

**Report of the Acting Clinical Director**

**National Advisory Environmental Health  
Sciences Council Meeting**

**September 2009**

## NIEHS Clinical Research Program Updated Organizational Chart

Since the last NAEHS Council meeting in May 2009, several changes were made to the NIEHS Clinical Research Program's organizational chart (Figure 1). First, the Digital Infusions contract which provided support to the Office of Human Research Compliance was phased out. Second, initial staff was hired for the Clinical Research Unit (mostly through contract mechanisms) including a Clinical Research Manager, Research Nurse, Receptionist, Clinical Laboratory Technician and two Post-baccalaureate IRTAs. Third, the Environmental Autoimmunity Group had two positions re-instated (Staff Clinician and Postdoctoral IRTA) after an outstanding BSC Review in June 2009. Forth, several research groups which have primary affiliations within other DIR Programs were given secondary affiliations within the Clinical Research Program.

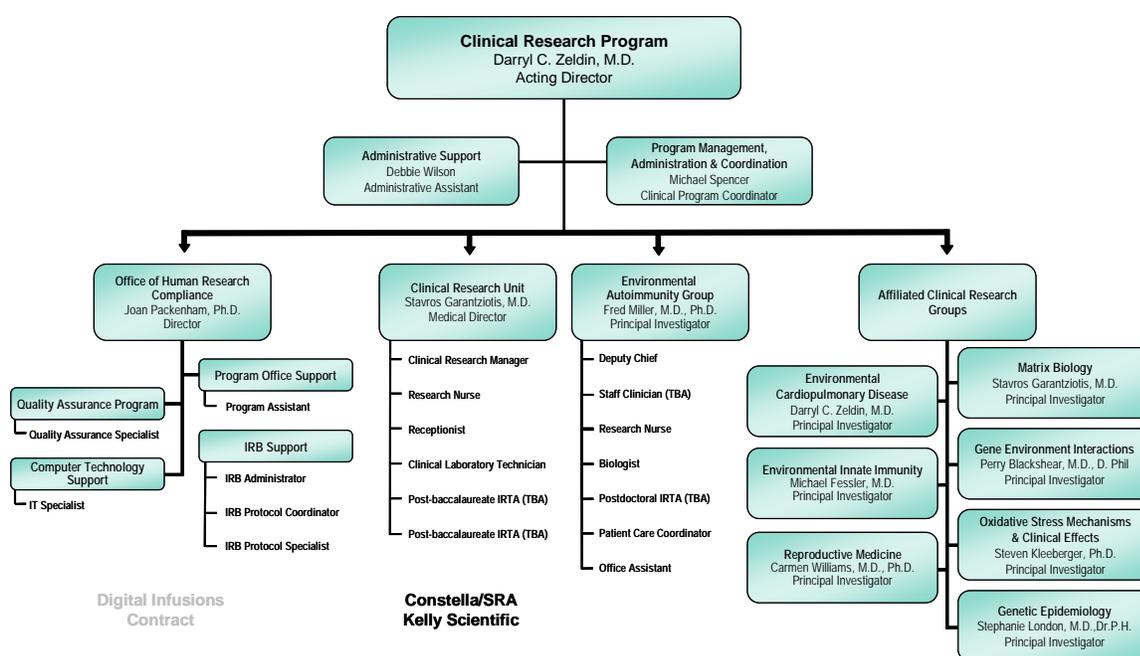


Figure 1. Organizational Chart of the NIEHS Clinical Research Program (updated September 2009)

## NIEHS Clinical Research Unit (CRU) Update

The NIEHS Clinical Research Unit (CRU) held its Grand Opening on July 27, 2009. The event, which was emceed by Joe Graedon (The People's Pharmacy), consisted of opening remarks from Dr. Linda Birnbaum, greetings from Drs. Michael Gottesman (NIH) and Robert Califf (Duke), remarks from numerous national, state and local officials, award presentations to individuals who were instrumental in the successful completion of the project, and a formal ribbon cutting ceremony. The event culminated with a Clinical Research Symposium consisting of three outstanding translational research talks. A copy of the program is appended below.

The National Institute of Environmental Health Sciences (NIEHS) is located in Research Triangle Park, North Carolina, and is one of the National Institutes of Health (NIH), the nation's premier biomedical research agency. The mission of the NIEHS is to reduce the burden of human illness and disability by understanding how the environment influences the development and progression of disease. As a part of this effort, the NIEHS has built a new Clinical Research Unit.

The NIEHS Clinical Research Unit is a 14,000 square foot facility specifically designed to host collaborative research that moves laboratory science into applications for improving human health and preventing disease. The facility will advance partnerships between NIEHS scientists and other scientists from local North Carolina universities and research institutes, and will also serve as a point of interface with the NIH Clinical Center in Bethesda, Maryland.

The new Clinical Research Unit is situated adjacent to the main NIEHS building, which houses the Institute's research laboratories, and will provide an easily accessible on-campus site to collect human tissue and fluid samples, carry out analysis, and conduct functional assessments of study participants. The Clinical Research Unit will accommodate outpatient research only, and will offer routine patient evaluation as well as specialized diagnostic and analytical capabilities, such as pulmonary function testing and various imaging procedures.

Scientists who will utilize the new facility have proposed a diverse array of research studies involving pulmonary diseases, medical genetics, cardiovascular diseases and reproductive health. And, the Clinical Research Unit will allow for advanced training opportunities for students and postdoctoral fellows whose research interests require access to clinical samples and patients.

Darryl Zeldin, M.D., is the Acting Director of the NIEHS Clinical Research Program and Stavros Garantziotis, M.D., is the Medical Director for the Clinical Research Unit. Together with the NIEHS leadership, Drs. Zeldin and Garantziotis have put in place a thorough scientific, human subjects protection and resource utilization review process to make certain that only the highest quality research is conducted at the facility, and to ensure patient safety at every step of the research process.

To learn more about the NIEHS Clinical Research Unit, visit our website at [www.niehs.nih.gov/clinicalunit](http://www.niehs.nih.gov/clinicalunit).






## Grand Opening

of the

## NIEHS Clinical Research Unit

**July 27, 2009 • 11:00 a.m.**

National Institute of Environmental Health Sciences  
David P. Rall Building • Rodbell Auditorium  
111 T.W. Alexander Drive  
Research Triangle Park, North Carolina



### I *Order of Service*

#### MASTER OF CEREMONIES

**Joe Graedon**  
The People's Pharmacy

#### OPENING REMARKS

**Linda Birnbaum, Ph.D.**  
Director, National Institute of Environmental Health Sciences  
and National Toxicology Program

#### GREETINGS FROM NIH

**Michael Gottesman, M.D.**  
NIH Deputy Director for Intramural Research

#### A LOCAL PARTNER'S PERSPECTIVE

**Robert Califf, M.D.**  
Vice Chancellor for Clinical Research, Duke University

#### OFFICIALS

**Kay Hagan, U.S. Senator from N.C.**  
**David Price, U.S. Representative from N.C., 4th District**  
**Bob Etheridge, U.S. Representative from N.C., 2nd District**  
**Brad Miller, U.S. Representative from N.C., 13th District**  
**Walter Dalton, Lieutenant Governor of N.C.**  
**Lanier Cansler, N.C. Secretary of Health and Human Services**  
**Michael Page, Durham County Commissioner**  
**William Bell, Durham Mayor**

#### AWARD PRESENTATIONS

**Darryl Zeldin, M.D.**  
Acting Director, NIEHS Clinical Research Program

ADJOURN TO NIEHS CLINICAL RESEARCH UNIT  
FOR RIBBON-CUTTING CEREMONY

### *Clinical Research Symposium*

#### SYMPOSIUM MODERATOR

**Stavros Garantziotis, M.D.**  
Staff Clinician  
Medical Director, Clinical Research Unit

1:30 P.M.

**Robert Califf, M.D.**  
Vice Chancellor for Clinical Research, Duke University

"Addressing Key Issues on Evaluating Mechanisms of Disease in Humans"

2:00 P.M.

**Philip Landrigan, M.D., M.Sc.**  
Professor and Chair of Community and Preventive Medicine  
Mt. Sinai Medical Center

"The National Children's Study — The Need and the Promise"

2:30 P.M.

**Franck Mauvais-Jarvis, M.D., Ph.D.**  
Associate Professor of Medicine  
Division of Endocrinology, Metabolism and Molecular Medicine  
Northwestern University

"Estrogen Receptors and Pancreatic Islet Survival in Diabetes:  
An Example of Bidirectional Translational Research"

The CRU saw its first patients under an IRB approved protocol titled *Innate Immunity Signal Transduction in Human Leukocytes* (Principal Investigators: Mike Fessler, Mike Resnick, Ron Mason, Doug Bell and John Cidlowski). A second protocol titled *Pathogenic Studies In Families With Twins Or Siblings Discordant For Systemic Rheumatic Disorders* (Principal Investigator: Fred Miller) was approved by the IRB and will begin to enroll patients in the near future. Several additional protocols are being developed and are in various stages of the approval process. The plan is to have 10-12 active CRU protocols by summer 2010.

### **NIEHS External Clinical Advisory Council**

An External Clinical Advisory Council was assembled by the Acting Clinical Director to provide valuable input to the NIEHS Clinical Research Program as it matures. Members of this Council are experienced clinical investigators, with proven credentials as leaders in their respective fields, who possess a vision and global approach to clinical-translational research. Council members include representatives from the NIH Medical Executive Committee (MEC), the NIEHS Board of Scientific Councilors (BSC) and the National Advisory Environmental Health Sciences (NAEHS) Council. A full list of Council members is shown in Appendix 1.

The first meeting of the External Clinical Advisory Council was on July 28, 2009 (coincident with the CRU Grand Opening). The Council was consulted about, and provided suggestions on, three major issues: 1) the overall direction of the Clinical Research Program; 2) how the Clinical Research Program can best interact with NIEHS intramural and extramural investigators; and 3) the best strategies for programmatic growth of the Clinical Research Program. The summary below succinctly reviews the Council's suggestions on these important issues. A more detailed list of the Council's suggestions is shown in Appendix 2. Minutes of the Council meeting are shown in Appendix 3.

Regarding the overall direction of the Clinical Research Program, the Council's suggestions focused on the following four concepts: a) creation of one or two "signature" programs, focused on an environmental health topic, which will distinguish the Clinical Research Program from other clinical research programs at the NIH and nationally; these programs should take full advantage of existing expertise at the NIEHS and should emphasize public health promotion/disease prevention; b) collaboration with the National Toxicology Program (NTP), and other governmental agencies such as the U.S. Environmental Protection Agency (EPA) or the Centers for Disease Control and Prevention (CDC) for optimal translational impact; c) optimal utilization of existing NIEHS databases and established cohorts, and development of the Environmental Polymorphism Registry as a new environmentally focused database and biobank; and d) development of a research program that seeks to better understand health disparities and identifies environmental exposures which contribute to disproportionate prevalences and morbidities of certain diseases in the population.

Regarding the best model for interaction with NIEHS intramural and extramural scientists, the Council suggested the following six strategies: a) approach established NIEHS basic science leaders and collaborate on the development of clinical research projects that address interesting clinical questions; develop multi-disciplinary clinical-translational research studies at NIEHS in order to broaden and strengthen both the basic science and human studies research portfolios; b) encourage the recruitment of additional junior level, tenure-track investigators with training in clinical-translational research at the M.D. or M.D./Ph.D. level; c) provide incentives for clinical-translational research success during the tenure process; d) provide a competitive funding mechanism to support investigator-initiated, clinical-translational research projects (e.g. Clinical IRA, bench-to-bedside award program); e) offer workshops and seminar series in order to increase awareness among NIEHS basic scientists that they are already an integral part of the clinical-translational research enterprise at NIH; f) provide necessary administrative and operational support for development and implementation of clinical research studies at NIEHS.

Regarding the best strategies for programmatic growth, the Council had the following four suggestions: a) provide additional training opportunities for undergraduates, medical students and clinical fellows; b) create a visiting clinical scholar program; c) hire a physician-scientist with expertise in Environmental or Occupational Medicine and develop a clinical-translational program in this area which is highly relevant to the NIEHS mission; d) use short- and long-term benchmarks to gauge success of the program and track progress.

Finally, the Council members recommended the following six key items for future development and expansion of the Clinical Research Program: 1) distinguish the new NIEHS CRU from other governmental clinical research units by emphasizing its environmental focus; 2) begin with small, highly achievable projects and develop larger, more complex studies over time; 3) raise internal awareness of the types of research studies that are being conducted in the CRU; 4) develop incentives and inducements to encourage participation in clinical-translational research by NIEHS investigators; 5) develop clinical-translational protocols in selected areas of strength such as respiratory medicine, reproductive/developmental medicine and medical genetics; 6) take a leadership role in developing a new model for conducting environmentally relevant clinical-translational research studies.

### **NIEHS Office of Human Research Compliance (OHRC) Update**

In July 2009, OHRC staff moved into the new NIEHS CRU. This move merged the office from three locations on two campuses into one central location on the main NIEHS campus. This move will facilitate interactions between OHRC staff, CRU staff, the IRB Chair, and NIEHS clinical investigators.

Currently, NIEHS has 54 active clinical protocols that are handled by OHRC. Forty-eight protocols are reviewed by the NIEHS Institutional Review Board (IRB) and eight

protocols are reviewed by outside IRBs (3 at NIAID IRB, 3 at NIDDK IRB). Nineteen of the 54 protocols are reviewed by the full board and 28 protocols undergo expedited review. The total number of active Epidemiology Branch protocols is 36 whereas the total number of active Non-Epidemiology Branch protocols is 18. Since the last Council meeting in May 2009, the NIEHS IRB conducted 3 initial reviews, 15 continuing reviews, reviewed 11 protocol amendments, reviewed 2 protocol deviations/violations, and facilitated 2 protocol terminations.

Currently, the NIEHS has 14 IRB Members. There are 10 affiliated members and 4 non-affiliated or community members. Two new members were added since the last Council meeting (Drs. Robert Sills and Adelaide Siegl). The list of current members, their affiliations and their areas of expertise is shown in Appendix 5.

Since the last Council Meeting in May 2009, the OHRC has worked closely with the NIH Office of Human Subjects Research (OHSR) to establish reliance agreements for two NIEHS clinical protocols. A reliance agreement is between the NIH and another Federal Wide Assurance (FWA)-approved institution and acknowledges that a single IRB review will suffice. Reliance agreements help to simplify the IRB review process by limiting the number of IRBs that will review a particular clinical protocol.

In May 2009 and August 2009, the OHRC Quality Assurance/Quality Improvement Program performed two due-diligence audits. Due-diligence audits are an important safeguard to allow the IRB to have confidence that remote study sites understand and enforce human subjects' protections. The two sites that were audited were Duke University Medical Center and Social and Scientific Systems (SSS).

Since the last Council meeting, OHRC offered a number of training opportunities including a retreat for IRB members and OHRC Staff. This retreat included presentations by Sara Hull, Ph.D. (NHGRI IRB Vice-Chair) titled "Confidentiality of genomic data: Ethical and Scientific Issues" and by Charlotte Holden, JD (Acting Director, Office of Human Subjects Protections, NIH) titled "What's going on in the NIH Office of Human Research Compliance." In addition, there was a panel discussion on "The Authority of the IRB: Protecting Human Subjects vs. Overreaching." The panel consisted of Joan Pakenham, Ph.D. (Chairperson), Charlotte Holden, JD (NIH Perspective); Pat Chulada, Ph.D., M.S., (Investigator Perspective); Donna Baird, Ph.D. (Investigator/IRB Member Perspective); Daniel Nelson, M.S., CIP, Director, Office of Human Research Ethics, University of North Carolina (University Perspective). OHRC Staff also attended a workshop at Duke University titled: "Human Research Protections Program (HRPP) Workshop: Improving Research Quality" and a workshop with Family Health International IRB titled "Challenges of International Research."

On July 23, 2009, OHRC launched its new Sharepoint website. This website contains two sections, one for Principal Investigators and their staff and the other for IRB Members. The Principal Investigator section has 4 major sub-sections: Resources and References, Investigator Information, People, and News & Events. The Resources and References sections contain information regarding governmental regulations and

guidance, NIH policies, NIEHS policies and procedures, definitions and terms, and a Quick Reference Guide for Investigators. The Investigator Information section contains all the necessary SOPs and PDF fillable forms for the pre-IRB review process, the IRB review process and the process for obtaining IRB exemptions. The People section contains information on OHRC Staff, NIEHS IRB Members and NIH/NIEHS affiliated offices. The section on News & Events contains the quarterly IRB Newsletter, education and training information, and a calendar for continuing review deadlines.

## **Appendix 1 - NIEHS External Clinical Advisory Council Members**

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## **Appendix 2 – NIEHS External Clinical Advisory Council detailed suggestions.**

### **A. Overall Direction of the Clinical Research Program**

- Develop and validate internal and external biomarkers of exposure.
- Collaborate with the NTP to develop expertise in the area of human toxicology (note: the NTP does not currently have a clinical toxicologist on staff).
- Collaborate with and provide expertise to the CDC and EPA. The CDC and the EPA have the ability to quickly place experts in the field when environmental emergencies occur (e.g. chemical spills) but they lack knowledge of the physiological impact of those exposures. A generic protocol to study acute exposure incidents can be developed. The CDC already has similar protocols in place.
- Develop one or more “signature” project(s) to define the Clinical Research Program or focus on a “signature” disease similar to the NIAID’s focus on HIV and bioterrorism. Utilize both the NIEHS CRU and NIH CC in Bethesda in this effort. Consider current clinical strengths and expertise in developing these projects.
- Take the lead in developing a model or paradigm that focuses on the principles of environmental exposure assessment and disease prevention. Encourage pilot projects with existing cohorts to improve existing methodology.
- Collaborate with existing epidemiological cohorts such as the National Children’s Study, the Agriculture Health Study, and the Sisters Study, or with investigators at Duke or UNC to access their electronic medical record databases. Collect new information on environmental exposures in these cohorts. This is also an opportunity to develop and validate exposure assessment tools.
- Collaborate with the Genes, Environment, and Health Initiative (GEI) investigators that are developing new methodologies and sensors. The Environmental Polymorphism Registry (EPR) could provide a cohort to test these sensors. This would also be an opportunity to compare external exposure measures to internal exposure measures.
- Develop a CRU biobank by collecting additional samples from study participants when they are seen at the CRU. Utilize a standardized health assessment tool such as the NHANES questionnaires to obtain additional health and exposure data from individuals.
- Utilize the EPR initially for *ex vivo* basic research studies and later attempt to translate the findings into clinical prevention/intervention studies with diseased patients.
- Develop a research program that seeks to better understand health disparities. Identify environmental exposures which contribute to the disproportionate prevalence and morbidity of certain diseases in the population (e.g. asthma).

- The following represent examples of suitable research for the new NIEHS CRU:
  - Genetic, epigenetic and serologic biomarkers studies
  - Exercise treadmill studies with exclusions for certain medical conditions (e.g. unstable heart disease)
  - Endometrial biopsies
  - Allergy skin testing
  - Pulmonary function testing with methacholine challenge
  - Induced sputum collection
  - Restrict use of the CRU to populations that are at relatively low risk for complications (this is only necessary for procedures with some risk, e.g. methacholine and exercise challenges, induced sputum, etc.)
  - Review community standards for the types of procedures the CRU is considering; explore what is and is not permitted at other clinics that are located apart from a major medical center

## **B. Interaction with NIEHS intramural and extramural investigators**

- Promote the relevance of clinical research to NIEHS basic scientists. The NIEHS stakeholders expect NIEHS to conduct clinical-translational research that will address major public health concerns.
- Approach basic scientists with expertise in areas identified as clinical research priorities. Take the initiative to incorporate the basic scientist's work into research questions and encourage them to develop their own clinical hypotheses.
- Increase awareness among basic scientists that they are already an integral part of the clinical-translational research enterprise.
- Recruit junior level, tenure-track scientists trained in clinical-translational research.
- Add a clinical research component and/or reward clinical-translational research success during the tenure process. Develop incentives by supporting promotion criteria that incorporates clinical-translational research relevance.
- Establish a mechanism to fund pilot projects in the area of clinical-translational research (e.g. Clinical IRA) and provide an opportunity for them to develop into a larger program if successful (e.g. Director's Challenge). Develop a roadmap for grant development similar to that found in the extramural world (e.g. K-award, R21, R01, SCCOR). Encourage collaboration by requiring research teams to include both physician-scientists and basic scientists.

- Encourage submissions to the NIH Bench-to-Bedside program. Consider funding high quality projects with NIEHS funds, even if they are not funded through the program.
- Increase the number of IRB meetings and establish performance metrics similar to other IRBs. Speeding up the internal review time and minimizing obstacles to clinical research are essential to attracting basic scientists into the clinical research enterprise.
- Conduct a social network analysis to map interconnections between intramural scientists and investigators in the extramural research community. This can be a useful tool in identifying nodes/hubs that can spawn collaboration.
- Collaborate with CTSA programs to bring clinical-translational research expertise to NIEHS.
- Provide opportunities and structure for basic scientists to collaborate with external investigators on clinical research projects.
- Develop mechanisms to collaborate with other government organizations (e.g. EPA, CDC), academic institutions (e.g. Duke, UNC) and the private sector to obtain expertise or facilities that the NIEHS CRU does not currently have access to.
- Enhance ongoing communications with the NIEHS research community about progress, resources, and opportunities by developing a twice yearly CRP Newsletter with the following objectives: a) heighten awareness of the importance of clinical-translational research at NIEHS; b) provide examples of ongoing CRU successes; c) provide updates on CRU resources to facilitate clinical-translational research; d) provide examples of improvements in the IRB review process; and e) provide updates on new clinical-translational opportunities such as grant programs, visiting clinical scholars program, training opportunities, etc.

### **C. Clinical Research Program Growth**

- Provide training opportunities for undergraduates and medical students to be involved in clinical-translational research at NIEHS
- Provide clinical fellowship training opportunities at NIEHS. Match clinical fellow with bench scientist and encourage collaboration on clinical-translational projects. Collaborate with the local universities (UNC and Duke) to develop a training program in Environmental Medicine.
- Recruit additional Staff Clinicians to develop a human environmental exposure assessment program. Consider hiring a tenure-track investigator in the area of Occupational Medicine.
- Develop a visiting professor program to attract senior clinician scientists to work on clinical-translational research projects at NIEHS.

- Collaborate with Duke and UNC to establish training program for PhDs in clinical research.

#### **D. Benchmarks**

- Develop evaluation criteria to measure the CRU's short term and long-term success.
  - First year benchmarks should include:
    - Number of new clinical research protocols, number of protocols that align with the NIEHS mission, number of subjects enrolled
    - Number of PIs and Co-PIs that utilize the CRU
    - Development of a symposium or workshop on clinical-translational research
    - Development of a clinical research pilot program (e.g. Clinical IRA)
    - Development of plans for a clinical research training program
  - Long term benchmarks should include:
    - Implementation of a clinical research training program
    - Establishment of methodological standards for exposure assessment in humans
    - Number of publications in clinically relevant journals
    - Reduced time from conception to approval of a clinical research protocol
- Establish an internal committee to review the CRU's success. The committee is also a way to engage basic scientists at the NIEHS in the CRU's work

## Appendix 3

### NIEHS External Clinical Advisory Council Meeting Minutes

NIEHS Executive Conference Room  
Research Triangle Park, NC

July 28, 2009

#### Attendees:

External Clinical Advisory Council Members	Attended Yes/No	Other Attendees	Attended Yes/No
Richard Boucher, M.D., University of North Carolina at Chapel Hill	Y	Linda Birnbaum, Ph.D., NIEHS	Y
Nancy Brown, M.D., Vanderbilt University Medical Center	Y	Marc Hollander, NIEHS (Observer)	Y
Robert Califf, M.D., Duke University Medical Center	Y	Darryl Zeldin, M.D., NIEHS	Y
Garret FitzGerald, M.D., University of Pennsylvania	N	Stavros Garantziotis, M.D., NIEHS	Y
Philip Landrigan, M.D., Mount Sinai Medical Center	Y	Fred Miller, M.D., NIEHS, NIH Clinical Center	Y
Cliff Lane, M.D., NIAID/NIH	Y	Patricia Chulada, Ph.D., NIEHS	Y
Grace LeMasters, Ph.D., University of Cincinnati College of Medicine	Y	Michael Spencer, NIEHS (Observer)	Y
Andrew Liu, M.D., National Jewish Medical and Research Center	Y	Neha Mehta, SRA International (Observer)	Y
Jerome Strauss, M.D., Ph.D., Virginia Commonwealth University	Y	Brenda Yingling, SRA International (Observer)	Y
		Lila Schweins, SRA International (Observer)	Y
		Rich Cohn, Ph.D., SRA International (Observer)	Y
		Lisa Murphy, SRA International (Observer)	Y

**Welcoming Remarks:** Linda Birnbaum, Director of NIEHS, welcomed council members and stated it was an honor to have the members here today for their insight and recommendations. She reported the Clinical Research Program (CRP) and the Clinical Research Unit (CRU) received local, state and national recognition during the grand opening on July 26, and expressed enthusiasm and support for the CRU. The CRU is a resource for partnership and collaboration with the mission to bridge the gap between basic research and clinical care. Translational research at the NIEHS is broadly defined as bench to public health and will be achieved by conducting studies that provide insight on how we can prevent environment related diseases. The CRU will also provide a training ground for scientists in clinical research focused on environmental exposures. Dr. Birnbaum also noted that the CRU will not be limited to cardiopulmonary issues. Due to the lack of proximity of emergency medical facilities, she has decided to limit the CRU to minimally invasive procedures.

**NIEHS Clinical Research Program:** The following program overviews were presented by the Clinical Research Program members. Please refer to PowerPoint presentations for details.

1. Overview of the Clinical Research Program mission and vision was presented by Darryl Zeldin, Acting Clinical Director, NIEHS.
2. Overview of the Clinical Research Unit mission and vision was present by Stavros Garantziotis, Medical Director, Clinical Research Unit, NIEHS.
3. Overview of the NIH Clinical Center in Bethesda and opportunities and challenges was presented by Fred Miller, Senior Investigator, NIH Clinical Center (NIH CC) in Bethesda.
4. Overview of the Environmental Polymorphism Registry (EPR) was presented by Patricia Chulada, Principal Investigator, EPR, NIEHS.

**Panel Discussion:** The external clinical advisory council was provided a list of questions for their insights, ideas and recommendations. The following ideas were generated for each set of questions provided.

### **Recommendations regarding overall direction of the Clinical Research Program**

- Develop and validate internal and external biomarkers of exposure. Currently, validation and standardization of exposure assessments are lacking in environmental research. This is an opportunity for the Clinical Research Program (CRP) to take the lead in validating biomarkers and to establish themselves as experts. Take advantage of toxic spills and exposures by obtaining samples and utilizing these extreme examples to develop and validate exposure markers and assessment tools. Collaborate with the National Toxicology Program (NTP) to broaden this area of expertise since the NTP does not have a human toxicologist on staff.

- Collaborate with and provide expertise to the CDC and EPA. The CDC and the EPA have the ability to quickly place experts in the field when environmental emergencies occur such as chemical spills but they lack knowledge of the physiological impact. A generic protocol to study acute exposure incidents can be developed. The CDC has similar protocols in place.
- Determine signature project(s) to define the Clinical Research Program or “Signature” disease similar to the NIAID’s focus diseases. The intramural program can focus on cohorts of rare diseases that may be related to environmental exposures. Utilize both the NIEHS CRU and NIH CC in Bethesda to develop a signature program. Decide on specific exposures, populations, and health outcomes to focus on. Consider current clinical strengths and expertise in this decision.
- Take the lead in developing a methodological model or paradigm that focuses on the principles of environmental exposures and disease prevention. Currently, many published environmental studies have flaws in methodologies. This is an opportunity to be creators of a new methodology. Establishing a model will also provide structure for basic scientists to design future translational studies. Encourage pilot projects with existing cohorts to utilize and improve the methodology.
- Develop a position similar to a staff clinician at NIAID. At the NIAID, the staff clinician is a non-tenure track investigator providing 50% service and 50% research. Council members expressed concern that this type of position may create the notion that clinical investigation is less valuable than basic science because it is not a tenure track position.
- Recruit staff physician to build a model environmental exposure assessment program. This could be a scientist that has chosen a non-tenure career path or a post-doc position with a clinical focus. Consider hiring an occupational health physician.
- Work towards embedding translational research into the basic science program. Recruit junior level scientists trained in translational research to focus on developing the clinical research program and also assign them to a research lab that best fits their expertise and interest.
- Provide pulmonary fellowship opportunities for junior level clinical trainees. Match clinical fellow with bench scientist to collaborate on clinical translation projects.
- Develop a visiting professor program. Attract scientists to focus on a particular project with clinical translation.
- Collaborate with the National Children’s Study at the UNC Population Center (Director, Barbara Entwisle). Conduct adjunct assessments to obtain data related to environmental factors. This is also an opportunity to develop and validate exposure assessments with additional samples. The study recently

started recruitment with the goal of enrolling 10,000 children. They are also recruiting women within 20 weeks post conception.

- Collaborate with the Genes, Environment, and Health Initiative (GEI) programs that are developing new methodologies and sensors. The EPR could provide a cohort to test their sensors. This would also be an opportunity to examine and compare external exposure measures to internal measures.
- Collaborate with the National Cancer Institute (NCI) on their agriculture cohort studies. The primary end points are cancer but there may be an opportunity to access specific exposures and outcomes with questionnaires. The study is currently in the process of obtaining samples from their cohort.
- Develop a CRU Biobank by collecting additional samples from participants when they are present at the CRU. Utilize a standardized health assessment tool such as the CDC questionnaire to obtain additional health data. Characterization consent will be required to populate a recruitment registry. Andrew Liu can provide a copy of a characterization consent they use at his center.
- Collaborate with the National Children's Study (NCS) to focus on pregnancy outcomes, exposure assessments and environmental impact on risk of chronic disease. Utilize EPR cohort of reproductive age women.

### **Strategies to engage PhD basic scientists at NIEHS in translational research**

- Take leadership roles in initial studies at the CRU to establish standards and develop quality research. The initial studies need to be successful to show the value of translational research.
- Promote the relevance of clinical research to basic scientists. The NIEHS constituents expect the NIEHS to produce translational research that will address public health concerns. The NIEHS needs to emphasize that all research at the NIH should have clinical relevance.
- Approach basic scientists that have expertise in areas relevant to the CRU's current research projects or areas identified as priorities. Take initiative to incorporate the basic scientist's work into research questions rather than waiting on them to develop a hypothesis. Include basic scientists as collaborators rather than initiators of the translational research.
- Increase awareness among basic scientists that they are already part of the integral cycle of translational research.
- Add a clinical research component to the tenure process or add a clinical position that has a clinical tenure track. Concern was expressed that the basic scientist seeking tenure may not be interested in pursuing or taking the lead on clinical research projects because clinical research would not be considered in the tenure process. Currently, the NIEHS scientist is allocated 80% to lab research and there is no incentive for a tenure track scientist to focus on clinical translation. Develop staff incentive by developing promotion criteria that includes

translational research. Contribution to clinical translation could be considered in promotions but not a requirement. Develop hiring plans similar to NIAID. NIAID recruits three clinical staff physicians for every one tenure tracked basic scientist.

- Collaborate with CTSA funded program to bring in expertise in translational research.
- Establish fellowship training opportunities in translational research. Collaborate with the UNC and Duke Medical Centers in developing the training program.
- Provide opportunities and structure for internal basic scientists to collaborate with external investigators.
- Establish grants for three to four pilot projects. If one of the pilots is successful, consider adding a program similar to the former director's challenge grant program to provide an incentive to expand their program. Develop a plan for this grant funded pilot program that includes a roadmap to the director's challenge grant program or Program Project Grant (PPG) program. Encourage collaboration by requiring the teams to include both a clinical physician and basic scientist. The grant proposals could be new submissions or resubmissions.
- Provide "Studios" similar to the program at Vanderbilt University Medical Center. The studios provide a two to three hour block of time for young scientists to receive feedback and ideas on their grants and protocol develop from senior staff.
- Encourage submissions to the NIH's Bench to Bedside program. The program provides young investigators structure and support to initiate their ideas. Expand "bedside" to human subject research. Consider funding highest scoring projects directly with NIEHS funds if they are not funded through the program.
- Increase the number of IRB meetings to speed up the review process and establish performance metrics similar to other IRBs. Speeding up the internal review time is essential to attracting basic scientists and that in the absence of such acceleration, clinical research at the NIEHS will be severely hampered. Young investigators will be deterred with the currently long review cycles. Track time from protocol development to IRB approval to determine if review cycles improve over time.

### **Interactions with extramural researchers (academic and private sector)**

- Collaborate with local academic institutions to utilize their expertise in select focus areas.
- Propose cost sharing or collaborative agreements with extramural researchers to address concern of NIEHS funds going to outside projects rather than to internal projects.
- Collaborate with Duke and UNC to establish training program for PhDs in clinical research.

- Develop mechanisms such as interagency agreements or memos of understanding with other government organizations, academic institutions and other private researchers to utilize their expertise or facilities that the CRU does not currently have.

### **Best Utilization of the Environmental Polymorphism Registry (EPR)**

- Link subjects that obtain health care at Duke and UNC to their medical records for additional data.
- Obtain additional samples to phenotype them. Determine specific hypotheses and genotypes of focus before calling participants in for additional samples. Utilize mapping models and county level health statistics to determine health outcomes of interest, perhaps associated with issues such as health disparities and environmental exposures.
- Utilize reproductive age women for pregnancy outcome measures.
- Utilize registry for ex vivo basic research studies and later translate into clinical study.
- Consider demographic subpopulations and examine confounders with biostatisticians to determine sample size in light of biologic plausibility.
- Contact research group at Duke that has collected information on regional environmental exposures.
- Select specific gene functions to study from the list of 104 and group together into one study for IRB review.
- Utilize standardized questionnaires such as the CDC's questionnaire to obtain additional information on participants.

### **Recommendations about acceptable research risk in the NIEHS CRU**

Due to limited time, Dr. Zeldin will contact the council via email for additional input on acceptable research for the CRU. The following recommendations were generated:

- Exercise treadmill challenge with parameters for certain medical conditions.
- Endometrial biopsies following existing standards.
- Allergy skin testing following existing standards.
- Induced sputum.
- Restrict use of the CRU to certain low risk populations.
- Review standards for the types of procedures the CRU is considering as part of their program to determine if the procedure would be safe to perform at the unit. Also, explore what is permitted and not permitted at other remote sites.

## Other Suggestions

- Develop evaluation criteria to measure the CRU's short term and long-term success.
  - First year benchmarks generated include: number of new protocols that align with the CRU mission, number of PIs and Co-PIs that utilize the CRU in new protocols, offer half-day symposiums on clinical translation projects every 3 – 6 months, number of subjects enrolled, develop plan for research grant pilot program, develop strategic plan for a training program and determine best journals for publications.
  - Long term benchmarks generated include: implement training program, establish methodological standards for exposure measurement, number of publications and reduced protocol approval time.
- Establish an internal review committee to review the CRU's success. The committee is also a way to engage scientists at the NIEHS in the CRU's work
- Explore the NIH CC recruitment group services. They develop recruitment plans but do not implement them and do not conduct screening.
- Explore electronic study management software utilized by CTSA to share data across institutes.

## Summary and Next Steps

The following final suggestions were generated from the council members.

- Richard Boucher: Distinguish the CRU through an environmental focus. Start off with small projects. Raise awareness internally of what types of research is being conducted at the CRU. Set an algorithm for grant mechanisms. Take advantage of the expertise at the EPA.
- Philip Landrigan: Determine level of enthusiasm across institute. Debrief with Linda Birnbaum and develop incentives with leadership's support. Don't be inhibited by internal politics.
- Andrew Liu: The basic scientists at NIEHS are a strong national resource. If a couple of basic science leaders were to have a positive experience and implement a pilot study with great success, that would instigate other basic scientists to get involved.
- Cliff Lane: Get protocols launched in your selected focus areas. Provide leadership to ensure the initial projects are successful.
- Nancy Brown: Define CRU's success as you would like it to be measured. Make it clear that the research is environmental. Develop fellowship and training programs.

- Jerome Strauss: Emphasize the importance of the basic scientist's work and how it is essential to the circle of translation research. Take a leadership role in developing a methodological model for conducting environmental research.
- Grace LeMasters: Establish how you are going to evaluate your success over the short term and long term so yearly benchmarks can be reviewed.

**Closing Remarks:** Darryl Zeldin thanked everyone for their time and contributions. The minutes will be circulated to the council for review. Darryl encouraged everyone to email additional comments and suggestions to him.

## Appendix 4: Current NIEHS IRB Members

Member name	Degree	Email address	Term end	Minority/ Gender	Speciality	Affiliation
Baird, Donna	PhD	baird@niehs.nih.gov	09/30/2011	N / F	Epidemiology	NIEHS
Bishop, Jack	PhD	bishop@niehs.nih.gov	06/01/2010	N / M	Toxicology	NIEHS
Blackmon, Betty	--	bettyblackmon@csallc.com	01/30/2010	Y / F		Community Member
Fessler, Michael	MD	fesslerm@niehs.nih.gov	01/30/2010	N / M	Respiratory Biology	NIEHS
Hoppin, Jane	ScD	hoppin1@niehs.nih.gov	07/01/2010	N / F	Epidemiology	NIEHS
Lee, Craig R.	PharmD, PhD	craig_lee@unc.edu	04/22/2010	N / M	Pharmacology	NIEHS
Moore, Alicia	MS	moore5@niehs.nih.gov	03/31/2010	Y / F	Biology	NIEHS
Packenham, Joan (IRB Vice Chair)	PhD	packenhm@niehs.nih.gov	09/30/2010	Y / F	Pathology	NIEHS
Ramirez, Rey	BA	rey2@gte.net	01/30/2012	Y / M		Community Member
Resnik, David (IRB Chair)	JD, PhD	resnikd@niehs.nih.gov	09/30/2010	N / M	Research Ethics	NIEHS
Roberts, Michael	DDS	Mike_Roberts@dentistry.unc.edu	01/30/2010	N / M	Pediatric Dentistry	Community Member
Siegl, Adelaide	PhD, ThM	docs3boys@yahoo.com	7/23/2010	N / F		Community Member
Sills, Robert C.	PhD, DVM	sills@niehs.nih.gov	06/11/2010	Y / M	Pathology	NIEHS
Williams, Carmen	MD	WilliamsC5@niehs.nih.gov	01/30/2012	N / F	Reproductive & Developmental Toxicology	NIEHS