

Building Patient Trust: A New Era in Parkinson's Clinical Research Rights & Responsibilities

January 24, 2007

Roundtable Summary and Recommendations



Parkinson's
Disease
Foundation

TABLE OF CONTENTS

Executive Summary and Recommendations	02
Agenda	05
Participants	06
Presentation: Engaging the Community in the Clinical Research Process	08
Presentation: Enhancing the Informed Consent Process	14
Presentation: Encouraging Clinical Research Data Translation and Transparency	20
Listing of Roundtable Briefing Materials	27

Dear Friend,

On January 24, 2007, the Parkinson's Disease Foundation (PDF) convened its first in a three-part roundtable series at the New York Academy of Sciences aimed at addressing barriers to clinical research participation among people with Parkinson's disease (PD). Entitled *Building Patient Trust: A New Era in Parkinson's Clinical Research Rights and Responsibilities*, the meeting offered a unique opportunity for stakeholders in the Parkinson's clinical research enterprise — scientists, government, industry sponsors and people with Parkinson's — to engage in a collaborative dialog on strategies that could heighten patient trust, increase knowledge and awareness of clinical research, and ultimately increase participation in clinical studies. The Roundtable is part of PDF's Advancing Parkinson's Therapies (APT) initiative, our multi-project program that is designed to identify and address non-science barriers to the acceleration of Parkinson's treatments and therapies.

Based on the presentations and discussions of the day, PDF developed a set of summary recommendations and is now looking toward next steps in 2008, including:

- The creation of a clinical research learning institute — a multi-day training that will provide a core group of engaged, active leaders with Parkinson's disease with the information and tools necessary to take on roles as informed and knowledgeable patient representatives within the clinical process; and
- The staging of a second roundtable, this one focusing on the relationship between engaging community physicians in clinical research and increasing study participation by people with Parkinson's.

PDF thanks the three national experts who led the discussion on the issues, including Christine Brunswick, the Vice President of the Board of Directors at the National Breast Cancer Coalition; Ruth Fischbach, Ph.D., M.P.E., the Director and Co-Founder of the Center for Bioethics at Columbia University; and Kenneth Getz, M.B.A., the Co-Founder and Board Chair of the Center for Information and Study on Clinical Research Participation.

We would also like to thank a core group of people with Parkinson's, including members of the Parkinson Pipeline Project, for serving as advisors on this project. We also thank Vernalis Pharmaceuticals as the primary underwriter and Teva Neuroscience for their support.

Our hope is that in sharing information and recommendations from this Roundtable, we are reaching a larger audience of organizations and individuals who are interested in becoming engaged in addressing barriers to clinical trial participation — thus aiding in the advancement of Parkinson's treatments and therapies and bringing us that much closer to a cure.

Sincerely,



Robin Anthony Elliott
Executive Director



Veronica L. Todaro
Director of National Programs



Executive Summary

ISSUE PRESENTATIONS

Engaging the Community in the Parkinson's Clinical Research Process

Christine Brunswick, Vice President of the Board of Directors for the National Breast Cancer Coalition (NBCC), spoke about the organization's belief that consumer advocates, if involved in research as substantive collaborators, offer important insights in designing clinical trials and invaluable assistance in increasing awareness and knowledge of clinical research within the breast cancer community. NBCC's commitment to ensuring that the patient perspective is incorporated into the clinical research process is demonstrated through a series of integrated programs, such as their Clinical Trials Initiative. A core component of the Clinical Trials Initiative is an intensive training for consumer advocates — Clinical Trials Project LEAD® (Leadership, Education, and Advocacy Development) — which provides intensive training to prepare individuals to become participants in all levels of the clinical trial process, from evaluating trial design to serving on institutional review and data safety monitoring boards.

Enhancing the Informed Consent Process for People with Parkinson's

Dr. Ruth Fischbach, Ph.D., M.P.E., Professor of Bioethics and Director and Co-Founder of the Center for Bioethics at Columbia University, spoke of the need to balance concern about the cognitive decline that can accompany Parkinson's disease with an individual's desire to participate in a clinical trial, suggesting that no particular group, especially the vulnerable, should be systematically selected for, or excluded from, clinical research.

Dr. Fischbach provided a set of principles to govern the inclusion and protections of participants in research who are, may be, or may have their capacity impaired, and stressed that an individual with impaired capacity should have the ability to create an Advance Directive indicating his or her interest in participating in clinical research and employ a legally authorized representative who would be informed and provide permission in the event that the individual is unable to provide informed consent for him or herself.

Encouraging Parkinson's Clinical Research Data Translation and Transparency

Ken Getz, M.B.A., Co-Founder and Board Chair for the Center for Information and Study on Clinical Research Participation (CISCRP), Senior Research Fellow at the Tufts Center for the Study of Drug Development, and former CEO of CenterWatch, spoke about how recent activity calling for greater public disclosure and transparency in clinical research is not producing the desired effect — to raise awareness and improve clinical trials literacy among patient communities and the public. Mr. Getz stressed that transparency and disclosure of research information alone will not move public sentiment and patient education in the desired direction. Education needs to begin with what he refers to as “pre-education.” This pre-education is necessary to counter the way in which the public currently receives information about clinical research.

- **Develop a clinical research leadership training program that provides people with Parkinson's with the skills and resources necessary to represent the PD community in the clinical research process.**

The Parkinson's Disease Foundation (PDF) will launch the Clinical Research Learning Institute in 2008. Inspired by the NBCC LEAD[®] initiative, this training for people with Parkinson's disease (PD) will provide participants with the tools they need to serve as leaders and knowledgeable representatives within the clinical research process and empower people to contribute beyond the passive role of trial participant. The multi-day Institute will prepare graduates to take part in such activities as educating other people with PD about the importance of clinical research; serving on Institutional Review Boards (IRBs) and Data Monitoring Safety Boards (DMSBs); and providing research sponsors, investigators and government with input on trial design, implementation, and evaluation. Leaders from all sectors of the clinical research enterprise will be invited to serve on the Institute's faculty.

- **Develop and implement strategies and tactics to increase the engagement of community physicians in clinical trials.**

PDF will focus the second of three roundtables on exploring the barriers to clinical research participation by discussing ways to better engage community physicians in Parkinson's clinical



KEY RECOMMENDATIONS AND ACTIONS

research. This includes communicating with their patients about clinical trials as well as serving as study investigators and utilizing their facilities as collaborative research sites. Roundtable participants will include clinical research scientists, foundation and government specialists, representatives of industry, and patient-advocate leaders. The Roundtable will take place in February 2008.

- **Address the specific informed consent needs of people with PD who will have, currently have, or may intermittently have diminished cognitive capacity, while protecting their rights and respecting their special needs.**

PDF will initiate further investigation among experts and stakeholders into ways in which informed consent can best meet the needs of people with PD. This includes the role of IRBs in shaping the informed consent process and examining the use of Advance Directives and the assignment of a legally authorized representative for people with PD who wish to participate in clinical research (for example, the existence and success of state laws that define a legally authorized representative — such as the current law in California — will be explored as a model for states such as New York).

- **Develop mechanisms to increase education and awareness about clinical research among people with PD and ensure ongoing communication throughout the clinical trial process on a one-on-one as well as community-at-large basis.**

PDF is leading and supporting the *PDtrials* clinical research education and awareness initiative in collaboration with other national Parkinson organizations. The project includes a website — www.PDtrials.org — that provides general information about clinical research in addition to a listing of clinical studies that are currently seeking participants. The distribution of free print informational materials and presentations on clinical trials to professional and patient groups are also part of the initiative. The recommendations presented at the Roundtable will be incorporated into the thinking about the future direction of the *PDtrials* initiative, including an increased focus on "pre-education" and examining the scope and content of information currently provided on www.PDtrials.org. PDF will also examine ways to work through its Advancing Parkinson's Therapies (APT) initiative to facilitate consistency and expansion of clinical trial information sharing and communications.

Roundtable Agenda

10:30 AM – 10:45 AM	Welcome and Introductions – Robin Anthony Elliott, M.A.
10:45 AM – 11:15 AM	Why is Building Patient Trust Important to the Parkinson’s Community and to Clinical Research? – Veronica Todaro, M.P.H.
11:15 AM – 12:15 PM	<p>Presentations and Discussion – Facilitator: Ira Shoulson, M.D.</p> <ul style="list-style-type: none">• Engaging the Community in the Parkinson’s Clinical Research Process <p>Christine Brunswick <i>Vice President, Board of Directors, National Breast Cancer Coalition</i></p> <p><i>Discussion:</i> Researcher/Sponsor Commentary – Christopher Gallen, M.D. Person with Parkinson’s Commentary – Perry Cohen, Ph.D. Open Discussion</p>
12:15 PM – 12:45 PM	Lunch Break
12:45 PM – 1:45 PM	<ul style="list-style-type: none">• Enhancing the Informed Consent Process for People with Parkinson’s <p>Ruth Fischbach, Ph.D., M.P.E. <i>Professor of Bioethics and Director and Co-Founder of the Center for Bioethics, Columbia University</i></p> <p><i>Discussion:</i> Researcher/Sponsor Commentary – Kathleen Shannon, M.D. Person with Parkinson’s Commentary – Peggy Willocks, M.Ed. Open Discussion</p>
1:45 PM – 2:45 PM	<ul style="list-style-type: none">• Encouraging Parkinson’s Clinical Research Data Translation and Transparency <p>Kenneth Getz, M.B.A. <i>Co-Founder and Board Chair, Center for Information and Study on Clinical Research Participation (CISCRP), Senior Research Fellow, Tufts Center for the Study of Drug Development, Founder and former CEO of CenterWatch</i></p> <p><i>Discussion:</i> Researcher/Sponsor Commentary – Jean Hubble, M.D. Person with Parkinson’s Commentary – Jean Burns, M.A. Open Discussion</p>
2:45 PM – 3:00 PM	Break
3:00 PM – 4:15 PM	Identifying Core Issues and Action Items – Facilitator: Robin Elliott
4:15 PM – 4:30 PM	Closing Remarks

List of Presenters and Participants

PRESENTERS

Christine Brunswick
Vice President
Board of Directors
National Breast Cancer Coalition

**Roundtable Topic: Engaging the
Community in the Clinical Research Process**

Ruth Fischbach, Ph.D., M.P.E.
Professor of Bioethics and
Director and Co-Founder of the Center
for Bioethics, Columbia University

**Roundtable Topic: Enhancing the
Informed Consent Process**

Kenneth Getz, M.B.A.
Co-Founder and Board Chair, Center for Informa-
tion and Study on Clinical Research Participation
(CISCRP), Senior Research Fellow, Tufts Center
for the Study of Drug Development, Founder
and former CEO of CenterWatch

**Roundtable Topic: Encouraging Clinical
Research Data Translation and Transparency**

PARTICIPANTS

Constance Woodruff Atwell, Ph.D.
PDF Board Member
Director, Division of Extramural Research (retired)
National Institute of Neurological
Disorders and Stroke

*David Banks, R.Ph., Ph.D.
Captain, US Public Health Service
Office of Special Health Issues
US Food and Drug Administration

Ray Bartus, Ph.D.
Senior Vice President and Chief Operating Officer
Ceregene

Jean Burns, M.A.
Person with Parkinson's

Perry Cohen, Ph.D.
Person with Parkinson's
Director, Parkinson Pipeline Project

Robin Anthony Elliott, M.A.
Executive Director
Parkinson's Disease Foundation

Marian Emr
Director, Office of Communications
and Public Liaison
National Institute of Neurological
Disorders and Stroke

Mary Ellen Esgro
Associate Director, Marketing
Vernalis Pharmaceuticals

Christopher C. Gallen, M.D., Ph.D.
President and CEO
Neuromed Technologies, Inc.

Jean Hubble, M.D.

*Vice President of Medical Affairs
Vernalis Pharmaceuticals*

*Danna Jennings, M.D.

*Clinical Research Director
Institute for Neurodegenerative Disorders*

Jorge Luis Juncos, M.D.

*Associate Professor of Neurology
Movement Disorders Program
Emory University*

Maria Lagera, R.Ph., M.S.

*Associate Director, Project Management
Quintiles, Inc.*

Karen Marder, M.D., M.P.H.

*Sally Kerlin Professor of Neurology,
Columbia University Medical Center –
Sergievsky Center
(Co-Chair, Parkinson Study Group)*

Phyllis Salzman, Ph.D.

*Director of Medical Research
Teva Neuroscience, Inc.*

*Kapil D. Sethi, M.D.

*Director, Movement Disorders Program
Medical College of Georgia
Fellow, American Academy of Neurology*

Kathleen M. Shannon, M.D.

*Associate Professor, Neurological Sciences
Rush University Medical Center*

Ira Shoulson, M.D.

*Louis C. Lasagna Professor
of Experimental Therapeutics
Professor of Neurology,
Pharmacology and Medicine
University of Rochester
(Co-Founder and former Chair,
Parkinson Study Group)*

Veronica L. Todaro, M.P.H.

*Director of National Programs
Parkinson's Disease Foundation*

Mickie D. Welsh, R.N., D.NSc.

*Assistant Professor, Department of Neurology
Keck School of Medicine
University of Southern California*

Peggy Willocks, M.Ed.

Person living with Parkinson's

OBSERVERS

David Eger, Ph.D.

*Co-Chair, PDF People with Parkinson's
Advisory Council
US Food and Drug Administration
Patient Consultant*

Daniel Gersen, Esq.

PDF Board Member

Marshall Loeb

*PDF Board Member
US Food and Drug Administration
Patient Consultant*

*Unable to participate the day of the Roundtable.

“NBCC believes that consumer advocates, if involved in research as substantive collaborators, can offer important insights in designing clinical trials and invaluable assistance in increasing awareness and knowledge of clinical trials within the breast cancer community.”

Christine Brunswick
Vice President, Board of Directors
National Breast Cancer Coalition



Engaging

the Community in the Clinical Research Process

Ms. Brunswick spoke about the commitment of the National Breast Cancer Coalition (NBCC) to issues surrounding clinical trials and ensuring that the patient perspective is incorporated into the clinical research process. She outlined the components of the NBCC Clinical Trials Initiative, which is charged with engaging activists in all aspects of clinical trial design, implementation and oversight; increasing the number of clinical trials in breast cancer and helping improve their design; and enhancing women's ability to access quality clinical trials, breast cancer treatment and care. The primary elements of the program include research partnerships with clinical trial sponsors, legislative strategy and an educational training program.

NBCC works with research organizations to collaborate on and publicize particular trials that meet certain criteria:

- The study must be designed to answer an important, novel question relevant to breast cancer;
- The study must be well-designed, scientifically rigorous, and employ appropriate and meaningful outcomes;
- The study must be conducted in an ethical manner. There must be sufficient data supporting efficacy and safety to provide meaningful informed consent, and the study must be approved by an Institutional Review Board (IRB). The trial must employ mechanisms to provide adequate protection for the privacy of participants and the confidentiality of participant information. There must be a system in place for evaluating protocol and patient safety as the trial proceeds;
- The research agreements between the sponsor and investigators must adhere to the guidelines for sponsorship, authorship and accountability outlined by the 2005 International Committee of Medical Journal Editors', "Uniform Requirements for Manuscripts Submitted to Biomedical Journals." The research institutions participating in the study must be involved in the design, recruitment and data interpretation for the trial;

NBCC CLINICAL TRIALS INITIATIVE	
Research Organization Collaboration Responsibilities	NBCC Collaboration Responsibilities
<ul style="list-style-type: none"> ✓ Afford advocates opportunities for meaningful input into study design and implementation throughout the entire process, not just at occasional points. ✓ Continuously provide trial participants and breast cancer advocates with updates on the progress, status, and results of the trial, even if it is canceled or ends early. ✓ Publish primary results in full form in a respected peer-reviewed journal, including negative results. 	<ul style="list-style-type: none"> ✓ Assure that knowledgeable, trained patient advocates provide meaningful input on study design and implementation. ✓ Actively provide assistance to investigators in designing outreach materials to educate the public and potential trial participants (e.g., ensuring that it is understandable, readable and culturally sensitive). ✓ Provide assistance to investigators with participant accrual. ✓ Assist in the design, if needed, of an expanded access program and a compassionate access protocol.

- There must be a mechanism in place to address concerns about the payment of medical costs for trial participants; and
- The trial must adequately address concerns about ensuring diversity among trial participants and guarding against inappropriate exclusion of specific populations.

NBCC PROJECT LEAD® (LEADERSHIP, EDUCATION AND ADVOCACY DEVELOPMENT)

Ms. Brunswick described Project LEAD®, a program that has been providing intensive training for consumer advocates for more than a decade. Project LEAD teaches the concepts of science to advocates who then help influence the research and public policy processes. The four-day training is designed by NBCC in collaboration with scientists, academics and consumers, and includes lectures, study group sessions, case studies and role-playing on content that include basic science, epidemiology, clinical medicine and advocacy development.

Participants learn about the research process, what is involved in serving on an IRB, critical appraisal skills and the principles of evidence-based medicine. NBCC works with Project LEAD graduates — about 1,000 to date — to identify opportunities for them to use their skills. It also provides continuing education classes and maintains an online journal club for sharing information and issues discussion.

NBCC ensures that advocates who engage with industry and government are not just “window dressing.” A specific example of how this was accomplished was the announcement of an annual appropriation of over \$200 million in federal funds for breast cancer research through the Defense Appropriations Act in 1993. This advocacy success in turn strengthened NBCC’s hand with research sponsors and researchers, which was extremely helpful when NBCC requested to be included in clinical research design.

“The Project LEAD program builds the credibility and confidence of the advocate to participate and really move the [clinical research] process forward. Advocates become part of the clinical trial team – building bridges and trust.”

Christine Brunswick

Clinical Trials Project LEAD is an advanced three-day course for Project LEAD graduates. The course provides intensive training to prepare students to become participants in all levels of the clinical trials process from evaluating trial design to serving on institutional review and data safety monitoring boards.

PROJECT LEAD: WHY IS IT IMPORTANT TO BREAST CANCER ADVOCATES?

- It enables advocates to play an integral role in breast cancer decision making in research, policy and healthcare systems;

CASE STUDY FROM THE BREAST CANCER COMMUNITY: GENENTECH

In 1996, NBCC partnered with Genentech, the biotechnology company, to design and implement a Phase III clinical trial of the drug Herceptin®. Herceptin had been shown to improve survival and slow disease progression in women with metastatic breast cancer who over-express the protein HER2. NBCC helped design an expanded access program for the drug, served on the Data Monitoring Committee and served on the Steering Committee of the trial. Advocates reviewed and revised the trial protocol, and attended all major principal investigator meetings. Finally, NBCC used its networks in the breast cancer community to raise awareness about the trial and to facilitate patient accrual. In this groundbreaking collaboration, advocates and industry worked together to bring a breast cancer treatment to market. This is just one of several clinical trial collaborations in which NBCC has been active.

- It gives advocates tools to critically appraise research proposals and science news;
- It builds bridges between the consumer advocacy and science communities; and
- It builds credibility for the consumer advocacy community.

WHAT ARE PROJECT LEAD GRADUATES DOING?

A 1997 impact survey of Project LEAD graduates found that as a result of participation in the training program:

- **76 percent serve** on Institutional Review Boards;
- **65 percent work** on clinical trial recruitment issues;
- **58 percent assist** in the development of research protocols/design;
- **58 percent use** science to become more involved in breast cancer advocacy;
- **55 percent are involved in developing** consumer oriented information; and
- **50 percent participate** in scientific review grant proposals.

FOCUS ON THE PD COMMUNITY: The FDA Patient Consultant Program

The US Food and Drug Administration's (FDA) Patient Consultant program for Parkinson's research is an example of how people with Parkinson's, who are knowledgeable about the clinical research process, can formally work with government. The program selects and trains people with Parkinson's to serve as consultants on the research phase of development that precedes approval and general release of a treatment. Patient Consultants are involved in pre-approval meetings and help to bring key issues to light, such as how trial participants should be informed when a trial is suddenly halted.

“ Being involved in all stages of the clinical trial process builds our trust in trial design and helps us to go out into the community and really advocate for individuals to be entered into these trials.”

Christine Brunswick

Engaging the Community in the Clinical Research Process

RECOMMENDATION

Develop a clinical research leadership training program that provides people with Parkinson's with the skills and resources necessary to represent the community in the clinical research process.

Explore the development of a training program similar to the NBCC Clinical Research Project LEAD® initiative. This type of primer for people with PD will provide participants with the tools they need to serve as leaders and knowledgeable patient representatives within the clinical research process – advocating for the role of the patient in the pathway that brings medications and medical devices from research to market and empowering people to contribute in ways that extend beyond the passive role of trial participant.

ACTION

Creation of the PDF *Clinical Research Learning Institute*

PDF will be launching the *Clinical Research Learning Institute* in 2008. This multi-day training will prepare its graduates to take part in such activities as educating other people with PD about the importance of clinical research; serving on Institutional Review Boards (IRBs) and Data Monitoring Safety Boards (DMSBs); and providing research sponsors, investigators and government with input on trial design, implementation, and evaluation. Leaders from all sectors of the clinical research enterprise will be invited to serve on the Institute's faculty.

“In our successful effort to protect those with questionable or limited autonomy, have we also successfully precluded the participation of those who would most benefit from research?”

Ruth Fischbach, Ph.D., M.P.E.
Professor of Bioethics and Director and
Co-Founder of the Center for Bioethics
at Columbia University



Enhancing

the Informed Consent Process

Dr. Fischbach spoke of the need to balance legitimate concerns about the cognitive decline that can accompany Parkinson's disease with an individual's desire to participate in a clinical trial, suggesting that no particular group, especially the vulnerable, should be systematically selected or excluded in research. She argued that in conducting research with persons of limited capacity, emphasis should be placed not simply on protecting participants from research risks, but on promoting the right of interested individuals to explore participation in clinical trials. She also stressed that some research questions may only be answered through studies that involve persons with impaired decision-making capacity, such as testing an investigational drug to address late-stage Parkinson's disease dementia.

CAPACITY TO CONSENT: A HISTORICAL PERSPECTIVE

Dr. Fischbach began her brief historical perspective on the capacity to consent by discussing the 1947 Nuremberg Code that stipulated four requirements of informed consent, namely consent must be given by a competent person; based on adequate information; based on the person's understanding of that information; and given voluntarily, without coercion or undue influence.

She also reviewed the historical basis of current informed consent practices and standards, referring to the 1979 Belmont Report that established three ethical principles that are the philosophical

underpinnings for federal laws governing research involving human subjects and vulnerable populations:

- Recognition of the autonomy and personal dignity of individuals, and assurance that they give informed consent for participation in research;
- Recognition that there are certain persons who, because of their potential vulnerability, should be given additional protections. These include the mentally disabled, prisoners, children and pregnant women; and
- Commitment to ensuring that research risks are always justified by the expected benefits of the research.

Dr. Fischbach concluded her historical review by referring to the Common Rule agreement of 1991 in which all federal agencies that conduct research are required to abide by regulations that identify certain populations as especially vulnerable to coercion or undue influence. While the statute explicitly covers groups such as pregnant women, children and prisoners, there is no mention of those with cognitive impairment. However, there is acknowledgement of times when research subjects cannot consent for themselves and in these instances, the Common Rule provides for the research participant to have a legally authorized representative who has the ability to consent on behalf of the prospective participant. However, the term "legally authorized representative" is not defined. In addition, there is no specific guidance as to what constitutes appropriate safeguards for a person with capacity impairment.

PROPOSED PRINCIPLES TO GOVERN CLINICAL RESEARCH INVOLVING INDIVIDUALS WITH IMPAIRED CAPACITY

Dr. Fischbach outlined core principles to govern the inclusion and protections of participants in research who are, may be, or may have their capacity impaired. They include:

- The autonomy of individuals with impaired decision-making capacity should be respected. Their assent to participate in research should be obtained whenever possible and their decision to withdraw from a study at any time should be honored;
- Communication among the members of the research team, participant family members or other representatives is key to successful research participation. Model informed consent forms and procedures should be developed that expressly require that research participants and their surrogates are present during discussions regarding clinical trial participation;
- Individuals who are cognitively impaired may need more time to consider the information they are given about a research protocol. Among the ways to facilitate this is to provide information to promote understanding and to build waiting periods into the informed consent process so that participants have time to consult family members and other representatives about whether or not to participate, or continue to participate, in a clinical trial;
- Informed consent is a continuous process. Participants and their representatives should be kept informed regularly about the status of the study and its implications throughout the course of the research. For example, it would be helpful to have single-sheet summaries of information about key elements of the study and the informed consent protections provided on a regular basis;
- Both IRBs and clinical investigators must recognize that decision-making capacity may fluctuate. Because of this, on-going assessment of the informed consent process during the course of the research is critical;

- There should be clearly indicated differences between research and treatment, and between the role of the investigator and the role of the clinician. These distinction should be reinforced continuously;
- Researchers and IRBs must strive for a balance that maximizes potential benefits and opportunities, recognizes and extends individual autonomy, and minimizes risks associated with scientific inquiry;
- IRBs should include at least one voting member who is independent of the research investigators, and who has appropriate professional background, knowledge and experience in working with individuals of questionable capacity; and
- IRBs should include representatives from the local community. This includes representatives of patient advocacy groups and individuals who are not affiliated with the research institution.

CREATING A SLIDING SCALE FOR RISK ASSESSMENT AND PROTECTIONS

Dr. Fischbach outlined four commonly used standards for assessing the capacity to consent, with higher level of cognitive function corresponding to increased study risk. These standards are: the ability to communicate a yes or no decision, that is, to evidence a choice; the ability to understand relevant information; the ability to appreciate the nature of the situation and its likely consequences; and the ability to manipulate the information rationally.

With these standards in mind, Dr. Fischbach presented a concept that she promoted while Senior Advisor for Biomedical Ethics in the Office of the Director of Extramural Research at the National Institutes of Health. The concept, simply put, is that as impairment and risk increase, safeguards also should increase. Protections should be proportional to the severity of capacity impairment or the magnitude of risk or both. IRB members should insure that this sliding scale of safeguards is in place before approving a study that proposes a greater-than-minimal risk to the study participant who has questionable decision-making capacity.

UNCHARTED TERRITORY: THE USE OF AN ADVANCE DIRECTIVE AND SURROGATE IN CLINICAL TRIAL CONSENT

Dr. Fischbach proposes two changes in state law that would greatly aid an individual with diminished cognitive capacity who wishes to participate in clinical research. The first proposed change would be the creation of an Advance Directive that would communicate the desire to participate in clinical research, outline an individual's philosophy and guidelines for participation and designate a legally authorized representative to serve as surrogate in providing informed consent.

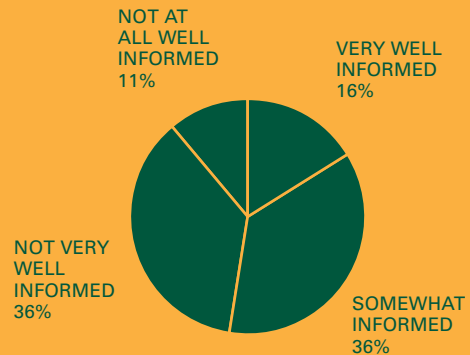
The second proposed change would be to formally codify the definition of "legally authorized representative" so that there is clarity as to who may be designated as a surrogate to give permission to enter into a research protocol on behalf of another individual. Dr. Fischbach cited

a California State law enacted on January 2003 that many hope will serve as a model for other states. The new law expands surrogate consent beyond those with advanced health care directives and those with court-appointed conservators and now includes one's spouse; domestic partner; custodial parent; adult son, daughter, brother, sister or grandchild, and closest available relative.

Unfortunately, the use of an advance directive and surrogate for consent to clinical research has been met with controversy as some feel that allowing a surrogate to enter a person lacking capacity into clinical research promotes a lower standard of protection for the vulnerable, presenting a clear and present danger to those who have the potential to be coerced. This sentiment has prevented the passage of laws that would allow potential clinical research participants from fulfilling their desire to possibly benefit from, and contribute to, science.

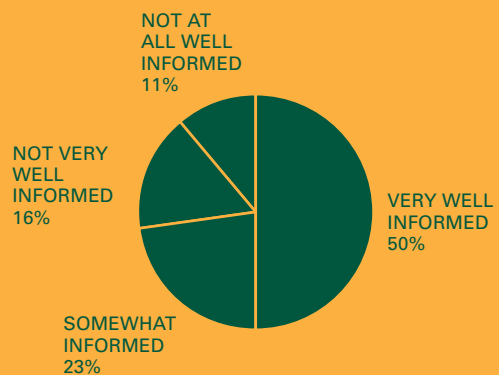
FOCUS ON THE PD COMMUNITY: Parkinson's Clinical Trial Participants' Attitudes About Being Informed

How well were you informed about the potential of the trial?



Source: Harris Interactive® Survey, March 2005

How well were you informed about the risks involved in trial participation?



Source: Harris Interactive® Survey, March 2005

Enhancing the Informed Consent Process

RECOMMENDATIONS

Address the specific informed consent needs of people with Parkinson’s who will have, currently have, or may intermittently have diminished cognitive capacity, while protecting their rights and respecting their special needs.

The issues surrounding clinical research participation by individuals who may experience diminished cognitive capacity are complex. However, it is in the best interest of people with PD as well as to the advancement of Parkinson’s treatments and therapies to address these issues and develop solutions. One solution is for people with PD who are interested in clinical research to have the ability to create an Advance Directive outlining their desire to participate in trials. This Advance Directive would include the conditions in which participation would apply, as well as the appointment of a legally authorized representative who, in the case of cognitive impairment, would be designated to make decisions on their behalf. Another solution is clearly defining “legally authorized representative” so that a surrogate may be appointed to make decisions regarding clinical research participation on behalf on an individual who is cognitively impaired.

Informed consent for a person with Parkinson’s should include re-consent and re-education over time — particularly where the study extends over several years. In addition, the IRB should be viewed as an opportunity for continuous improvement of the informed consent process. This includes encouraging people with Parkinson’s to participate in IRBs at the highest level possible and providing the necessary outreach and education to foster this level of involvement.

ACTION

Initiate further dialog on meeting the informed consent needs of people with PD.

PDF will initiate further investigation among experts and stakeholders into ways in which informed consent can best meet the needs of people with PD. This includes policy considerations, such as examining the use of an Advance Directive and the assignment of a legally authorized representative for people with PD who wish to participate in clinical research (for example, the existence and success of state laws that define legally authorized representatives, such as the current law in California, will be explored as a model for states such as New York), as well as examining the role of IRBs in shaping the informed consent process.

“As an enterprise, we are asking the wrong question. The question is not what information do we want to provide for the public and the patient community, but what do *they* want and what will *they* use?”

Kenneth Getz, M.B.A.

Co-Founder and Board Chair, Center for Information and Study on Clinical Research Participation (CISCRP), Senior Research Fellow, Tufts Center for the Study of Drug Development, Founder and former CEO of CenterWatch



Encouraging

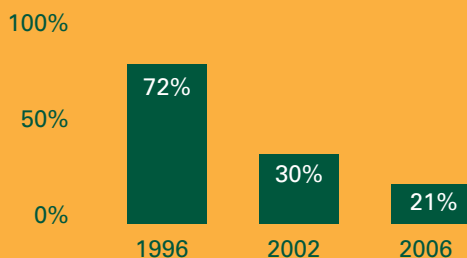
Clinical Research Data Translation and Transparency

Mr. Getz delivered two key messages. One: Since 2003 there has been significant activity calling for greater disclosure and transparency in clinical research, such as university-based clinical research degree programs, professional certification programs, site accreditation, privacy and conflict of interest guidelines, and data translation and transparency vehicles. And two: all of the activity to date is not producing the desired effect.

There is a critical need to raise awareness and improve clinical trials literacy among patient communities and the public. If clinical research awareness and literacy is not improved, we cannot expect the transparency and disclosure of research information alone to move public sentiment and patient education

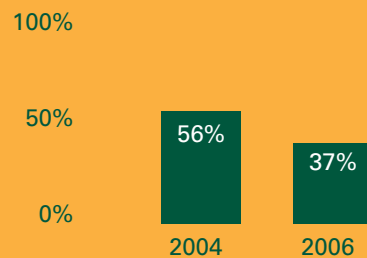
in the desired direction. Increasing clinical research awareness and literacy is essential if we are to effectively address the current lack of trust that the public has in the pharmaceutical industry, which funds over 85 percent of all clinical trials, and in the US Food and Drug Administration.

Public Trust in Clinical Research Information from Pharmaceutical Companies has Significantly Declined



Sources: ResearchAmerica!, Harris Interactive® Survey 2002 and 2006

Public Belief in the Effectiveness of the FDA in Ensuring Consumer Safety has Declined



Sources: ResearchAmerica!, Harris Interactive® Survey 2004 and 2006

REGISTRY CONCERNS: FRAGMENTATION AND ASKING THE WRONG QUESTION

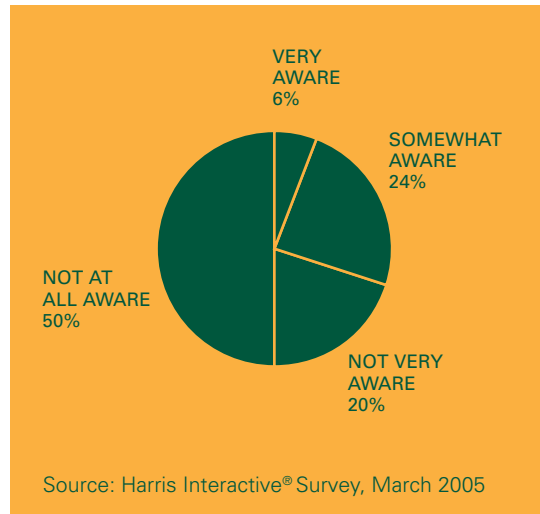
Mr. Getz stated that there are more than 40 registries of clinical trial results or clinical trial listings supported by for-profit companies, in addition to sites run by the federal government (www.clinicaltrials.gov), and the World Health Organization (www.who.int/ictcp/en). These registries represent important ways to gather information about clinical research, but the fragmentation of multiple sources of information can be very confusing for an individual who is desperately trying to find specific information.

Mr Getz cited that the clinical research enterprise is asking the question, “What data should we provide to the public and the patient community?” and has focused on examining the kind of content or information that should be provided; the type of medium that should be used (single source/multiple source); and the means of enforcing compliance with measures vehicle(s) created to promote disclosure and transparency.

Mr. Getz said that the question is not, “What information do we want to provide for the public and the patient community,” but, “What do they want and what will they use?” Once the question is asked in this manner, a totally different set of guidelines, input and insights into the research process emerges. These in turn will provide useful guidance on such issues as the information to be provided and the services to be offered to support individuals who are trying to wade through what is typically technical and difficult material.

FOCUS ON THE PD COMMUNITY:

People with Parkinson's Lack Awareness About Clinical Trials



LACK OF CLINICAL TRIAL AWARENESS AMONG THE GENERAL PUBLIC

While the public comprehends the need for clinical research to understand the safety and efficacy of treatments before they come into the market, most people do not draw the personal connection about their role in the process. The public has a fair amount of recall of clinical trial advertisements and announcements of breakthrough treatments. For example, 69 percent say that they can recall recently seeing or hearing an ad and 80 percent report having heard a recent announcement of a breakthrough. Yet only 20 percent believe that they have even a simple understanding of what clinical research is all about and fewer than five percent report that they are confident enough to even know where to go to get information. (Source: CISCRP, 2005)

DO CLINICAL RESEARCH WEBSITES BUILD KNOWLEDGE AND TRUST WITH THE PUBLIC?

To assess the impact of clinical research data registries on public trust in the research community, the Center for Information and Study on Clinical Research Participation (CISCRP) administered a poll in June 2005 to individuals who recently used a clinical trial registry, generating nearly 5,000 responses. Key findings include the following:

- Most users wish it were easier to find the information and want the information to be easier to understand. They also want to know about the essential features of each trial, such as its location, the reputation of the research center and the investigator, how they can contact an actual individual and ask questions and how they can have more interaction with the study staff;
- A high percentage of people (87 percent) want suggestions on what to do with the information they find on a registry and how to evaluate and make sense out of the content to determine whether a particular trial is a good fit for them (84 percent);
- Over 95 percent of users said that it is important that the registry lists all trials that are currently going on around the country;
- Most users acknowledge that no single place today has all of the information that they are looking for (this is the nature of the Internet);
- The typical user will go to an average of four different registries and spend almost five minutes on a single registry;
- People come to the online registries through search engines (41 percent) or another website (38 percent); and

- Only nine percent of respondents bookmark the registry (signifying the immediacy of their search to address critical questions quickly).

Mr. Getz suggested that we need to find ways of either integrating registries or creating more of a "one-stop shop" opportunity for users.

He also reminded roundtable participants that only 58 percent of Americans use the Internet and 24 percent of Americans today do not have online access. (Source: Pew Internet American Life Project, 2003) There are huge use disparities in special populations that must be taken into account in communicating with and informing the public about clinical research.

WHY ARE DATA DISCLOSURE AND TRANSPARENCY NOT DELIVERING THE DESIRED EFFECT?

Mr. Getz argued that while registries will play a role in informing the public, there is a need to address the larger issue of building trust, raising awareness and improving clinical trial literacy. Education needs to begin with what he refers to as "pre-education." This pre-education is necessary to counter the way in which the public currently receives information about clinical research. For example, people learn about research through such means as hearing about a specific trial that is actively enrolling volunteers; aggressive product marketing on a breakthrough therapy; or media play on clinical research related to human error, greed and corruption. What is needed are consistent, general messages that recognize the gift that a clinical research participant provides to the processes of advancing medical knowledge and improving public health.

THE ROLES OF CLINICAL TRIAL PARTICIPANTS, HEALTHCARE PROVIDERS, RESEARCHERS, AND SPONSORS

- Clinical Trial Participants:** An integral piece of the clinical research education puzzle is the role of the study participant. Mr. Getz noted that over 90 percent of study volunteers rate the level of research staff professionalism and the quality of care received as excellent. (Source: CenterWatch 2003) Exit surveys with volunteers show that 88 percent of participants would be willing to do so again if it made sense. (Source: Harris Interactive®, 2005) In addition, 87 percent of participants say that they want to know the results of their study, but 80 percent of volunteers state that they receive no follow-up whatsoever. (Source: CISCRP, 2006)

- Health Care Providers:** Health care providers are widely trusted by the public when it comes to disseminating information about clinical research, with a fairly high percentage of volunteers stating that they would prefer to learn about clinical research first from their primary or specialty care physician. And yet only 17 percent of these providers report having given such information to their patients. The rate of referrals among practicing physicians is remarkably low. The typical community-based physician will see an average of 7,000 patients in a year and his or her typical referral rate is less than 20 patients annually. (Source: Tufts Center for the Study of Drug Development, 2007) This lack of engagement, Mr. Getz argues, has led to potential clinical research participants being forced to "self advocate," relying on themselves for seeking out clinical research opportunities.

FOCUS ON THE PD COMMUNITY:

Few Physicians Talk with Patients about Clinical Trials and Few Refer Patients to Clinical Trials

Percentage of physicians who have talked with 10 percent or less of their PD patients about clinical trials

76%
PCPs/
Gerontologists

74%
Neurologists

Percentage of physicians who have referred a PD patient to a clinical trial

17%
PCPs/
Gerontologists

47%
Neurologists

Source: Harris Interactive® Survey, March 2005

- Sponsors and Researchers:** Academics and corporate research sponsors do not take advantage of negative media coverage in communicating information about clinical research to the public. This is because it is traditionally believed that responding provides legitimacy to bad press. Unfortunately, this has backfired over the years as remaining silent has allowed the media to lead the discussion and debate.

Another hindrance to providing the public with complete and accurate information about clinical research is that corporate sponsors do not have the internal expertise — nor do they take advantage of external clinicians, researcher or patient advocacy groups — to deliver clinical trial information. CISCRP has found that the news media have been receptive to its message acknowledging the contribution that clinical study volunteers make to advancing public health. It would bode well for the academic community and corporate sponsors to do more in the clinical research “pre-education” arena.

Encouraging Clinical Research Data Transparency and Translation

RECOMMENDATIONS

Develop and implement strategies and tactics to increase the engagement of community physicians in clinical trials.

Physicians play a significant, if not primary role in educating people with PD about clinical research, and engendering trust in the process. The general sentiment of Roundtable participants was that physicians are interested in clinical research as a means of generating new knowledge that could be of use in their practice but they lack awareness of trials and will often have competing demands and concerns. These include the fear of a patient not returning to the clinician's practice once referred and the lack of a feedback mechanism for informing the referring physician about the outcome and/or status of the patient's study participation.

Some suggested strategies are as follows: identify the competing demands and concerns that interfere with the communication between a physician and patient through discussions, questionnaires, focus groups, and/or polling; advocate for formal education on clinical research as part of medical professional curricula as the vast majority of clinical training programs do not contain a formal module on clinical research; and encourage research sponsors to take on a more prominent role in educating physicians — not only academic leaders, but also family practice physicians — on the benefits of knowing about clinical research as part of good clinical practice and the benefits of participation to their patients.

Develop mechanisms to increase education and awareness about clinical research among people with Parkinson's and ensure ongoing communication throughout the clinical trial process on a one-on-one as well as community-at-large basis.

There is a need to ensure that people with PD are provided with consistent and timely information about clinical research. Education programs need to include general information about clinical research and information on specific trials that is in language understandable by people with PD, including guidance on key questions one should ask when considering participation in a clinical trial.

There is also a need to develop mechanisms for the provision of consistent and continuous information to individuals who participate in a specific clinical study as well as assuring that there is a plan for the provision of study data to the larger Parkinson's community. This plan needs take into consideration all constituencies (the investment community, study participants, and the public at large). The sharing of data in a timely manner through a range of communications mechanisms available — media press releases, clinical research registries, national, regional and local Parkinson's organizations — helps to increase the knowledge and education of people with PD about clinical research while contributing to the overall acceleration of therapies as information is shared with other researchers.

ACTIONS

Roundtable on Engaging Community Physicians in Clinical Research

PDF will focus the second of three roundtables exploring the barriers to clinical research participation on ways to better engage community physicians in Parkinson's clinical trials. This includes communicating with their patients about clinical trials as well as serving as study investigators and collaborative research sites. Roundtable participants will include clinical research scientists, community physicians, foundation and government specialists, representatives of industry and patient-advocate leaders. The roundtable will take place in February 2008.

The *PDtrials* Clinical Research Education and Awareness Initiative

PDF leads and supports the *PDtrials* clinical research education and awareness initiative in collaboration with other national Parkinson organizations. The project includes a website — www.PDtrials.org — that provides general information about clinical research in addition to a listing of clinical studies that are currently seeking participants. The free distribution of print informational materials and on-site presentations on clinical trials to professional and patient groups are also part of the initiative's efforts. The recommendations presented at the Roundtable will be incorporated into the thinking about the future direction of the *PDtrials* initiative, such as an increased focus on “pre-education” and examining the scope and content of information currently provided on www.PDtrials.org. PDF will also examine ways to work through its Advancing Parkinson's Therapies (APT) initiative to facilitate consistency and expansion of clinical trial information sharing and communications.

Resources

The following briefing materials were provided to roundtable participants.

ENGAGING PATIENTS IN CLINICAL RESEARCH

- Applied Clinical Trials. *Educating the Public: A Critical, Unmet Need: Informing the Public and Clinical Study Volunteers through Broad-Based Outreach and Advocacy.* (March 1, 2005). Getz, K. & Kremidas J. Retrieved January 20, 2007, from <http://www.actmagazine.com/appliedclinicaltrials/article/articleDetail.jsp?id=149965>
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- National Institutes of Health. *Report and Recommendations on Public Trust in Clinical Research for the NIH Director from the Directors Council of Public Representatives (COPR).* (January 2005). Retrieved January 20, 2007, from http://copr.nih.gov/reports/public_trust.asp
- Institute of Medicine of the National Academies. *Engaging the Public in the Clinical Research Enterprise: Clinical Research Roundtable Workshop Summary, pp 1-8.* (2003). Retrieved January 20, 2007, from http://books.nap.edu/openbook.php?record_id=10757&page=1

TRIAL DESIGN AND RESEARCH PRIORITIZATION

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- National Breast Cancer Coalition Fund. *Clinical Trials Initiative Research Partnership Criteria for Trial Evaluation.* Retrieved January 20, 2007, from <http://www.natlbcc.org/bin/index.asp?strid=150&btid=1&depid=7> – check - date
- National Breast Cancer Coalition Fund. *Position Statement on Core Values for Breast Cancer Research.* (October 2003). Retrieved January 20, 2007, from <http://www.natlbcc.org/bin/index.asp?strid=591&depid=9>
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- Human Research Protections Program. University of Wisconsin-Madison. *The Eight Elements of Informed Consent*. Retrieved January 20, 2007, from <http://www.grad.wisc.edu/research/compliance/humansubjects/4.informedconsent.htm>
- Applied Clinical Trials. *Opportunities to Improve Informed Consent: Frequently Observed Problems in Processes and Content*. Mackintosh, D. & Molloy, V. (May 2003). Retrieved January 20, 2007, from <http://www.actmagazine.com/appliedclinicaltrials/article/articleDetail.jsp?id=88095>

DATA RESULTS AND TRANSPARENCY

- Applied Clinical Trials. *Forgotten Voices in the Transparency Debate: Online Trial Registries Alone Will Not Succeed in Rebuilding Public Confidence*. Getz, K. (April 2006). Retrieved January 20, 2007, from <http://www.actmagazine.com/appliedclinicaltrials/article/articleDetail.jsp?id=316473>
- Dana-Farber Cancer Institute Press Release. *Sharing Clinical Trial Results Strongly Favored by Participants, Though Misunderstanding and Anxiety Are Risks*. (June 2005). Retrieved January 20, 2007, from <http://www.danafarber.org/abo/news/press/2006/sharing-clinical-trial-results-strongly-favored-by-participants-though-misunderstanding-and-anxiety-are-risks.html>
- Journal of the American Medical Association Vol. 294, No. 6. *Disclosing Individual Results of Clinical Research: Implications of Respect for Participants*. (August 10, 2005). Retrieved January 20, 2007, from <http://www.actmagazine.com/appliedclinicaltrials/article/articleDetail.jsp?id=149965>

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THE GDNF EXAMPLE

- The Lancet Neurology, Vol. 4, 787. *The hard way to a bill of rights*. Editorial. (December 2005). Retrieved January 20, 2007, from <http://neurology.thelancet.com>
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PARKINSON'S DISEASE FOUNDATION

The Parkinson's Disease Foundation® (PDF®) is a leading national presence in Parkinson's disease research, education and public advocacy. We are working for the nearly one million people in the US who live with Parkinson's by funding promising scientific research and supporting people with Parkinson's, their families and caregivers through educational programs and support services.

Since its founding in 1957, PDF has funded over \$70 million worth of scientific research in Parkinson's disease, supporting the work of leading scientists throughout the world.

MAIN OFFICE

1359 Broadway, Suite 1509
New York, NY 10018
P: (212) 923-4700
F: (212) 923-4778

COLUMBIA UNIVERSITY OFFICE

710 West 168th Street
New York, NY 10032

MIDWEST OFFICE

833 West Washington Blvd.
Chicago, IL 60607
P: (312) 733-1893



(800) 457-6676 | info@pdf.org | www.pdf.org



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