

# **Supporting Diversity in Research Participation: A Framework for Action**

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## **EXECUTIVE SUMMARY**

Members of minority groups have often been underrepresented in clinical trials, which represents a major challenge to CIRM-funded researchers, given that California is the nation's most diverse state. Among the reasons given for low minority participation are:

- Lack of awareness by members of minority groups and their community-based physicians of clinical trials
- Limited recruitment of members of minority groups by trial sponsors
- A general lack of trust in the health care system and especially in clinical research
- Logistical barriers, such as lack of transportation, child care, and/or elder care; inability to take time off work; lack of means of communication; the time required; costs of participation not covered by other entities; and confusing processes
- Literacy issues, including lack of English-speaking ability, lack of health literacy, and lack of literacy in clinical jargon
- Cultural considerations, including lack of understanding or acceptance of concepts such as double-blind trials using placebos

There are other issues that are specific to certain minority groups. African-Americans tend to have the lowest level of trust in the health care system because of historical abuses. Chinese-Americans also have trust issues, as well as problems with English and, for older members of the community and recent immigrants, a lack of understanding of the underlying concepts of clinical research. Latinos also face language barriers, as well as a fear on the part of immigrants – legal or otherwise – that participation could bring negative consequences for them and their families. Southeast Asians share many of these issues, along with, for many groups, a fear of authority bred by a variety of traumas.

Given CIRM's commitment to supporting diversity in clinical research, it is suggested that opportunities for participation be enhanced by supporting the following activities in the context of clinical research supported by the institute:

- **Early Outreach:** Engage community partners at an early stage and perform a formative evaluation to identify possible literacy issues and understand the questions and preferences of potential study participants.
- **Involve Familiar Faces:** Involve celebrities, community leaders or other credible spokespersons, including patient advocates, to facilitate communication.
- **Involve Community-based Physicians:** Support health care provider outreach and education to inform community-based physicians and health care workers of opportunities for trial participation

- **Community Advisory Boards:** Establish advisory bodies, comprised of representatives from the above groups, to provide ongoing interaction with the research team to support educational material development, community outreach, recruitment, results interpretation and reporting.
- **Patient Support:** Support mechanisms to improve participant access including use of research funds to support transportation, child care, and compensation for lost wages.
- **Provide Feedback:** Synthesize results for all audiences and develop mechanisms to recognize the contributions of participants.

If members of minority groups are going to participate in CIRM-funded clinical trials now and going forward, actions must be taken to ensure long-term partnerships with them, their community-based providers, and their communities.

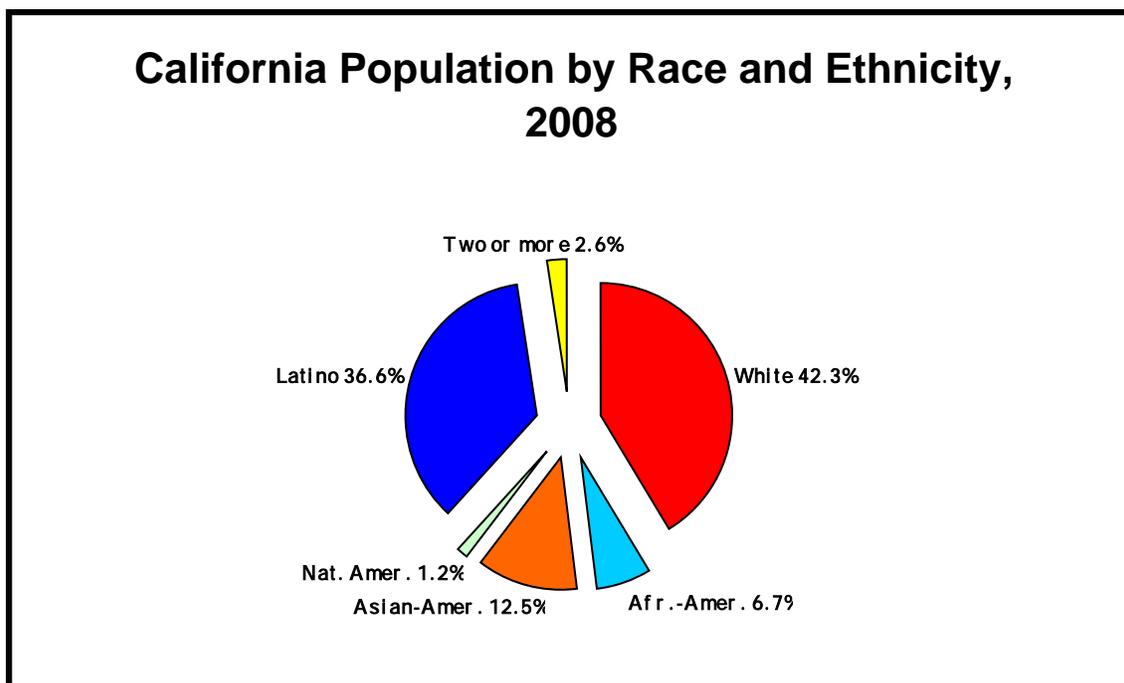
## Supporting Diversity in Research Participation: A Framework for Action

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### Introduction

The California Institute for Regenerative Medicine (CIRM) has a legal and an ethical obligation to ensure that the products of the research it funds have the potential to improve the health of all Californians. At the very least, CIRM-funded products should not be ineffective in certain groups because members of those groups were not adequately represented in research, including clinical trials designed to develop therapeutic products. Although this is an issue wherever clinical trials are conducted, it is a particular imperative in California, which is now a “minority-majority” state (along with Hawaii, New Mexico, and Texas).



*Source: U.S. Bureau of the Census, 2009*

As Mona Newsome Wicks, R.N., Ph.D., professor and associate dean for research at the University of Tennessee Health Science Center, has observed, “If trials do not include minorities, then there is a question of whether or not the results of the studies are relevant to everyone across the board.” Adds Robert Wong, M.D., resident physician at California Pacific Medical Center in San Francisco, who conducts research on racial and ethnic health care disparities: “The cohorts that are being left out of clinical trials are also the ones who generally receive suboptimal care. So the ones who need optimal care the most are the ones at greatest risk of being excluded.”

In addition to the demographic and clinical realities, there is also the prospect that if CIRM-funded products are found not to be effective for certain minority groups *because those groups were not sufficiently represented in the clinical trials*, there is potential for CIRM to fail to achieve its core objective of developing therapies for all Californians.

## **The Problem**

Racial and ethnic minorities, historically, have consistently been underrepresented in clinical trials. This pattern has continued despite the passage in 1993 of the National Institutes of Health (NIH) Revitalization Act, which mandated that women and minorities be included in NIH-funded research, unless the clinical condition involved excludes some or all of those groups. Most other entities that fund research have either mandated or recommended a similar policy, and the CIRM Medical and Ethical Standards regulations incorporate the NIH policy.

Nonetheless, disparities persist. In their extensive study, Murthy and others found that in clinical trials funded by the National Cancer Institute that were being conducted in 2002, 86.6% of participants were white, 7.9% were African-American, 3.0% were Latino, 2.2% were Asian-American or Pacific Islanders, and 0.3% were Native Americans or Native Alaskans (Murthy). These figures are reflected in numerous other studies that document underrepresentation of all minority groups in clinical trials. Although the proportions vary, of the largest ethnic and racial groups, Latinos and African-Americans tend to be the most underrepresented.

There are many theories as to why this situation developed and persists. They range from accusations of racism on the part of researchers to distrust in the system on the part of minorities to more specific issues that include lack of insurance, immigration status, insufficient English-language skills or literacy, and lack of transportation to the site of the trial. All of these explanations, and many others, have some validity.

## **The Literature**

There is an extensive literature concerning low rates of minority participation in clinical trials. It includes literature searches, data collection and analyses, surveys, and discussion of why the problem exists and what might be done to remedy it. There is also a contrarian literature that argues that members of minority groups are often willing to participate in studies if someone bothers to ask them, makes it easy for them, and addresses problems that could complicate their participation.

In addition, there is a small but impressive literature focused on the issue of minorities' level of trust in the health care system; these studies discuss historical factors and current attitudes.

A representative list of articles and studies is appended to this report. Where these sources are quoted in the report, a reference is provided.

## **Why Is Minority Participation in Clinical Trials So Low?**

### **General Issues**

Several issues appear to cut across most or all racial and cultural lines. One is whether members of minority groups are even invited to participate in clinical trials. Wendler and his colleagues, after an extensive search of the literature, found that although consent-to-participate rates did not vary all that much by race or ethnicity, the proportion of minorities invited to participate did (Wendler).

A second issue, cited in published research and by several informants, is that a person usually has to be a patient in the health care system before he or she can be invited to participate in a trial. Mary Medina, a social worker, attorney, and executive of the Greater New York Hospital Association, points out that "If they don't have a primary care physician or an actual medical home, and they harbor some anxiety about going to the emergency department and therefore avoid it, they will likely not be in the pool of potential participants."

Furthermore, the question has been consistently raised of whether many potential participants are even aware of the existence – and sometimes the concept – of clinical trials. Elliott C. Roberts, Sr., a professor at the Louisiana State University Health Sciences Center, suggests that "general lack of participation [by minorities] may well be related to a lack of knowledge, involvement, and concern." He adds that even when many members of this group are aware of trials, they may not be aware "that there is more positive than there is negative in terms of participation."

Beyond lack of knowledge is lack of trust. This appears to be characteristic of all ethnic minorities, but is most prevalent among African-Americans, probably because of that group's singular historic experience in the United States. Distrust is often compounded by negative personal experience, undocumented immigration status, and/or a history of abuse at the hands of government, whether in the United States or elsewhere.

There are also issues that researchers might consider more mundane, but that constitute powerful disincentives. These include:

- **Transportation to the site of the trial.** In a portrait of Julius Phillips, an African-American who recruits potential minority participants for trials at the University of California-San Diego (UCSD), Pablo Jaime Sainz quotes Phillips as saying, "UCSD is so isolated from the people it wants to serve. Many times people don't have the transportation to go to La Jolla [the upscale community where UCSD is located, some 15 to 20 miles from downtown San Diego]. Taking the bus? If getting them to participate in a clinical trial was a problem, now imagine telling them that in order to participate, they also have to be on a bus for hours." (Sainz)
- **Access to child care**
- **Access to care for elderly relatives**
- **Needing to take time off work.** Although many clinical trials schedule patient visits during "off hours," researchers may not be sufficiently sensitive to the fact that minority workers are far more likely to work evening and overnight shifts, making it difficult, if not impossible, for them to participate during scheduled times.
- **Lack of telephones or other means of communication.** Given the disproportionate poverty rate among minorities, it is not surprising that a significant proportion of them do not have telephones, and even fewer have computers or Internet access. The growing reliance on the Internet for recruitment of participants almost guarantees that minorities will continue to be underrepresented. Dr. Wong reports, "I had a patient being discharged who lives in a single-room-occupancy hotel and has no means of communication. I decided to make an appointment for him at a community health center, and it took me an hour to make the appointment! And I don't even know if he will be able to keep it." If it is that difficult to make a primary care appointment, one can hold out little hope that people who lack telecommunications capacity will be able to join, and stay the course of, most clinical trials.

- **The time required.** Most people lead busy lives, and, depending on the nature of the trial, it can require a significant amount of the participant's time. Dale Sandler, Ph.D., chief of the Epidemiology Branch of the NIH's National Institute of Environmental Health Sciences, describing recruiting efforts for the Sister Study, which follows the sisters of women who have developed breast cancer, emphasizes this point. "We were asking a lot from people; it demanded a lot of time. It required that you participate in a two-hour phone interview, fill out three questionnaires, and have an at-home blood draw. And we want to follow them for ten years! If you are a single parent and can't take time off work, that's asking a lot."

This challenge is underlined by David Weir, Ph.D., of the Institute for Social Research at the University of Michigan, who is principal investigator for the NIH Health and Retirement Study, who observes that the more that is asked of participants, the higher the drop-out rate is likely to be, especially among minorities.

- **Cost to the participant.** "The burden of the cost of clinical trials is an issue," write Jacob Beverage and Dale O'Brien of the Lorenzen Cancer Foundation. "Third-party insurance providers have been reluctant to offer reimbursement for such services, thereby leaving the burden of payment to others." This may not be a major issue in California; the authors remind us that for cancer patients, at least, California law requires that insurers "provide coverage for all routine patient care costs related to the clinical trial if the enrollee's treating physician, who is providing covered health care services to the enrollee under the enrollee's health benefit plan contract, recommends participation in the clinical trial" (Beverage).

Nonetheless, there may well be costs associated with participation in the trial that are not covered by the study or by insurance, and that could be a major disincentive for lower-income potential participants.

- **Confusing processes.** Ho Luong Tran, M.D., president and CEO of the National Council of Asian and Pacific Islander Physicians, emphasizes that almost everything involved in a clinical trial is confusing to a lay person. "The entire process is so difficult that for a person in the community to receive the information - when everything is put into one message - that message is very hard to understand. The forms tend to be long, complicated, and hard to fill out." Dr. Wong adds, "If the process of making one appointment with a community health center is so confusing, how can we expect vulnerable patients to make and keep clinical trial appointments?"

In addition, some concepts that are second nature to researchers are alien to many potential participants; one of these is the notion of a placebo. For people who presume that all health care is intended to cure, the idea of taking something useless is not only strange, but in some cultures may be considered borderline unethical.

- **Literacy.** These confusions can be exacerbated by a lack of understanding of clinical language. Mah Hussain-Gambles conducted a study of British South Asians who were approached about clinical trials, and found that “lack of fluency in the English language led to uncertainty and confusion.” One respondent reported, “I understood bits of it; some things I didn’t understand. When I visit the doctor, I occasionally take my daughter because of the terminology used” (Hussain-Gambles).

Dr. Weir, who, in conducting the Health and Retirement Study, necessarily works with older participants, reports that “with mail surveys, there are issues of vision and of reading and filling out forms, which will produce different results in groups with lower than average education.”

Also, conversational literacy in English (or Spanish, or whatever language is being used) is different from health literacy, and both, in turn, are different from literacy in the often arcane language of clinical trials.

- **Cultural considerations.** There is also the issue of cultural attitudes toward illness. Some cultures can be quite fatalistic when it comes to chronic and/or life-threatening disease. For example, among Cambodians, especially those who are not acculturated to U.S. health care, there is often a tendency not to want to hear “bad news,” which can result in individuals dying long, slow, painful, and often unnecessary deaths (Friedman August 2009). Among the Hmong, as Anne Fadiman recounted in her 1997 book, *The Spirit Catches You and You Fall Down*, epileptic children are considered to be blessed (Fadiman). Varying attitudes about the need for treatment will obviously affect participation in trials.

In addition, the severity of the illness matters in many situations. Lillian Lew, director of a program at St. Mary’s Medical Center in Long Beach, California, that serves a largely Cambodian population, reports that “If someone in this group is diagnosed with Stage 4 breast cancer, perhaps she would participate; but if it is Stage 1, participation is highly unlikely.”

There are also issues on the provider side of the equation that can affect participation. These include:

- **Whether community providers, especially physicians, even know that trials are available.** Dr. Tran asks, “Who is encouraging minorities to participate in clinical trials? One reason that it is not happening may be that the physicians treating these patients may not even be aware of what trials are being conducted. The system is so fragmented that it’s hard for information to get around. And even if physicians know about the trials, why should they add that burden to their already full schedules?”
- **Constraints on physicians.** Indeed, Dr. Wicks has pointed out that all physicians, and especially community-based physicians, face major time constraints. In addition, the locations of trials can be some distance from where these physicians practice. As Claudia Baquet, M.D., professor and associate dean of the University of Maryland School of Medicine, told an interviewer, “There aren’t enough trials in community settings where people affected by disparities often live” (Hightower).

Furthermore, points out Professor Roberts, there are not enough minority physicians or medical school faculty involved in research “to begin to make a dent in terms of exposure of minority communities to the concept of clinical trials and orienting minorities to participate.”

- **Researchers’ priorities.** Obviously, most researchers have their own patches of turf, and they often jealously guard that turf. Although this may be necessary in order to retain the purity of the research, and may be considered necessary for reasons of ego, professional advancement, or protection of what may become proprietary trade secrets, it also creates yet more silos. As a result, “best practices” in recruitment and retention of trial participants are often kept private, which does not advance the overall inclusion of minorities in clinical trials.

Study design is also an issue. Dr. Baquet has pointed out, as have others, that many studies, in their design, specifically exclude those groups that are most likely to participate – and benefit. She told an interviewer of one trial of dietary supplements that might reduce the risk of prostate cancer in high-risk men, including African-American men. “While national accrual to this study went well,” she says, “patients who had uncontrolled hypertension were not eligible and were excluded. Some of the communities that are at most risk for higher incidence of prostate cancer also have a higher prevalence of hypertension. Minority populations can be restricted from clinical trials just because of how the trial is designed and eligibility criteria developed” (Hightower).

However, obviously, there are many instances in which inclusion criteria do reasonably limit participation in order to protect the integrity and usefulness of the clinical trial.

However, given that activist patients during the earlier days of the AIDS epidemic forced revolutionary changes in the classic model of the randomized double-blind clinical trial, perhaps a reassessment of study design might be in order, if it increases the participation of key minorities.

In addition to these general issues, there are specific challenges associated with particular minority groups.

## **How Can Minority Participation in Clinical Trials Be Increased?**

### **General Issues**

Researchers must have sufficient knowledge of the minority groups whose participation they seek. Ms. Hansen advises that one way to increase minority participation is to “show that customized medicine can really be targeted appropriately to racial and ethnic subgroups. It is so much better to be able to identify the characteristics of the subgroup going in, rather than to try to refit something after it has been developed.” She gives the example of the On Lok project, which has been much emulated: “On Lok worked locally first, then it became a national program. We built it from the ground up.”

Also, differences among subgroups must be known. Rinaldo Z. Juarez, Ph.D., professor and president emeritus of Texas A&M University, Kingsville, points out, “Ethnicity is an important variable; there are differences between Mexican-Americans and Puerto Ricans.” Dr. Tran says similarly, “Asian-Americans are very diverse, and Pacific Islanders are a very different group altogether.” These differences include not only language and culture, but also history: In some cases, there are very old enmities between subpopulations, and their members do not at all appreciate being lumped together.

Diabetes researcher Wilfred Y. Fujimoto, M.D., observes that “Investigators may not adequately understand important differences within a population. ‘Southeast Asian,’ for example, does not take into account major differences among the peoples from this region (e.g., Filipino, Vietnamese, Thai, Indian, Laotian). Moreover, there are considerable differences even within a seemingly homogeneous Asian ethnic group. For example, consider ethnic Chinese coming from northern China, southern China, Hong Kong, Taiwan, or Vietnam. Besides differences in cultural customs and norms, there are differences in dialect. In addition, there may be differences in socioeconomic level, education, literacy, and health beliefs and knowledge” (Fujimoto).

Not understanding the nuances of a subpopulation can lead to major problems. Dr. Sandler says that her team made a serious commitment to recruiting Native

Americans for the Sister Study. “We were doing well with Native American recruitment overall, but the Navajo nation has its own institutional review board, which they insisted we use. In the end, they declined to participate in the study, and then insisted that we screen out all Navajos, including anyone who lived on the reservation or within a set number of miles of the reservation. [Their resistance] apparently had to do with taking blood and tissue samples and testing for DNA; that is a an issue for them.”

It is also necessary to understand – and confront - widespread lack of trust in the health care system generally, and often in research, particularly. Professor Boulware advises, “Two key aspects of the trust issue are transparency and historical memory of lack of trustworthiness. It is necessary to create institutional transparency, conduct efforts to reach out, achieve true informed consent, get the community involved, and own up to the fact that wrongs have been committed and that there have been poor relationships with the community.” She adds that such commitments must be sincere and must constitute much more than lip service in pursuit of a research goal.

Rochelle Rollins, Ph.D., director of the Division of Policy and Data in the Office of Minority Health, U.S. Department of Health and Human Services, has been quoted as saying, “You don’t ask any population to get over what has happened in the past, because you need to remember. I think progress is being made, and people should not forget, but aiming low should not be accepted” (Curley).

In both the literature and interviews conducted for this report, community relations is a constant theme. Among the suggestions:

- **Outreach to communities is key.** Dr. Baquet reports in her published interview that in the model that she helped develop for residents of the eastern shore of Maryland, “We use a multi-pronged approach that includes public education on what clinical trials are and their potential benefits. Methods for ensuring human research participant protections are always a part of these lectures. We get involved in going into neighborhoods, attending community events, [visiting] churches, and getting support from the leaders of different faiths to get the word out.”

An ongoing relationship with community members – that is, avoiding a hit-and-run approach of recruiting and then disappearing – is also recommended by many researchers. Giselle Corbie-Smith and her colleagues, who have conducted research on minorities and trust in the health care system, advise, “To counteract the distrust that has been documented... and to demonstrate trustworthiness, we suggest that recruitment in the African-American community be thought of as an ongoing process of engagement, dialogue, and feedback.... Trust is generated and maintained through repeated interactions in a long-term relationship. Community members become skeptical, and distrust

possibly reinforced, when researchers approach communities only when recruiting subjects” (Corbie-Smith 2002).

The establishment of community advisory boards is widely recommended; Fujimoto writes that members of these boards can be a powerful positive influence in recruiting, as well as in study design: “Creation of advisory boards should be considered to review the research plans, recruitment, and retention. Advisory boards can also judge whether incentives are appropriate, coercion is used, and materials are appropriate in terms of language and literacy levels. Our own study has benefited immensely from the participation of our community advisory board because of the partnership with the community that the members of the board have promoted” (Fujimoto).

Involving key community leaders is also considered to be an effective approach. Ms. Medina advises, “It helps to have the involvement of people who are respected members of the community. Get them to help promote the trial and recruit participants.” Dr. Sandler adds that partnering with respected community organizations can make a difference; the Sister Study’s partners in recruitment included breast cancer expert and author Susan Love, M.D., and the Avon Foundation, sponsor of the highly successful Avon Walk for Breast Cancer.

- **Involve celebrities.** Use of familiar faces can extend beyond community leaders. Dr. Sandler says, “The approaches that were successful were use of celebrities and the media, although it cost a lot of money. We used BlackAmericaWeb.com [and its celebrity representative, radio host Tom Joyner]. Mr. Joyner does not have a personal tie to breast cancer, but he is highly respected. We also worked with Robin Roberts, the ‘Good Morning America’ anchor, who has breast cancer. Her sister joined our study and they served as spokespeople, as did the wife of the governor of Puerto Rico. We also worked with Latino musicians and television stars.”

Mr. Pablo added that it need not be a celebrity face. In 1996, both he and a 2-year-old girl named Alana Dung, both residents of Hawaii, were diagnosed with leukemia. Both Mr. Pablo and the Dung family learned that there were few Asian bone marrow donors in the United States or anywhere else. They began a campaign to encourage Asian-Americans to sign up as donors; Alana, who was a beguiling little girl, became the “poster child.” Both she and Mr. Pablo found donors; both transplants were successful, but she succumbed to complications. By the time she died, the campaign had attracted more than 30,000 donors. [He died in December 2009.]

- **Involve community-based physicians.** Park and colleagues note that “Community oncologists are in an excellent position to recruit minority patients into clinical trials. Community-based practices offer minority

patients easy access to clinical trials under the supervision of their local oncologist” (Park). The authors go on to offer a series of recommendations that include making a priority of having a racially and ethnically diverse staff within the medical practice.

Professor Roberts adds, “When trials become available, it is usually through a relationship with the clinician. That would thus require that the medical profession itself be more active in establishing relationships and working with minority patients, so that there is goodwill and patient trust in the physicians who bring the information to them. I don’t think there has been enough effort made by the clinical community to encourage participation by the minority community. That can also influence the minority physicians who should be involved in these efforts.”

- **An integrated approach may remove obstacles.** Reporting at the 2009 meeting of the American Association for Cancer Research on a highly successful effort to recruit African-American patients for clinical trials, Debra Wujcik, Ph.D., R.N., director of clinical trials at Meharry Medical College, emphasized an integrated approach. For trials being conducted at Nashville (TN) General Hospital, a public hospital that treats large numbers of low-income African-Americans, a team approach is used. There are permanent clinical trial staff employed at the hospital, who are fully integrated into the clinical treatment team. Every patient with a possible cancer diagnosis is identified and, if a trial is available, that patient’s physician is contacted. “Clinical trials are discussed with the patient during the first conversation about treatment,” Dr. Wujcik explained (Stuart). “The trial is not offered as an afterthought, and patients can participate in a trial in their own cancer center and be cared for by the staff and doctor they know.”

In addition, “nurse navigators” assist patients in making their way through the system, including helping them keep appointments and working to remove barriers, such as making child care available and arranging transportation. Through this approach, Dr. Wujcik said, over a six-year period, 68% of all patients eligible for trials agreed to participate; 61% of them were African-American.

A number of recommendations involve actual recruitment strategies. Among these are:

- **The recruiter should preferably be of the same race, ethnic origin, gender, and/or language group as the potential participant.** It is generally believed that recruiters who are similar to potential participants will receive a more positive response. Dr. Juarez believes that with Latinos, language facility is the most important factor: “If the [recruiter] is bilingual, I don’t think race or ethnicity is necessarily a factor. But gender is a different question. If you are trying to recruit a female subject,

you should use a female interviewer/recruiter. And the reverse could apply; if your research involves a drug or medication for prostate cancer, you might want to have a male interviewer.”

However, says Ms. Medina, a perfect match may not always be necessary: “For African-Americans, I think it is essential; perhaps not so much so for Latinos. For Asian-Americans, however, it is it is critical.”

Dr. Weir also suggests that recruiters also be from the same area as potential participants: “We use people from the area. If you are working in Chicago, use someone from Chicago. That has helped.”

- **Successful recruiters have “been there.”** Ms. Lew believes that the recruiters who achieve the best results “are people who have been through it” – that is, who have participated in clinical trials themselves and have had a good experience. Mr. Pablo believed that his being a patient in need of a bone marrow transplant gave him extra credibility as an advocate for Asian-American marrow donation. Ms. Hansen adds, “A good story, a positive outcome that can be conveyed, can be very important. Have someone tell the story who is credible.”
- **Results are likely to improve if recruiters and participants establish a relationship over time.** Dr. Weir says of the Health and Retirement Study, “We try to link the interviewer over time with a given cohort. That is not always possible; subjects shift around and interviewers leave. But this does help the response rate. It helps in any study with repeated contacts. In our second round of interviews, all the response rates went up, but especially with Black respondents. I think that is partly due to greater familiarity with the study, and with the interviewer.”
- **In-person recruiting is best.** Professor Juarez advises that face-to-face recruiting is preferable to other types of approaches, especially use of telephones. “This is better than saying that ‘somebody will call you’ or calling potential participants directly. There are so many scams over the telephone.” Professor Boulware adds, “I would be wary about contacting people out of the blue.”
- **The dilemma of incentives.** The pros and cons of using incentives, financial or otherwise, are complex. On the one hand, writes Dr. Fujimoto, “Incentives are sometimes helpful, although they should never be used to substitute for [other approaches]. Free medical tests are usually possible. In some cases, free medical care may also be feasible. Gifts that serve as symbols of participation in the study are often quite effective and need not be expensive. In many studies, honoraria for participating are also used. Attention should be given, however, to assure that these cannot be interpreted as being coercive. Incentives should never be overemphasized at the expense of other components of the program.” He

adds that incentives that have proven successful in his diabetes research include the timely return of laboratory test results, tee shirts, coffee mugs, pot luck socials, newsletters that include interesting features and recipes, and honoraria.

On the other hand, says Ms. Amatul-Haqq, offering cash payments can backfire. “People sometimes get paid to participate. That is not what would motivate me, and I would think that if they are offering to pay, that must mean lots of risk is involved.”

But in Professor Juarez’s experience with the Hispanic Health and Nutrition Examination Survey, payment was sometimes a necessity. “When we were working with the Cuban population – it cropped up more with them than with other groups – if we did not pay them, they would not participate. It wasn’t a huge amount – something like \$60 – and some of them said that was not enough. And when I was doing research in south Texas, some people said, ‘You guys come and do research and you get publications and you get famous, and we get nothing.’ I think we should remember that when we ask people to participate in surveys or research, we are taking their time, and one way to look at it is that you are paying them for a service. Perhaps the approach should be, ‘We aren’t asking you to do this for free, and we know we are imposing on your time, and your schedule, and so, because of that inconvenience, we will pay you.’ Or you can put it in more concrete terms: ‘We will pay you \$100 toward this month’s electric bill.’”

If researchers do promise payment, says Ms. Medina, they must keep their word. “There are instances of trials in which participants are promised payment. I know of situations when subjects were paid the first time, and after that, they were not paid. They were told that they would receive transportation, a meal, and a stipend every month, but after the first month, they did not receive these things. And they dropped out of the study.”

Addressing logistical challenges can also increase minority enrollment. Wendler and his colleagues advise, “Health research trials should try to include sites that are accessible to minority groups, and identify and attempt to address factors that may undermine minority groups’ participation in particular, such as the need for child care and reimbursement for travel expenses” (Wendler). Dr. Weir goes further, saying, “Transportation is an issue with most clinical trials; in our study, we go to them. If people don’t have cars and have to take public transportation, it will likely lower participation.”

The issue of treatment for other conditions (whether related to the condition for which the trial is being conducted or not) comes up often. If a diabetic patient, for example, has a comorbidity, offering to treat it could make participation more likely. Treatment of any and all clinical consequences of participation in the trial should be a given.

Volunteer participants also should not suffer adverse financial consequences as a result of the trial. Although California law mandates insurer coverage of reasonable expenses associated with cancer trials (as discussed above), this may not apply to all conditions for which trials are conducted. Indemnifying patients against their personally incurring expenses as a result of being in a trial would seem to be an obvious means of increasing participation.

And as Professor Boulware points out, *all* written materials associated with the study should be “tailored to the appropriate level of health literacy, and tailored to a lay population.”

Finally, there is the appeal to altruism, which appears to be a powerful motivation. This was cited by informants in all groups. Certainly, self-interest is likely to come first; Mr. Pablo said of his successful recruitment of bone marrow donors, “We told them, ‘It’s there for you; it will be there for you in the future.’ The idea was, ‘Somebody of my race has this condition, and I might get it one day.’ So self-interest is part of the message. But so is altruism.”

The idea of helping family members who might be at risk of developing the same disease – breast cancer or diabetes, for example – is a major incentive. Dr. Tran advises, “Talk in terms of, ‘What if it were your son or your wife?’ Use the culture, use the values – and the value is the family. They may or may not care about the community, but they always care about family members. It can be presented as a win-win situation: If you test the drug, the drug might benefit your family and other loved ones in the future.” Professor Juarez adds, “The predisposition for certain diseases, such as diabetes, is much higher if it has occurred within a family. So the appeal should not only be to the individual who has the condition, but also to the family: ‘We need your help, not just for you, but also to try to aid your children or grandchildren, because the chances are high that they may get this disease.’”

Dr. Wong believes that there can be a strong desire to serve one’s ethnic community: “Among Asian-Americans, there is a strong sense of community, of togetherness, because often they are exposed to the same obstacles and trials together. It’s a bond of suffering that breeds a sense of togetherness. So they are often interested in doing things that will benefit the community as a whole.”

But even beyond community is service to humanity. Hussain-Gambles, in discussing the reasons that South Asians resident in Britain gave for participation in clinical trials, found that “Altruism was a prominent feature in the majority of the interviews, where taking part in clinical trials was perceived as helping society” (Hussain-Gambles). Furthermore, for this population, which at times has been subject to discrimination and attack, participation in trials could provide “a sense of purpose and of belonging to British society” (Hussain-Gambles).

One informant for this report, who has breast cancer, agreed to participate in a trial of a new form of breast imaging that, it is hoped, will detect breast cancer and pre-cancerous lesions earlier. She explains, “I agreed to do so, not for myself, but because it would benefit other women. And even with the inadequacies of the system, if you appeal to people on the basis of service to others, I think that approach can work. People of color, even with their suspicions and their doubts, can be appealed to on the basis of service to humanity, even though, ironically, that is the level on which the health care system fails them.”

## African-American Issues

African-Americans generally have the lowest rate of participation in clinical trials of all minority groups. Time and time again, in both the literature and in interviews, one phrase recurs with regard to African-American reluctance to participate in clinical trials: “Can you spell ‘Tuskegee’?” Conducted from 1932 to 1972 by the U.S. Public Health Service, the "Tuskegee Study of Untreated Syphilis in the Negro Male" was a morally insupportable experiment that left the disease untreated in poverty-stricken sharecroppers in order to glean information on how the disease ravages an African American body, testing the theory that somehow it caused less neurologic damage than in whites. The experiment continued for years after effective treatment became available. When this barbaric study was finally ended in 1972 – long after some of the subjects had died and all had suffered greatly – reporter Harry Reasoner described it as an exercise in “using human beings as laboratory animals in a long and inefficient study of how long it takes syphilis to kill someone” (Brunner). The Civil Rights Act had been in effect for eight years when the experiment was finally terminated.

The Tuskegee study, according to Johns Hopkins associate professor L. Ebony Boulware, M.D., M.P.H., who has done extensive research on African-American trust of the health care system, “is the big sentinel example. But within African-American culture, there are stories handed down among generations about mistrust of institutions – medical and otherwise – and poor institutional relationships with African-Americans.” Says John Bluford, CEO of Truman Medical Centers, Kansas City, MO, “African-Americans have long been used as research and teaching subjects without the population necessarily benefiting from the results.”

Indeed, some surveys have found that younger African-Americans who have never heard of the Tuskegee experiment are still distrustful of the health care system – and especially of research - because of real or perceived negative experiences. Some of these suspicions are deeply held, such as the perception, which Professor Roberts cites, that in terms of organ donation, African-American organs almost always go to white recipients, whereas white organs never go to African-American recipients. Neither is true, but the belief persists.

Taalibah Amatul-Haqq, a hospital trustee, says that most African-Americans enter the health care system with a predetermined belief that they will be treated “differently.” She is an alternative healer as well as a trustee, and she relates the story of the time she had two clients, both attorneys, one white and one African-American, both of whom had cardiac problems. It became obvious to her, in listening to them, that “the level of care for the white man had simply been more aggressive than for the African-American man.”

She adds that because of the unsettled relationship between African-Americans and the health care system, “People of color can also read things into situations that simply aren’t there. I am aware that sometimes we overreact to things, in that

if the phrase had been spoken by someone who is of the same race as you, you wouldn't interpret it in such a negative light."

There is also a pervasive belief that researchers have a fairly cavalier attitude about African-American research participants. Charles Mouton and his colleagues, in a study of participation in clinical trials by African-American women, found that "Black women were more likely to feel that clinical research was unethical, that researchers did not care about them, and that by participating in research, they would not have access to better care" (Mouton).

There is also the institutional question. Mr. Bluford is CEO of a major teaching hospital, but he nonetheless observes that "People think of institutions like Grady Memorial in Atlanta, or Cook County Hospital in Chicago, as being minority or African-American hospitals. But these are only minority hospitals in terms of their patient populations, not in terms of their decision makers or researchers. That can produce a major negative trust factor."

This is borne out by the work of Professor Boulware and her colleagues on African-American trust of hospitals. They determined that although 73% of white respondents believed that "patients have sometimes been deceived or misled at hospitals," 80% of African-Americans did (adjusted for socioeconomic and other factors). When asked if "hospitals have sometimes done harmful experiments on patients without their knowledge," 29% of white respondents agreed, whereas 59% of African-American respondents did (Boulware).

There is also often suspicion among African-Americans that any type of "medical testing" may seek to identify persons who are HIV-positive or who have AIDS, which could have a negative impact on the individuals involved.

In terms of increasing African-American participation in clinical trials, the first three issues would appear to be trust, trust, and trust.

### **Increasing African-American Participation**

In recruiting African-American participants, the trust issue must always be paramount. With this population, probably more than others, acknowledging the troubled history of research and providing assurances that things have changed may enhance interest in participation.

Such acknowledgement should include recognition that the health care system still may not deal with African-Americans particularly well. As Ms. Amatul-Haqq says, "It's going to be a problem to get people of color to participate in these types of clinical trials until we deal with the reality of their medical experience outside of that arena, because that has a major impact on the decisions they will be making."

Mr. Bluford suggests that one way to confront that reality is to “facilitate the research activity through local community hospitals that have large minority patient populations and a largely minority medical staff.”

Cordelia Russell, M.P.H., project coordinator for the Black Women’s Health Study (BWHS), conducted by Boston University, cites several approaches that worked well for the study, which was launched in 1995 and is ongoing, with an average annual participation rate of 80%. From the beginning, she says, “We have stressed over and over that African-Americans are involved, including the people on our advisory board – who are all African-American women – and the organizations they represent” (which include many prominent African-American groups). In addition, the study leaders made it clear from the beginning that they had acquired potential participants’ names from the mailing list of *Essence* magazine.

In addition, the BWHS keeps in touch with participants through semi-annual newsletters that report general study results, and also through its web site. “That gets us in touch with them a couple of times a year, and keeps them aware of the study and acknowledges their contributions.”

BWHS participants are not paid for their overall contributions, which consist largely of filling out questionnaires. However, the study now includes a mail-in DNA mouth swab (also without compensation), for which participation has been about 60%. The study is piloting the drawing of blood samples in two communities, and, says Ms. Russell, “We did see some dropoff in participation. We don’t know if it was travel inconvenience, or something else. We pay for the blood samples – approximately \$75 – to cover costs and any expenses associated with getting to the lab.”

## Chinese-American Issues

For many Chinese-Americans, a triple play of difficult challenges confronts both researchers and potential participants: Language, immigration status, and cultural/religious issues.

In terms of language, although younger Chinese-Americans generally are likely to speak English well (especially if they were born in the United States), older members of the same family may well not do so, if they speak English at all. As a result, for them, participation in clinical trials can be a more complex affair.

As for immigration status, although the vast majority of Chinese-Americans are legal residents of the United States, there is an unpleasant history – largely forgotten outside the Asian-American community – of discrimination against people of Chinese heritage. Two particularly nasty pieces of legislation – the Masters and Servants Act of 1850 and the Chinese Exclusion Act of 1882 – made it perfectly clear that Chinese people – immigrant or native-born in the United States – were second-class citizens. As is true in other cultures, the memories and stories linger.

Cultural and religious issues are also complex. Jennie Chin Hansen, who for 25 years was the executive director of On Lok, an innovative program of comprehensive care for fragile Chinese seniors in San Francisco, explains that for many Chinese-Americans, especially older ones, “The frame of reference, especially for immigrants, is just very different than for those who grew up with allopathic medicine. In the perception of many Chinese-Americans, solutions in health care come from word of mouth, and also from trusted sources in the community – neighbors’ reports of efficacy, or information from people who have established themselves with credibility in the neighborhood.”

Henrietta Ho-Asjoe, director of community development for New York University’s Center for the Study of Asian-American Health, adds, “The attitude is, ‘I don’t know who you are, and I don’t want to be a guinea pig.’ Especially for new immigrants, the reaction to recruitment is, ‘Who are *you* to be testing *me*?’”

Dr. Wong adds, “For many Asian-American and especially Chinese immigrants, in their home countries, medicine is very different. It is rooted in community-based care, where you know the people who are providing your care. Moving to a more urban, institutionalized system of care, where you might not even see the same physician twice, contributes to a lack of bonding, a lack of trust.”

Ms. Hansen also observes, “Being part of a clinical trial is not a framework that is familiar. Being in a double-blind study seems weird. The thinking is, ‘Why should I participate in a study when there is a 50-50 chance that I won’t get anything useful?’” Dr. Wong has encountered the same questions: “I know that the traditional model of double-blind randomized clinical trials is supposed to be

the pinnacle of research, but many patients come to us and say, ‘Yes, there is a theoretical benefit for *someone*, but what will it do for me?’”

Ms. Hansen emphasizes that age and generational identity also matter a great deal. “In California, a Chinese family can have six or seven living generations. Attitude varies by generation and by how recently the family immigrated. For some of those who are older, even giving blood is a no-no. Receptivity to participation in clinical trials will vary enormously by generation cohort.”

Given that among the conditions that stem-cell innovations may address are macular degeneration, arthritis, and diabetes, attention to the specific concerns of older subgroups within the Chinese-American community will be necessary.

### **Increasing Chinese-American Participation**

Community considerations are extremely important to Chinese-Americans. Dr. Wong suggests the idea of “brokers,” be they physicians or community leaders. “A primary tool or avenue to make recruitment more successful might be for representatives of the research effort to come to the community themselves, and to recruit local leaders to be brokers within the medical system. Using that avenue – going to the community, bringing the information to them – might be a more effective approach. It is easier for us, as providers, to do that than for them to come to us. That also might be more beneficial for us, because we can provide the full gamut of information in a more comfortable environment. And then it isn’t just a group of doctors or clinical trial recruiters trying to convince them, but rather a request coming from their community leaders.”

Ms. Hansen echoes this thought: “Go to people who are trusted sources in the community, who understand biculturalism and who can be credible sources of information. If they, too, believe in the study, they can encourage support and help develop the correct way to frame it. But the reverse can be true – they can have a negative impact. The risk and the reward are both there.”

Dr. Wong sees Chinese-American physicians – who are widely viewed with respect – as key players. “Chinese physicians are perceived as leaders within the community. They are also perceived as experts; their advice – whether medical or general – is likely taken in a better light because of that aura of respect.”

Ms. Ho-Asjoe adds that other community-based health care professionals – social workers, nurses, community health and outreach workers – can also be productive partners in explaining the notion of clinical trials.

However, Dr. Wong adds, combining a recruitment invitation with a clinical encounter may not work well with many Chinese-American patients. “It is likely best to recruit in a more neutral environment, not during the clinical encounter. Perhaps it is better done in a group setting, such as a group counseling session.”

## **Latino Issues**

One of the most paramount issues for the Latino community is that “Latino” and “Hispanic” are general terms for people of Spanish-speaking descent. The broad categories used by the Census Bureau to describe minority groups are not particularly useful when it comes to true cultural sensitivity. Indigenous people from Guatemala have little in common (even language) with urban immigrants from Mexico City, or fifth-generation Latino Californians.

Language is, of course, a controlling issue. Although most Latinos speak both Spanish and English, research shows that nearly 25% of Latino-Americans over the age of 5 do not speak fluent English (Beverage). In addition, as Ms. Medina points out, “Medical translation is very different from conversational knowledge of the language.”

And although it is an issue for all minorities – as well as for many whites – insurance status is a particular concern for Latinos. In California, 29.8% of Latinos are uninsured. As a result, mandates that insurers cover appropriate expenses associated with clinical trials are often meaningless. Latinos with no insurance are unlikely to participate in clinical trials that might cost them money.

Immigration status is an additional challenge, in several ways. Undocumented residents have a profound (and often justified) fear that interaction with anything resembling authority could result in deportation. Dr. Weir admits that it’s a difficult issue: “I would certainly suspect that undocumented residents are less likely to participate in studies. But if it becomes generally known that trials included this population, there will be all kinds of negative reactions.”

Furthermore, the sometimes frenzied political battle over the status and role of immigrants – documented or otherwise - has created a major disincentive for Latinos to participate in clinical trials. Ms. Medina says, “Many immigrants ask, ‘Why would I want to volunteer for a research study when everyone hates me?’ Even if you are here legally, even if you are a citizen, many immigrants may think, ‘I am here legally, I participate in my community, I have a right to be here. But I am still treated badly. So I’m good enough to be a study subject, but not good enough to live peaceably in this country?’”

## **Increasing Latino Participation**

In the case of Latinos, says Professor Juarez, several factors can present obstacles to participation, and one of these is, simply, fear of the unknown. “There is a sense of ‘What am I getting myself into?’ How do you overcome that? I think that it takes a long-term process of continuous education about the safeguards that are in place and what is being done to protect patients and ensure that no harm is done. That has to be laid out as the bottom line - that this will cause no harm. You can’t guarantee that a hundred per cent, of course, because that’s why we

have clinical trials in the first place. But trying to figure out a way to overcome the fear is at the top of the list.”

He adds that the decision to participate in a trial, if it involves an older member of a family, involves everyone. “In the case of the elderly, the challenge is not so much to convince the elderly person. You have a family surrounding the elderly person like mother hens, and the decisions, for the most part, are made by the family member who is considered to be the lead caretaker of that person. The elderly person will not make a decision without consulting the elder son or daughter who is looking after him or her.

“Yet researchers want to go directly to the subject, and sometimes it doesn’t work that way in this culture.”

Ms. Medina warns that proficiency in Spanish may not be enough to convince potential participants. “One necessity is to have recruiters who are respectful, knowledgeable, and culturally competent – and who are willing to be held accountable. In my experience, if the recruiter speaks the language, and has these other qualities, then he or she need not even be Latino.”

Edward L. Martinez, a consultant who focuses on organizations that serve diverse communities, says that more Latino researchers is the key to higher participation in trials by members of this community. “They have to see their face in that researcher’s face. Then they feel that their language is going to be respected, that their culture and practices are going to be respected, and that the people they are working with are knowledgeable about where they come from.”

Another group that is influential in the Mexican-American community, Ms. Medina says, is *promodoras* – lay community health educators who also help Latinos navigate the sometimes impenetrable labyrinth of the health care system.

And as important as anything – indeed, more important than most other factors, for Latinos – is reporting the results of the trial back to the community. This is apparently not common practice, and may well be a major reason for low Latino participation in clinical trials.

“If you want successful long-term participation, and especially participation in future trials, go back to the community and tell them what happened,” says Ms. Medina. Community leaders who were asked to help promote participation in the trial can help inform the community about the results. “You can also use community health forums, local newspapers, churches – which are very important in the Latino community – and community health centers. But of all forms of communication, word of mouth is the most powerful: It can kill a study – all you need is one bad experience – and it can also make a study. But if you do not go back to the community and report the results, you can kiss any future participation goodbye. It will be perceived as a breaking of trust.”

## **Southeast Asian Issues**

Southeast Asians in the United States face the same triple whammy as Chinese-Americans and Latinos: Issues of language, immigration status (although to a lesser extent), and culture. But with these populations, the challenges are far more diverse. There is no common language, and there are few strong common cultural threads. Furthermore, many Southeast Asians - especially immigrants from Burma (Myanmar), Cambodia, Laos, and Vietnam - have as part and parcel of their cultural memory a horrific legacy of war and other violence.

As Dr. Tran observes, “We are different. We do not have the baggage that African-Americans or Latinos have, but we have our own issues.”

Among those issues is a distrust of formal authority. For many Southeast Asian immigrants, the recent history of their home countries has been marked by war, violence, genocide, ethnic fighting, and political repression. One informant, who serves a largely Cambodian and Lao population, says starkly that he would never ask any of his patients to participate in a clinical trial: “It’s too risky; there is a general lack of trust and a specific lack of trust in government, any government. It takes such a long time to build up trust.”

Leakhena Nou, Ph.D., an assistant professor of sociology at California State University in Long Beach, who has extensively studied survivors of war, genocide, and torture in Cambodia who are now resident in the United States, reports that there are widespread psycho-emotional and social health issues in this population. She says, “People who are put into situations over which they have no control learn to live with it, and they hope it will go away, whether the symptoms are of mental or physical health problems.” But this is only suppression of severe conditions that sooner or later will manifest themselves.

Ms. Lew adds that the level of trust and potential willingness to participate in clinical trials varies greatly by age. Traumatized older generations of Cambodians are unlikely to be willing; members of younger generations, more familiar with Western medicine and not haunted by horrific memories, might be more accessible candidates.

Cultural and religious beliefs are also extremely important, especially among older people. As Dr. Tran explains, in traditional Southeast Asian philosophy, “It is very important to be healthy; it is equivalent to being rich, to having gold. Being wealthy means that you are being fed. Health is gold.”

This may seem quaint to most native-born Americans, but during the 1975-79 Cambodian auto-genocide that killed nearly two million people, access to food was equivalent to survival. Most of those who died did not succumb to torture or murder – although there was a lot of that - but rather to ill health and especially starvation (Friedman June 2009). The interrelationship of food, health, and

wealth for Southeast Asians must be taken very seriously by those who wish to involve them in clinical research.

Dr. Tran also warns that the notion of a double-blind randomized clinical trial can be alien: “The concept of probability is not familiar; in most Southeast Asian cultures, everything is supposed to be 100% clear. People may wait all day, but they will be able to see the doctor. They may travel for two days, but sooner or later, they will receive a medication that should ease their pain. To tell them that they will receive a medication, but it is not for sure that it is a real medication, makes no sense to them. It goes against the culture of certainty.”

Religious considerations are also complicated. Christopher G. Pablo, a leukemia survivor and attorney [who died of cancer shortly after he was interviewed for this report], said that in Filipino Catholic culture, “In order to be ‘raised up’ after your death, in order to go to the next level, your body has to be intact.”

And religious leaders can have a profound impact, for better or worse. One Southeast Asian informant, a highly educated health care professional, tells a story about her mother, who is diabetic and who is also a devout Buddhist. Her mother must be on a restricted and carefully controlled diet. There is a time of year, in their branch of the faith, when the devout are expected to follow a pristine vegetarian diet for ten days. This would have played havoc with her mother’s medications and health status. “I went to the monks and said, ‘She has to follow a certain regimen.’ One monk replied, ‘This is for karma.’ As a physician – and this monk knows I am a physician – I begged him not to put my mother on a vegetarian diet for ten days. He refused. And my mother would not listen to me, because my advice went against the teachings.” She adds, “The churches of Asian groups are very different from each other; there are even significant differences among Buddhist teachings.”

### **Increasing Southeast Asian Participation**

Because of the profound diversity within this population, there are many challenges for researchers. Dr. Sandler reports that in recruiting for the Sister Study, “We had Asian advisers – both scientists and community people – on our board. But they were upset that we weren’t going to translate the materials into all relevant languages. And the information is complicated enough that we knew it would not work to try to study women who aren’t generally acculturated. Community advocates also wanted live [language] interpretation for all participants, which just wasn’t practical for all these different language groups.” In the end, the study was unable to recruit as many Southeast Asians as had been hoped.

Mr. Pablo said that in seeking bone marrow donors for himself and other Asian-Americans, “I knew that I had a greater likelihood of matching if I could find someone from my ethnic group” [Mr. Pablo was Filipino]. He went on, “So I had to focus on that, and use communications that had credibility in that community.

This included Filipino doctors, who as a group worked together to communicate with the community about the need for donors and why they should be involved. We also had to address cultural barriers, such as the fear of desecration of the body. We went to the major radio outlet for the Filipino community. But I don't speak the dialect. So I partnered with a legislator who was Filipino-born and who spoke Ilocano, a major Filipino dialect in Hawaii. There are also Tagalog speakers [another Filipino dialect] on the radio. I spoke in Catholic and Methodist churches. A major part of our message was that bone marrow replaces itself, and the body can regenerate. It's important to dispel myths."

Ms. Lew adds that verbal community history and gossip can make or break a recruitment effort. "Gossip never dies," she says. "Everyone hears about a mistake" – and everyone will remember.

Several informants stress that it is critical to report the results of clinical trials – whether positive or negative – back to the community, preferably through pathways that already exist. Dr. Nou explains, "Researchers and scholars must go back to the community, so that they know what the results are and how they benefited research subjects. This is very important; the experience cannot be unidirectional. Community follow-up is critical, not just in print, but also in dissemination to community leaders, so there is not fear that people have been exploited for the benefit of others, but not themselves."

She adds, as have other informants, that acknowledging the contribution of those who participated in a trial is extremely important. "The more you can honor what they did, the more likely it is that they and others will participate in the future."

## Framework for Action

The challenge is mighty, the stakes are high, and the tasks are formidable. But, given current and future population patterns in California and the United States as a whole, conducting clinical trials in a business-as-usual environment is simply not an option. It is not acceptable that the vast majority of clinical trial participants are still white, insured, and of higher socioeconomic status, 16 years after the NIH Revitalization Act called for greater diversity. The time to act is not now; it was a long time ago. Clinical research must now play catch-up in a rapidly changing society.

To that end, a framework for action for CIRM and its grantees should include these priorities:

- **Acknowledge that mistakes have been made in the past, and work to ensure that patients are fully informed and protected**
- **Be as transparent as possible in all activities**
- **Learn as much about the target groups and subgroups as possible**
- **Tailor recruitment – and the trials themselves - to the target groups**
- **Help participants navigate the process from beginning (filling out forms) to end (telling them the results of the trial)**
- **Involve minority community leaders, physicians, and recruiters**
- **Develop relationships that last over time, avoiding a “hit-and-run” approach**
- **Use varied approaches; the Internet is a useful tool, but at this time, overreliance on it will exclude many minority patients**
- **Prepare for a higher drop-out rate among minorities, so oversample if possible**
- **Report the results back to the communities involved**
- **Publicly acknowledge the contributions of participants**
- **Share what has been learned about minority recruitment and participation**

“The need is there – no question,” says Dr. Tran. “We just have to figure out how to fill it.”

Ms. Hansen believes that the potential for improvement is very real. “If CIRM and its research partners can learn how to do this, they could produce a workable model and create a prototype for the nation, which would be incredibly important, given the demographic future.”

## **ADDENDUM: ETHICS, INFORMED CONSENT, AND FUTURE MINORITY PARTICIPATION IN CLINICAL TRIALS**

The ethics of recruitment for clinical trials and protection of participants occupies a large space in the biomedical ethics literature, which is easily accessible. However, many informants and several written sources brought up important points in terms of the ethics of recruiting minorities for clinical trials. Those points are summarized here.

- **The “therapeutic misconception.”** Bioethicist Judith Swazey, Ph.D., elucidates that the “therapeutic misconception” occurs when potential clinical trial participants believe – or are told – that the trial might bring a therapeutic benefit, as opposed to its simply seeking information for *future* therapies. This situation often occurs in recruitment. Indeed, the director of one successful recruitment program told an audience in 2009 that potential participants in cancer clinical trials were offered the trial as “a therapeutic option.” Clinical trials, by their nature, are not therapeutic and cannot ethically be presented as such, especially to members of minority groups for whom language, cultural, education, and literacy issues may exist.

It is therefore ethically imperative that researchers and recruiters make it very clear what a clinical trial might accomplish – and what it might not. This includes addressing privacy concerns of potential participants who may believe that the research will be used in ways other than what they have been told.

- **Passivity of potential participants.** Although the U.S. patient population is increasingly described as “consumerist,” for many who are new to this country, who do not speak English fluently, or whose cultures are not so self-expressive, pleasing persons perceived to be in authority is natural. “[Such] patients often trust Western physicians and act in very passive ways,” says one informant. Indeed, in one published study, participants often reported that they wanted “to please the doctor.” Another informant observes, “Many Latino Americans would never think of questioning a nurse or a physician, so [providers] hold great power over the patient.” “[Patients] must know that it is okay to decline, which requires countering their innate respect for authority,” says one researcher.
- **A sense of obligation, or a fear of “losing face.”** A related issue is that some patients may feel a sense of obligation toward the physician or recruiter who seeks to enroll them in a trial. They might also believe that refusal to participate could constitute “losing face,” or being embarrassed within their community or in front of persons who are viewed as being in a position of authority. Such situations might be inherently coercive and must be avoided.

- **The potentially coercive effect of incentives.** Although incentives are important in many clinical trials, there is concern that they might be coercive, either in a positive sense (in essence, bribing people who need the money), or a negative one (if money is offered, the potential participant may feel bound by conscience to accept it – and participate in the trial). Understanding of the effects of incentives, especially financial ones, is extremely important for ethical recruitment.

Fortunately, at least one study of incentives has found that few participants felt that they had been coerced or that their involvement was anything other than voluntary, but some did, and that should set off at least mild alarm bells (Appelbaum).

- **The trustworthiness of institutional review boards (IRBs).** IRBs are entrusted with much of the power to ensure that participants in clinical trials are protected against abuse. However, a series of reports in recent years has raised serious questions about the ability and willingness of IRBs to fulfill this obligation. One government study obtained approval for oversight of a phony clinical trial of a phony product by a phony IRB (Kutz). As one informant observes, “IRBs bury you in paperwork on the front end, but then they never follow up.” Furthermore, the underlying priorities of for-profit IRBs, which are an increasing presence in clinical research, are questionable. Although this is an issue for all clinical research, when potential participants are members of minority groups, and might have problems with literacy, language, education, and understanding of the basic concepts of clinical trials, the threat of shoddy enforcement is even greater. “IRBs were never intended to be formal regulatory bodies,” writes Elliott (Elliott). “The prevalence of private-sector drug research and the push to commercialize every facet of medical research makes the original model hopelessly outdated. Research subjects need a watchdog to protect them.”
- **Insufficient informed consent, or worse.** Informed consent of participants is the basis of ethical research, yet it is often less than what it should be. One informant states, “In order to block passive agreement, the researchers have to inform the patient fully and make sure he or she knows what is going on, what the researchers are aiming to achieve, and what are the benefits and risks and costs. Informed consent must be meticulous. Patients must know what their options are.”

Issues of literacy and understanding of the process are also crucial. Dr. Swazey emphasizes that “what counts is the *oral* transaction, not the written transaction,” as many people will sign almost anything, and “most informed consent forms are unreadable.”

As George Annas, J.D., chairman of the Department of Health Law, Bioethics, and Human Rights at the Boston University School of Public Health, states, “The most important ethics consideration in recruitment of human subjects is that people understand that it’s research and not treatment. The second most important consideration is that the patient has his or her own physician who can advise him or her about this, and who has no stake in whether they enroll or don’t enroll. Too many researchers will do anything to make it look like it’s a good deal.”

- **Rank violations of the ethics of clinical research.** Although, fortunately, it is a rare event, massive violations of the basic ethics of clinical research still do occur, and, sadly, they tend to disproportionately involve minority populations. One informant cites a study that would never have passed muster by a U.S. IRB, so the researchers conducted it in a developing nation with no oversight whatsoever, while claiming that a reputable U.S. IRB had approved it. Another informant cites the use of “scare tactics” to intimidate members of a minority group into participating. A third tells a harrowing story of unethical informed consent within her own family: “My grandmother developed a very rare form of cancer.... I am a highly educated person, and yet in conversations with the oncologists and other physicians, I couldn’t really get a clear understanding of what was involved in the treatment they were offering her. One of the discussions I had with the oncologist, who was a specialist in this area, involved the fact that they were trying this new treatment - was she willing to participate? Here you have a woman who has been told that she has from three days to two months to live, and she does not speak English, and I’m translating back and forth, and when you’re sick, you aren’t processing information optimally, in any case. I tried to explain to my grandmother that this was a clinical trial, that she might get a placebo, that the trial was to gather information and not to provide a cure. The physicians offered none of that information. I didn’t want her to do it, but she overruled me and participated. She always said, ‘You don’t say when I will die; God says when I will die.’ She lived for another six months or so.” The family was never told the results of the clinical trial.

Such practices, although uncommon, are a violation of basic patients’ rights, and can also poison the prospects for future research.

- **Accountability and future participation in trials.** If the research community is committed to involvement of minorities in clinical trials, then that commitment must be long-term, and everyone involved in the research effort must be accountable to those who participate, to their families and other loved ones, and to the communities involved. It seems obvious that it does not take much - in terms of dishonesty, lack of feedback, and/or lack of long-term involvement with the community - to produce a distaste for future participation.

In their “road map” for the conduct of ethical clinical trials, Fleischhacker and Cohen offered the following key elements (Fleischhacker):

- Protection for “whistleblowers”
- Recourse for participants who are injured or otherwise harmed
- Protection for all human research subjects, even in trials exempt from federal oversight
- Reform of IRBs
- True monitoring of informed consent
- Restrictions on comparative and non-inferiority drug trials
- Sufficient federal funding for clinical trials, to lessen the influence of private funding
- Tighter oversight of conflicts of interest

One informant, who has been involved in minority participation in clinical trials as both a recruiter and as a family member of a participant, makes it very clear what can happen if unethical practices are allowed to go unchecked: “These are heartfelt issues for me because of things I have seen, experiences I have had, and episodes that I have been involved in. That’s why I am so skeptical now. I’ve had personal experience with it, and unless I have solid, solid, experience with the principal investigator and the co-principal investigator, frankly, I will stay as far away from clinical trials as I can.”

**PROJECTS DEDICATED TO IMPROVING MINORITY PARTICIPATION IN CLINICAL TRIALS (NOT A COMPREHENSIVE LIST)**

CancerPACT (Cancer Patients' Alliance for Clinical Trials)  
Lorenzen Cancer Foundation  
312½ Fountain Ave.  
Pacific Grove, CA 93950  
(877) 647-0400  
[www.CancerPACT.org](http://www.CancerPACT.org)

EDICT (Eliminating Disparities in Clinical Trials)  
Chronic Disease Prevention and Control Research Center  
Baylor College of Medicine  
1709 Dryden, Suite 1025  
Houston, TX 77030  
(713) 798-4614  
[edict@bcm.edu](mailto:edict@bcm.edu)  
(Four-year funding from Genentech ended in 2009.)

Project I.M.P.A.C.T. (Increase Minority Participation and Awareness of Clinical Trials)  
National Medical Association  
1012 10<sup>th</sup> St. NW  
Washington, DC 20001-4492  
(202) 347-1895, ext. 261  
[www.impact.nmanet.org](http://www.impact.nmanet.org)

San Diego EXPORT Center  
UCSD Division of Community Pediatrics  
9500 Gilman Drive - MC 0927  
La Jolla, CA 92093-0927  
(619) 681-0660  
<http://meded.ucsd.edu/sdexport/contact.html>

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