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# Policy *primer*

## ELIMINATING DISPARITIES IN CLINICAL TRIALS

### *EXECUTIVE SUMMARY*

*Cutting-edge clinical trials may constitute the last, best hope for some cancer and respiratory patients. So how do we make sure that everyone has equal access to this precious resource?*

## Why should everyone have needs-based access to trials?

For many years, the underprivileged were exploited for the ends of medical research. In the Nineteenth and Twentieth centuries, women, racial and ethnic minorities, the poor, children, those without decisional capacity, orphans and other groups were systematically forced or coerced into risky medical research either without their knowledge or informed consent.<sup>1</sup> While some of these benefitted physically from the experimental interventions, many did not, most were harmed, and all were wronged.

Fortunately, codes of conduct,<sup>2</sup> laws,<sup>3</sup> and regulations<sup>4</sup> were passed in the second half of the Twentieth century to help prevent these wrongs in the future.

Unfortunately, when it comes to the inclusion of the underprivileged in beneficial clinical trials, there has been a pendulum swing in the opposite direction. While human subject protections now prevent the abuse of certain populations in medical research, these populations are now, for the most part, *under*represented in clinical trials. This contributes to health disparities by keeping the newest techniques and drugs out of the reach of disadvantaged groups, and by making approved drugs more dangerous for these populations because they may not have been tested on a sufficiently diverse participant pool to detect population-specific contraindications.



## Our Purpose



Herein is included a compendium of thought pieces, personal essays, and opinion articles compiled to prepare each of you for the "Eliminating Disparities in Clinical Trials (EDICT): Formulating Policies" Roundtable, September 6-8, 2006 in Houston, Texas. Part of preparing for any meeting, discussion or notable event is to develop an understanding not only of the issues that will be discussed and addressed, but also the purpose of the meeting. *(continued)*



*“Human progress is neither automatic nor inevitable... Every step toward the goal of justice requires sacrifice, suffering, and struggle; the tireless exertions and passionate concern of dedicated individuals.”*

*– Dr. Martin Luther King.*

This meeting is a “round table conference” or a meeting of peers to exchange views regarding a topic which is agreed to be serious.<sup>5</sup> Undoubtedly, an issue—such as health disparities—that is an intersection of quality of life issues such as health, equality, progress and justice merits serious consideration by a group of informed, dedicated and compassionate individuals.

However, it is important to remind ourselves that the true goals of this meeting move beyond having a discussion. Namely, over the two days we spend together in Houston, we plan to discuss the issues of disparities in clinical trials so that we may:

1. build a common understanding of current policies;
2. review model programs and policies from the public, private and non-profit sectors;
3. identify feasible policy strategies to enhance underrepresented groups’ access to clinical trials; and
4. reach consensus on policy recommendations and create an action plan for implementation with concrete action steps.

As with any discipline, the science of clinical trials includes multiple dimensions of expertise. Even as we focus specifically on the area of disparities and clinical trials, it is important to recognize and weigh the various areas of knowledge. To help each participant become versed in some issues of particular relevance to EDICT, a panel of experts—your peers—have contributed a series of articles on a broad range of topics, including what helps and hampers “minority” participation in clinical trials, policies that exist, policies that are needed, distributive justice, global responsibility,

and the impact of genomics on clinical trials. Authors have shared their experience so that we may begin the meeting with some common understandings of the issues at hand, solutions we have tried, and ideas for future action.

## Organizing Framework

### The Three R’s

For too long, the clinical trials enterprise has lacked a holistic framework for questions of equality policy. As Amy McGuire notes in her article, “it is essential that current and future policy development be grounded in a coherent conceptual model that defines and distinguishes the various phases of research, including recruitment, informed consent, enrollment, participation, and post-trial treatment and follow-up care.”

For this reason, Dan Bustillos will introduce an organizing framework in his essay “The Three “R’s” of Clinical Trial Participation” that will serve to orient our discussion at the September 2006 EDICT Roundtable meeting as well as serve as a broader policy framework for our entire project. We feel confident that it will also serve as a useful heuristic for the broader policy discussion in the field of equity in clinical trials.



We’ve named the framework “The 3 R’s” since they represent, we think, the fundamental facets of the policy issues revolving around eliminating disparities in clinical trials. As might be expected, the first “R” of clinical trial participation is **recruitment**. However, unlike much of what has been written about the problem of diverse recruitment, we hope to look at each of the three R’s more holistically both within themselves and in relation to the other R’s. Thus, when identifying specific policies to address problems of recruitment disparities in clinical trials, our framework begins with threshold questions upon which the more obvious problems might be predicated.

The second “R” stands for **retention**. Certain underserved populations tend to drop out of clinical trial participation at a higher frequency than majority populations. The unexpected drop-out of patients is a costly problem and a symptom of the failure to

design and operate clinical trials in ways that adequately address some of the problems for which answers are being sought by underrepresented populations.

The area of clinical trials that gets the least attention is the post-trial period. This is one of the reasons that our third “R” stands for **return**. What level of duty, if any, do researchers, sponsors, pharmaceutical companies, etc., owe the people whose self-sacrifice allowed for the private, intellectual, and societal benefits that are reaped from clinical trials? Should the populations that helped test new therapies have access to these after the trial is over? Should those who reap the financial rewards from others’ sacrifice “give something back” to those participants and their communities? Our “3 R” framework will set the stage to answer such policy questions.

## The Landscape Today

In discussing the landscape of the issues of disparities and clinical trials, there are a few important dimensions to consider. This includes reviewing the status of clinical trial participation in the United States, particularly emphasizing issues that influence not only whether patients participate in clinical trials, but also whether they are recruited.

### *Landscape in the United States*

In the article, “Developing Responsible Policies for Recruitment into Clinical Research,” Amy McGuire outlines some of the specific challenges to participation. Some issues can be described as *individual level* challenges, such as barriers to patient notification and low patient interest due to limited understanding of benefits of participating. Others are found more often at the *organizational* or *institutional* level, including inconsistent recruitment policies across and within institutions, confusing IRB requirements, and inconsistent interpretation of HIPAA and other regulations.

### *A Case Study*

Linda Burhansstipanov and Linda Krebs provide an important foundation for understanding the issues that discourage or prevent successful recruitment and enrollment of underserved participants in clinical trials in “Reaching Populations labeled as ‘hard-to-reach.’” Using experiences from research with Native American populations, the authors illustrate challenges to recruitment beyond “barriers” such as economics, travel, and culture on the part of the patient and encourage us to consider the role of biases of the researchers—such as assuming more research needs to be conducted to identify barriers. The article also emphasizes the importance of understanding the health literacy level of (potential) participants and how we can improve unnecessarily complex IRB / consent forms for these individuals.

### *The International Landscape*

Addressing disparities in clinical trials also requires that we understand clinical trials research from a global perspective. In “Developing Responsible Policies for International Clinical

Research”, Nick Iammarino describes the clinical trials disparities from an international perspective. The holocaust and concentration camps of WWII led to the development of the Nuremberg Code, human subject protection policies, and the requirements of informed consent. As Iammarino illustrates, these steps have been necessary but insufficient. Financial motivations and desires to make new treatments available to the public more quickly has put pressure upon pharmaceutical companies to conduct clinical trials in locations with fewer regulations and oversight—especially poorer and less developed countries. Sadly, despite tremendous sacrifices in the name of clinical trials, many communities from the under-developed world do not benefit from the treatments they help test. Additionally, the priorities of many drug companies are treatments for diseases most prevalent in the US and the developed world rather than for those suffered by populations in the under-developed world.

### *The Legal and Regulatory Landscape*

In this non-comprehensive preview of current laws, regulations, and agency guidelines, Dan Bustillos will lay bare some of the contours of the policy landscape that will allow the participants at our EDICT Roundtable to better navigate the pitfalls as well as the opportunities afforded by existing rules and regulations. Hopefully this will also orient our discussion towards areas ripe for policymaking.

#### Goals of the EDICT Roundtable:

1. Build a common understanding of current policies;
2. Review model programs/policies from all sectors;
3. Identify feasible policy strategies to enhance underrepresented groups’ access to clinical trials; and
4. Reach consensus on policy recommendations and create an action plan for implementation.

With the article, “The Role of State Legislation and Policy in Addressing Disparities in Clinical Trials,” we take a closer look at specific policy initiatives designed to make clinical trials more accessible to poor and/or underserved communities. The author, Claudia Baquet, describes some common barriers to participation in clinical trials (such as lack of insurance or fear of adverse events) and approaches adopted by several states to address these barriers. Baquet then grounds the discussion in a concrete example of a policy approach adopted by the State of Maryland to remove financial barriers by including clinical trial costs in health insurance plans offered in the state. She follows with recommendations for future policy endeavors based on the experiences of Maryland.

## Why we need a solution

### *The Scientific Rationale*

In his commentary, “The Scientific Rationale for a Diverse Study Population in Biomedical Research”, Charles Rotimi encourages us to consider the role of our changing understanding of genetics and race. The Human Genome Project has helped to illustrate that “race” is a social construct and not science. While genetics is important, the National Human Genome Center (NHGC) at Howard University expert panel suggests that genotype-environment interactions are more important in explaining group differences in health than genotype, environment, or any factor called “race.” The challenge remains to better understand how to

use the information from the Human Genome Project in endeavors such as pharmacogenomics. It is, therefore, important to include multiple ethnic groups in clinical trials not because these are distinct biological groups but rather because there are subtle differences in allele frequencies between groups that may be important in how members of these groups respond to drugs at the individual levels. Thus, Rotimi argues that the future may lie in developing “groups” for clinical trials based more on specific biological differences rather than imprecise and dynamic concepts such as “race” and “ethnicity.”

#### *The Social Justice Rationale*

Colin Soskolne presents several ethical principles related to clinical trials in “The Equitable Inclusion of All Populations Into Clinical Trials From A Distributive Justice Perspective.” As part of the principles of individual rights, beneficence, non-maleficence, and justice, the research community must be willing to honestly determine whether a new treatment is an improvement over existing treatments. Issues like this force us to consider the more subjective side of science, wherein our personal values influence how we perceive the problem, understand the extent of, and approach the problem at hand. Scientific research requires that we balance the four ethical principles mentioned above, understanding that they can compete with one another. Thus, when undertaking research endeavors, we must be very specific about the nature of the problem, whom it affects, and who can benefit most from treatment. From there, it is our obligation to ensure that the treatments are accessible to those in need.

Margo Michaels’ article, “Access to Cancer Clinical Trials: An Issue of Social Justice” is a close examination of community-based issues and social justice in clinical trials. Michaels offers five challenges to socially just practices in conducting clinical trials. These include inequities in certain populations being approached regarding clinical trials, lack of access to state-of-the-art care often associated with clinical trials, lack of efforts to engender community trust by researchers and institutions, protocols inconsistent with community needs, and benefits of research not being translated to the communities who participated. The author continues by offering concrete recommended solutions which require the efforts of all who are involved in clinical trials research, including institutions, communities, individual researchers, and individual community members. The solutions are grounded in community-based approaches, including community-based participatory research (CBPR) practices as part of the clinical trial design.

#### **Possible solutions**

As several of our authors attest, while our population both in the U.S. and globally is becoming more diverse, we have been unsuccessful at resolving the problem of under inclusion of women and racial/ethnic groups in studies despite many efforts to improve our performance in this area. In his article, “Creating a Community-based System of Care That Promotes Health Through Innovation,” Robert Valdez discusses recent efforts such as the Food and Drug Administration’s (FDA) Guidance for the Industry on the Collection of Race and Ethnicity Data in clinical trials and the National Institutes of Health (NIH) policy including Women and Minorities as Participants in Research Involving Human Subjects. Despite these encouraging efforts, many groups

continue to be underrepresented in clinical trial research. Valdez challenges the research community to move outside of their comfort zone and to develop innovative partnerships with agencies and institutions that have access to the underserved. Valdez suggests that one particularly viable partner (though not without its own challenges) is the national system of Federally Qualified Health Centers (FQHCs). These clinics and centers specialize in providing care to the poor and underserved. As such, working with the FQHCs as partners represents a viable option by using an existing infrastructure to increase recruitment efforts with underserved groups.

Paula Kim, (“The Clinical Trial is Complete, Now What?”) encourages us to consider that opportunities to improve clinical trial recruitment also occur after a trial concludes. This is due to how poorly many underserved patients perceive the clinical trial experience and outcomes. Issues such as lack of insurance, limited health care access, and financial strain are exacerbated by concerns about the extra time burden involved, side effects and lack of a guaranteed of the outcome for many underserved patients. Those who do participate in clinical trials cite altruistic motives, such as the desire to “further scientific progress” and “helping others with the same disease.” But this reflects the motivations of the very small fraction of patients that choose to participate in clinical trials. What will influence others? Perhaps offering successful treatments to those who participated and their communities or coordinating continued health care after the clinical trial concludes will fit this bill. As part of any efforts to improve the status quo, Kim emphasizes the importance of partnerships with community members, community caregivers, to continue our learning after a trial ends. Above all we must balance research interests with patient-centered needs.

Similarly, in “A Look at Clinical Trials from the ‘Patient’ Side” Deborah Collyar emphasizes the importance of patient-focused medicine and its role in clinical trial recruitment. Of which culturally appropriate care is a major part of the solution. A patient centered approach requires that we also tackle the issues of access and literacy regarding not only clinical trials, but health care in general. This includes ensuring that research is conducted in an ethical manner with consistent policies for protection of the participants, including clear interpretations of HIPAA and universal application of informed consent and IRB requirements. Collyar argues that practitioners must learn to view things from the patient’s perspective. Patient-centered approaches will also give attention to the impact of the clinical trial experience on the patient after it is complete, thereby setting a stage for future participation by the individual participants or perhaps others in their communities.

#### **Conclusion**

*“The pursuit of peace and progress cannot end in a few years in either victory or defeat. The pursuit of peace and progress, with its trials and its errors, its successes and its setbacks, can never be relaxed and never abandoned.” – Dag Hammarskjöld*

**O**n June 10, 1993, President Bill Clinton signed into effect the NIH Revitalization Act of 1993, PL 103-43 to establish guidelines for inclusion of women and

minorities in clinical research.<sup>6</sup> This Act not only emphasized the importance of ensuring adequate representation of women and minorities in research, but also laid a framework for accomplishing this goal. The authors of this act laid out a plan of implementation, assigning roles and responsibilities and a framework for assessment. In January of 1997, some 7.72% of NIH research applications were considered to have unacceptable inclusion of women and/or minorities.<sup>7</sup> By 2003, this had decreased to 5.16%.<sup>8</sup>

These figures reflect a promising trend in our *intentions* regarding recruitment and inclusion of women and minorities into clinical trials. The challenge remains, as Hammarskjold suggests, in staying committed to the pursuit of progress. Above all, the goal of equal access, treatment and opportunity is one that should never “be relaxed and never abandoned.” ●

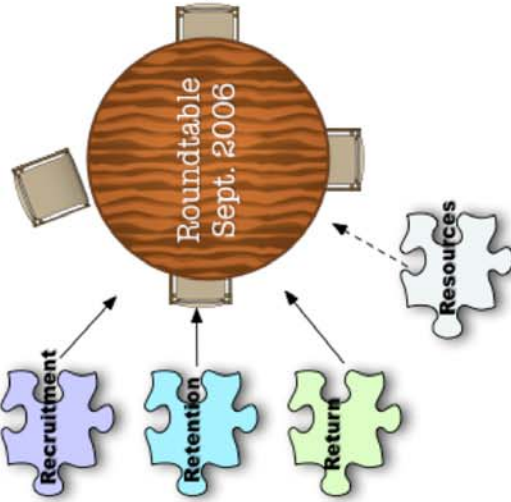
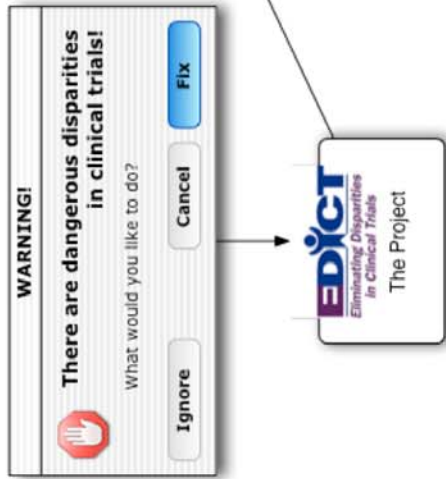
*By Dan Bustillos JD, PhD(c) and Rachel Shada MHR.*

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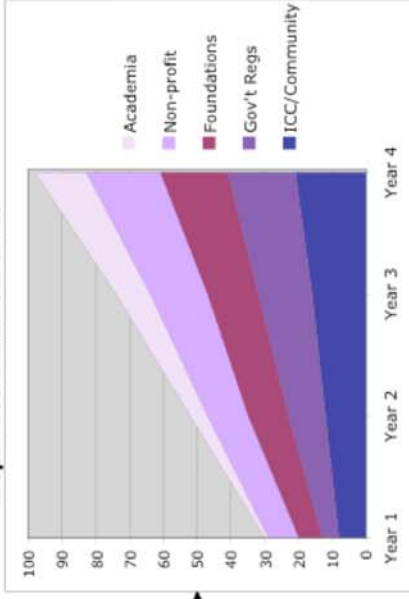
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**Striving for the Elimination of Disparities in Clinical Trials**



Introducing the EDICT project's new online Reading Room. Your one-stop resource library for articles, news, and links about overcoming disparities in clinical trials. Be sure to bookmark: <http://chronic.bcm.tmc.edu/edict/readingroom.html>

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**EDICT**  
Eliminating Disparities  
in Clinical Trials

## Reading Room

The first offering of the Eliminating Disparities in Clinical Trials Reading Room is the **2006 Roundtable Meeting Policy Primer**, a compendium of thought pieces, personal essays, and opinion articles compiled to acquaint the reader with some of the more salient policy questions and their historical, ethical, and legal context. We suggest that you start with the **Policy Primer Introduction and Executive Summary** as this serves as an orientation to the problem of the under-representation of certain groups in clinical trials, and also gives short descriptions of the following articles.

### 2006 Roundtable Meeting Policy Primer

#### Essential Reading . . .

- [Policy Primer Introduction and Executive Summary](#)
- [The Three "R's" of Clinical Trial Participation](#)
- [Policy Landscape](#)
- [Developing Responsible Polices for Recruitment into Clinical Research](#)
- [The Equitable Inclusion of All Populations Into Clinical Trials From a Distributive Justice Perspective](#)
- [Understanding and Using Human Genetic Variation Knowledge in the Design and Conduct of Biomedical Research](#)
- [Cancer Clinical Trials: Participation by Underrepresented Populations](#)

#### Additional Reading . . .

- [Creating a Community-based System of Care That Promotes Health Through Innovation](#)
- [Reaching Populations Labeled "Hard-To-Reach"](#)
- [Developing Responsible Policies for International Clinical Research](#)
- [The Clinical Trial is Complete. Now What?](#)

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## EDICT Project Overview

The Chronic Disease Prevention and Control Research Center (CDPCRC) at Baylor College of Medicine and the Intercultural Cancer Council (ICC) in Houston are conducting a four-year (2005-2009) research program that addresses problems and solutions related to improving participation of minority and underserved patients in oncology and asthma clinical trials. The four-year study is funded by Genentech, Inc. To maximize the impact of this effort, the study has two arms coupling research on strategies to improve healthcare policy together with conducting actual field research:

**Policy Research Arm.** The Policy Research Arm focuses on health policy and patient advocacy affecting clinical trial recruitment and retention efforts in the targeted populations. The end products will be both a consensus document outlining health policy priorities and also educational materials for advocacy to improve national policy affecting minority recruitment to clinical trials.

**Field Research Demonstration Arm.** The Field Research Demonstration Arm addresses barriers and facilitators to clinical trial recruitment and retention in the targeted populations, including methods and educational materials for outreach to researchers, referring physicians, patients, and the general public. In this arm, demonstration research is being aimed at increasing minority accrual to oncology and asthma clinical trials.

***For more information please contact the Chronic Disease Prevention and Control Research Center at 713-798-4614 or [cdrc@bcm.edu](mailto:cdrc@bcm.edu).***



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