which are necessary steps in the development of new malaria interventions.

P01 NS38475 (Volpe) 12/10/99-11/30/04
NIH/NINDS
Periventricular Leukomalacia in the Premature Infant
To study the pathogenesis of periventricular leukomalacia in premature infants and to use the results to formulate innovative preventative and therapeutic interventions.

R03 MH65152 (Woods) 07/01/03-06/30/05
NIH/NIMH $50,000

HIV Prevention: Providers as Agents of Change
The goals of this new initiative will include developing and testing culturally and developmentally sensitive measurement tools specifically for adolescent girls being treated for STD's concerning the association of provider-patient relationships and mutuality of exchange of information with return for subsequent health care visits.

B. NIH Career Development Grants

K01 DK62237 (Ebbeling) 08/15/02-06/30/05
NIH/NIDDK $111,400

Motivating Obese Adolescents to Reduce Risk for Diabetes
The Mentored Research Scientist Development Award provides support for an intensive, supervised career development experience in one of the biomedical, behavioral, or clinical sciences leading to research independence. The aim of this particular project is to evaluate a directive, patient-centered counseling style for assisting obese girls in modifying diet and physical activity behaviors and equipping their mothers to provide needed support.

K08 HS13333 (Landrigan) 09/01/02-08/31/03
DHHS/AHRQ $116,500

Effects of Sleep Loss and Night Work on Patient Safety
The major goal of this Mentored Clinical Scientist Development Award is to develop the investigators' expertise in the impact of sleep deprivation and night work on patient safety. The proposal aims to study the manner in which interns' work schedules and sleep deprivation affects patient safety.
K23 HL074202 (Levy)  07/01/03-06/30/08
NIH/NHLBI                  $116,500
Family Based Analysis of Modifiers of CF Lung Disease
The purpose of this mentored patient-oriented research career development award is to support the career development of investigators who have made a commitment to focus their research endeavors on patient oriented research. This particular project is to identify key associations between genetic variation and clinical inflammatory markers that are responsible for pulmonary disease severity in cystic fibrosis.

K08 HS013675 (Lightdale)  06/01/03-05/31/07
DHHS/AHRQ                  $116,500
Improving Safety of Pediatric Sedation
Mentored Clinical Scientist Development Award, goals of which are to define adverse outcomes associated with pediatric sedation and to develop prediction rules to help avoid adverse events during sedation for pediatric gastrointestinal endoscopy.

K23 HL075502 (Ordonez)  07/01/04-06/30/09
NIH/NHLBI                  $118,225
P. aeruginosa Virulence in Cystic Fibrosis Lung Disease Progression
The purpose of this mentored patient-oriented research career development award is to support the career development of investigators who have made a commitment to focus their research endeavors on patient oriented research. The goal of this project is to use a functional genomics approach to identify virulence factors associated with progression of CF lung disease.

K08 HS11660 (Porter)  07/01/02-06/30/05
DHHS/AHRQ                  $115,805
Informative Technology Linking Parents and Providers
Test of a computer-based system for improving health communication in the emergency department in cases of pediatric asthma. The hypothesis is that by transmitting parents’ data directly to care providers, the system will improve parents’ satisfaction in the domains of communication and partnership as well as asthma-specific process measures of quality of care.

K01 DP000089 (Rhodes)  09/30/04-09/29/07
DHHS/CDC                   $277,708
Health Values and Treatment of Pediatric Type 2 Diabetes
The goal of this mentored research scientist development award is to provide training in health services research, and to develop expertise in research methods and disciplines that will be used to develop health promotion and disease prevention strategies for children with, and at risk, for type 2 diabetes. The study proposed will evaluate the role of health preferences in the treatment of type 2 diabetes in children.
K23 DK02729 (Rufo) 09/30/99-06/30/04 NIH/NIDDK $116,500

Clotrimazole Therapy for Human Diarrheal Diseases
The purpose of this mentored patient-oriented research career development award is to support the career development of investigators who have made a commitment to focus their research endeavors on patient oriented research. The specific goal of this translational research project is to evaluate the efficacy of orally and topically administered imidazole antibiotic clotrimazole in the treatment of secretory and inflammatory diarrheal disease.

K23 RR016080 (Schachter) 08/01/00-07/31/05 NIH/NCRR $116,200

Nuclear Factor Kappa B in Pediatric Nephrotic Syndrome
The purpose of this mentored patient-oriented research career development award is to support the career development of investigators who have made a commitment to focus their research endeavors on patient oriented research.

C. Glaser Pediatric Research Network: Design, Analysis and Coordinating Center

(Wypij) 09/01/02-08/31/05
Glaser Pediatric Research Network $150,856
Design, Analysis, and Coordinating Center (DACC) for the Glaser Pediatric Research Network
The DACC provides leadership in protocol development and statistical design for GPRN, a consortium of pediatric academic medical centers performing multi-center research, and conducts training in clinical research methods for the GPRN Fellowship program.

(Wilson/CHB subcontract: Lenders/DACC: Osganian) 12/01/02-02/28/07
Glaser Pediatric Research Network $90,414
Design, Analysis, and Coordinating Center (DACC): A Multi-center, Randomized, Placebo Controlled, Double Blind Trial of Metformin in Overweight Adolescents
The purpose of the study is to determine if the drug Metformin will result in decreased obesity among obese adolescents.

(Neufeld/DACC: Feldman) 12/01/02-5/31/05
Glaser Pediatric Research Network $51,646
Design, Analysis, and Coordinating Center (DACC): Open Label, Phase I/II Trial of Rituximab for Chronic, Severe Idiopathic Thrombocytopenic Purpura in Children and Adolescents
This is a pilot phase open label study to evaluate the effectiveness of rituximab in severe or refractory pediatric ITP and to obtain further safety information on rituximab.

(Moss/CHB subcontract: Jaksic/DACC: Wypij) 12/01/02-11/30/06
Glaser Pediatric Research Network $78,424
Necrotizing Enterocolitis (NEC) Surgical Database
This study will develop a multi-center prospective data collection process for necrotizing enterocolitis in order to provide accurate data regarding practice of treatment and variability of care between different centers.
D. Foundation/Association/Other

(Bennett)  
St. Giles Foundation  
Genetic Modifiers of Childhood Chronic Immune Thrombocytopenic Purpura (ITP)  
This study has two specific aims: 1) to collect precise and detailed phenotypic data from the North American Pediatric Chronic ITP Registry to study a large cohort of patients with chronic ITP in a prospective manner, and 2) to analyze the association of candidate genes to the clinical severity of chronic ITP and its response to therapy.

(Curley)  
Gustavus and Louise Pfeiffer Research Foundation  
Sedation Management in Pediatric Patients Supported on Mechanical Ventilation  
The purpose of this two-year project (randomized controlled clinical trial of two matched pediatric intensive care units in two different hospitals) is to pilot test an intervention to change sedation management in pediatric patients supported on mechanical ventilation for acute respiratory failure in the pediatric intensive care unit (PICU). The hypothesis is that pediatric patients managed per sedation protocol will experience fewer days of mechanical ventilation than patients receiving usual care will.

(Duggan)  
Mass Vitamin Litigation Fund  
Body Composition in Cancer Patients Undergoing Stem Cell Transplantation  
A randomized trial in children undergoing stem cell transplantation, who typically lose muscle mass as a side effect of chemotherapy, designed to test whether reduced parenteral nutrition and vitamin E supplementation will result in better tolerance of chemotherapy and their reduced levels of resting energy expenditure.

(Grand)  
Crohn's & Colitis Foundation of America  
Use of Intranasally Administered Calcitonin in the Treatment of Osteopenia and Osteoporosis in Children, Adolescents, and Young Adults with IBD: A Pilot Study  
The goals of this pilot trial are to compare the effect of treatment with nasally administered calcitonin plus calcium and vitamin D supplementation to that of treatment with placebo plus calcium and vitamin D supplementation on the lumbar bone mineral density of patients with the diagnosis of IBD and low lumbar bone mineral density.

(Harris)  
Aerosmith Foundation  
A Needs Assessment of Health Risk Behaviors and Protective Factors among Students attending Two Boston High Schools  
This study is part of an ongoing collaboration between Children’s Hospital adolescent health clinicians/researchers and two nearby high schools to identify, and develop strategies to address, student health needs. The first collaborative project is an anonymous needs-assessment survey of all students in both schools.
(Hirsch, CHB subcontract: Osganian) 01/01/02-12/31/06
Robert Wood Johnson Foundation $7,930
Injury Free Coalition for Kids of Worcester at the University of Massachusetts Memorial Hospital
This study proposed to evaluate a community-based injury prevention program that targets youth ages 19 years old and younger. The intervention will target the more prevalent injuries in the Greater Worcester area and the evaluation will consist of an injury surveillance program to monitor trends in the incidence of hospitalized injuries and fatal injuries in the communities that define the Greater Worcester Area.

045222 (Knight) 5/1/02-10/31/05
Robert Wood Johnson Foundation $251,088
Implementation of Medical Office Screening for Adolescent Substance Abuse
The major goal of this project is to determine how screening is best implemented in different clinical settings and, most importantly, how pediatric clinicians can best respond to those who screen positive.

049207 (Levy) 6/1/03-5/30/04
Robert Wood Johnson Foundation $91,624
A National Survey of Physicians' Adolescent Drug Testing Practices
The major goals of this project are to determine drug-testing practices used by physicians, to compare these with existing policy guidelines, to compare practices used by physicians in different specialties, and to inform policy makers of the results.

047191 (Mooney) 11/15/02-11/14/06
Robert Wood Johnson Foundation $52,720
Injury Free Coalition for Kids of Boston
The purpose was to become the Injury Free Coalition for Kids of Boston site. The planned intervention was based upon the needs expressed by the community and data concerning injuries to children. The surveys indicated that families perceived home, fire, and pedestrian safety as their top three concerns. The interventions will include a home safety program, a community safety program, and a pedestrian safety program.

(Nugent) 10/02/02-02/27/04
Deborah Munroe Noonan Memorial Fund $60,090
The First Assessment: Using the CLNBAS to Promote the Development of At-Risk Infants and Families in Early Intervention Settings
This study will test the effectiveness of the Clinical Neonatal Behavioral Assessment Scale (CLNBAS) (Nugent and Brazelton, 2001), as an assessment and intervention system for infants who are at-risk for developmental delay. The CLNBAS is a neurobehavioral examination, applicable for infants from birth to three months adjusted age, consisting of 18 items and designed to examine the infant’s reflexes, motor behavior, crying and consolability, and social interactive capacities.
(Porter) 07/01/02-06/30/04
Charles H. Hood Foundation $41,782
Informative Technology Linking Parents and Providers
The project investigates outcomes of health communication and quality of care for pediatric asthma, a disease condition notable for its differential and negative impact on urban poor and minority youth. The hypotheses are 1) the provision of parents’ data to providers alters parents’ satisfaction in the domains of communication and partnership, and 2) the provision of parents’ data to providers alters asthma-specific process measures of quality.

(Shrier) 09/01/04-08/31/05
Harvard Medical School 50th Anniversary Program $ 24,611
Affective States and Sexual Behavior in Depressed Adolescents
The primary goal is to demonstrate the feasibility of recruiting depressed adolescents to participate in a momentary sampling study of mood and HIV/Sexually Transmitted Infections (STI) risk behavior. The secondary objective is to explore the associations of antecedent, concurrent, and subsequent positive and negative affect, and affect variability with sexual thoughts, desires, and risk behaviors among depressed adolescents.

(Taveras) 09/01/04-08/31/05
Deborah Munroe Noonan Memorial Fund $68,182
Improving Clinical Practice to Prevent and Manage Obesity in Children
This cross-sectional study of parents of overweight children and their pediatric clinicians will collect information regarding the 1) current delivery system for overweight prevention and management in primary care, 2) services available to parents and clinicians to support overweight management, and 3) type of overweight prevention interventions that parents and clinicians think most feasible. Knowledge obtained from this study will be used to design a clinical intervention to improve prevention of pediatric overweight and management of its associated complications and disabilities.

GERAFF (Ward) 07/01/02-06/30/04
GE-AUR Radiology Research Academic Fellowship $65,000
The objective of this health services research project is to prospectively evaluate whether, after a fetal chest mass has been discovered on US, MRI provides additional and more accurate diagnostic and/or prognostic information.

E. Industry

(Laufer) 05/01/03-06/30/06
Personal Products Worldwide $58,955
Assessment of the Utility of Salivary Hormonal Assays for the Determination of Menarche
The purpose of this study is to determine if consistent changes in the selected hormonal markers, introital pH, and body mass index could be used to predict menarche.
VIII. Staff Accomplishments and External Contributions

This section highlights some of the independent and external contributions of the CRP faculty to research and teaching as well as participation on national committees.

**Stavroula Osganian, M.D., Sc.D.**

**Presentation**
School Nurse Delivered Tobacco Cessation Intervention for Adolescents; sponsored by The National Conference on Tobacco or Health, Boston, MA; December 2003

**External Teaching**
Small Group Leader; sponsored by Harvard School of Public Health, Clinical Effectiveness Program; Summer 2004

**National Committee**
Chair, Data and Safety Monitoring Board for the Girls Health Enrichment Multi-site Studies (GEMS); sponsored by The National Heart Lung and Blood Institute; 2003-present

**Sion Kim Harris, Ph.D.**

**Presentation**

**Leslie Kalish, Sc.D.**

**Presentation**
Stop Hypertension with the Acupuncture Research Program (SHARP): Clinical Trial Design and Screening Results; sponsored by The Harvard Pediatric Health Services Research Fellowship Program; November 2003

**National Committee**
Data and Safety Monitoring Board for multicenter clinical trial: Program to Reduce Incontinence by Diet and Exercise (PRIDE); sponsored by NIDDK; 2004

**Mei-Chiung Shih, Ph.D.**

**External Teaching**
Course Developer and Lecturer; Regression and Analysis of Variance in Experimental Research (BIO 211); Department of Biostatistics, Harvard School of Public Health; January-May 2004.

**Presentation**
Measuring the strength of association at candidate genes for family-based association studies; sponsored by The International Conference on Analysis of Genomic Data; May 2004

**Henry Feldman, Ph.D.**

**National Committee**
Scientific Review Panel: Overweight and Obesity Control at Worksites; sponsored by The National Heart, Lung, and Blood Institute, Bethesda, MD; Jun. 18, 2004.

National Symposium
Invited workshop: Research Designs for Complex, Multi-Level Health Interventions and Programs. Presentations on Quasi-Experimental Designs for Promotion of Physical Activity, with Deborah Cohen and Ross Brownson; Time Series Design and Analysis: An Overview; sponsored by The National Institutes of Health and Centers for Disease Control, Bethesda, MD; May 4-5, 2004.

National Training Seminar

Clarissa Valim, M.D., Sc.D.

External Teaching
Course developer and Lecturer; Short Course on Introduction to Biostatistics; Albert Schweitzer Hospital, Lambarene, Gabon; September 2004.

David Wypij, Ph.D.

External Teaching
Course Developer and Lecturer; Methods II (BIO 233); Department of Biostatistics, Harvard School of Public Health; January-May 2004.

Course Developer and Lecturer; Short Course on Case Studies in Biostatistics; Treviso, Italy; June 2004
Introduction to Clinical Trials; Servico de Bioestatistica e Informatica Medica, Faculdade de Medicina da Universidade do Porto, Portugal; September 2004.

Course Developer and Lecturer; Short Course on Repeated Measures and Longitudinal Data Analysis; Servico de Bioestatistica e Informatica Medica, Faculdade de Medicina da Universidade do Porto, Portugal; September 2004.
IX. Program Resources

There has been a substantial institutional commitment to the Program, in terms of both space and operating budget, which has facilitated the growth and visibility of the Program. The Program presently occupies 3,300 square feet of office space located on the Fourth Floor of 333 Longwood Avenue with fourteen offices, thirteen cubicles, and one conference room.

Institutional and other sources of support for the Program are shown in Table IX-1. Institutional support for the Clinical Research Program (CRP) has increased substantially since the inception of the Program and now totals $1.8 million. Equally exciting has been the rapid growth in funding from collaborative relationships with clinical investigators and CRP extra-mural funding, which now totals nearly $1 million.

<table>
<thead>
<tr>
<th>FISCAL YEAR</th>
<th>INSTITUTIONAL BUDGET</th>
<th>GRANT SUPPORT/OTHER FUNDING</th>
<th>TOTAL</th>
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</table>

*projected

Figure XI-1

Clinical Research Program Funding

- Grant Support/Other Funding
- Institutional Funding
- Budget
Appendix A - Program Description and Request for Assistance Form
Clinical Research Program
333 Longwood Ave., – 4th Floor
Phone: 617-355-2463 / fax: 617-355-2312
cr@childrens.harvard.edu

Program Description and Application

Mission:
The mission of the Clinical Research Program is to enhance the quality of clinical research at Children’s Hospital by providing to members of the research community scientific support, education, and collaborative assistance in the design, conduct, and analysis of clinical research. We also closely interact with the Children’s Hospital General Clinical Research Center (GCRC) and provide some support to GCRC-funded studies.

CRP Personnel: [Staff Biographies]

- **Directors:** Senior clinical researchers with extensive experience in conducting clinical research studies.
- **Biostatisticians:** Skilled in protocol and grant development, study design, and data analysis.
- **Survey Epidemiologists:** Skilled in the design and analysis of surveys.
- **Clinical Research Specialists:** Skilled in the design of case report forms and questionnaires, quality assurance procedures, and the development of manuals of operations.
- **Applications Specialists:** Skilled in data management system design, including database and web application development.
- **Budget Specialists:** Experienced in budget development and the grant submission process.

Funding Sources:
The CRP receives a portion of its support from the hospital as part of the institution’s commitment to clinical research. The majority of our funding comes from federal, foundation, and other awards that are obtained by either our staff or the investigators with whom we collaborate. The CRP can offer limited consultative services at no cost (up to 10 hours per project) to all clinical research investigators, but assistance that is more extensive will require a collaborative effort and funding. As we plan our role in your research, we will estimate your requirements and a realistic budget will be developed to formalize our collaboration. We also strongly encourage investigators to consider seeking GCRC support for their clinical studies wherever possible.

Core Resources:

Consultative Services:
- Protocol/Grant Proposal Development
- Study Design
- Sample Size and Power Calculations
- Analysis Methods
- Randomization
- Case Report Form and Survey Design
- Data Management and System Design
- Data Interpretation
- Budget Development
- Mentoring

Educational Seminars:
- Introduction to Clinical Research (for Junior Investigators)
- Career Development Block (for Residents)
- Coordinating Clinical Research (for Project Coordinators)

Collaboration:
- Grant Proposal Development
- Study Implementation
- Data Analysis and Manuscript Preparation
**Assistance Procedures:**

To be eligible for CRP assistance, you must have an appointment at Children’s Hospital or be a Children’s Hospital employee. For assistance with any aspect of study implementation or with data analyses, you must have a written study protocol with IRB approval to conduct the research.

- For each request, complete the CRP Investigator Request Request for Assistance form and submit by interoffice mail or e-mail: crp@childrens.harvard.edu. We will respond within 10 business days to schedule an initial planning meeting.
- Along with your request form, send all pertinent background materials (including a draft of your research aims, draft protocol or grant proposal, guidelines for submission of the grant application, draft data forms, etc.). These materials should be sent to the CRP at least one week before your meeting.
- At the initial planning meeting, CRP staff will meet with you (and your mentor, if applicable) to assess your request. At the initial planning meeting, we will begin to discuss feasibility and resources. This includes an evaluation of tasks to be performed, assignment of responsibilities, and the need for budgetary support.
- At a follow-up meeting, we will develop a mutually agreed-upon written plan of action and an estimate of costs, when needed.
- Consultative and collaborative work will proceed according to an agreed-upon timeframe.

**Timeframes:**

Grant proposal applications as well as study protocols vary in complexity and length. Most National Institutes of Health (NIH) applications (R01’s, K23’s and other funding mechanisms) as well as applications to major foundations require significant time and effort to prepare. Furthermore, the CRP provides assistance to many investigators at any given time. Therefore, we ask that investigators adhere to the following timeframes when requesting assistance from the CRP on a grant proposal or study protocol.

- We recommend beginning to work with us at least 90 days before the submission deadline or due date and require a minimum of 60 days.
- We also require a complete first draft of the grant proposal or study protocol and preliminary budget a minimum of 30 days before the submission deadline or due date.
- If this timeframe is not met or we feel there is not adequate time to assist you, we may recommend delaying submission to the next cycle.

We also ask that you plan ahead for assistance with study implementation and data analyses for manuscripts, abstracts, or presentations. Most studies require **6 to 12 months** of planning prior to recruitment of subjects. Therefore, for assistance with study implementation, we ask that you begin working with us well in advance of your anticipated start of recruitment. Similarly, data analyses require sufficient time for data cleaning, statistical programming, interaction with the investigators, and writing and review of manuscripts. Therefore, we recommend beginning to work with us **60 to 90 days** before any deadline, depending on the scope and complexity of the analyses.

**CRP Contact Information:**

- The CRP Offices are located on the 4th floor at 333 Longwood Avenue. We can be reached by phone at 617-355-2463 or by e-mail at crp@childrens.harvard.edu.
Investigator Request for Assistance

Instructions: Please complete our Request for Assistance questionnaire to help us better assist you with your project. Submit this form via e-mail, fax, or interoffice mail (see above). **A CRP staff member will contact you within the next week to schedule a meeting.**

1. Requestor:
   Last Name ___________________________________________ First Name __________________________ CH ID# ______________________

2. Title: [ ] Prof. [ ] Assoc. Prof. [ ] Asst. Prof. [ ] Instructor [ ] Fellow [ ] Resident [ ] Nurse [ ] Other (specify): __________________________

3. Department: __________________ Division: __________________ Office Location __________________

4. E-mail __________________________ Phone/Ext# __________________ Page # __________________

5. Research Mentor (if applicable) __________________________

6. Principal Investigator: [ ] Check if same as name of requestor
   Last Name ___________________________________________ First Name __________________________ CH ID# ______________________

7. Title (same as on protocol):
   __________________________

8. IRB Information
   a. Has the protocol been submitted to the IRB?
      [ ] Yes (Protocol #__________________________)
      [ ] No (GO TO Q. 9)

   b. What is the current status of your protocol with the IRB?
      [ ] Full Approval
      [ ] Conditional Approval
      [ ] Deferred

9. What type of assistance are you requesting [see program description for explanation]? (check one)
   [ ] Collaboration
   [ ] Consultation
10. What do you require assistance with...? (check all that apply)

a. Grant Proposal / Protocol Development
   - Grant Proposal Preparation
   - Protocol Preparation
   - Statistical Analysis Plan
   - Power and Sample Size Determination
   - Data Monitoring Plans (DSMB) / Interim Analysis Plan
   - Concept Proposal Development
   - Budget Assistance

b. Study Implementation
   - Case Report Form Development
   - Survey/Questionnaire Design
   - Randomization
   - Database Development
   - Data Management
   - Assistance with Existing Database

c. Data Analysis/Interpretation
   - Presentation (MM/DD/YYYY): ___/___/______
   - Manuscript (MM/DD/YYYY): ___/___/______
   - Statistical Analysis/Interpretation of Results

d. Other (Specify below)
   - 

11. Funding Status

a. Is your project currently funded?  [ ] Yes  [ ] No

b. Are you presently applying for funding?  [ ] Yes  [ ] No; Skip to Q. 12

c. If Yes, what type of application is it? (check one)
   - [ ] New Submission
   - [ ] Resubmission
   - [ ] Competing Renewal
   - [ ] Non-Competing Renewal

d. When is the deadline for submission? (MM/DD/YYYY): ___/___/______
12. Funding Sources

☐ NIH

a. Name of institute / Center: ____________________________

b. Type of funding mechanism (check one): 
   ☐ R01  ☐ R03  ☐ R21
   ☐ K01  ☐ K08  ☐ K23  ☐ K24

c. Is this a response to an announcement? ☐ Yes ☐ No
   i. If Yes, what is the type? ☐ RFA ☐ RFP ☐ PA
   ii. If Yes, what is the number? ____________________________

☐ Other Federal Agency: _______________________________________________________________________

☐ Foundation / Association: 1) __________________________________________________________________
                                2) ___________________________________________________________________

☐ Industry Sponsor: ___________________________________________________________________________

☐ Internal Award: _____________________________________________________________________________

☐ Department/Division/Program Funds: _______________________________________________________________________

☐ Other (specify): _____________________________________________________________________________

13. Will data need to be submitted to the FDA? ☐ Yes ☐ No

14. Will this protocol utilize the GCRC or its resources? ☐ Yes ☐ No

   a. If Yes, what is the current status?
      ☐ Approved
      ☐ Pending
      ☐ Not yet submitted

15. Other Requests / Comments
____________________________________________________
____________________________________________________

NOTE: Make certain that you send all pertinent background materials (including a draft of your research aims, draft protocol or grant proposal, guidelines for submission of the grant application, draft data forms, etc.) to the CRP along with your request form at least one week before your meeting. This will lead to a much more productive first session. Thank you!
Appendix B – Staff Publications

2004 Publications


Ebbeling CB, Sinclair KB, Pereira MA, Garcia-Lago E, Feldman HA, Ludwig DS. Compensation for energy intake from fast food among overweight and lean adolescents. JAMA, 2004; 291:2828-2833.


McGrath E, Wypij D, Rappaport LA, Newburger JW, Bellinger DC. Prediction of IQ and achievement at age 8 years from neurodevelopmental status at age 1 year in children with D-transposition of the great arteries. Pediatrics, 2004; [Epub ahead of print]


2003 Publications


Cullen KW, Baranowski T, Owens, E, de Moor C. Availability, accessibility, and preferences for fruit, 100% fruit juice, and vegetables influence child's dietary behavior. Health Education and Behavior, 2003; 30:615-626.


2004 Abstracts


2003 Abstracts


2004 Chapters/Reviews


2003 Chapters/Reviews


2003 Books

Appendix C – Course Agendas

A. Introduction to Clinical Research

Introduction to Clinical Research Schedule
Tuesday, July 13, 2004

8:00 - 8:30  CONTINENTAL BREAKFAST

8:30 - 8:45  Introduction and Course Overview
             Voula Osganian, MD, ScD
             David Wypij, PhD

8:45 - 9:30  Overview of Clinical Research
             Voula Osganian, MD, ScD
             David Wypij, PhD

9:30 - 10:30 Data Analysis I: Descriptive Statistics
              David Wypij, PhD

10:30 - 10:45 BREAK

10:45 - 11:30 Data Analysis II: Precision and Accuracy of Measurement
               David Wypij, PhD

11:30 - 11:45 The General Clinical Research Center (GCRC)
               Richard Grand, MD
               Kristine Jordan

11:45 - 12:00 Clinical Research at Children’s Hospital
               James Mandell, MD

12:00 - 1:00  LUNCH

1:00 - 1:30  Scientific Presentations
             Jonathan Finkelstein, MD

1:30 - 2:15  Ethical Issues in Pediatric Research
             Walter Robinson, MD

2:15 - 3:00  Designing Surveys and Questionnaires
             Sion Kim-Harris, PhD

3:00 - 3:15  BREAK

3:15 - 4:00  Observational Study Designs
             Voula Osganian, MD, ScD
Introduction to Clinical Research Schedule  
Wednesday, July 14, 2004

8:00 - 8:30  CONTINENTAL BREAKFAST

8:30 - 9:00  The Research Mentor  
Jordan Kreidberg, MD

9:00 - 10:00  Writing for Scientific Publication  
Jean Emans, MD

10:00 - 10:15  BREAK

10:15 - 11:30  Data Analysis III: Comparing Two Groups  
Henry Feldman, PhD

11:30 - 12:15  Clinical Trials: Design and Monitoring  
Jane Newburger, MD

12:15 - 1:15  LUNCH

1:15 - 2:45  Human Subjects, Institutional Review Board, and HIPAA  
Susan Kornetsky, MPH

2:45 - 3:00  BREAK

3:00 - 4:00  Data Analysis IV: Correlation and Regression  
Henry Feldman, PhD
Introduction to Clinical Research Schedule
Thursday, July 15, 2004

8:00 - 8:30  CONTINENTAL BREAKFAST

8:30 - 9:45  Statistical Issues in Study Design
             David Wypij, PhD

9:45 - 10:30  Bias and Confounding
              Clarissa Valim, MD, ScD

10:30 - 10:45  BREAK

10:45 - 11:45  Operational Issues in Conducting Clinical Research
               Christopher Duggan, MD

11:45 - 12:45  LUNCH

12:45 - 2:45  The Drug Development Process and Application of Good Clinical Practice (GCP) in Clinical Research
              Alberto Grignolo, Ph.D.

2:45 - 3:00  BREAK

3:00 - 3:30  Writing a Grant and Applying for Funding
              Voula Osganian, MD ScD

3:30 - 4:00  The NIH Scientific Review
              Voula Osganian, MD, ScD

4:00  Wrap-up
      Voula Osganian, MD, ScD
      David Wypij, PhD
**B. Coordinating Clinical Research**

**Coordinating Clinical Research Schedule**
March 25, 2004 8:30am-12:00pm/ March 30, 2004 1pm-5pm/ April 6, 2004 1pm-5pm

*Farley 1 Classroom*

**March 25, 2004: Human Subject Protections**

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>8:30-9:00</td>
<td>Continental Breakfast</td>
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<tr>
<td>9:00-9:10</td>
<td>Welcome and Course Overview</td>
<td>Stavroula Osganian</td>
</tr>
<tr>
<td>9:10-11:20</td>
<td>Human Subject Protection Responsibilities for Research Nurses/ Study Coordinators</td>
<td>Susan Kornetsky and IRB staff</td>
</tr>
</tbody>
</table>

- Before the Research Begins
  - Training Requirements
  - Protocol Submissions
  - Writing Informed Consents

- During the Research
  - Research Subject Recruitment
  - Continuing Renewals
  - 3 Year Re-writes
  - Amendments/ Revisions
  - Adverse Events

- After the Research
  - Working as a Research Team

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<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Presenter</th>
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</thead>
<tbody>
<tr>
<td>11:20-11:30</td>
<td>Quality Improvement and Human Subject Protection</td>
<td>Eunice Yim-Newbert</td>
</tr>
<tr>
<td>11:30-12:00</td>
<td>Obtaining Consent/Assent: Practical Techniques</td>
<td>Kristi Thomas</td>
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</table>

**March 30, 2004: Clinical Research Study Implementation**

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>1:00-1:30</td>
<td>Resources for Conducting Clinical Research</td>
<td>Stavroula Osganian</td>
</tr>
<tr>
<td></td>
<td>• Introduction to the CRP</td>
<td>Meg McCabe</td>
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<tr>
<td></td>
<td>• Introduction to the GCRC</td>
<td>Kris Jordan</td>
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<td></td>
<td></td>
<td>Christine Clark</td>
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<tr>
<td>1:30-2:00</td>
<td>Designing Clinical Research Studies</td>
<td>David Wypij</td>
</tr>
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2:00-2:45  Study Implementation and Data Management

- Operationalizing the Study Protocol:  
  **Manuel of Operations and Training**  
  Amy Kroepin
- Case Report Form Design and Completion  
  Amy Kroepin
- Managing the Data:  
  Database Design, Data Entry, Reports, and Error Resolution  
  Amy Kroepin

2:45-3:00  BREAK

3:00-3:30  Quality Control of Data Collection  
  Carol Sweeney

- Internal Study Performance Monitoring and External Study Audits
- Source Documentation (What, Why and How)

Study Closeout and Records Retention  Carol Sweeney

3:30-4:00  Clinical Research Financial Management  
  Kris Jordan
  Paula Longden

4:00-4:15  Training and Certification Resources  
  Maureen Clark

4:15-5:00  Questions and Discussion

April 6, 2004: Clinical Trials: FDA regulations and ICH Good Clinical Practice

This session will provide a general understanding of the drug development process and the US regulatory environment. You will be provided with commonly used clinical research definitions, abbreviations, acronyms, and resources. The regulatory historical framework, which is the underpinning of how clinical research is practiced today, will be discussed and the Code of Federal Regulations emphasized. The organizational structure and the roles of the Food and Drug Administration will be enumerated. The definition, purpose, origin, and importance of the International Conference on Harmonization (ICH) Good Clinical Practices will be discussed as well as the key elements of the phases of clinical research.

1:00-5:00  Regulatory historical framework  
  Code of Federal Regulations (ICH) Good Clinical Practices  
  Terry Himmelmann PA, MA, CCRA
C. Glaser Pediatric Research Network Symposium

Building a Career in Pediatric Clinical Research
Views from Academia, Government & Industry

A symposium sponsored by
Children's Hospital Boston
Clinical Research Program and General Clinical Research Center
Glaser Pediatric Research Network
Johnson & Johnson Family of Companies

HIM Lecture Room (Rm 138), Harvard Medical Conference Center
77 Avenue Louis Pasteur, Boston Friday, July 16, 2004

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>7:30–8:30</td>
<td>Registration, Continental Breakfast</td>
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<tr>
<td>8:30–8:45</td>
<td>Welcome</td>
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<tr>
<td>8:45–9:30</td>
<td>Philip A. Pizzo, MD, Stanford University School of Medicine</td>
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<td>Academic Careers in Pediatric Research</td>
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<td>9:30–10:15</td>
<td>Stephen P. Spielberg, MD, PhD, Dartmouth Medical School</td>
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<td>Industry-Academia Interface in Pediatric Research</td>
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<td>10:15–10:45</td>
<td>Refreshment Break</td>
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<tr>
<td>10:45–11:30</td>
<td>Dianne Murphy, MD, U.S. Food and Drug Administration</td>
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<td>Role of the FDA in Pediatric Drug Research</td>
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<td>11:30–1:00</td>
<td>Lunch: Roundtables</td>
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<tr>
<td>1:00–1:45</td>
<td>Yvonne Maddox, PhD, National Institute of Child Health and Human Development</td>
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<td></td>
<td>Federal Sponsorship of Pediatric Clinical Research</td>
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<tr>
<td>1:45–2:30</td>
<td>James Ware, PhD, Harvard School of Public Health</td>
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<td>Publishing Pediatric Research</td>
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<td>2:30–3:00</td>
<td>Refreshment Break</td>
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<tr>
<td>3:00–4:00</td>
<td>Charles Prober, MD, moderator, Glaser Pediatric Research Network</td>
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<tr>
<td></td>
<td>Panel Discussion: How Can I Make Best Use of Academic, Government, and Industry Resources?</td>
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<tr>
<td>4:00</td>
<td>Adjourn</td>
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