

IECRN



Inventory and Evaluation of
Clinical Research Networks

Summary Report of the IECRN National Leadership Forum

July 28, 2006



TABLE OF CONTENTS

<u>Topic</u>	<u>Page</u>
May 31, 2006	1
Welcome and Introductions.....	1
NIH Roadmap Update.....	2
IECRN Objectives	6
IECRN Overview.....	7
Findings from the Descriptive Survey and Best Practices Study.....	12
Management and Governance and Financial Practices	12
Network Operations, Recruitment and Retention, and Training and Professional Development	14
Information Technology and Data Management	16
June 1, 2006	24
Welcome	24
Keynote Speaker.....	25
Breakout Sessions	
Management and Governance	31
Network Operations	35
Data Management	37
Information Technology.....	41
Financial Practices	45
Recruitment and Retention.....	49
Training and Professional Development	53
Comments and Closing Remarks.....	56

MAY 31, 2006

Welcome and Introductions

Stephen Katz, M.D., Ph.D., Director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

Dr. Katz welcomed attendees and provided an historical overview of the development of the Roadmap initiative and other factors that contributed to the origin of the Inventory and Evaluation of Clinical Research Networks (IECRN) project. According to Dr. Katz, eliminating roadblocks to moving science forward was a recurring theme in earlier discussions almost 4 years ago, particularly in relation to the difficulty of sustaining clinical research networks across multiple studies. Many of the National Institutes of Health (NIH) directors and others in the community were committed to the concept of trying to develop a system where the network infrastructure does not have to be rebuilt every time a new study is launched, which is inefficient and enormously expensive. Key participants in early efforts to reengineer the clinical research enterprise, along with Dr. Katz, included Claude Lenfant; Steve Straus, Director of the National Center for Complementary and Alternative Medicine; Larry Friedman, a renowned clinical investigator formerly of NIH; Jim Kiley, from the National Heart, Lung and Blood Institute (NHLBI); and now Jody Sachs. Dr. Katz expressed appreciation to Dr. Sachs for her efforts to conduct and publicize these meetings and to led this effort. In addition, Dr. Katz thanked the Westat project team, particularly Nancy Dianis, project director and Smita Amin, project coordinator. He also thanked Dr. Barbara Alving, acting Director of the National Center for Research Resources (NCRR).

Dr. Katz commented that he had read the executive summary and other available IECRN reports and believes that, in their totality, the findings provide a blueprint for the development of strong and sustainable networks that can address questions not only in terms of clinical trials but also for other types of clinical research that are so critical to the health of our nation.

A critical component of the success of the Forum, according to Dr. Katz, is the response of attendees to the findings of the studies, including the identification of networks with a semblance of best practices. In closing, Dr. Katz commented that IECRN is a culmination of many activities that have been going on at NIH in recent years, and that he looks forward to the results of the meeting's deliberations.

NIH Roadmap Update

Elias A. Zerhouni, M.D., NIH Director

Dr. Zerhouni thanked Dr. Katz for his leadership, along with Jim Kiley from NHLBI and Dr. Barbara Alving. Next, he addressed the purpose of the meeting and why it is occurring now. Several drivers of the biomedical research enterprise existed when Dr. Zerhouni became NIH Director 4 years ago, including the sense that there was a loss of energy in the translational clinical science areas, as well as the impression that translation was more difficult and costly, due in part to the exploding demand in clinical services.

Three fundamental issues pervade the process that came to be known as the Roadmap Initiative, which was launched in 2003. One was systems biology, the sense that biological systems have emerged as very complex entities. Looking at molecular pathways and trying to validate a target, molecular pathways are really embedded in very complex, interacting networks. Questions arose about how to tease out, for example, what are called hub molecules to determine those that really are controlling the behavior of the system. In addition, the population is not suffering as much from acute diseases as from chronic diseases. Chronic diseases, which are 75-80 percent of the disease burden today, utilize different types of analysis and study, including clinical epidemiology, clinical trials, and observational trials, with a different timeline than for acute disease. To perform experiments that are statistically valid and observationally solid, we need to have long clinical trial times. These observations led to investments in structural biology, systems biology, and molecular libraries, and to giving tools to the research community that are easily accessible to conduct very fundamental research.

Second, the scale, scope, and complexity of science had reached such a level that interdisciplinary teams were needed, leading to collaboration among computer scientists, with physical scientists, and across the life scientists themselves. This has led to the concept of the research teams of the future and investment in what is called high-risk, high-impact research. An example of this is the Pioneer Award, which is a completely different review mechanism for really far out ideas that need to be tested. Interdisciplinary research is also a difficult issue, because collaboration should be created, not forced. Interdisciplinary research should be allowed to self-assemble.

The third fundamental roadblock is being addressed as part of re-engineering the clinical research enterprise. Along with the loan repayment program and career and mentoring awards, NIH began to focus on the sociology of how we conduct clinical research, both within institutions or within networks. NIH then realized the need to create a stimulus for change that would challenge the community to find better ways to conduct translational and clinical science and to train the new generation of clinician scientists. The complexity of regulation, experimental design, and biostatistics requires a supportive infrastructure as well as a supportive intellectual environment. And while NIH knew that there were hundreds of clinical research networks, questions of how they operated, how efficiently they were integrated, and how interoperable they were rose to the top of our concerns. Dr. Zerhouni commented that he looked forward to seeing how members of the clinical research community can improve the tools used by clinical and translational scientists, and at the same time create a new vision of how to conduct human-oriented research, patient-oriented research, effectively and appropriately without the rigidity of the system standing in the way. Dr. Zerhouni also noted that some trials cannot be conducted without a strong community-based infrastructure, and that means a good

information system, and appropriate ways of training and developing constant, trusted leadership around the issues of whatever network you are participating in.

In conclusion, Dr. Zerhouni reminded the attendees that these are the issues that have led to the IECRN project and to the Forum. In reflecting on the project reports, Dr. Zerhouni noted that, while some of the project findings were expected, others, such as the finding that 60 percent of clinical research is still paper-driven, were enlightening. Especially important is to consider how to integrate new investigators in this clinician scientist pathway, and to create a robust force of clinical investigators that will make it possible to test the new therapeutic and preventive strategies more quickly than is currently possible. Dr. Zerhouni commented that he was pleased to see so many people in attendance at the Forum and opened the floor for questions.

Dr. Zerhouni responded to four questions:

Question #1 to Dr. Zerhouni

Speaker: Carlos Camargo, Boston, Mass. General Hospital

Question/Comment (paraphrased): Very often we hear the phrase “bench to bedside” and I’m concerned whenever I hear that the academic medical center bedside is actually very far from our country’s needs. I’d appreciate your comments on the idea of bench to bedside to population, because I think that really speaks to the issues you raised in your talk.

Dr. Zerhouni’s response (paraphrased): Science is good science, whether it is population, whether it is bench to bedside, or basic. The key thing is you can’t rigidify our enterprise and sustain the creative, innovative models that people can come up with. So my view is that progress can come from any area of science and you have to have a balanced view of that, including the other end of the so-called pipeline, and you have seen that with many examples. The Framingham study is the one that always comes to mind, but there are many others.

Question #2 to Dr. Zerhouni

Speaker: Kevin Peterson, University of Minnesota

Question/Comment (paraphrased): I completely agree with that, the bench to bedside. We used to sometimes call it from bedside to bookshelf. I also really like the comments you have about involving the community and bringing some of this information out into the community. We have actually set up a demonstration across the hall of some of those new tools that we are using in networking, and I would be happy to show you around some of those tools.

Question #3 to Dr. Zerhouni

Speaker: Alan Morris, University of Utah

Question/Comment: You point out in your very nice emphasis on translational research the need to move back and forth, and I am glad you didn't use bench to bedside as the model. But the bidirectional movement across scales of research, for example, from bedside to bench, is largely dependent upon the quality of research conducted at the bedside. We usually think of so-called "reductionist" or bench research as very high-quality scientific research and then when we get to medical research and intact patients, we think in much more fuzzy terms. So my question to you has to do with the generation of tools to make the inquiry at the clinical level more scientifically robust. We don't have mechanisms right now to establish replicable methods across different community and academic clinical institutions. Do you think it would help the roadmap, which I think is a terrific movement, if it also embraced the inclusion of tools that focused on the clinician-patient encounter and on the decision support that would be necessary to make clinicians do replicable things in different environments?

Dr. Zerhouni's response (paraphrased): I totally agree with your view and, actually, the Roadmap does do that. There is a program in the Roadmap called "PROMIS"—patient reported outcome medical information system. However, there is no one body of validated tools that you can use in all communities, in all cultural environments, with the appropriate language. So that was one example.

The other point that you make, which is absolutely on target, is the need for bidirectional exchange, which means that you have to have a cadre of scientists who are absolutely trained to be able to bridge all the worlds of science that are needed. For example, if you look at proteomics or you look at genomics and the tools that have been developed in the laboratory and how you need to translate that into population research, you have seen, for example, the genome-wide association studies that are ongoing right now in many areas of science. One of the main stumbling blocks is you don't really have good phenotyping tools. So the development of understood, standardized phenotyping strategies, environmental measures is a good example of a lack of that, as well. If you think about just a simple problem such as obesity, how do you measure food intake and caloric intake? We do not have a good measure of that right now. There isn't a strategy to measure the environmental impact of just caloric intake at an individual level, so that you can correlate that against any particular trial, and on and on. If you look at individual measures of exposure for particular agents at the individual level, you can do it, and it can be done at the regional level and the local level. So those are tool developments that need to occur, in addition to what you talked about; that is, the concept that the whole is greater than the sum of the parts. So that you can, in fact, exchange and analyze, through registries, for example, events that occur in large populations. You have seen an example of that with the detection of adverse events, cardiovascular events in the use of Vioxx through the mining of the database at the Kaiser Permanente network in California, and this is what picked up the finding and drew the attention of people to that, in part.

Question #4 to Dr. Zerhouni

Speaker: Chet Fox, University of Buffalo, part of a practice-based research network, where our questions are not really the “what” questions, what works, but how.

Question/Comment (paraphrased): Whatever we are doing we need to focus on how is this going to benefit the patient, not maybe 10 years, 20 years, 30 years, but how is it going to benefit the patient. But the question I have is in this age of evidence-based medicine and standards and other things like that, the randomized control trial has become sort of the gold standard of how we do things, but as we work out in the field, creating research, patients are not interested in being randomized. They are interested in being improved. Wouldn't studies that looked more rigorously at longitudinal observation over time, looking at quality improvement or patient improvement, maybe, rather than quality improvement, be a better model for studying?

The partners that we have, like we build community collaboratives and there are a lot more partners out there. HMOs have huge databases, as you mentioned with Kaiser, that can help us with research without having us rebuild it. But, also, when you get patients involved, if something works, they want it now. They don't want to wait.

Dr. Zerhouni's response (paraphrased): Very good question. When you look at translational clinical sciences, a lot of the fundamental concepts haven't been researched in their own ways in terms of validation in the context of a changing landscape of disease. The randomized double-blind clinical trial, prospective clinical trial is a gold standard, no question about it. But as you deal with chronic diseases that last a long time, where you have patient loss, you have multiple diseases and morbidities at the same time, we need to engage the research community in thinking about different models. For example Bayesian statistics is getting now the sort of treatment that I would like to see more of in both information systems and other biostatistical areas, and that can change, in fact, the way you look at what some people call population surveillance strategies, where you really accumulate data.

IECRN Objectives

Jody Sachs, D.P.M., IECRN Project Officer, NCRR

Dr. Sachs provided an overview of the agenda for the Forum and of the IECRN project. She discussed the two components of the overall initiative – the IECRN – and a group of 12 contracts that are examining the feasibility of integrating and expanding clinical research networks. The IECRN contract, awarded in September 2004, has been led by a Westat team, including Lockheed Martin Aspen Systems Corporation, Social and Scientific Systems, and Borland. It also is led by an external advisory committee of clinical research networks experts and it has oversight by the Trans-NIH Roadmap Steering Committee. The major goals of the IECRN were to develop a fully searchable inventory and database of clinical research networks, to describe operational and organizational clinical research network characteristics, and to examine existing CRNs that allow achievement of goals through efficient operations and promotion of successful interactions both internally and externally; and to conduct today's National Leadership Forum to discuss these findings. Additional information can be found at <https://www.clinicalresearchnetworks.org>

Dr. Sachs noted the many accomplishments associated with this contract. It has produced the first inventory of clinical research networks, and the first to gather information on the infrastructure of CRNs. This information is helpful to assess where we are and the data on barriers and facilitators will help us to move forward. Finally, this is the first time a meeting like this has been convened, filled with a wide range of clinical research network stakeholders, for exchange of ideas toward the goal of optimizing the clinical research enterprise.

Dr. Sachs reiterated the primary purpose of the meeting—to review the IECRN survey findings and results—and reviewed the 2-day agenda.

IECRN Overview

Stephen Durako, Vice President, Westat

Mr. Durako, principal investigator for the IECRN project, introduced himself and provided a context for why participants have gathered at the National Forum. He expressed optimism that this opportunity to share ideas and make recommendations to NIH will lead to improvements in the use, efficiency, and effectiveness of the clinical research network infrastructure in this country, as well as around the world.

Mr. Durako noted that, due to several important features, CRNs are one of the most effective vehicles for translation of basic science into clinical medicine. First, they are composed of already existing groups of investigators who have made some commitment to conduct collaborative multicenter research. In addition, they are generally formed around a dedicated, multiproject, integrated agenda dealing with either a particular disease or a particular patient population, providing a sense of coherence and cohesiveness to a full agenda that is trying to address a particular problem. A third important feature of CRNs is that there is already sort of organizational structure in place that allows for rapid development and implementation of studies, and does not require having to start from scratch. Finally, by their very nature of having multiple organizations involved, multiple clinical sites, CRNs generally have much greater access to patient populations than do studies conducted in a single site environment.

Mr. Durako provided an overview of the four goals for the Forum. First, the project team will communicate to attendees the findings that we have obtained from our study. The second goal is to engage the group in discussion of these findings and what they mean for the clinical research enterprise. Next is the goal of developing recommendations that will enhance the translation of research findings through the use of clinical research networks. The fourth and last goal is to engage members of the research community in implementing these recommendations.

Information about the four components of the IECRN data collection was presented by Mr. Durako. The first, referred to as the Core Survey, was the effort to create an inventory of all the clinical research networks in existence throughout the world. The second component, the quantitative component of the Descriptive Survey, was intended to develop a baseline of current practices in many different areas that addresses how clinical research networks carry out their work. The third component was a follow-up to the descriptive survey, utilizing qualitative telephone-based interviews to assess barriers and facilitators to CRNs carrying out their work and accomplishing the missions set for the clinical research network. The final component was the Best Practices Study, the identification of networks that could demonstrate particular accomplishments in achieving their goals and in achieving important accomplishments that NIH has recognized. For this study, the project team conducted intensive telephone interviews with representatives of these networks to examine their successes and to determine what approaches they had used to accomplish them.

At the onset, the project developed an operational definition of a clinical research network. First, a CRN is a multiorganizational entity composed of clinical field sites and investigators. Second, it is organized to conduct multiple research protocols, sometimes consecutively, sometimes concurrently. Finally, a clinical research

network can either be a formal or informal structure, as long as it had demonstrated some collaborative accomplishments.

Core Survey. The three primary objectives were to confirm whether entities first identified as candidate CRNs met the project criteria, to collect some basic characteristics about each network, and to create the public web-based resource by putting all of the network profiles in a publicly accessible inventory. With no available list of clinical research networks in existence, project staff utilized a range of methods to identify potential CRNs, including making contact with experts in the field and with government agencies, consulting the medical literature, and searching the internet. These efforts yielded more than 700 entities that could possibly be clinical research networks. Additional followup contact and investigative work reduced the number of potential CRNs to a total of 294, each of which was contacted to complete the Core Survey. Of these, 262 are actually clinical research networks, and the project staff achieved a response rate of 95 percent, or 249 of the 262 networks contacted.

Core Survey Results. The results showed that some networks have been in existence for up to 50 years, while others are as young as 6 months; the median network age was about 6 years. The U.S. Federal Government is a major funder of clinical research networks, with more than 60 percent of CRNs reporting the U.S. Government as their primary funding source. The most common type of study done by clinical research networks is, not surprisingly, clinical trials (39 percent). However, 28 percent of CRNs are also doing some kind of observational research. The majority of clinical research networks (52%) are U.S. based, most likely because the U.S. Federal Government is a primary sponsor of clinical research networks. About one-third reported both U.S. and international sites in their networks, an interesting development especially in the areas of infectious diseases, HIV, tuberculosis, and others, but also for other chronic diseases, suggesting an increased interest in dealing with these health problems, not just in the U.S. population, but worldwide, which is a credit to NIH for supported this so aggressively. The smaller number of CRNs with only foreign sites is due in part to the fact that most other governments do not provide the kind of support that the U.S. Government does for clinical research; nonetheless, there are some dedicated investigators out there who have established networks and are conducting research. Despite these interesting findings from the Core Survey, Mr. Durako emphasized that the CRN inventory is actually the most important accomplishment resulting from this data collection, and he encouraged attendees to use the inventory as a resource and as a tool for greater external interactivity among research networks. Mr. Durako recommended that Forum attendees visit the inventory web site demonstration that is ongoing in the Randolph Room throughout the meeting. Web site usage statistics show that, on average, the site is getting about 800 hits a week, with the average length of visit about 12 minutes.

Descriptive Survey. For this component, the project sampled networks based on the Core Survey inventory; roughly 40 percent of the networks were in the Core Survey sampling frame. Clinical trials networks and NIH-funded networks were oversampled and international networks undersampled international networks. The survey was comprised of seven domains related to networks operations and practices: management and governance, financial practices, network operations, recruitment and retention, training and professional development, information technology, and data management. Within each of the domains (except financial practice), open-ended interviews conducted by telephone focused more closely on barriers and facilitators

associated with effective CRN functioning. Mr. Durako expressed appreciation to the respondents who completed the survey components, many of whom were in attendance at the Forum.

Best Practices Study. A call for nominations was developed and distributed through advertisements in journals, mailings to Core Survey respondents, and contacts with agencies that sponsor clinical research networks. Individuals could nominate their own or others' networks, based on demonstrable accomplishments in one or more of the following eight achievement categories. Particularly fruitful were the areas of internal interactivity within the network, external interactivity across the network, informatics, training, and expanding the research agenda. A selection and review committee, consisted of IECRN project team members who were content evaluation experts, members of the project's evaluation team, and several members of the outside expert advisory panel. In-depth telephone interviews were used to explore the practices of the networks with demonstrated accomplishments in the specified outcome areas. In closing and before opening the floor for questions, Mr. Durako expressed his appreciation to all of the members who participated on the IECRN Advisory Panel, to Nancy Dianis, project director, to the leaders of the evaluation and qualitative research team, Susan Berkowitz, from Westat, and Darcy Strouse, from Lockheed Martin, Aspen Systems Corporation, as well as the many other staff members who contributed to the project.

Mr. Durako responded to five questions:

Question #1 to Mr. Dukako

Speaker: Linda Brubaker, Assistant Dean of Clinical and Translational Research at Loyola in Chicago

Question/Comment (paraphrased): I find this really fascinating and am hoping that in your future plans or future contracts, you will be able to begin to work to integrate this registry with the registration of clinical trials that are open for enrollment. Is that going to be a possibility?

Mr. Durako's response (paraphrased): That is a very interesting and important question. In fact, we had some discussion about that during the course of the project. Dr. Sachs and I were working together to see if we could directly link from our inventory into <http://clinicaltrials.gov>, so that you could actually see the trials that a network is doing. It's complicated, due to the names of the networks, and that the way to link to them is not the same. I think we actually now do let you jump into Clinicaltrials.gov, but it doesn't give you that network specifically. It gives you a list of studies that seem to be related to the disease that you were interested in. Dr. Sachs would like to make a comment.

Dr. Sachs: Thank you. We are trying to make that process streamlined so that you can actually link and look at what networks do what trials, and I think that is what is essential and needed.

Question #2 to Mr. Dukako

Speaker: Carol Hamilton, Duke University and Duke Clinical Research Institute

Question/Comment (paraphrased): I have a couple questions and comments. One, it was very interesting, the graph that showed how many of the networks were U.S.-based versus elsewhere. Is it true that you only searched in English so there could be sites that are totally listed in other languages? Also, did you have an opportunity to talk to any of the pharmaceutical industries, because they also fund and coordinate various networks, and I didn't know if they would show up in your survey.

Mr. Durako's response (paraphrased): Yes, only searched in English, although we certainly found networks, like the Netherlands-Australia HIV Network. We did not have the capability to search in other languages and felt that, particularly due to the U.S./NIH orientation of the project, those networks probably would be a little bit difficult for us to be able to work with at this point. We tried to contact pharmaceutical industries, and found, much to our amazement, that there seemed to be no actual clinical research network, according to our definition, that is totally sponsored by the pharmaceutical industry. As Dr. Katz mentioned, they are usually one-study groups of clinical sites. Pharmaceutical industries are not necessarily in the business of continuously funding a general research agenda but are targeted to approval of particular products.

Question #3 to Mr. Dukako

Speaker: Gregg Gilbert, University of Alabama at Birmingham

Question/Comment (paraphrased): Of the 264 or so clinical research networks that you inventoried, what percentage of those would also classify themselves as practice-based research networks?

Mr. Durako's response (paraphrased): I am not sure of the exact number, but there are probably at least 60 or so (of the 80 – 90 in the Federation of Practice-Based Research Networks).

Question #4 to Mr. Dukako

Speaker: Carlos Camargo, Mass. General

Question/Comment (paraphrased): You mentioned that this initiative will be going into the future, with plans of integrating with other databases. What kinds of outcomes will you be tracking to measure the success of the enterprise?

Mr. Durako's response (paraphrased): That has not yet been defined. We plan to meet with NIH after this Forum to review the recommendations from the meeting. Some outcomes that I would like to try to measure include how many networks start working together, and whether we start seeing individual investigators who are applying for research funding being directed toward clinical research networks to support and facilitate their work. Important outcomes in the information technology area include whether we start making improvements in some areas, such as the use of electronic systems for data transfer.

In addition, I would like to see whether the support for practice-based research networks actually increases in some fundamental and measurable way. We found in our research that many of the practice-based research networks do not have an infrastructure and are funded study-by-study. It is important to get into the practice community and make it easier for investigators or clinicians to practice as investigators.

Question #5 to Mr. Dukako

Speaker: Jim Mold, University of Oklahoma, with the Oklahoma Physicians Resource/Research Network

Question/Comment (paraphrased): I now belong to three registries, that I am aware of: the Federation of Practice-Based Research Networks Registry, the AHRQ, the Agency for Healthcare Research and Quality's resource center registry, and now your registry. The last two of these required a fairly lengthy survey and more is coming. So I would argue that we need to sort of coordinate our efforts, at least in the Federal Government. My question pertains to the observation that the results show a tremendous nonhomogeneity among the networks surveyed, anywhere from ICU to nursing home to hospice to primary care practice. How did you deal with that nonhomogeneity with regard to analysis of the data or even coming up with the right survey questions?

Mr. Durako's response (paraphrased): First, I would say that we did hear as we were doing this survey that AHRQ had beat us to the punch for the practice-based research networks, and we appreciate your tolerance for participating. I agree that this points, again, to the need to link databases before there are too many of them. On the issue of homogeneity, we tried to find everything that was a clinical research network, and we defined clinical very broadly as conducting any kind of research in humans, any kind of health-related research in humans, which did lead to some difficulty asking questions broadly enough that everybody could answer them. We addressed this partly by spending a lot of time on survey design, conducting pilots with a group of networks, and consulting with our expert advisory panel.

Findings from the Descriptive Survey and Best Practices Study: Management and Governance and Financial Practice

Stephen Durako, Vice President, Westat

Mr. Durako presented an overview of the findings pertaining to two of the seven practice domains: management and governance, and financial practice.

Management and Governance. The areas encompassed by management and governance, and associated practices, include the organization of the network, whether it has bylaws, policies, and procedures; who participates in the leadership and the operational management of the network; how networks determine membership; whether the clinical research network is open to expansion and inclusion of new networks, and setting the research agenda. Also key is to the effort to expand the use of clinical research networks is the CRN's ability and current practices of internal collaboration, that is, interactivity among investigators within the network, and external collaboration, that is, either cross-activity with other networks or with other clinical research investigators.

In two-thirds of the clinical research networks, the primary funder is highly or somewhat involved in overseeing the governance of that network. Furthermore, among networks funded by NIH, the sponsor is involved in setting the scientific agenda. Compared to networks conducting other types of studies, those conducting primarily clinical trials have a more complete staffing arrangement for their networks in terms of leadership, with more project directors and managers, other health professionals, and more information technology staff available to support the network. NIH-funded networks also tend to be more committee intensive, though clinical trials CRNs are more likely to have budget and finance committees. More than half of all CRNs reported some sort of scientific planning committee which helps to bring in all the strengths of the members of the network in establishing a broad and cohesive research agenda.

Summary of themes/outcomes. Mr. Durako presented the four themes associated with the management and governance findings: internal interactivity, external interactivity, expanding or broadening the research scope, and the effectiveness of the clinical research network in changing clinical practice. Regarding *internal interactivity*, the findings emphasize the importance of bringing investigators together, establishing rules for interaction and collaboration among investigators, and mediating differences or disagreements among investigators who are tasked to work together. The findings show that a vast majority of networks (86%) have some information sharing going on across network partners, within their own network. There is a considerable amount of interactivity within the networks in the development of publications from their research. And, again, NIH-funded networks are more likely to actually have policies, formal policies on the sharing of research data within the network. *Barriers to internal interactivity* are typically related to the career needs of the investigators who participate in the research. Many respondents felt there was insufficient investigator commitment to full collaboration and lack of willingness to contribute to the greater good. Particularly from more junior investigators in academic environment, the Findings revealed that the pathway to promotion can be a barrier to collaboration. *Best practices associated with internal interactivity* include the establishment of a sense of collegiality among the people who are in that network, developing trust, acknowledging everyone's contribution, and having a common focus for the network. Mr. Durako discussed

examples of how strong sponsor involvement and providing governance opportunities, particularly for new investigators, were found to facilitate interactivity.

External interactivity, or working with other people or networks outside one's network, was also discussed. For NIH-funded networks, 72 percent of the sponsors encourage cross-network collaboration; at least 73 percent of all networks indicated that they do have some current connection with another clinical research network. The study did not probe, however, as to how strong those connections are, but there is a sense that people are willing to talk to other clinical research networks. On the negative side, 29 percent of networks reported a failed attempt at collaboration, and nearly half are currently working to establish new cross-network collaborations. Funding was identified as one of the *barriers to external interactivity*, along with lack of investigator time to foster these collaborations, and lack of sponsor support. Sponsor support, such as an organizational vehicle that helps to manage the collaboration, was found to facilitate interactivity outside of the network. Collegiality was again found to be a *best practice*, as well as the identification of shared goals and the ability to resolve differences through either informal or formal means. The practice-based research networks, for example, have seen the value of external interactivity and have created a federation to establish alliances and to provide support to their research networks.

Mr. Durako next presented the findings pertaining to *expanding research scope*. The study found that non-clinical trial networks have conducted an average of 5.8 studies, with clinical trials networks conducting, on average, over 20. This raises the question of how much more can CRNs do without additional resources, since the study also found that networks apply for an average of two to four grants per year. *Barriers to expanding research scope* are obvious and include lack of time, not having protected time (important for investigators to work on new ideas), and not having enough research infrastructure to support the expansion of the research agenda.

The last theme briefly addressed was *changing clinical practice*. Older networks, not surprisingly, were found to report a greater impact on changing clinical practice. In conclusion, the highlights include the importance of academic reward, sponsor involvement in encouraging collaboration, and having enough of both funds and time.

Financial Practices. Mr. Durako also provided information on the findings associated with financial practices; qualitative data were not collected on this practice domain, which addressed sources of funding, how those funds are used, whether those funds are adequate to conduct the work, and how cost overruns are handled. One of the most important findings is that 73 percent of networks report that they have some secondary funding sources other than their primary funding. This is important to the success of clinical research networks to be able to get out and to actually look for secondary funds to supplement their primary funding sources. In terms of raising funds, the majority of CRNs only respond to funding announcements that are put out by sponsors; few actually conduct separate marketing or private fund-raising or any other kind of fund-raising activities. Given that the average number of applications is only two to four per year (50% are funded), perhaps there is some room for CRNs to get more aggressive in terms of seeking additional funding to supplement the work that they are doing. In terms of how funds are allocated, 85 percent of CRNs spend some funds on their management and leadership and 83 percent contribute funds to statistical and data management entities. In addition, 45 percent of the networks (likely primarily the practice-based research

networks) report that funding is on a study-by-study basis. Almost half (40%) of the networks indicated that they have cost overruns all or most of the time. Most are related to increases in scope as opposed to misestimating the cost in the beginning, and are typically absorbed by the networks. *Barriers to funding* are that funds are generally insufficient to cover all the costs, and the lack of a core infrastructure. Furthermore, there are usually no funds for secondary analysis of the data, which can maximize research output. Working at off-campus facilities, with different and lower indirect cost rates, was found to be a *facilitator*, for off-campus facilities, along with being able to collaborate and tap into other awards. Best practices associated with financial management includes setting clear priorities and then seeking funding, as well as combining funds from multiple sources, centralizing activities, and looking at ways in the information technology or other fields to achieve efficiencies.

Network Operations, Recruitment and Retention, and Training and Professional Development

Nancy Dianis, R.N., MS, Associate Director, Westat, and Project Director, IECRN

Ms. Dianis presented the IECRN project findings pertaining to three practice domains: network operations, recruitment and retention, and training and professional development.

Network Operations. This domain addressed the conduct of the business of the network, including managing site selection and study protocol development, regulatory practices, and network communications. The study found that almost half of all CRNs use standard time lines for protocol development and are able to meet those time lines almost all the time. Fewer than half of the networks were found to provide training on study design and development, and fewer than half use tracking tools for either the regulatory process or for tracking protocols. Those who used tracking tools reported that they help them manage and simplify the protocol renewal process.

Summary of themes/outcomes. Ms. Dianis introduced the themes and results associated with network operations, incorporating relevant comments and examples from survey respondents. Respondents reported that the protocol development process is often protracted, with many review steps along the way to approval. NIH-funded networks, compared to networks receiving primary funding from other sources, reported undergoing a higher number of protocol reviews. One network addressed this issue by identifying the number of steps in the protocol review process, adopting a “lean thinking” approach, and eliminating redundant or unnecessary steps. The importance of effective communication is another theme related to network operations, and is considered by many to be a critical factor in the success of research. Particularly for the many CRNs with wide geographical dispersion, methods such as extranets and e-rooms are essential for communication, along with regularly scheduled face-to-face meetings. *Best practices* in communication include the use of new or alternative modes of communication to increase efficiency and to reduce costs. They try to streamline communication by eliminating unnecessary communications. Key to communication is developing and supporting methods whereby stakeholders can provide feedback effectively and efficiently. These methods will vary by networks, as not all CRNs are alike or have the same communication needs. In conclusion, Ms. Dianis reiterated the need to address operational issues associated with protocol reviews and regulatory issues, with approaches such as identifying someone within the network who is dedicated to

managing these efforts, streamlining the process by developing standard procedures and formats, and encouraging collaboration and consensus building.

Recruitment and Retention. This area pertains to strategies and procedures for planning, implementing, and monitoring and evaluating recruitment and retention of study participants. About two-thirds of the CRNs report recruitment relationships with community-based physicians, emphasizing again the importance of drawing those providers, as well as participants, into the research process. The challenge, once the patient is eligible and is enrolled, is to keep the person in the study. About two-thirds of CRNs report that they contact inactive participants when retention is lower than expected. This finding implies that people actually monitor recruitment and retention, which is worth doing, especially with the aid of tracing methods to locate inactive participants. Commonly used recruitment strategies include seeking subjects from their own institutions and providing recruitment materials. A recurring theme for this practice domain is the importance of staff commitment. Adequate time to devote to recruitment and retention activities, in the context of other clinic responsibilities, was also frequently discussed by respondents. In addition, communication and a sense of partnership among all stakeholders are key to being effective in this area. The results of the *Best Practices Study* also point to the role of partnerships and to the ability to adapt recruitment strategies to meet the site's needs. It also helps to have a dedicated recruitment coordinator. One example of success was an international network that leveraged local knowledge and cultural norms to help develop recruitment strategies. The key elements in successful recruitment and retention include establishing links between PIs and community-based physicians, and careful selection of sites, and fostering relationships between participants and site staff.

Training and Professional Development. Ms. Dianis noted that a distinction was made between activities and practices associated with training and those associated with professional development, which builds on and enhances previous skills. The study results show that inadequate funding is a major challenge. As expected, newer networks are more likely to provide financial support for site level professional development and NIH clinical research networks place a greater emphasis on training and monitoring these activities. Overall, professional development activities are not emphasized at the network level; although CRNs report that they encourage the pursuit of professional activities, they generally do not provide financial support for these efforts. Compared to non-clinical research networks, the findings show that clinical research networks were significantly more likely to provide professional development opportunities for data management staff than for other types of staff. The most frequent type of program participation was investigator awards and new investigator training programs. Key themes for this practice domain are staff buy-in and having adequate time. Ms. Dianis presented an example of a network that recognized the importance of staff buy-in and designed a simple and effective staff training program that incorporated the provision of technical and resource support. With regard to time, staff need to balance the priorities between taking care of the patients clinically, conducting research, and having time to learn more about the research protocol. In summary, Ms. Dianis reviewed the importance of training that is timely, focused and relevant, as well as the finding that, overall, professional development is not a key network-level priority.

Information Technology and Data Management

James E. Smith, Ph.D. Senior Vice President, Westat

Dr. Smith provided results pertaining to the information technology and data management practice domains.

Information Technology. Dr. Smith noted that proponents of IT are encouraged by the idea that it can create efficiencies in the research process, new capabilities, and various kinds of interoperability and communication collaboration. The IECRN project addresses the computer and electronic means for collecting, storing, processing, using, and communicating information. About two-thirds of the clinical networks responding to the survey reported that they do not have any sort of standing IT committee or borrowing of seats on another committee, which leaves approximately one-third of CRNs with out much committee structure to address IT issues. About half reported some kind of dedicated IT director. Dr. Smith commented that clinical trial networks face regulatory requirements and that NIH is often promoting, if not requiring, an emphasis on IT without corresponding funding. Approximately half of the networks utilize a combination of in-house and outside services, with about a quarter of the CRNs relying solely or very heavily on outside services, and the remaining quarter tending to conduct all IT in-house or everything significant in-house. It appears, then, that the most general model of IT functioning within network organizations is a mix of in-house, with some significant use of, in some areas, outside resources. However, there is wide variation around that model. In addition, networks vary in the number of IT staff or staff that are identified as IT, with a mean of four, most networks reporting less than two, and a mode of zero. In smaller networks, it may very well be the case that no one is consistently dedicated to IT functions.

Information technology themes. Dr. Smith addressed the themes associated with the information technology study results. It can be presumed that IT is a facilitator of internal interactivity, and the results show that two-thirds of the networks have some kind of web-based infrastructure as their kind of major architecture. The remaining networks use client server architecture and many have major applications primarily at the desktop level. Dr. Smith noted that the interesting thing about web architecture nowadays is that it can be introduced incrementally, and does not have to be a major, one-time, very large investment. Although the architecture itself may not always be web-based, most networks have web sites and a good share of those have some kind of a member portion, which means there's some kind of log-in security and only members of the network can access it. The primary activities taking place in the member-only areas of network web sites include sharing materials, protocols, organizational directories and scientific information. Dr. Smith also discussed IT-related barriers to internal interactivity, which includes hardware/software upgrades; compatibility factors; and staff willingness and knowledge. As one might expect, facilitators of internal interactivity include the use of web-based systems and tools that foster interaction, gradually adopting standards, recognizing the clear value of the software, and responding to users' needs. Identified best practices also acknowledge the importance of knowing what users want, and the idea of focusing on "high tech and right tech." High-tech solutions often require more dedicated staff and support, as well as the finances to move into the higher tech types of technologies. Explicitly recognizing the network's barriers and then addressing them is another IT best practice. Many of the components, particularly the adoption of standards, also apply to external interactivity between networks. The data shows that 41 percent using common data elements, 40 percent are using ontologies and vocabularies, 6 percent using LOINC, 11 percent SNOMED. Sixty percent of networks

reported using no data interchange standards. These results suggest that a lot of work is needed to get the kinds of standard adoptions that would bring about more effective external interactivity. Thirty-eight percent report using XML for data transfer and storage, which is actually a technology rather than a standard. Barriers reported by networks are lack of time and funding; limited use of standards; and lack of active sponsor support, as well hardware/software issues. The best practices results suggest the importance of motivating factors (not the technology per se), such as commitment to core principles of open development, open access, and open source.

In terms of IT efficiencies, Dr. Smith reviewed the findings on the adoption of standards and web-based distribution and communication, which was not very high among IECRN survey respondents. The most prevalent elements that IT seems to be contributing in efficiency for CRNs involves online training and saving travel costs; in participant randomization happening; and in clinical trials data management. Barriers include lack of funding and inadequate staff. In summary, Dr. Smith noted that information technology has a lot to offer CRNs, although overall they are a long way from state-of-the-art, and that proponents of IT need to understand what is going on in the research process to develop and apply the appropriate solutions.

Data Management. Dr. Smith also presented the findings pertaining to data management, an area which is closely related to information technology. Data management involves activities related to capturing, processing, storing, exchanging, and presenting information. An encouraging finding, according to Dr. Smith, is that about two-thirds of the CRNs report centralized data management, which is more efficient and secure. Furthermore, the findings show that more of the networks have data management committees than have IT committees. Almost two-thirds of the CRNs in the IECRN study also have a dedicated data management director. Networks primarily conducting clinical trials and those funded by NIH are more likely to use private contractors for data management. For others, academic centers are their predominant data management organizations. For data capture, which is part of data management, the most common data transfer methods are hard copy, though multiple methods appear to be used by the organizations. With regard to standards, 61 percent of networks have developed some kind of common data standards related to their data management practice. Only about 18 percent are using CDISC. Overall, standards are viewed positively and are generally seen as improving data quality and increasing operations and shortening time lines. Dr. Smith also noted that, while the use of external standards is fairly low, it is encouraging that 42 percent of CRNs report they are participating in some kind of standards development efforts; 62 percent, or nearly two-thirds, plan to participate in additional standards development efforts; and, again, the NIH-funded networks report that they are more likely to plan to participate. The results also show that that data management barriers are staffing and defining common data elements. Key to success is the belief in the value of data management standards and common data elements. Facilitators in data management are electronic data capture, valued as a solution to labor shortages in a number of organizations, and use of common data elements. In conclusion, Dr. Smith observed that data management standards are coming but that there is a long way to go.

Dr. Smith concluded that flexibility and diversity of approaches is part of what information technology should support. The floor was then opened for questions for IECRN project staff.

The IECRN project staff responded to 12 questions:

Question #1 to Project Staff

Speaker: Elizabeth Hager with Balan Biomedical Analytics

Question/Comment (paraphrased): I take from your presentation the definition of data management did not include data analysis, and, presumably, that is because first order analysis will be focusing on the research questions. Is there an initiative to look at second order analysis of the data sets being created? Also, with regard to the financial side, is there a best practice for the financial business model, the business plan itself, because most companies would never exist, given the numbers you gave.

Mr. Durako's response (paraphrased): You are correct that we did not include the statistical analysis of data in what we consider data management. On the point of secondary analysis of data, this is actually something that was not highlighted enough. Several people have told us there is no resource available, generally, to use the data after you have done your primary publication for the study. So one of the recommendations is the need for set aside funding for secondary data analysis that will both lead to better use of the data in terms of answering multiple questions; and that will help inform the development of research agendas. I don't think the study identified a financial best practice.

Question #2 to Project Staff

Speaker: Doug Miller, from St. Louis University

Question/Comment (paraphrased): It is interesting that this important survey is taking place contemporaneously with the release and response to the CTSA RFA, and I expect that more than 95 percent of those responses include something to do with bio informatics, data management and IT. Is there anything about this survey that will inform the evaluation of the CTSA proposals when they are evaluated? That is perhaps a question for Dr. Sachs.

Dr. Sachs' response (paraphrased): This is a good question, and I would like to address it. I think we need to see where we are in IT, and that is why we are here today. The CTSAs and the future awards will have to look at a lot of issues that we are dealing with through the breakout sessions, especially in the informatics area and interoperability. So the timing is right, as you said, for seeing where are and using that information to go forward with the CTSAs and actually applying it is really of great value.

Question #3 to Project Staff

Speaker: Alan Morris, University of Utah

Question/Comment (paraphrased): I would like clarification of what you meant by internal interaction and open membership, because, in fact, contracts and grants are not open unless you are talking about the joining of a young investigator to an institution that already is a contractee.

Mr. Durako's response (paraphrased): That is a very important question. Bringing new people and ideas in the stream for clinical research networks is very important to promote interaction and the discussion of fresh ideas. You have recognized a barrier that needs to be addressed in some way; that is, if your grant is fixed, how do you make it possible for new people to come in? In my opinion, one solution may be for sponsors to encourage new investigators with new ideas to partner with research networks in their applications, where the network can bring a lot of the infrastructure and the force behind this, but the new partner is able to generate the scientific idea and to basically bring funding for both him or herself and the network to conduct that research. I can't speak for NIH, but I hope that that is something we will consider.

Question #4 to Project Staff

Speaker: audience member

Question/Comment (paraphrased): Regarding external interactivity, I think the way this was structured did not necessarily recognize a lot of the reasons the best practices became best practices and I want to say two things. First, AHRQ has done really yeoman's effort to create infrastructure for networks, to have methods conferences for networks, to have annual conferences for networks. This has greatly promoted external interactivity and I am concerned that there not be a bright wall or a line or a border wall between AHRQ and NIH in terms of promoting interactivity. The second is the specialty societies, such as the Federation of Practice-Based Research Networks, which is basically funded by secretariat support by the American Academy of Family Practice, and PROS, which is one of the best practice networks, is supported by the American Academy of Pediatrics. So, there are partners out there beyond the research community that we need to look at. My question is how do we make sure that these collaborations are honored and brought in?

Dr. Sachs' response (paraphrased): I want to acknowledge that you brought up some really good issues and really good points, and I think the future looks toward collaboration with HHS, with other agencies, as well as with societies. And I think we see that as very crucial and evolving in the future because we have to form these partnerships and collaborations.

Mr. Durako's response (paraphrased): I'd like to add that AHRQ stands for the Agency for Healthcare Quality and Research; they are the main sponsor of much of the practice-based research, and we did encourage their networks to participate in the IECRN study. This reminds me of a point I'd like to make that it is very important for different sponsors to try to figure out ways to pool their resources or to at least judiciously combine resources in certain areas to make things happen, because it isn't just NIH versus AHRQ or NIH versus CDC or others. Each of these agencies struggles to find adequate funds and the combining of those initiatives is important, even with sponsors outside of the United States and other governments, as well.

Question #5 to Project Staff

Speaker: Janet Holbrook, from the Johns Hopkins Center for Clinical Trials

Question/Comment (paraphrased): Information that was missing was who was in your study? We have three networks running in our center and only one of them is in your database.

Mr. Durako's response (paraphrased): I don't know how we missed them, but if we did miss, we are certainly interested in having them in our inventory. We tried every method we could to identify potential networks, including reading the literature, searching the internet, and asking people if they knew of other networks that we might have missed. The inventory is ongoing so it is not too late to join. We do recognize, as one of the limitations of our study, that we may not have identified every network during this phase of the project.

Dr. Sachs' response (paraphrased): Yes, the collection of networks is ongoing and, certainly, on our web site, we have an opportunity, if you think your network complies with our definition of a network or you know of other networks, please submit that.

Question #6 to Project Staff

Speaker: Linda Brubaker, Chicago

Question/Comment (paraphrased): Are there any plans for looking at the finances at the practice or institutional level for the unique aspect of clinical trials, where you have clinical costs and research costs and variable third party payers? And, without being able to have the practice or institution identify those as research costs and bill the grant or the Medicare for research, when it is appropriate, or the appropriate third-party payer, the finances may not get cleaned up, which impacts so many of the other aspects of the best practices. I think that it is information technology that needs to be able to identify the costs, but if this is out of the project's scope, are there are any plans to look at it?

Mr. Durako's response (paraphrased): You're right, it was not in our scope, although tomorrow morning we are going to have a plenary session from a representative of the Office of the National Coordinator on Health Information Technology, which is clearly oriented to sort of the universal health record, which I think we all hope will include research components. I think that is an area where there is great potential for being able to delineate clinical tests that are part of the research enterprise and actually be able to take advantage of what clinical tests and visits are covered by third-party payers.

Question #7 to Project Staff

Speaker: Bob Harrington, Duke University

Question/Comment (paraphrased): Did you question networks about ownership of data? In particular, for the NIH-sponsored networks or projects, did you talk about when data becomes publicly available and available to other researchers? And on the industry-sponsored side, what percent of these networks actually have true independent ownership of the data that allows all the other things, including secondary analyses, building of careers for junior investigators, et cetera?

Mr. Durako's response (paraphrased): I don't recall if we asked the question explicitly that way, but we did address issues such as publication policies and data sharing policies in the management and governance survey. The issue of who owns the data is an important one, and many of you are aware of NIH's push to have plans in every application for how you are going to share the data. But in our study we don't have any

data on ownership by network at this point, though it is certainly is important to external interactivity, as well as secondary data analysis.

Question #8 to Project Staff

Speaker: Barbara Calabrese, the American Medical Directors Association Foundation

Question/Comment (paraphrased): First, let me commend you on all the work that you have done and all the information you have provided. I was wondering if there are any opportunities to begin to look at those organizations that are more society-based rather than academic and then to compare and contrast them with the academics to see what differences and similarities they may have.

Mr. Durako's response (paraphrased): That is an excellent question and suggestion. Because this project moved along very quickly and collected a large amount of information, we made our first very broad-brush cuts at just presenting some fairly simple and straightforward findings. We hope to dig deeper into questions like the one you raise. What we have done so far is compare networks that conduct primarily clinical trials with others, and those funded primarily by NIH vs. those with other sources of funding.

Question #9 to Project Staff

Speaker: audience member (from NYU)

Question/Comment (paraphrased): You mentioned that these CRNs have been around for over 50 years. What was the initiative that had the greatest impact, and was this a randomized control trial and what is the percentage of these CRNs that can handle a true RCT versus other forms of clinical research?

Mr. Durako's response (paraphrased): Well, as a politician, I won't answer the first question. I think there are probably many CRNs who have had an impact. Examples of success include the cancer cooperative groups (some of the oldest networks are in the cancer field) as well as the National Surgical Adjuvant Breast and Bowel Project, which may be the oldest network in our inventory. Regarding clinical trials, 40 percent of the networks are doing true randomized clinical trials.

Question #10 to Project Staff

Speaker: Andy Nierenberg, Massachusetts General Hospital and NIMH-sponsored bipolar trials network

Question/Comment (paraphrased): I wonder if you have given thought to the minimal requirements that a network must have in order to function and, related to that, have you thought about coming up with metrics to assess networks?

Mr. Durako's response (paraphrased): Developing metrics is a good idea. Although it was not part of our project, if you wanted to look at effectiveness and efficiency, metrics would be necessary. I am not sure I can answer the question about the minimum needed to have a network function. I think, obviously, you need some kind of scientific or medical leadership, because you need some kind of agenda. Clearly, you need to have access to some sites, whether they are dedicated sites or whether you get them on a study-by-study basis. My own personal belief is the you need funding for infrastructure. How much infrastructure is debatable, but if

you don't have some core that is there that can maintain the network and, in particular, can continue to generate ideas and obtain funding, you can't do the work. As I said earlier, we interviewed a few network that are dormant, they don't have core funding. So once one study ends, if they didn't get another one funded, they basically are out of business for the time being. They are technically still a network, but nobody is doing anything because nobody has any time.

Question #11 to Project Staff

Speaker: audience member

Question/Comment (paraphrased): We have heard repeatedly about the importance of community involvement in various medical research networks and we heard something about family involvement. Were you able to identify best practices in terms of involving the community of patients, participants? Not the clinicians, but the patients involved.

Mr. Durako's response (paraphrased): There are a number of networks, particularly in the HIV field, and now moving into the cancer field, that have what they call community advisory groups and in the HIV field, this started with, basically, advocates from the affected population groups. That has extended into advice from organizations, advice from actual real geographic communities. I am working on an HIV network where part of what we are trying to do in order to pave the way for HIV vaccine studies is to go out and engage the community and all the community groups and help them understand what we are trying to do and what it is about and that it is not just experimentation. The cancer community has certainly developed many, many patient advocacy groups, as well as associations that advise the agenda, and I would say that is an important thing to do. If the patients don't want to participate, if they don't think it is relevant to them, if they are afraid they are being experimented on, then you are going to have trouble with recruitment and retention.

Dr. Sachs' response (paraphrased): I would like to add that the HIV community and the HIV networks are a good example of doing something a little bit different and doing care based on their doing it in developing countries, family care. So it is women who can come in pre-pregnancy, post-pregnancy, prenatal care, postnatal care, and, also, their family can come in and get care. This is a network based on total care, age span across the board, rather than delineating different network groups, like pediatric care or maternal care or the elderly. It is across-the-board family care community and it is based on a community type care system and it works well, I think, in the developing countries, where they usually come in and they come in collectively as a group.

Mr. Durako's response (paraphrased): I think that is a very important example that Jody mentioned. It is something that is usually called PMTCT Plus. Prevention of Mother-to-Child Transmission is the PMTCT. The Plus is you are not just trying to prevent transmission to the child, but you are trying to deal with all of the healthcare issues of the mother, the baby, and the extended family. That adds value and it makes people understand or appreciate you are not just coming in to experiment on them, you are trying to take care of them.

Question #12 to Project Staff

Speaker: audience member

Question/Comment (paraphrased): I want to endorse your notion of core funding as key to success and ask the question about whether you observed anything differences between whether that core funding was internal or external and if that makes any kind of difference.

Mr. Durako's response (paraphrased): We did not address that. There are different models for that, one of which (the Cancer Trial Support Unit) we are working on now, where NCI has attempted to take some administrative functions and totally centralize them within one contractor as opposed to putting them in every single cancer cooperative group. While I am biased in thinking that that is a good model because I am working on it, I do not know if everyone would think that that is a good model, though it has potential if you have many networks doing the same kind of thing or needing the same kind of core infrastructure, like regulatory support and other kinds of things that are not really specific to the network's scientific agenda.

JUNE 1, 2006

Welcome

Barbara Alving, M.D., Acting Director, NCCR

Dr. Alving welcomed participants and reviewed the agenda for the day. She commented on the interesting poster session on the first day of the meeting and how pleased she was to observe the many and productive interactions among attendees. To clarify why many of the Roadmap Initiatives are housed at the National Center for Research Resources (NCCR), she explained the difference between categorical and noncategorical ICs [NIH Institutes/Centers]. A categorical institute/center focuses on specific diseases (e.g., National Heart, Lung and Blood Institute), whereas a noncategorical IC provides infrastructure throughout the NIH. Thus, NCCR, a noncategorical IC, reaches out and works with all the other institutes of NIH. The NCCR, Dr. Alving commented, has four divisions. The Division of Research Infrastructure is responsible for the Institutional Development Award (IDeA) Program, which Fosters health-related research and enhances the competitiveness of investigators at institutions located in states in which the aggregate success rate for applications to NIH has historically been low. Some very robust informatics efforts are taking place in some of these states that are challenged by low population and vast distances. This is an ideal setting for the challenge of informatics and connectivity. Dr. Alving also described the activities related to informatics and connectivity in other NCCR divisions. For example, the Division of Comparative Medicine funds eight national primate centers, where they are using informatics to link up the research, and the Division of Biomedical Technology has developed new ways to do research with large instrumentation, and improvements of instrumentation. Finally, the Division of Clinical Research has been heavily involved in the CTSA's, the Clinical and Translational Science Awards. NCCR's informatics efforts are led, in part, by Dr. Peter Highnam.

NCCR is also very interested in how to connect clinical research informatics with health IT and is greatly interested in what is being done in the Department of Health and Human Services. Dr. Alving urged the research community to continue working in these domains. She then introduced Kelly Cronin, Director of the Office of Programs and Coordination in the HHS Office of the National Coordinator for Health Information Technology, the office responsible for achieving the President's vision of interoperability of health care information systems. Ms. Cronin is responsible for ensuring complete integration of all efforts across the Office of the National Coordinator and supports the dissemination and adoption of the administration's policy on health IT. Dr. Alving also provided an overview of Ms. Cronin's accomplishments prior to this assignment.

Keynote Speaker

Kelly Cronin, Director, Office of Programs and Coordination, Office of the National Coordinator for Health Information Technology (ONCHIT)

Ms. Cronin expressed appreciation for the opportunity to attend the Forum and noted that clinical research is one area that really stands to benefit from widespread adoption of interoperable electronic health records and personal health records and, the deployment of a nationwide health information network. First, she presented an overview of the Office of the National Coordinator and its major initiatives to try to reach the President's goal of having most Americans by 2014 have their own electronic health records:

- American Health Information Community
- Standards Harmonization Process
- Compliance Certification Process
- Privacy and Security Solutions
- Nationwide Health Information Network Prototypes
- Health Information Technology and Health Care Anti-Fraud
- Health IT Adoption Initiative
- Proposed Changes to Self-Referral and Anti-Kickback Rules

The Office was established through an executive order a little over 2 years ago, creating a new position of a national coordinator for Health Information Technology (HIT), similar to some of the other what's commonly referred to as czars, the drug czar or the AIDS czar, with broad responsibility across the executive branch, yet they are typically housed within one particular department or agency. David Brailer, who has recently stepped down, served in the role over the last 2 years. The broad vision put forth by the administration was to try to have a fully electronic healthcare system, with widespread adoption of electronic health records and personal health records, and a way to connect clinicians and patients across settings of care. This will allow medical information to follow the consumer and not necessarily be stuck within a skilled nursing facility or just within a hospital or in an outpatient clinic. It was also considered an opportunity to start the transition from a payment system, at least in the federal government, with Medicare and much of Medicaid, which is based on fee for service to a quality-based or performance-based system. Thus, the infrastructure will serve a variety of purposes, not only in delivering evidence to the point of care, but also being able to get the right data out of clinical care, not only for better performance measurement or quality measurement, but also for public health.

Ms. Cronin presented a slide that identified four Offices within the Office of the National Coordinator:

- Office of Health Information Technology Adoption
- Office of Interoperability and Standards
- Office of Programs and Coordination
- Office of Policy and Research

Ms. Cronin also discussed four major goals of the Office:

- Inform clinical care, essentially trying to get the right kind of electronic health records fully integrated into the system.
- Interconnect clinicians so that the data flow from one setting or one clinician to another in a seamless way.
- Personalize healthcare, so that personal health records are interoperable and longitudinal, and can serve as a tool for health self-management, as well as to share with clinicians across the lifetime.
- Improve population health, though improvements in quality of care and the surveillance system for public health.

Anecdotal data, Ms. Cronin commented, suggests that as recently as a couple years ago, roughly 70 to 80 percent of the system, both public and private sector, was still primarily paper-based. Ms. Cronin described efforts over the past years to make the market more efficient and interoperable. This work has been done with Federal partners not only within HHS (NIH, FDA, CMS, the Agency for Healthcare Research and Quality, CDC, HRSA), but also the VA, the Department of Defense, the Department of Commerce, Treasury, and Office of Personnel Management. Outreach has also been conducted with vendors and with states, as well as international partners.

Ms. Cronin reviewed the initiatives underway, including the American Health Information Community, chaired by Secretary Mike Leavitt, which is an advisory committee made up of leadership across the public and private sector, all the major stakeholders of healthcare, to advise the secretary on how to move forward. The Office has also supported a standards harmonization process, recognizing that there is a lot of activity going on across standards development organizations that is not coordinated, and has efforts underway to improve the quality of products in the market, so that they become interoperable over time and incorporate privacy and security features. The Office is also funding four nationwide health information network prototypes, has projects that examine the impact of health IT on fraud and abuse in healthcare, and has a research initiative to standardize methodology on how to measure adoption of health IT.

The concept of National Health Information Network (NHIN) has existed for some time. About 1½ years ago the Office requested information and received 500 responses from various experts across the country. Some of the concepts that emerged are that the NHIN should be a nationwide utility that allows for secure and seamless health information exchange; a decentralized architecture that is built using the Internet, but linked by uniform communications and a software framework of open standards and policies; and should be governed by both public and private stakeholders. In particular, there needs to be sufficient safeguards so that the data cannot be tampered with.

Ms. Cronin also noted that there are many regional efforts going on across the country, and from these we can learn what works and doesn't work. She also mentioned that they have already proposed some regulatory changes and are in the process of finalizing two regulations to allow for hospitals and other designated entities, through Medicare, to donate electronic health records to physicians. Many large hospital systems would like to do this now, but they are prohibited under current law.

Ms. Cronin commented that the Office is off to a good start, and that she expects each year to be able to introduce more rigorous criteria for interoperability, for functionality, and for privacy and security. After work is completed on ambulatory electronic health records, the focus is going to move to inpatient. In 2008, ONCHIT will be taking on the certification of the NHIN to make sure that everything connects together, so that the interoperable or certified EHRs can share information with the NHIN.

The advisory committee chaired by Secretary Leavitt (for the American Health Information Community) has high level leadership across HHS, as well as hospitals, physicians, nursing groups, and other major stakeholders, though not all federal agencies are currently represented (including Dr. Zerhouni) due to a cap on the number of members that could be appointed. The committee has been convening for the last 8 months and their initial recommendations were to come up with some short-term priorities. They have guided the Office to focus on four different areas, each with its own workgroup:

- **Biosurveillance;** this is line with Secretary Leavitt's priorities around pandemic flu preparedness;
- **Consumer empowerment;** relates to how we get information out to consumers in personal health records and what types of information would be most valuable to them;
- **Electronic health records;** involves trying to get lab data exchange in a patient-centric manner;
- **Chronic care monitoring;** aimed at connecting both patients with their physicians through structured email or secure messaging.

Ms. Cronin then introduced the broad and the specific charges for each of workgroups associated with these breakthrough opportunities. She presented a slide depicting Health Information Technology Deployment Coordination to illustrate what the Office is doing to support the long-term transformation of the industry through standards harmonization, certification, and the development and deployment of the NHIN.

Next, Ms. Cronin presented information on the Regional Health Information Organizations (RHIOs), which are regarded as a good first step to getting something accomplished on a local level that will make it meaningful to the local healthcare market. These organizations are meant to be nongovernmental, multistakeholder, and they provide the policy and technical framework that is needed for health information exchange. They bring to the forefront the issue of a sustainable business model for health information exchange. Ms. Cronin also discussed the principles guiding the implementation of RHIOs, some specific examples of success within the program, and next steps in supporting these regional program.

Ms. Cronin presented information on barriers and solutions to the secondary use of data. She discussed how HIPAA [The Health Insurance Portability and Accountability Act] has solved some problems but perhaps has caused some confusion about sharing of health data for research purposes, and the importance of setting the right policies that will oversee the access and aggregation of this data for a variety of purposes, including clinical research, health services research, population health monitoring, and vital statistics.

Ms. Cronin next discussed opportunities for clinical research and commented that many in the audience are already involved in exciting activities to try to use informatics to improve the quality and ability to do robust clinical research. Some of the efforts already underway through CDISC, NCI, and the FDA, in particular, have helped to bridge what is happening in industry, academia, and government. More coordination across

sectors in terms of standards for clinical research will enable the health IT standards panel to name standards for clinical research and to identify the right implementation guides.

In closing, Ms. Cronin announced that a public meeting is being held the end of June (28th and 29th) for people interested in knowing more about the functional requirements for the NHIN. She particularly encouraged participants to attend the meeting if they feel that clinical research needs are important to be represented.

Next, Ms. Cronin addressed four questions from the floor.

Question #1 to Ms. Cronin

Speaker: Jim Mold, University of Oklahoma

Question/Comment (paraphrased): If you are going to use this kind of data for clinical care, I think one of the most important issues is capturing outcomes. I have not heard much about capturing important outcomes; for example, mortality. It is traditionally very difficult to find who is dead. You would think you would care about that, but that's a whole different data set. Cost is another issue and while we can capture costs through the national health information infrastructure, we should be able to capture all the costs. Right now we can capture our own charges from our own office, but to capture overall costs is difficult. So outcomes like mortality and cost would be nice to incorporate in this for clinical researchers. I would think it would also be helpful for clinicians.

Ms. Cronin's response (paraphrased): Those are great points. There is a keen interest in trying to determine how electronic health records and the various data sources that will be sort of the backbone of the NHIN, so to speak, can be collected, aggregated and analyzed in such a way so that we can understand the health outcomes of given patients. As I mentioned before, the performance-based or quality-based payment system that we want to move to is going to be dependent on that. So there are a lot of efforts underway now through the Ambulatory Care Quality Alliance and other organizations to determine how we can use these electronic data sources in such a way that we will be able to accurately measure health outcomes. I don't know that the mortality issue is going to be resolved anytime soon, because there are obvious problems around death certificates and registries. However, more people are talking about the need to integrate vital statistics into the agenda. Part of the challenge is that there are so many needs in so many areas, and it will take our small office time to prioritize all of the needs and make sure they are addressed.

Question #2 to Ms. Cronin

Speaker: Bob Harrington, from Duke University

Question/Comment (paraphrased): Thanks for the presentation. When you showed your diagram of the organization within the Office of the National Coordinator, you list these four divisions that are led by a director, but I didn't see one for research. I'm wondering where the research responsibility lies and who is it that takes responsibility for making sure that the research agenda is being considered in all of these efforts. I wonder if thought has been given to creating a division at director level for research responsibility.

Ms. Cronin's response (paraphrased): It's a great point. The Office of Policy and Research is supposed to be looking after the research needs of the office. We have not gotten to the point through the American Health Information Community that they have agreed to prioritize research, but it is very likely that over the next 6 months, we are going to do some type of priority setting process where we would get testimony from the research community for them to express their opinion and communicate the benefits that could be achieved if, in fact, this were made a shorter term priority.

Question #3 to Ms. Cronin

Speaker: Jim Hunt, University of California-San Francisco

Question/Comment (paraphrased): How does your office view clinical research and clinical care and the differences with that data. We are often informed that clinical research has a different granularity or reliability of the database that they use versus what clinicians use. Do you or does your office have views of the differences in data that clinicians need and clinical investigators need or do you think that can be harmonized and how would you propose to do that?

Ms. Cronin's response (paraphrased): It's a great question. I don't think we've thought enough about the issue, to be honest. I think that over time, the intention is to have standardized nomenclature. So that, ideally, SNOMED will be adopted in all electronic health records and we will have the terminology that will be sensitive and specific enough to not only allow for really robust clinical decisions to support health care delivery, but, also, that can transfer into the right type of database for a variety of different research purposes. Right now we are probably not at a point where we have consistent granularity across the system that's emerging, but we hope, over time, to progress to that. Part of the challenge is that physicians and clinicians using these tools don't necessarily want to be slowed down by choosing all the terms and taking that extra time away from patient face-to-face time to really make sure that he has the perfect terminology captured in his EHR. I think there will be a balance that we will have to achieve over time to make sure that we not only improve clinical care, but also have the data available for all these important secondary uses. One of the things that I think is clear is that I don't think the clinical research community has been engaged enough to date in many of the activities that are going on. Over time it is going to be important for the voice to be heard at the certification commission, the health IT standards panel, and, to the extent that NIH can make their views known, too, to the department.

Question #4 to Ms. Cronin

Speaker: Kevin Peterson, University of Minnesota

Question/Comment (paraphrased): You have mentioned many things that reflect some aspects of the English system, a single system with birth-to-death records. One of the things they have in England that we do not have in the United States is a national medical insurance number. Is the identification of a universal ID a solvable problem here?

Ms. Cronin's response (paraphrased): That is probably one of our most challenging issues right now. The Federal Government, at least HHS, is probably not going to be pursuing a unique identifier. I think we're prohibited by law to do that right now. But we can be looking at a standardized way to identify patients and to also match patients to their records. There are algorithms that are being fielded and piloted in a couple regions in the country to determine how we can maximize the success rate in matching patients to their records using a certain number of data elements that uniquely represent that patient. Over the next several months, we're likely going to be taking this on through a variety of public meetings, to figure out how to move this forward, because it is a critical and time-sensitive issue.

Breakout Session: Management and Governance

The content experts for this session were Dr. Ira Shoulson, Louis C. Lasagna Professor of Experimental Therapeutics and Professor of Neurology, Pharmacology and Medicine at the School of Medicine, University of Rochester, and Dr. Andrew Nierenberg, Associate Director of the Depression Clinical and Research Program, Massachusetts General Hospital and Associate Professor of Psychiatry, School of Medicine, Harvard University. The session moderator was Dr. Patricia Dolan Mullen, Professor of Behavioral Sciences and Health Education and Training Director at the Center for Health Promotion Research and Development, School of Public Health, University of Texas-Houston Health Sciences Center.

Dr. Mullen presented the findings from the Management and Governance breakout session regarding the characteristics of attendees and barriers and facilitators discussed by the group. She presented slides showing that session attendees were primarily identified with academia and government, with some representation from clinical research and organizational networks, and that many held positions of leadership within their networks. Facilitators identified by the group included the following (in rank order):

- Scientific agenda
- Funding
- Communication
- Collegiality
- Sponsor direction
- Community support
- Protected time
- Diversity

Barriers, in rank order, included the following:

- Funding
- Communication
- Collegiality
- Sponsor direction
- Protected time
- Scientific agenda
- Community support
- Diversity

Next, Dr. Shoulson reported that the group felt a lot could be learned and gleaned from the business world, including dimensions of strategic planning, milestone-based engineering types of models, and end-driven mission versus enhancement of an academic career. There was also a great deal of discussion on performance metrics, which are gradually evolving and taking shape. The idea of a toolkit, something that could be a common resource not just for clinical research networks, but also for sponsors, was a concept that emerged from the breakout session. Project officers from NIH attending the session agreed that a toolkit could be a

valuable way to share information. Dr. Shoulson reported that there was consensus that this would be a public access tool for network management and governance. Possible elements of a toolkit include the following, in rank order:

- Committee functions and organization
- Common NIH resources
- Constitutions and by-laws
- Publication policies
- Conflicts-of-interest policies
- Web site (clinical research)
- Publications of clinical research
- Web site (contract research)

Dr. Nierenberg spoke about the issue of leadership that was discussed in the breakout session, including the question of how to develop effective communication and collegiality. Dr. Nierenberg noted the lack of leadership training currently available centrally through NIH or other organizations. He presented a slide that depicted Hackman's "Leading Teams," a resource that provides skills and principles to follow. We could also benefit from sharing our leadership lessons – addressing what has worked well and what mistakes have been made. In summary, Dr. Nierenberg presented a slide with the main issues addressed during the Management and Governance session:

- Sociology of CRNs
- Borrow from business models
- Share between CRNs and among sponsors
- Leadership training
- Research and development and practice
- Address unmet needs of those affected by or at risk for the condition (disease; illness); will it improve patient outcomes?

The floor was opened for questions and comments:

Question/Comment #1

Speaker: Susan Berkowitz, Westat

Question/Comment (paraphrased): In the discussion that occurred yesterday, there were a lot of very specific examples that different networks gave about how they handle their publication policies, and I would hope that that would somehow be captured in the write-up because I think people were very interested in the specifics of how different networks have actually dealt with those issues.

Response (paraphrased): That was a topic that people have struggled with to make sure that everyone feels good about what they participate in and there have been, I think, both problems and opportunities with different approaches. Thanks for bringing that up.

Question/Comment #2

Speaker: audience member

Question/Comment (paraphrased): I have a question about the research agenda setting. I assume that “unmet need” in the bar chart means public health need. As there wasn’t any mention of innovations, I was wondering whether that was part of the discussion because in our network, our PIs have conceded early on that our product will probably never win a Nobel prize, but they are comfortable with that because the purpose of the network is different. So I am wondering whether the panel or the group has discussed innovation, one of the reviewing criteria for NIH.

Response (paraphrased): There was not much discussion in the group about that. Of course, innovation as a review criterion, as applied to clinical research, has been modified, as we know, by NIH in the past year or two to better accommodate the nature of clinical research. There are certainly many innovating aspects of clinical research but not in the traditional way in which innovation is applied to science in general.

Question/Comment #3

Speaker: Alan Morris, University of Utah

Question/Comment (paraphrased): I saw a number of interesting things in your list of items for NIH project officers. As someone just mentioned, I didn’t see publications and I wonder if linked to publications there might not be some consideration of what one does to assure proper ends and not just academic career advancement for new investigators. Also, did you discuss the consent document among those tasks for the new NIH project officer? That’s another very important issue that might benefit quite well from a more standard and uniform approach.

Response (paraphrased): I agree that consent documents would be a great toolkit issue and, in fact, those of us involved in clinical research know if you really want to get at the nitty-gritty of what somebody is talking about, read the model consent form. However, we did not discuss it at great length. We did spend a lot of time discussing publication policy. One of the concerns raised is that publication policy is very interesting, but a bit self-serving; however we realize that issues such as authorship are an important part of clinical research networks.

Question/Comment #4

Speaker: Jonathan Tobin, Clinical Directors Network, New York

Question/Comment (paraphrased): The strategies for disseminating research results were an area that I think has been under addressed both in the conference, as well as in the session yesterday. I think we create the new knowledge, the innovations, but fall short at the point at which we disseminate and translate them. I wonder if there is a strategy or opportunity to build that into the requirements, or into the evaluation of the adequacy and the effectiveness of the performance, and make it part of demonstrating whether or not something works.

Dr. Sachs' response (paraphrased): That's a great point. Thank you.

Breakout Session: Network Operations

Content experts for this session were Kevin Peterson, Associate Professor, Department of Family Practice and Community Health, University of Minnesota, and David Schoenfeld, Professor, Department of Biostatistics, Harvard School of Public Health. The session did not have a moderator.

Dr. Schoenfeld provided an overview of the presentation and noted that 78 percent of the session attendees reported that they had participated in the descriptive survey. Regarding their level of research experience, most people self-identified as advanced, with a few people as experts and intermediate. Most reported that they were involved with NIH-funded trials.

Dr. Schoenfeld next presented barriers and solutions identified with the four components of network operations: protocol development, protocol implementation, regulatory procedures, and communication. Four points were discussed pertaining to *protocol development*: that funded grant proposals are not protocols; the use of protocol templates, the use of consent form templates, and the concept of “measure twice and cut once.” The key message is that the time it takes for protocol development is time well spent and shouldn’t be shortcut. In the discussion of *protocol implementation*, a session attendee described how their network conducted a patient recruitment survey before the study started to get a better idea of expectations for recruitment. Another suggestion was to maintain a database of all past and concurrent studies. The discussion of *regulatory procedures* focused on how IRB approval for multisite studies can be a barrier and that the current system can be confusing and difficult to navigate, due to inconsistent reviews and many levels of review. Strategies for improving *communication* were also raised, including a coordinating center with two shifts to cover time zone differences; conducting regular meetings, and using a central web site.

Next, Dr. Peterson provided a summary of the group’s discussion of *best practices*. He observed that many of the best practices discussed in the session reflected the barriers that were discussed earlier. In the context of site selection, about half of the session attendees selected sites based on performance-based criteria (i.e., who did well in the previous study, in contrast to others who seemed to be applying the idea of bringing people in and nurturing them along through training. Best practice for the development of protocols was standardization and simplification, as well as selection of the appropriate protocol. Other suggestions included polling membership to assess their interests and streamlining the data collection. Also discussed, Dr. Peterson reported, was the importance of staff training. The next topic in the session was how networks conducted site monitoring. The IECRN findings emphasized the importance of having a local relationship with the site, which is facilitated by aligning the incentives of the sites with the incentives of the central organization.

With regard to attendees’ impressions of the IECRN findings, some expressed surprise that the study primarily provided a description of what currently exists rather than prescriptions for best practice. The attendees expressed interest in more specificity regarding what works for networks with different characteristics or purposes. The group also discussed the importance of emphasizing the need to develop metrics for health improvement rather than the metric for the network itself. Using the electronic audience response system, the group also provided recommendations on what practices should be adopted. Resources and mentoring were considered the most important, as well as most likely to be adopted. IRB and regulatory

reform, along with resources and mentoring, were the areas that most participants would like to see changed.

The floor was opened for questions and comments:

Question/Comment #1

Speaker: Janet Holbrook, Johns Hopkins

Question/Comment (paraphrased): Did you discuss data and safety monitoring boards? One of the issues that we're facing in our asthma network is we have funding from different places and sometimes the funders want different DSMBs. It is quite onerous to be reporting to more than one DSMB, and they aren't able to integrate all the research we do and we get very mixed messages.

Response (paraphrased): DSMB issues did not come up specifically, although the group indicated that IRB issues are a hot topic and a real barrier with no easy solution. We did not discuss any specific DSMBs.

Question/Comment #2

Speaker: Alan Morris, University of Utah

Question/Comment (paraphrased): Did you discuss the attributes of networks with regard to some of these important issues? In particular, did you focus on what networks were specifically intended to accomplish?

Response (paraphrased): No. We focused in our session on getting the ideas of the group, which agreed with you and asked the same questions.

Question/Comment #3

Speaker: Bruce Pihlstrom, National Institute of Dental and Craniofacial Research, NIH

Question/Comment (paraphrased): Could you expand on the discussion regarding a metric of health information or health improvement rather than specific operations of the network?

Response (paraphrased): One of the comments raised was that we are looking at network operations, but we also need to look at the overall effect on health improvement; that the purpose of the research is to influence healthcare and we haven't been measuring our practices related to our ability to change clinical practice.

Breakout Session: Data Management

Content experts for this session were Elsa Villarino, Chief, TB Trials Consortium Team, Clinical and Health Systems Research Branch, Centers for Disease Control and Prevention, and Meredith Nahm, Director of Clinical Data Integration, Duke Clinical Research Institute. The session was moderated by Therese Brown Gibson, Program Director, Health Communications, Aspen Systems/Lockheed Martin.

Ms. Nahm began the presentation by introducing the group's overarching observations about the survey. One was that the absence of clear definitions limited its value, and that participants wanted to delve down into the more detailed aspects of data management and how it was done in different networks. The participants were also concerned that the findings would be utilized to mandate requirements for future RFAs and RFPs, which would limit an organization's ability to be creative or innovative in how they approach operational aspects of trials. Another overarching comment was that there was no evidence base with quantitative information for data management operations and that in lieu of an evidence base it is not possible to identify best practices.

Topics discussed in the session included data center placement, management and oversight of the data center, policies and procedures, methods used to transfer data, and utilization, adoption and implementation of data standards within networks. The audience response system results indicated that there were approximately 90 participants; an average of 52 persons responded to the polling questions; the range was from 41 to 72 respondents in the room. Seventy-three percent of the individuals in the room declared that they were associated with a clinical research network.

The group discussed whether *centralization* is a best practice. Eighty-three percent agreed that centralizing data operations in one center is a best practice overall; 67 percent agreed it was also a best practice in global and international trials, and 88 percent said—in the absence of constraints such as funding, politics, existing structure, roles and responsibilities—they would implement this in their own networks. Ms. Nahm mentioned several relevant comments from participants, including that centralization can improve data quality as far as the fidelity in the data processing; that there also needs to be consideration of standardization of procedures implemented at the site; that industry sponsors tended to maintain or want to maintain data ownership, which may mean a difference between centralization or not for data centers who did industry versus government trials; and that curating data or applying certain standard terminology sets or coding should maybe be done at the sites. The overarching comment was that if poor quality data is integrated at a central center, it is still poor quality data.

The next topic discussed by the group was *data management and oversight*. Eighty-eight percent said that it is a best practice to have an individual responsible for data management on the network. An overwhelming 100 percent said that they would like to implement this in their own networks. Fifty-nine percent said that having a standing committee dealing just with data management issues was also a best practice and 70 percent said that they would implement that practice within their networks. Regarding *policies and procedures*, 89 percent voted that documenting is necessary or helpful for data quality; and all (100%) of participants also said they would like to implement that practice. Ms. Nahm also noted that there was considerable discussion of who writes the SOPs—do you leverage the infrastructure of the organization providing the data center or should the network itself write the SOPs? The group concluded that it really did not matter who wrote the

SOPs, as long as all of the stakeholders had input and that the people who were going to use and implement the SOPs had input into those SOPs.

The use of *electronic data capture* (EDC) technologies was the topic of the next discussion. Seventy-six percent agreed that EDC is a best practice, and 88 percent would adopt this practice if there were no barriers to using it. Interestingly, half of the group believes that use of EDC would increase the total cost of trials, while the other half thought it would result in a decrease in costs. Ten percent reported that use of electronic data capture increased the total time from protocol to data lock, whereas 90 percent said it decreased the time. Important comments included that we need studies of the cost effectiveness of electronic data capture and, also, that we need studies to evaluate the impact of electronic data capture on data quality.

Ninety-eight percent of the session participants responded that they *measure site performance* and it was a best practice; everyone agreed they would implement this practice in the absence of barriers. Participants suggested that measuring site performance is most applicable and helpful when sites are in trouble, either with data quality, with timeliness of submissions or adherence to procedures; and that it is critical to have acceptance criteria stated in policies and procedures. *Data standards* were also discussed. The group was asked whether developing standards specifically tailored to the CRN is a best practice—81 responded that it is. Next, when asked if using nationally recognized standards (e.g., ANSI standards or CDISC or HL7 standards) is that a best practice, 78 percent said that it is, with 84 percent saying that they would implement nationally recognized standards in the absence of barriers. The group discussed how, in the absence of nationally recognized standards, it is helpful to develop local standards; but that national standards should be used and implemented where they exist.

In closing, Ms. Nahm thanked the participants, Dr. Villarino (content expert), and Ms. Gibson (moderator) and opened the floor to questions.

Question/Comment #1

Speaker: Mike Dean, University of Utah

Question/Comment (paraphrased): I would like to add something about how the votes and discussion about electronic data capture were in the context that no one could define what electric data capture meant. There was no discussion about FDA validation requirements when you did direct electronic entry. There was a lot of concern about not having source documents. So this was not about electronic transmission of data. Thus, I don't think there should be a conclusion that EDC—the way it's usually meant in the literature, which is there is no paper—should be the best practice. I don't think that's what the group agreed upon.

Response: Thank you.

Question/Comment #2

Speaker: Gregg Fromell, University of Pennsylvania

Question/Comment (paraphrased): I have one comment and one question. First, I think SOPs are critical, but I became concerned when there was mention that the group talked about SOPs specific to a protocol. In

my understanding, SOPs define overarching responsibilities and processes and policies, and that procedures or manuals of policies and procedures are specifics on how one *implements* SOPs. The other comment pertains to site performance. Did the group talk much about using site performance as a way to identify those sites that need more mentoring or infrastructure? All of us involved in research long enough know that a site that is stellar one year can perform poorly the next, because they don't have the right infrastructure, or they lost that key coordinator.

Response (paraphrased): There was a lot of discussion about having acceptance criterion or that bar that helps identify sites that are in trouble and need help. We will be sure to emphasize this topic in the write-up. However, it is important to point out that it does not mean dismissal of the site, but rather it's to identify where you could intervene early, get sites above those criteria so they are not lost. Your first comment about SOPs, illustrates how critical it is to use common terminology. Clear definitions are needed and that could help us with our current recommendations.

Question/Comment #3

Speaker: Julia Zachary, George Washington University

Comment (paraphrased): I would like to reinforce your comment that the questions were confusing and that many of them in the area of data management may be invalid. This relates to your observation that 30 percent of the people in the room were nonrespondents [did not vote] and that is exactly the reflection of the fact that the questions weren't there. Thank you.

Question/Comment #4

Speaker: Joyce Niland, City of Hope

Question/Comment (paraphrased): I have one suggestion about standards. I am involved with the bridge modeling process in caBIG and CDISC and would like to recommend indicating that we all move toward adopting national and international standards as we go into global research and multicenter studies across different countries, and HL7 is international. Another general comment is that I'd like us to begin to focus on information management rather than data management and information technology. We should look at technology as one of the tools, along with human, organizational and other resources.

Dr. Sachs' response (paraphrased): That's an excellent point, because there is so much overlap in both sections, and I appreciate that comment. Thank you.

Question/Comment #5

Speaker: Lynn Rose, Cystic Fibrosis Therapeutics Development Network

Question/Comment (paraphrased): Did you discuss the value of onsite monitoring from coordinating centers. In our network, we often have difficulty getting enough funding to do onsite monitoring of source data against the case report forms, which is an important part of data quality. I was wondering if people in the group had developed risk-benefit formulas for monitoring frequencies, both for EDC, as well as paper.

Response (paraphrased): We did not address monitoring or the source document verification part of monitoring directly. The discussion went towards the actual quality of data in the source and getting that data documented correctly and how technologies, like decision support, can help do that.

Question/Comment #6

Speaker: Alan Morris, LDS Hospital and University of Utah

Comment (paraphrased): If one uses, at the bedside, an electronic tool for establishing quality and decision support, it becomes the source document and the monitoring demands diminish dramatically, because the data that are transmitted electronically are, in fact, the data that drive decisions. So these issues are tightly linked, the quality of the data, and the quality of the interaction and monitoring.

Response: Thank you.

Breakout Session: Information Technology

Content experts for this session were Charles Jaffe, Senior Global Strategies for the Digital Health Group at Intel Corporation, and Rebecca Kush, President of CDISC. The session was moderated by Wayne Kubick, Senior Vice President with Lincoln Technologies. The leaders of this session opted not to use the electronic audience response system technology.

Mr. Kubick, session facilitator, began the presentation by providing some of the demographics of the group. There were approximately 60 people in the session; about 30 indicated they were IT professionals, 5 were principally clinical, 10 data management, and 10 statisticians. The group initially spent some time clarifying what is meant by out-sourcing, with the key conclusion being that out-sourcing is considered to be desirable and commonly practiced. To provide clarity, the group tried to discuss infrastructure and application as separate concepts. According to Mr. Kubick, there was genuine concern expressed by the group that the results of the survey and the Forum overall might be misinterpreted by the NIH, and that these findings do not clearly point to specific recommendations. However, there is the need to achieve more commonality across networks to improve efficiency. There was also discussion of the desire for a common level of proficiency that could extend over all networks, which might be in the form of a toolkit or provided or funded somewhat by NIH. caBIG was mentioned as the most prominent example of trying to provide shared infrastructure for a federation of networks.

Some participants said that the field may be too immature to be going into out-sourcing, partly related to the communication gap between the general technology world and the general research world. Skilled people, such as informaticians, are needed to bridge that gap. With regard to applications, while everyone had a web site, it was difficult to identify which applications were most important.

When asked what was missing from the survey, the group discussed the association between clinical data management and IT. They observed that specimen tracking systems, for example, were not included in the surveys, and adverse event tracking was also noted as a gap. The results showed that data standards were not used in most cases, despite their importance for interoperability. With regard to standard vocabularies, the NCICDEs are probably used most commonly. The session participants discussed the finding that NIH funded networks had better IT, and whether it might be because NIH tends to fund networks who have better IT infrastructures rather than those who are funded to build better infrastructures. A barrier to IT was how difficult it may be for CRNs to know what to buy and where to start. Web-based tools have probably presented the biggest change in technology in the last 10 years. People tend to make web-based tools very easy, which makes it possible for technology to be adopted, but it is key to play to the lowest common denominator, because some technology is out of reach for some users.

The session devoted considerable discussion to best practice, particularly what was value-added to IT. They talked about whether one can do things top-down and bottom-up at the same time and what types of examples might have shown ways to improve communication. The following networks shared their experiences – OKPRN, ARDSnet, CaReNet, The George Washington University network on high-risk pregnancy, MAFPRN, SWOG, and the Buffalo primary care research network.

When the group was asked what they found surprising in the study, they mentioned that some of the more advanced IT architectures for bio informatics and micro array data were overlooked. The group discussed the importance of interoperability to their networks. Operability enhances the ability to expand the number of trials that could be done and to do multiple trials. Even if data are interoperable, however, the group agreed that it is important to ensure it is useful and of sufficiently high quality. When asked impressions of the impact of the electronic healthcare record, the group discussed the potential to “collect once and use often,” a concept of having one system support both internal primary care needs, as well as research needs.

The last topic discussed, according to Mr. Kubick, was whether all CRNs should be brought up to a basic level of IT. There was talk about the NIH-FDA interagency task force that should be working together to try to encourage both a basic level of proficiency, as well as to the sharing of data, which is really the critical issue with regard to improvements in public health. One of the concluding comments was that it is important to bridge clinical and IT gaps with informatics and business analysts. To make the move from EDC to electronic health records, it is also important to ensure that research needs are captured and that the industry architecture is in place. Also emphasized was the importance of continued conversation among networks that have much to learn from each other through both collegiality and collaboration.

The floor was opened for questions.

Question/Comment #1

Speaker: Joyce Niland, City of Hope

Question/Comment (paraphrased): I have two comments. caBIG was discussed as a good initiative to follow although it does not involve pharma and it is only oncology oriented. However, caBIG has joined forces in the bridge modeling process, which has taken a year or two but now it is a joint modeling effort—the biomedical research integrated domain group model—between caBIG, CDISC and HL7, all of which were ongoing initiatives already and which span FDA, pharma, and other types of disease. So it has become a joint effort, and I think there is an impetus to move everything forward. My second comment is, given that there are so many initiatives already ongoing, I would encourage NIH to participate, collaborate, and leverage initiatives that are already ongoing rather than starting another swirl of activity. So much momentum is already there and so much has already been started, so that joining forces would be the optimal way to make progress.

Dr. Sachs’ response: Well said. Thank you.

Question/Comment #2

Speaker: Victoria Pemberton, from the National Heart, Lung and Blood Institute, NIH

Question/Comment (paraphrased): Currently we are working on an initiative that I think was brought up in the management and governance committee, which is looking at a clinical trial web site or a web site that could encompass a lot of clinical trial information, clinical research networks, and those individual investigators who may be conducting clinical research. The idea of a toolkit is an excellent one and we hope to vet this in the NHLBI community. I would like to get some feedback from those of you who are here as to

specifics that would be included in the toolkit. I think you have given us some really good information about templates, protocol templates, and consent form templates. But we would like to put it into the community to do some testing, as well, and those who may be interested in doing that. We'd like suggestions for specifics that can be included in the web site, as well as those of you who may be interested in doing some testing of the site itself.

Dr. Sachs' response (paraphrased): Would you like to suggest having a subcommittee help you with this?

Dr. Pemberton: That would be an excellent idea, to form a group who has a vested interest, obviously, in seeing something like this be provided to the public.

Dr. Sachs: Maybe we can post that on the web and ask for participants or volunteers to work on this effort.

Question/Comment #3

Speaker: audience member

Question/Comment (paraphrased): I would also like to echo some of the comments about not starting over but joining in with efforts that are going on. We tended to have a lot of discussions in the breakout groups about what certain words meant and what questions we're really asking, and I think there are still a number of words that we ought to be defining. CDISC started an effort, when it first was initiated in 1997, to do a glossary around clinical trials and clinical research and that glossary was combined with the applied clinical trials glossary that is published every December in their research issue, and that is published on the CDISC Web site. It has definitions for electronic data capture, for e-source, which means no paper is being used, and for a number of the words that we have been using, but not all of them. And every year we update that. So anybody who wants to provide suggestions or comments on the words that are defined or new definitions, we would like to have that collaborative effort. We have made a plea to caBIG to combine their glossary with ours and to provide it as a service to the community. It can be found on the CDISC Web site at CDISC.org; there are a number of other resources we can add to help collaborate on that.

Dr. Sachs' response: Thank you. I have a question for you. Would you agree to have that glossary put on the forum web site, in addition?

Audience member: That glossary can certainly be there or you can put a link to it and every time we update it, you could have the updated version.

Dr. Sachs' response: Thank you. I appreciate that.

Question/Comment #4

Speaker: Kevin Peterson, University of Minnesota

Comment (paraphrased): I'm really big on community involvement and getting networks into the community and into providers' offices. I thought I would mention just a word of caution with Dr. Pemberton's announcement. NHLBI is a great group, and they have some great networks already, as do

NIDDK, the NCI, and the asthma group. Sometimes with networking it's nice to get some of these groups to work together. I think I would be a little cautious about having each of the institutes now reinvent the whole networking solution. We have a great and new initiative here in the roadmap and it's being concentrated here under NCCR. I would encourage the institutes to maybe work a little bit more closely with NCCR in creating maybe a single forum or network, so that people do not have to join lots of them.

Breakout Session: Financial Practices

Content experts for this session were Deborah Roth, Chief Operating Officer, Duke Clinical Research Institute, and Donna Marinucci, Vice President, Operations, Coalition of Cancer Cooperative Groups. The session was moderated by Sadie Bennett, Project Manager, Lockheed Martin/Aspen Systems. The electronic audience response system technology was not used for this session.

Ms. Roth began the presentation with an overview of the nature of the discussion. There were approximately 40 participants who demonstrated a shared passion about the topic of financial practices for clinical research networks, and a strong desire to share their own experiences. She reminded the audience that the financial practices domain did not include the qualitative component. Ms. Roth reported that the focus of the session was on providing a brief summary of the findings, getting reactions and assistance in interpreting the data, and attempting to identify some best practices.

The participants did not find the results to be very surprising. Overall, they thought they were reflective of their own experiences. The findings indicate that cost overruns are clearly a significant issue that most networks are struggling with. It was unclear whether the finding that only one-fifth of the networks reported billing third-party payers was a function of the types of activities that these networks are involved in, or if this is not yet sufficiently a common practice.

The group did express surprise at the overall youth of the networks. The average age of the networks was actually 9.6 years. The median was 6. A finding from the financial practices survey was that the average duration of funding from the networks' primary funding source was 5.2 years. Given the average age of many of these networks and the average duration of funding, there was a concern about the extent of the challenges that face many of these networks in terms of getting their initial funding, getting organized, building their infrastructure, putting their process in place for developing protocols, implementing the protocols, completing the protocols, getting data, having demonstrated output from their process, and then needing to go into the very next grant cycle of attempting to secure a renewal. There was recognition that there is a variety of different funding models among the existing networks. By this it is meant the extent to which networks are funded on a study-by-study basis, the extent to which some networks have funding for core infrastructure, and a recognition that there really are a variety of different configurations of how the basic funding is structured.

The participants attempted to drill down into the data to identify all of the various models that currently exist and then to explore further the pros and cons, the challenges and the advantages of those different models, with the hope of bringing forth a recommendation regarding the most optimal configuration and structure for funding. Participants noted that networks that are primarily funded on a study-by-study basis have a very challenging task, and the findings show that 45 percent of the networks indicated that they are funded on a study-by-study basis and of those, only 56 percent indicate that the funding was sufficient to carry out their mission. Thus, there was a general consensus that the lack of ongoing core infrastructure support is a very challenging and formidable task and that the absence of that ongoing funding is a significant barrier to the overall success of the networks that are part of our nation's clinical research infrastructure. Given the extent to which many networks face significant limitations in the available funding, many networks seek additional

funding sources. The recommendation of the breakout session is that networks aggressively pursue opportunities from a variety of sources for secondary funding. The survey found that older networks have a greater proportion of secondary funding compared to newer networks and that those networks appear to dedicate a significant amount of effort—particularly on the part of the network leadership and network financial development committees—to secure secondary funding. Perhaps there are some lessons learned that these older networks can pass on to the more newly established ones. The group also recommends development and describing the characteristics of the various models that have been used for both securing secondary funding and combining and leveraging various funding sources, identifying the types of activities for which secondary funding has been used, and providing more information, lessons learned, and assistance to various networks in understanding how to manage a combination of funding sources.

Ms. Roth also presented information about the group discussion of the issue of shared infrastructure. The group felt there were significant opportunities to identify sharing of infrastructure and core resources across networks. It was certainly noted that the vast majority of networks focus on a particular disease state or patient population. A question raised was whether or not it would be possible to effectively share resources and core infrastructure across networks that are focusing on different areas. The group also questioned the extent to which efficiencies and economies of scale could be realized by the utilization of centralized infrastructure.

Ms. Marinucci spoke next and discussed the issue of first cut feasibility. Once the protocol concept is developed, it would be important to have a first pass at the feasibility aspect to make sure it meets the test that could be set up as standards. There is also a desire to have a second pass at that same feasibility activity to be sure that those tests were met once the full protocol was developed. The need for a toolkit was again raised in the context of the observation that there are no tools available at the sites on a continuing basis to know how many patients need to be accrued to a study. It is astonishing that sites activate protocols without ever accruing a single patient, a waste of both money and time. The group had strong opinions about the involvement of leadership and the role and responsibility of leadership in setting priorities and decision-making and in controlling scope creep, one of the major reported culprits in cost overruns. The group also felt that the connotation of the term “cost overruns” was not exactly accurate and that it might be well worthwhile to consider other terms, such as underfunding.

The floor was opened for comments and questions.

Question/Comment #1

Speaker: Steve Reardon, Westat

Question/Comment (paraphrased): As far as toolkits goes, there is one that is worth looking at. As part of the caBIG program, there is a finance and billing special interest group that is developing use cases for doing financial modeling. Their work is not very advanced at this point, but the information is publicly available through the web site. As it is not specific to cancer it could be applicable to a lot of other disease areas.

Response: Thank you.

Question/Comment #2

Speaker: Martin Brown, National Cancer Institute, NIH

Question/Comment (paraphrased): I have a comment about the issue of shared resources across the sites. The cancer research network started as a cancer-specific enterprise, but it is across the network of HMOs who have very similar characteristics so it has gradually been expanding. Now the same sort of core data resources, informatics, et cetera, are shared across the cancer research network and the CERT project, which is our AHRQ sponsored project on pharmacology research. We also have interest from other institutes, Heart, Lung and Blood, genome, etc. I don't think there is anything intrinsic about disease categories as a barrier to sharing core resources, especially if the network has other features that it shares in common in regard to the nature of its institutional structure and its data structures.

Response: Thank you. I think everybody would agree that sharing resources is really essential. Thank you.

Question/Comment #3

Speaker: Bob Comis, president of the Coalition of Cancer Cooperative Groups and chairman of ECOG

Question/Comment (paraphrased): This is a grossly underfunded enterprise by the Federal Government and I think we cannot shirk away from that. Although it probably represents a greater level of funding than any country in the world, it is grossly underfunded. Dr. Zerhouni is in a position to go to Congress and say how underfunded this system is, but when you are talking about almost 70 percent of what all of us do being underfunded in some way or being unable to cover its expenses, no one would run a business like that. This entire enterprise is at risk and I think we, as investigators, and the public need to somehow point that out to Congress and get funding for this research infrastructure. It is the best infrastructure in the world, but it is probably the most at risk in the world.

Dr. Sachs' response: Thank you for your comment.

Question/Comment #4

Speaker: I'm Stephanie Zafonte, National Heart Lung and Blood Institute, NIH

Question/Comment (paraphrased): I was hoping for an explanation of scope creep.

Response (paraphrased): Often, when a contract is long-term, maybe over the course of 5 years or so, you have positive feedback from clients or stakeholders and then they ask for improvements or enhancements in the system that may or may not have been discussed up front and were not covered in the budget when you originally proposed it. For example, if you had a survey and the survey said that more education and training was needed in a particular area and the project officer suggested that that was a good idea, they may want you to implement that, but funding would not necessarily be available for that particular task.

Question/Comment #5

Speaker: Gregg Fromell, University of Pennsylvania.

Question/Comment (paraphrased): I can't really tell whether the enterprise is grossly underfunded, right funded, or overfunded at this stage, because I think going back to the CTSA concept, I'm not sure we've created the right home to do research in a clinical care setting. I think there are a lot of costly inefficiencies in the system, but that we can't control. Take approval delays—there's an article recently published in the Journal of Clinical Oncology by Dilts from Vanderbilt that focused on the number of non-value-added steps that exist in most academic centers and networks in getting research done. Removing some of these steps can save on costs, so I would be nervous about throwing money at something we haven't fully assessed on best operational practices. Maybe part of best financial practices might be that we do a better job of assessing the operations and how they can be more efficient.

Response (paraphrased): Your comment about assessment is absolutely warranted. However, I think the trick will be to maintain the system as it exists while we do the assessments. If we run out of money while we're doing the assessment, we're all in trouble. So I think there has to be some sort of balance here and I further agree that there needs to be assessment, but someone has to come forward and perhaps suggest ways of doing this in the interim.

Question/Comment #6

Speaker: Chet Fox, from University of Buffalo

Question/Comment (paraphrased): Most of this money is done at the university level, and we're talking about infrastructure that is underfunded. Yet, when someone receives a grant, whether it be AHRQ at 24 percent or NIH anywhere from 50 to 99 percent, none of that "infrastructure funding," which the NIH is giving to the university to provide infrastructure so that we can have core infrastructure to do future development, ever comes back to us. A best case scenario I heard of was 9 percent, but most principal investigators do not get a penny of this money. We have no idea where it goes, but it is a definite black hole. I wonder if NIH could do something to force the universities to be fairer in the sharing of the funds that they get from them for us.

Dr. Sachs' response: Comment duly noted. Thank you.

Breakout Session: Recruitment and Retention

Content experts for this session were Ken Getz, Chairman of CISCRP and Senior Research Fellow at the Tufts Center for the Study of Drug Development, and Jennifer Backhouse, Mid Anglia Cancer Research Network Manager. The session was moderated by Frances Heilig, Director of Health Communications, Aspen Systems/Lockheed Martin. The leaders of this session opted not to use the electronic audience response system technology.

Ms. Backhouse presented the key themes discussed in the breakout session, including the importance of careful and up-front planning, from protocol design to selecting the centers to participate in a given study through ensuring that the population is available. Many centers tend to overestimate how many participants they are likely to be able to put into a study. There was a call for a model to see whether or not people normally do overestimate study entrants, but that may vary too much across different disease sites and different patient groups.

The problems with recruitment and retention issues were consistent both within and across networks, regardless of what type of network it was, what type of study was being done, or what disease or population was being studied. While in some ways this was reassuring, it also meant that networks should be able to work together much better to find solutions for these issues. The group discussed tailoring recruitment strategies to communities, including those for reaching families in cases of genetic diseases, special communities, those of no fixed abode, and ethnic groups. They also provided information on different strategies for engaging a particular group, such as putting advertisements for recruitment into new studies in places where the mothers of some ethnic groups may see them rather than the study participants themselves. The group also discussed that it was essential to build and sustain strong relationships with stakeholders. For recruitment, this pertains to the study organizers building relationships with researchers at the individual sites and all the clinicians or the nurses or whoever may be recruiting patients. In terms of retention, the key relationship is between the individual researchers and the volunteers themselves. Some of the issues of *best practices* included maintaining those relationships after the point where active participation in studies was continuing, keeping in mind issues of coercion and sensitivity.

The group also discussed how to engage referring physicians and health providers. For example, where to find practical tips on the use of media, the appropriate use of advertisements, which groups are more likely to respond to Internet-based notices, or whether or not the best thing you can do is to go out into communities and talk to people directly. The group also acknowledged that there is not very much money available for these activities. Other topics discussed was whether or not recruitment in a small disease population has reached saturation point, which applies to genetic conditions where the population is actually relatively small and how to standardize recruitment and retention effectiveness.

Also discussed were the best metrics to effectively gather, manage, and recruit retention strategies. Five common techniques were identified by networks in the Best Practices Study:

- Establish a partnership with the affected community.
- Ensure that research offers a win-win scenario.

- Work with local experts in developing recruitment strategies.
- Adapt the recruitment strategy to the local context.
- Take advantage of economies of scale.

In conclusion, the group agreed that guidelines and standardized proven strategies and approaches to export across networks are needed, along with more opportunities like this [the Forum] to share successful strategies in practice. Recommended next steps included establishing an ongoing working group to share successful practices and valuable resources, and spending time reviewing the IECRN online profiles in the inventory. It may also be useful to learn some lessons from private sector networks and investigative sites and see what the differences are. Also recommended was the development of a clearinghouse for recruitment and retention resources and templates, as another way of sharing best practices.

The floor was opened for comments and questions.

Question/Comment #1

Speaker: Steve Durako, Westat

Question/Comment (paraphrased): I have one comment and two questions. I think when you said take advantage of what the private sector does and see how they're successful, I've worked on a number of private sector studies and they also tend to have recruitment problems. So what they do is increase the price from \$5,000 a patient to \$7,000 a patient and all of a sudden they get more recruitment. That technique is not available, in general, to us. In your situation with the National Health Service, you said you have a research physician in almost every hospital—are those people paid by the National Health Service? What is the source of funding to have people available in every hospital?

Jennifer Backhouse Response (paraphrased): All of the physicians are NHS employees. Most of their responsibility is clinical. At the NCRN (UK National Clinical Research Network) itself, which is Department of Health funded, we do employ research nurses, research pharmacists, and research radiographers within each network. We basically had free reign when the NCRN was set up as to how each network wanted to spend that funding. While it does vary quite a lot, basically they do it as an add-on to their general practice.

Question/Comment #2

Speaker: Barbara Calabrese, American Medical Directors Association Foundation

Question/Comment (paraphrased): I'd like to highlight a situation that happened when I worked at Johns Hopkins. After working with Head Start in Baltimore City we found, after a 4-year study, that we had ingrained ourselves in that community. They knew us, respected us, and felt comfortable with us; then there was a funding lag between one study and the next study and we dropped out of sight because there was no funding to continue that association and that partnership. NIH really needs to look at continuing some of those partnerships between studies so that you're not rebuilding them and to not reinforce the community feeling like you're doing a study to them rather than with them.

Response (paraphrased): Extensive discussion about continuity is also an issue that came through in the

report. It can't be focused on filling an individual project, per se, but on nurturing that relationship long term.

Question/Comment #3

Speaker: Alan Morris, LDS Hospital and University of Utah

Question/Comment (paraphrased): I was intrigued by your description of the autism study and the win-win strategy. Doing clinical trials in critical care, we don't have the opportunity for a win-win. We don't offer participants any benefit from the particular study, although they benefit from previous studies. I wonder if that's a common way to deal with more long-term trials. Enrollment randomization of subjects taken from a pool of screened potential subjects is tightly linked to the issue of generalizability, of how well the sample studied is linked to the population of interest, an issue that is very difficult to resolve. Even in the controlled setting of critical care trials in hospitals, we have had a great deal of difficulty identifying efficiencies in recruitment. For example, in the ARDS network, in the first round of the network, the original sites were paid \$90 a patient to screen. The additional sites were paid nothing to screen. It won't surprise you that the original sites screened more patients than the additional sites and, therefore, any estimate of efficiency would be clearly confounded by the payment. But beyond that, every hospital screening program had a different technique for identifying patients, which meant the general pool that was initially examined was very different from hospital to hospital. So, does anyone have any insight into how we could better identify the screened enrolled ratio and, thereby get a better sense of how the screened patients actually reflect the population of interest?

Response (paraphrased): To some extent, efficiency is tied to the center itself and the community it serves, the disease condition. In the private sector, we've seen many examples, and I will give you a few of them. There are some centers that, for years, were directing inquiries from a promotion, newspaper ad, to a switchboard operator who had not been informed about how to handle those calls and where to direct them. So there was a high dropout rate of those inquiring until they were able to reduce that intermediary step. Many sites now also look at the effectiveness of a recruitment strategy in the interim. Instead of waiting for a period of time, they look continuously, so that they can cancel or drop a program quickly and then reallocate those resources to a successful strategy. So they are able to make their dollars more efficient by allocating them to a more targeted set of approaches or strategies.

Though to some extent, it depends on how you define screening a patient. We [Dr. Backhouse] found enormous inconsistencies in the U.K. regarding screening; some people may record it as a half-hour chat with a patient to inform them and then they decide they don't want to be in a study, and someone else may say that screening occurred because they have been through the notes of every patient coming in to clinic that day and decided already which patients are suitable to be approached. Other times, it may be a multi-disciplinary meeting where each patient is discussed and somebody is sitting there ticking whether they're eligible for a trial or not. So it's important to define screening and how we then identify the reasons for patients not enrolling once they have been screened as being suitable.

Question/Comment #4

Speaker: Janet Holbrook, Johns Hopkins

Question/Comment (paraphrased): I would like to make a comment. One of the things that we have instituted is to have part of our training meeting as a consensus on what screening is, so we get a little more uniformity, but there is still going to be a lot of heterogeneity. My question was with regard to the best practices in the survey, were they based on empirical data about meeting milestones and retention rates?

Ms. Heilig's response (paraphrased): I can answer that. They were self-nominated based on solutions that they had encountered in successful recruitment and retention of patients. So we didn't measure their performance against a standard scale.

Dr. Holbrook: But you had in the self-nomination process that they met their recruitment target.

Ms. Heilig: Yes

Question/Comment #5

Speaker: Mark Friedman, Westat

Question/Comment (paraphrased): Could you expand a little bit about the slide that mentioned expanding the profile of the networks in terms of information available and what kinds of ideas come up in that discussion?

Response (paraphrased): That is really tied to the last question that was raised. A discussion of adding more quantitative information to the profiles that would provide metrics on recruitment success or process improvements that are related to recruitment and retention strategies. There were not a lot of questions about recruitment and retention specifically in this early survey. So the profiles could really be enriched by a broader profile along those lines.

Breakout Session: Training and Professional Development

Content experts for this session were John Hickner, Professor of Family Medicine at the University of Chicago and Founding Director of the AAFP National Research Network, and James Mold, Director, Oklahoma University Health Sciences Center. The session was moderated by Michael Davis, Westat consultant.

Dr. Hickner provided the summary of the training and professional development breakout session discussion. The group first discussed the IECRN survey. In the survey instrument, the definitions of network staff and site staff may not have been clear and differently structured CRNs may have put the same type of people into different categories. There was also omission of community educators, data management staff, and statisticians and economists as other important people on the research team. Finally, one of the session participants mentioned that the communities in which the research is being done should also be examined, as a group that needs ongoing education about the research effort.

The results showed that there are currently varying definitions of and targets for professional development activities, but again there were some definitional problems. The group thought it seemed fairly clear that professional development had to do with faculty, but there was less in the survey on professional development for site staff or perhaps staff themselves. They felt another subgroup analysis that might be informative is to look at the clinical research networks affiliated with academic centers versus those that are not, because it was assumed that the academic centers have much more training and professional development opportunities than those that are not in academic centers. The group also concluded that the survey questions appeared to be overly focused on the NIH-sponsored networks.

The group was unclear about how to interpret the finding that succession planning (i.e., training of future staff) in the older networks was less common compared to the young networks. The consensus was that perhaps training needs were not as great because these networks were more well established and knew what they were doing.

Dr. Hickner presented several implications of the study and suggestions for improvement, several of which, he noted, pertained to standardization:

- Standardize role definitions; e.g., what is a CRA (clinical research associate), site coordinator, project director, study coordinator. It might be helpful to develop standardized core competencies for specific roles and then perhaps some kind of a role certification. Standardizing training definitions for these various roles might assist then in planning educational efforts and training.
- Standardize required basic research training. Is there some standardized required GCP training, human subjects protection training, so site staff members do not have to take multiple courses? There is frequently redundancy in training requirements because staff have to go through the same training multiple times.
- Develop recommendations for CRNs on basic training competencies and techniques.
- Training material should be based on a needs assessment, so training would become relevant to site staff and clinical researchers, as well. Perhaps one could offer CME credit or reimbursement to community practitioners who participate in research training to get them more involved.

- Timing of training is important. What type of training can be provided at any time, and what training should be provided just before a study so people know what they need to do.
- Evaluate the effectiveness of training programs; before they can be improved it is important to know if and how they are effective.

The group also advised that sponsors should fund curriculum development, staff development, training and evaluation of training effectiveness. Dr. Hickner noted that this may be happening in many medical schools and health profession schools, and stressed the importance of incorporating research training into the basic curriculum of medical and other health profession schools. As a final thought, Dr. Hickner raised the question of whether clinical research networks should be a vehicle for improving practice. If so, how can the feedback loop be shortened so that the results of the trials get back to the clinicians who contributed to it? Is it possible to look at CRNs as a type of learning community, that tries to bring in the practitioners and link them more tightly with the clinical research networks?

The floor was opened for comments and questions.

Question/Comment #1

Speaker: Mike Dean, University of Utah

Question/Comment (paraphrased): With regard to distance learning, I think there is value in teaching trainees to attach to mentors, there's also face-to-face interaction through seminars that are weekly or biweekly. I am not sure how you replace that.

Response (paraphrased): Good point. I wouldn't want to replace that. The question is how to incorporate both, so we can also capitalize on distance learning and do both.

Question/Comment #2

Speaker: Stephanie Zafonte, from National Heart Lung and Blood Institute, NIH

Question/Comment (paraphrased): One of the points that I think is of value to bring out a little stronger is that industry and academia are really looking to NIH to set some standards for what is the minimum or acceptable training for PI staff, for study coordinators. I was at an OHRP-sponsored meeting two years ago at a training session and there was a very strong industry voice that was really looking to NIH to be able to set that standard, so that sites that are doing multiple-funded studies don't have to repeat the training multiple times for different funders.

Response (paraphrased): Thank you for that comment. I think the posting of the report will help toward that.

Question/Comment #3

Speaker: Alan Morris, LDS Hospital and University of Utah.

Question/Comment (paraphrased): I'm not sure there is much argument that research should be a vehicle

for improving practice, but the question is how. Education is not a particularly effective way to change human behavior, unless it's continual and very resource intensive. So you considered developing and utilizing tools that would be able to be then transferred to the clinical community in order to extend the application of protocols? The dependence upon human decision-making, given any information overload and short-term memory limitations, is going to be a constant weak link in transferring information to the community in a consistent manner.

Response (paraphrased): Instead of answering that, I'll make a couple very closely related comments. I think that the CCOPs, the clinical oncology group, have demonstrated quite effectively that involving community oncologists in studies raised the level of adherence to cancer protocols as those are being spread around the country, which illustrates that involvement in the study seems to raise awareness of what's new out there. The second issue is that at least in primary care practices, many of the issues tend to be systems issues and improving systems so that intelligent practitioners have a good system that supports their practice and have the necessary information technology and that is wedded with research is a very interesting issue.

Dr. Morris: I run a network and try to keep the practices interested in participating and it seems like there are three ways at least to try to keep people in a network. One is to pay them and you can do that for a while and you can do it with certain people, but it's not very satisfying as a way to sort of build what I consider a network. You can also appeal to their altruistic tendencies. You say, "Well, you know, you're going to help advance the field. We're going to learn things that are going to be helpful to everybody." There are some people who will stick with it for a while but it's not a terribly powerful incentive. The real powerful incentive is if they get something out of it, if it's a win-win situation, if they actually learn something through the process of doing the work or if they actually feel like it improves their practice directly. I realize that applies more to PBRNs, perhaps, than some of the clinical trials networks, but I think the concept is important and that the people in the PBRN world are concerned about NIH getting into this business, because we have this notion that what you're going to do is use our practices to find patients to put into clinical trials and that it's not going to preserve the relationship-based networks that we have tried so hard to develop, which are based upon the notion that everybody gains from participation.

Question/Comment #4

Speaker: I'm Harold Perl, National Institute on Drug Abuse

Question/Comment (paraphrased): I'd like to follow up by saying that I think the most powerful incentive is giving people answers to questions they really need and want the answers to, as opposed to the research community coming down and saying, "You know, you'll be better off if you do it this way."

Comments and Closing Remarks

Barbara Alving, M.D., Acting Director, NCRR

In closing, Dr. Alving commented on the extraordinarily dynamic meeting and extended her appreciation to the participants and particularly to Jody Sachs. She then provided a brief overview of how NIH gets its annual funding from Congress, and how it manages its budgets within its institutes and centers. She also emphasized the importance of work done in the area of clinical research and how NIH is very much focused on the community and on preventive medicine, as well as interventions in critical care. She also expressed her understanding that often studies require additional funding to carry out their work, and that these issues need to be considered in an era of tight budget constraints and competing demands for funds. Dr. Alving commented that she would like to continue to hear from the clinical research community, especially about strategies for improvement. She urged the participants to send ideas and suggestions to Jody Sachs to help provide direction for next steps, as well as to continue to work together. Next, Dr. Alving opened the floor for questions and comments.

Question/Comment #1

Speaker: John Hickner, The University of Chicago

Question/Comment (paraphrased): One of the other roadmap projects was the National Clinical Research Associates Group, which had to do with health manpower training. Can you let us know where that is in the process and if there are any decisions about outcomes for that program?

Dr. Alving: There are no decisions yet about that. There certainly have been decisions about the CTSA's and we're all taking a great big gulp, we at NIH, you in the community, as we move forward on that.

Question/Comment #2

Speaker: Isabel Melese-D'Hospital, EMSC National Resource Center.

Question/Comment (paraphrased): I have a question about dissemination. Is this going to be disseminated on the NIH guide to grants and contracts or something that has a very wide dissemination in terms of finding out what the results of the reports are and giving feedback?

Dr. Alving: We would like to do that and are planning to do that. And what I would also like to hear from you are ways that you think that needs to be done. For example, I think the Westat survey needs to be widely disseminated and I want to see many more hits on Web sites. I would really appreciate any thoughts that you have that aren't attached to dollars. I mean, there is a lot you can do without exorbitant sums of money. That's another thing when you talk about evaluation. We are very much for evaluation, but as you know, there is evaluation and then there is evaluation and sometimes contractors can come in and say, "Yes, we do this evaluation, we're experts, and that's a million dollars." And that's a million dollars you don't get. So we have to say how can we can do things in a very cost-efficient and useful manner.

Dr. Sachs: There are two ways you can help. One, fill out any comments and put them in the box, because

they are all going to be posted on the Web site. Two, fill out the evaluation form you received, because we want to know what your thoughts are for this particular meeting. And, three, when you go on the Web site, there is a forum box where you can put in your comments, where you want to see the results posted, what you suggest are next steps, what you suggest to us. We will take all those comments and we will also post them all, so they'll be publicly viewed. We need to hear back from you on a lot of those issues, what your needs are from this point on.

Dr. Alving: And be sure, for those of you who have funding from the other institutes and centers, NIDDK, NHLBI, NCI, please, be sure to let your project officers and program officers know what you are doing so that they are very aware of it. It's easy not to be aware of all the other activities that are going on and I'd like to say we do, as I've said before, have an NCRRI informatics committee and a trans-NIH informatics committee. We are very actively working with the caBIG effort and Ken Buetow. So it was very interesting to see your posters. They were excellent posters. And I'm glad they're on a disk, because we all don't see everything at once. So we can go back and read.

Again, thank you so much. You're a great group. You're doing very creative things.