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The Role of Community Review in Evaluating the Risks of Human Genetic Variation Research

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Summary

The practicality and moral value of community review of human genetic research has become a focus of debate. Examples from two Native American communities are used to address four aspects of that debate: (1) the value of community review in larger, geographically dispersed populations; (2) the identification of culturally specific risks; (3) the potential conflict between individual and group assessments of research-related risks; and (4) the confusion of social categories with biological categories. Our experiences working with these two communities suggest that: (1) successful community review may require the involvement of private social units (e.g., families); (2) culturally specific implications of genetic research may be identifiable only by community members and are of valid concern in their moral universes; (3) community concerns can be incorporated into existing review mechanisms without necessarily giving communities the power to veto research proposals; and (4) the conflation of social and biological categories presents recruitment problems for genetic studies. These conclusions argue for the use of community review to identify and minimize research-related risks posed by genetic studies. Community review also can assist in facilitating participant recruitment and retention, as well as in developing partnerships between researchers and communities.

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Introduction

Surveys of the ethical, legal, and social implications of the Human Genome Project often claim that genetic information requires special confidentiality and privacy protections (Annas and Elias 1992; Andrews et al. 1994; Murphy and Lappe 1994; Rothstein 1997). These protections are considered important ways to reduce the likelihood that genetic information will be used for discriminatory purposes (Gostin 1991; Billings et al. 1992; Rothstein 1993; Hudson et al. 1995). To date, discussions of genetic discrimination have focused on protecting individual human subjects; hence the bioethical models that have been advanced emphasize the importance of individual autonomy and informed consent (Beauchamp and Childress 1994). This focus has been appropriate to the initial goal of the Human Genome Project—namely, the elucidation of the basic genetic code common to all human beings.

Now, however, there is an emerging focus on population-specific genetic variation (Collins et al. 1997; Khoury 1997; Brown and Hartwell 1998; Schafer and Hawkins 1998; Collins et al. 1998). In this new context, genetic information about individuals may pose collective risks for all who share a social identity (King 1992; Caplan 1994; Kegley 1996; Rothman 1998). All members of a socially identifiable population may be placed at risk by the identification of genetic features linked with their common identity. Prominent examples are the associations of African-Americans with sickle-cell trait (Phoenix et al. 1995) and Ashkenazi Jews with specific *BRCA1* alleles (Stolberg 1998). The risks presented by research on genetic variation, however, are not limited to disease associations and are not purely economic. They also may include the contradiction of a population's sense of its own history (Grounds 1996), broader forms of discrimination and stigmatization (Wolf 1995), internalized psychosocial stress, or the disruption of a community's social equilibrium.

There is general agreement that research on human genetic variation can present genuine risks for socially identifiable populations (Committee on Human Genome

Diversity 1997; Greely 1997; Foster and Freeman 1998; Juengst 1998*a,* 1998*b*). Despite this agreement, however, a debate has emerged about how these potential risks should be evaluated and how human subjects can best be protected.

On one side of this debate are those who propose requirements for community involvement in the development and review of population-specific genetic studies (Greely 1997; Proposed Model Ethical Protocol for Collecting DNA Samples 1997; Foster et al. 1998; Freeman 1998*b*). In some communities, the social units on which community members already rely in making health-related decisions could be engaged in the evaluation of genetic research proposals (Foster et al. 1998; Freeman 1998*b*). In other communities, alternative approaches could be used to facilitate public discussion of the proposed research and ways in which research-related risks could be minimized (Moore 1996; Greely 1997; Proposed Model Ethical Protocol for Collecting DNA Samples 1997). Whatever method is employed, the aim of community review is to involve the community in the research process through a dialogue between researchers and community members. The underlying rationale is that community members are able to identify risks to themselves and, often, to develop ways to minimize those risks that outsiders cannot.

On the other side of the debate are those who question the practicality and value of requiring community review. Critics question whether it is possible to obtain community approval in culturally heterogeneous, geographically dispersed populations (Juengst 1998*a,* 1998*b;* Reilly 1998) and whether calls to do so confuse social and biological categories (Juengst 1998*b*). Others maintain that giving special consideration to the interests of certain groups is "paternalistic" and "inherently demeaning" (Reilly 1998, 684). Some have gone so far as to deny the very existence of collective risks to socially identifiable groups, arguing that most culturally specific concerns are "intangible (and largely undocumented) fears" (Reilly and Page 1998, 15).

Of special concern to critics of community review is whether researchers should be *required*—as a matter of regulatory policy—to consult with communities before beginning their research, and whether communities should have the authority to veto a research proposal (Juengst 1998*a,* 1998*b;* Reilly 1998). Critics suggest that, although researchers might be commended for seeking community approval, regulatory requirements that they always do so are too extreme (Committee on Human Genome Diversity 1997).

A significant difference between the two positions in this debate is that those who suggest a requirement for community review do so on the basis of their experiences with populations in which collective and culturally specific risks are of concern to community members. In contrast, those who criticize various forms of community involvement—particularly those that require institutional review boards (IRBs) to weigh community concerns as part of the review process—do so primarily on the basis of conceptual arguments and appeals to insurmountable practical problems. We believe that additional examples of successful community review can better inform this debate about its practicality and moral value.

More specifically, additional empirical examples can help shed light on four fundamental questions in this debate: (1) What is the value of community review in larger, geographically dispersed populations lacking established or readily identifiable moral leaders? (2) How can culturally specific risks best be identified? (3) Should collective social units be able to exercise a veto over an individual's choice to participate in genetic research? and (4) Are communities defined by social criteria the appropriate units to evaluate genetic studies that focus on biologically defined populations?

Here, we describe a study of health care decision making in two Native American communities. One hundred fifty members of each community were interviewed. Individuals were asked to describe how they recognized signs of their most recent illness and how they made decisions about its treatment. These interviews were then used to construct case studies about genetic research and genetic testing. These case studies were subsequently discussed in focus groups. Each community then went through a decision-making process about its participation in an actual genetic study. Through discussions both within these communities and between community members and genetics researchers, several collective and culturally specific risks were identified, and ways to minimize these risks were found. These examples illustrate the practical utility of community review and its moral value in assuring appropriate human subjects' protections for genetic research. (We do not reveal the identity of the two communities, because both wish to remain anonymous. Moreover, the human subjects approval of this research specified that community anonymity would be maintained in any reports of research results.)

Community A

Members of community A make use of both traditional Native and biomedical sources of health care. In making health care decisions, individuals attend closely to the collective implications of both the illness and its treatment options. They do so not only as autonomous social actors but also as members of social units that require individual participation in collective decision-making processes when signs of illness are recognized.

Individual health status is interpreted as an index of personal power within community A. Adults who seek

biomedical care are considered to lack control over their bodies and, therefore, to lack moral authority over other members. Consequently, most adults do not openly acknowledge illness and tend to seek biomedical treatment only in more advanced stages of disease. In contrast, traditional healing practices have the advantage of restoring one's personal power in the eyes of other community members and thus are preferred.

Within the family, individuals who are ill are required to consult all consanguineous kin of the same sex within three degrees of relationship. This consultation is carried out in a rank order, beginning with the most senior lineal kin. The decision to classify an individual's symptoms as a named disease and subsequent decisions about traditional or biomedical treatment are made through this collective process. Because many illnesses are thought to grow out of social conflict or inappropriate behavior, social dynamics within the family and political relationships with other families are prominent considerations in categorizing and responding to individual sickness.

Sickness is rarely viewed as confined to a single individual. Members of community A believe that the illness of a close relative has consequences for other family members. This belief reinforces the solidarity of family units. It also reinforces the obligation to consult appropriate kin when signs of illness appear and to involve them in decision making.

In the context of the community as a whole, disease is treated as a constant threat to the continuity of Native traditions. Diseases not only diminish the demographic viability of community A by decreasing the community's membership, they also diminish its internal social viability. If adult members are overwhelmed by illness and left without sufficient power to exert moral authority—as is threatened by the nearly 50% rate of diabetes mellitus—the community as a whole may no longer be able to maintain its distinctive social arrangements. Consequently, much of the discourse in the community as a whole focuses on promoting individual well-being through both biomedical and traditional means. Research is often advocated in public gatherings. The prevention or eradication of disease through biomedical research is seen as helping to preserve the long-term continuity of the larger community. Nonetheless, many of the culturally specific risks associated with biomedical treatment also apply to participation in research projects. By donating parts of their bodies for scientific study, community members' power may be diminished should those samples be misused. Misuse can include intentional as well as inadvertent actions that may pollute the sample and, by symbolic extension, its donor (Douglas 1966). These notions of "pollution" include a sample being handled by a menstruating woman or being placed in the same test tube rack as a sample from a member of another family. Simply being known to have donated a sample may be sufficient to affect perceptions of an individual's power.

For these reasons, community consensus in support of a genetic research project depends on support among the constituent family units. Thus, it is necessary to address culturally specific concerns within families before addressing broader concerns about genetic discrimination and stigmatization based on a shared communal identity. These are separate bundles of issues situated at different levels of social organization. In neither instance, however, is it culturally appropriate for an individual member to ignore the collective judgments of the family or community. Nor is it culturally appropriate for individual leaders to speak for the community as a whole in the absence of a consensus among families.

Discussions of the proposed research project led to a consensus among members of community A. Individual participation in genetic research came to be seen as a selfless act that individuals could choose, to help younger or future members reduce their risks of disease. As such, individual participation was seen as enhancing rather than diminishing personal power. This reinterpretation was made possible by genetics researchers' agreeing to limit the scope of their investigations to specific diseases of concern to community members, to recruit participants in accordance with the community's conventions governing requests for familial assistance, and to provide assurances both that samples would be safeguarded from outside pollution and that any unused tissue would be disposed of in a culturally appropriate way.

Community B

Members of community B make use of traditional and Christian religious organizations for preventive health care but rely almost exclusively on biomedicine for the treatment of illness. The importance of preventive care, delivered through a variety of traditional ceremonies, is emphasized in public discourses on health-related matters. Individual health status is interpreted as an index of the power of that person's religious organization. Individual illness is also believed to adversely affect the health of fellow members because of their close association through coparticipation in preventive ceremonies. Thus, when signs of illness are recognized, it is obligatory to inform fellow participants, and it is incumbent on them to visit and assist their ailing comrade. Their obligations often include facilitating access to biomedical care by providing encouragement, transportation, companionship, and other assistance. Failure to consult fellow participants or to seek biomedical treatment is viewed as a threat to the viability of the religious organization, prolonging the exposure of other members to the collective risks of illness.

Because identity in the larger community depends on

participation in one of its religious organizations, the stability of the constituent religious organizations affects the viability of community B as a whole. As in community A, the moral authority of constituent institutions also plays an ineluctable role in individual decision making about health care. To not adhere to collective decision-making processes is to violate the terms of membership in community B.

Within the religious organizations, choices are made in reference to the rituals and social dynamics unique to each unit. Illness is often attributed to inappropriate ritual or interpersonal behavior. Such explanations reinforce the interdependence of members and emphasize the necessity for a collective response. There are no adverse consequences for seeking biomedical care, but treatment choices are in part a result of collective decision-making processes.

Within the larger community, the religious organizations are implicitly evaluated with regard to the efficacy of their preventive care. Since each religious organization offers a slightly different approach to disease prevention, the success of their preventive efforts in part determines their overall status within the community. Providing assistance to members who become ill is a way to improve the image of the religious organization. Public statements about health, however, rarely make explicit comparisons between preventive rituals.

Increasingly, younger community members rely exclusively on biomedicine for all aspects of their health care. Doing so reduces both their motivations to participate in community activities and their adherence to an ethic of communal interdependence. Typically, individuals who do not rely on the constituent religious organizations for preventive care do not feel obligated to involve the community's collective decision-making processes when they become ill.

As in community A, community B as a whole is supportive of biomedical research, including research on genetic susceptibilities to disease. Scientific investigation is widely supported as a means to develop treatments for illnesses that threaten fellow members. The constituent religious organizations, however, are much more skeptical about the use of genetic information for disease prevention. Although biomedicine is considered necessary after an illness reaches the point at which ceremonial control is no longer appropriate, biomedical interventions sometimes stand in direct competition with the preventive ceremonies sponsored by religious organizations. Thus, community evaluation of genetic research in community B requires that these unique sociocultural implications be addressed within the constituent religious organizations.

After extensive dialogue with members of community B, genetics researchers asked the religious organizations to serve as recruitment centers, and the organizations agreed. This allowed the religious organizations to maintain their role as the primary health care sources in community B. Indeed, by making religious organizations the gateways for individual participation in the genetic research study—combining for the first time in this community both biomedical and traditional resources—the overall statuses of the religious organizations and of the scientific project were enhanced. There was no evidence that those younger members who relied exclusively on biomedicine considered the use of religious organizations as gateways to be inappropriate.

Discussion

Community Review in Larger, Geographically Dispersed Populations

In the two communities described above, consensus was reached within private social units, not through political organizations or established moral leaders. In this way, a number of private social units and their members were involved in reviewing the implications of genetic research. This broader engagement of community members is preferable to reliance on a small number of leaders who may have individual agendas that fail to reflect the full range of community concerns. When political organizations and their leaders were involved, their role was to formally ratify the consensus reached by the private social units, not to shape it. Thus, our experiences suggest that community review can take place in populations lacking established, inclusive political organizations and readily identifiable leaders.

Nonetheless, both of our examples involve relatively small, geographically localized populations. This calls into question the value of this approach in larger, more dispersed populations. We believe, however, that community review is possible in those populations as well. Such studies must inevitably recruit participants from a limited number of local research sites. Private social units at each of these sites can be engaged in dialogue about the proposed research. Those discussions, and subsequent discourse within each locality, have much to tell researchers about locally significant, culturally specific risks and possible ways to minimize them. Moreover, where views of the research differ substantially between localities, researchers may be able to create site-specific protocols that address local concerns.

The larger question is how to deal with differing views within a dispersed population that cannot be resolved by accommodations to local concerns. For instance, some national Native American advocacy organizations initially opposed all genetic research in Native populations (Rural Advancement Foundation International 1993; Indigenous Peoples Coalition Against Biopiracy

1996; National Congress of American Indians 1998), while some local communities agreed to take part in specific genetic studies. Those local communities were satisfied that their concerns had been taken into account by the researchers (Foster et al. 1998; Long et al. 1998). Nonetheless, some individuals who share a broader Native American identity with members of those local communities disagreed with their decision to participate in genetic research, maintaining that such research places all Native Americans at risk.

This problem of populations that are "nested" within other populations is one of the most difficult challenges for community review (Juengst 1998*a*). Although we do not have a comprehensive solution for this problem, we note that the concerns of local populations, such as those in the two communities described above, tend to be culturally specific, whereas the concerns of larger populations tend to be about broader forms of discrimination and stigmatization. Thus, one way to deal with the nesting of populations is to use several forums to assess the various risks presented at different levels of social identity. Efforts already have been made in this direction. For instance, Hadassah and the Jewish Council for Public Affairs recently initiated a dialogue between Jewish leaders and genetics researchers to review both the value of genetic research to Jews and ways to minimize potential harms to different segments of the Jewish population (American Jewish Congress 1998; Stolberg 1998). The aim of these discussions is to identify possible risks and concerns, not to formally approve or disapprove individual research proposals. Similar dialogues have recently taken place between genetics researchers and national Native American advocacy organizations.

The form that community review should take will vary between populations, depending on the pre-existing collective decision-making processes that are already in place. Thus, community review is a spectrum of different activities, including holding informal discussions with members of a community, involving community members in the planning stages of the research, asking the community to participate in the evaluation of human subjects protections, and negotiating a formal agreement with the community. Clearly, not all these activities are appropriate in every population.

Culturally Specific Risks

In both community A and community B, the risks that prospective participants focused on were specific to the existing social arrangements within each community. These culturally specific concerns are distinct from how a community is perceived and treated by outsiders. General concerns about discrimination and stigmatization, for example, are separable from the culturally specific concerns voiced by families in community A and religious organizations in community B. Indeed, members of both communities we studied were more concerned about culturally specific risks than about employment or insurance discrimination.

Although culturally specific risks can appear trivial to outsiders (Reilly and Page 1998), community members often perceive them as serious threats (Grounds 1996). Such perceptions could seriously reduce research participation by members of socially identifiable populations. Critics of community review, though, have argued that unique, culturally specific implications—such as contradicting a community's beliefs about its history or worldview—do not constitute harms that should be considered in evaluating risks to human subjects (Reilly 1998). In the two communities described above, however, the culturally specific harms that emerged as most prominent in discussions with community members involved fundamental disruptions of social life. Given that psychosocial stress and the disruption of family units are recognized by geneticists as harms (Fanos and Johnson 1995) and are regarded as legitimate risks to be considered and minimized by IRBs (National Institutes of Health [NIH] Office of Protection from Research Risks 1993; Andrews et al. 1994), consistency dictates that community stress and the disruption of a community's social arrangements also be treated as significant research-related harms.

The identification and evaluation of community-specific risks, however, is only one step toward protecting communities. The federal regulations that govern research involving human subjects emphasize that IRBs should go beyond merely documenting research-related risks and acknowledging them in the consent process (45 CFR 46.111[a][1]). Whenever possible, IRBs should take steps to ensure that those risks are minimized. In our experience, research proposals presented for community review were not simply approved or disapproved. Instead, through dialogues between the community and researchers, previously unforeseen risks were identified and steps taken to minimize those potential harms. After this dialogue, the community often approved the revised research plan. Community review thus helps both to identify and to minimize research-related risks. If this process is successful, accrual of volunteers to participate in the study is likely to be enhanced. Even genetic studies that investigate highly sensitive topics (such as alcoholism among American Indians) can gather long-term community support through a process of community review (Long et al. 1998), thereby reducing risks and improving the science by taking account of local knowledge that is relevant to a study (Freeman 1998*b*).

In contrast, relying solely on heightened IRB review to evaluate the collective risks posed by research on ge-

netic variation raises a number of moral and practical problems. Assessing the social and cultural implications of genetic research falls outside the usual expertise of IRBs, and most IRBs are not well prepared to assess population-specific risks. Even having IRB members from the study population is not sufficient to identify all research-related harms, much less to find ways to minimize those risks. For instance, the Indian Health Service (IHS) Headquarters IRB has 28 members, 20 of whom are Native Americans (including MD- and PhD-level researchers, health professionals, and laypersons from Native communities). Despite its unique composition, however, the IHS IRB sometimes is unable to predict what a specific Native community views as the primary risks to itself. Two recent examples include worries about the use of genetic research into migration history to attack tribal sovereignty and concerns about the use of mitochondrial DNA and Y chromosome research in claims about who is or is not "Indian." These risks were identified only by community review, not by any IRB. Similarly, it is doubtful that the unique concerns raised by families in community A or by religious organizations in community B would be anticipated by an outside IRB, technical review panel, or funding agency. Thus, given the wide range of culturally specific harms possible in genetic research, relying solely on IRB review to protect identifiable communities is insufficient.

Community Concerns and Individual Choices

The possibility that a community might strongly oppose a genetic research project has attracted much concern, both as a potential threat to autonomous decision making and as a nonscientific barrier to scientific progress (Juengst 1998*a;* Reilly 1998). Our experience, however, suggests that, in some populations, it may be morally inappropriate for individuals to substitute their judgments for those of their community or its constituent social units. Members of communities A and B are accustomed to consulting one another about health-related matters. To ask them to do otherwise is to ask them to deny their membership in a shared community. Individual choices about genetic research that are reached in isolation from such obligatory communal discussions evade the moral authority of families in community A, religious organizations in community B, the larger community in both, and the cultural grounding of individual members in those social units. In effect, asking subjects to make individual choices about collective issues requires them to disregard their affiliation with their primary cultural communities.

Moreover, in many communities the assumption that collective decision making conflicts with or undermines individual autonomy is not empirically grounded. Indeed, within the moral universes of communities A and B, collective processes are viewed as necessary prerequisites for individual decision making. For instance, the decisions made by families in A enable members who have become ill to take individual actions that restore their personal power. It is important to note that, although the path to moral renewal is determined collectively, the choice to take that path lies with the individual. Similarly, religious organizations in community B also enable and provide structure to individual decision making. In both communities, collective decisions necessarily prefigure individual actions and make genuinely autonomous individual decision making possible. The process of community review actively informs prospective individual participants about collective views of a genetic study. In the end, individuals, thus informed, have the ultimate "veto" on group participation.

By acknowledging the sociocultural role of constituent organizations within some populations, community review shows genuine respect for potential research participants, both as individual persons and as members of their community. In contrast, in some sociocultural traditions, genetic studies that rely solely on individual informed consent to judge collective and culturally specific risks evidence a lack of respect for the social and moral communities of which participants are members. Thus, in the same way that individual informed consent serves several functions apart from merely protecting human subjects (Faden and Beauchamp 1986), community review may be important to seek for reasons beyond protecting populations.

In addition, relying on individual consent alone could lead to morally problematic recruitment practices, such as "forum shopping" (Reilly 1998) or recruiting individuals who share the same genetic heritage but no longer subscribe to the moral authority of the community. Participants could even be recruited despite communal opposition to a specific study—taking advantage, for instance, of expatriates or geographically isolated emigrant populations (Committee on Human Genome Diversity 1997; Juengst 1998*a*). However, allowing individual autonomy to trump community concerns creates a situation in which individual choices could place entire categories of persons at risk. Collective harms do not disappear just because some individuals who share a community's identity do not recognize those harms. Indeed, an alternative phrasing of this issue might be, "Should individuals be able to exercise a veto over a community's concerns about the collective risks of genetic research?" Bioethics should help individuals and communities resolve such potential moral dilemmas rather than create them. Much work remains to be done to find ways to balance communal and individual rights and concerns.

Social Communities and Biological Demes

Biological demes rarely correspond to social identities (Juengst 1998*a,* 1998*b*). A simple approach for avoiding many of the risks presented by the reification of social categories is to maintain population anonymity—that is, neither to associate genetic findings with social identities in publications (Foster and Freeman 1998) nor to use social identities to recruit participants (Committee on Human Genome Diversity 1997; Juengst 1998*a*). Not linking the name of an identifiable population with specific findings minimizes many potential harms. Population anonymity helps prevent scientifically inaccurate representations of findings when genetic populations or demes do not correspond to social categories such as race or ethnicity (Freeman 1998*a*).

Population anonymity alone, however, may not protect against all collective or culturally specific risks. Studies that explicitly link social identity with genetic findings—for example, studies that use founder effects to investigate the genetic influences on disease—cannot avoid using social identity to recruit participants. However, even the use of social identity as a heuristic template for participant recruitment may disrupt a community's social equilibrium. For instance, the primary concerns of families in community A focused on the adverse consequences for individuals who were known to participate in genetic research, not on the implications of published findings or discrimination against the group or its members by external actors.

Moreover, the problematic fit between social and biological characteristics of populations is a general feature of the way in which genetic studies are designed and interpreted. The fact remains that, despite its biological imprecision, social identity often is used to recruit study participants and to analyze genetic findings. So long as that is the case, the social communities in question should be involved in assessing the risks such practices pose to their members.

Conclusion

Native American communities have developed a heightened awareness of the collective implications of genetic research. However, their concerns about those implications, and the collective decision-making processes they use to formulate those concerns, are not unique. Arguably, all socially identifiable populations have some culturally specific perspectives on genetic research and the significance of genetic information. Thus, many of our findings about community review in Native American communities are generalizable to other populations; specifically, (1) community review need not depend on the existence of recognized community authorities empowered to speak on behalf of the community as a whole; (2) the participation of community members in the review of genetic research may be essential for identification of population-specific risks; and (3) community discussions often help to define individual choices rather than usurp individual autonomy. Thus, we conclude that community review can be done in larger, geographically dispersed populations and may be helpful in identifying and minimizing research-related risks, particularly those that are culturally specific.

Community review does have limitations, however. Its findings can be locally variable in larger, geographically dispersed populations. The nesting of social identities can result in conflicting views about genetic research that are difficult to interpret. Nor does community review resolve the often imprecise fit between social identity and biological identity that is a problem common to many genetic studies. Nonetheless, just because community review has limitations, this does not obviate the collective risks of genetic research.

Research on population-specific genetic variation may play an important role in improving our understanding of common, complex diseases. To take full advantage of this research, we need the cooperation of various populations. Asking for their cooperation means that we must respect the diverse moral and social arrangements of those populations, must recognize diverse moral and social harms they could suffer as a result of their participation, and must take steps to reduce research-related risks so that both participants and nonparticipants with a shared social identity are protected.

The issues that have arisen in the debate about requiring community review are complex and will not be easily resolved. Both sides in the debate have made significant contributions toward development of an emerging standard for how members of one community should conduct genetic research that involves members of other communities. The population-specific risks of genetic research cannot be identified, let alone resolved, without first asking members of both sides to explain to each other their understandings of the issues in question. That is what community review does, and that is why it should be required in population-specific genetic research.

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