

Protecting communities in pharmacogenetic and pharmacogenomic research

C Weijer¹
PB Miller¹

¹Department of Bioethics, Dalhousie University,
Halifax, Nova Scotia, Canada.

Correspondence:

C Weijer, Department of Bioethics,
Dalhousie University, 5849 University
Avenue, Halifax, Nova Scotia, Canada B3H
4H7.

Tel: +1 902 494 6330

Fax: +1 902 494 3865

E-mail: charles.weijer@dal.ca

ABSTRACT

The existing EELS literature has usefully identified the scope of ethical issues posed by pharmacogenetic and pharmacogenomic research. The time has come for in-depth examination of particular ethical issues. The involvement of racial and ethnic communities in pharmacogenetic and pharmacogenomic research is contentious precisely because it touches upon the science and politics of studying racial and ethnic difference. To date, the ethics literature has not seriously taken account of the fact that such research impinges upon the interests of communities, and that taking such interests seriously requires that we both protect and empower communities in research. We propose a framework that rests upon the recognition that communities are heterogeneous human associations and differing policies are appropriate for differing communities. Community consent and consultation and community consultation alone are neither appropriate nor required for all pharmacogenetic and pharmacogenomic research. Rather, application of these policy protections must take into account particulars of both planned research and the communities involved.

The Pharmacogenomics Journal (2004) 4, 9–16. doi:10.1038/sj.tpj.6500219
Published online 2 December 2003

Keywords: pharmacogenetics; genetics databases; bioethics; human experimentation; culture; research standards

INTRODUCTION

While much has been written on the potential for pharmacogenetic and pharmacogenomic research to improve our understanding and treatment of disease, considerably less has been written on associated ethical, economic, legal, and social issues (hereinafter, 'EELS'). The EELS work published to date generally anticipates the issues in a broad outline.^{1–5} While such introductory work is essential for defining the range of issues that ought to be addressed, the time has come for detailed investigation of specific EELS problems. One set of problems open for study is the protection of communities in pharmacogenetic and pharmacogenomic research. These problems merit scrutiny in part on account of the increasing interest of scientists in conducting research on subjects or samples from named communities. They also deserve attention in light of the problems associated with the individualistic nature of existing moral, policy, and legal frameworks. Our analysis deals with current and anticipated pharmacogenetic research employing racial or ethnic classifications in tracking patterns in genetic variation and drug response, and pharmacogenomic research on samples identified with regard to race and ethnicity.

Received: 12 June 2003
Revised: 21 September 2003
Accepted: 14 October 2003
Published online 2 December 2003

RESEARCH INVOLVING IDENTIFIED RACIAL OR ETHNIC COMMUNITIES

A wide range of communities may be implicated in different ways by pharmacogenetic and pharmacogenomic research. Researchers and funding agencies have demonstrated a special interest in conducting research on subjects and DNA samples identified with respect to racial and ethnic origin. This research will directly implicate the interests of the wider racial or ethnic communities from whom subjects and samples are drawn. While pharmacogenetics and pharmacogenomics are relatively new fields, already studies have reported correlations between allele frequency and race and ethnicity,^{6–8} and between drug response and race and ethnicity.⁹ As more such studies are completed, researchers in pharmacogenetics and pharmacogenomics are likely to face heightened scrutiny.

The debates about the scientific relevance and moral justifiability of employing racial and ethnic categories in genetic research have already begun to take shape. Three distinct positions have been expressed to date. Schwartz argues that race and ethnicity are social constructs with no correspondence to biologically significant difference.¹⁰ Since 'race is a social construct, not a scientific classification' (Schwartz, p. 1392),¹⁰ and race has been used to discriminatory ends, he decries its use in practice or research. Schwartz and commentators¹¹ argue that the emerging era of genetic medicine, with its emphasis on individualized testing, will facilitate the end of the use of race and ethnicity in research and practice.

Others have begun a concerted effort to explain scientific interest in race and ethnicity, and to distinguish legitimate from illegitimate recourse to these categories. Burchard *et al*¹² allow that race and ethnicity are partly social constructs, but insist that this does not mean that they are devoid of biological significance. Racial and ethnic classifications do map onto patterns of genetic variation in disease susceptibility and drug response (Burchard *et al*, pp. 1172–1174).¹² These patterns emerge as a result of complex inter-relationships among a number of factors of scientific interest, including geographic isolation, reproductive insularity, shared lifestyle patterns, and environmental influences. Scientific questions concerning the interplay of these factors in the emergence of patterns of genetic variation and disease are, they argue, legitimate.

A third view is found in the work of Foster *et al*,^{13,14} who argue that self-reported claims of race or ethnicity are too imprecise to be employed legitimately. Self-reporting is unreliable and, further, distinct populations are often subsumed under broad classifications, for example, Caucasian, Latin American, European, Asian, and African-American. They argue that geneticists need to develop and employ categories that more closely map onto patterns of genetic variation through the careful construction of pedigrees. Foster and co-workers make the striking recommendation that socially mediated community identities be supplanted by identities devised and validated by scientists.

These arguments suggest three distinct policy directions for pharmacogenetic and pharmacogenomic research.

Schwartz's arguments incline to a policy prohibiting the employment of racial and ethnic distinctions in research. The position of Burchard and co-workers suggests that racial and ethnic distinctions may be used, conditional on finding that the study justification contains a persuasive explanation of the scientific or policy objectives served. The arguments of Foster and co-workers suggest a policy discouraging the use of conventional, self-reported racial and ethnic identities, and encouraging pedigree tracing.

While this debate continues to take shape, research involving racial and ethnic communities, identified in conventional ways, is already proceeding apace. The National Institute of General Medical Sciences (hereinafter, 'NIGMS') has established the Human Genetic Cell Repository, a collection of samples with limited phenotypic information from named ethnic and racial groups, including Caucasians, Han Chinese, and Mexican-Americans.¹⁵ The Pharmacogenetics Research Network at NIGMS has funded proposals to collect samples from Han Chinese-Americans and Mexican-Americans, as well as pharmacogenetic and pharmacogenomic studies of allele frequencies and drug response in and between racial and ethnic communities.¹⁶ Independently, Howard University has recently announced plans to collect and store DNA samples from 25 000 African-Americans for use in various forms of genetic research, including pharmacogenomics.¹⁷

PROTECTING COMMUNITIES: THE CURRENT STATE OF PLAY

The scope of potential benefits of pharmacogenetic and pharmacogenomic research to society is broad.^{18–20} First, the relationship between genetics, lifestyle, and the environment in influencing drug response may be better understood (Lindpainter, p. 223).¹⁹ Second, pharmacogenetic clinical trials could be smaller, safer for subjects, and more economically efficient for sponsors (Roses, pp. 1358–1360).¹⁸ Third, drugs may be safer to use by identification through genetic testing of those for whom the drug is unsafe (Roses, pp. 1358–1360; Tsai and Hoyme, p. 262; Noah, p. 2 and 8).^{18,21,22} Fourth, the efficacy in drug treatment could be improved as genetic testing identifies those unlikely to respond (Tsai and Hoyme, p. 262; Roses, p. 1358; Lindpainter, p. 227).^{18,19,21} Fifth, pharmacogenetics is promised to bring marked improvement in postmarketing surveillance of pharmaceuticals (Roses, p. 1359).¹⁸ Sixth, and finally, the identification of a genetic variation could lessen the risk of prejudice to the community and instead specify individuals who are at risk (and those who are not) for adverse or non response to treatment.

Nonetheless, the communities who are the subject of pharmacogenetic and pharmacogenomic research may be exposed to substantial risks. First, research results that link membership in a racial or ethnic community to a high rate of nonresponse to a conventional treatment may prejudice members of that community in obtaining insurance or employment. Second, the 'nonresponder' label may also foster or exacerbate society-wide discrimination against

members of the community. Third, where communities with high rates of nonresponse are economically disadvantaged, the pharmaceuticals industry may be reluctant to invest in alternative treatments. Fourth, where additional public funds are invested in research to find new treatments for communities with high rates of nonresponse to existing treatments, the perception that certain communities represent a 'drain on the system' may be damaging. Fifth, some pharmacogenomics research, intended to clarify the interaction between genes, lifestyle, and the environment, may present risks to community identity. Since western models of disease are not universal, the aims and results of the research may be in tension with culturally specific ideas about the meaning, causes, and treatments of disease. Sixth, the possibility for disruption of community identity would be even more pronounced if Foster and co-workers' call for the creation of genetically precise social categories were implemented, striking at the very heart of the legitimacy of self-reported claims of identity.

In light of these risks, we think it essential that communities be extended protections that allow for their respectful involvement in research. With adequate policy guidance, open and sensibly structured partnerships between researchers and communities can facilitate the gathering of information and samples as well as the recruitment of subjects, all of which is essential to scientific progress. Ongoing exchange of information between researchers and community representatives is conducive to the proper identification, assessment, and evaluation of the benefits and harms of the research to the community, and the development of strategies for harm minimization and benefit maximization.

The EELS literature on pharmacogenetics and pharmacogenomics raises important questions as to the adequacy of current consent procedures, and protections for privacy and confidentiality.^{1,23–25} Despite the fact that informational risks associated with genetics clearly implicate the interests of communities, many bioethicists are reluctant to recognize these interests as distinct from those of individuals. They presume that so long as the rights and entitlements of individuals are protected, the welfare of the community is secure. However, the interests of the community are separable from the interests of its constituent members. Consider Streuwing and co-workers' study of the prevalence of BRCA1 and BRCA2 mutations among Ashkenazi Jews in Washington, DC.²⁶ They found that 2% of Ashkenazi Jews carry a mutation in these genes, conferring a 56% risk of breast cancer and 16% risk of ovarian cancer by age 70. Although individual identifiers were destroyed, the community was identified in the publication. Thus, the study posed no risks to individuals, but posed substantial risks to the community, for instance, creating the false impression that Ashkenazi Jews are more susceptible to cancer.²⁷ Protections for individual subjects do little in and of themselves to protect or show respect for the community.

Most papers in the EELS literature on pharmacogenetics and pharmacogenomics have given the protection of communities only indirect or passing mention. Many EELS

commentaries, for instance, refer in general terms to the potential for genetic information to be received in such a way as to exacerbate pre-existing discrimination (Alcalde and Rothstein, p. 2240; Issa, p. 248).^{1,3} Others mention the possibility that the pharmaceuticals industry may engage in racial or ethnic profiling in their drug development and marketing strategies (Nuffield Council on Bioethics, p. 16).²⁸

The Consortium on Pharmacogenetics (hereinafter, 'Pharmacogenetics Consortium'), sponsored by a grant from the pharmaceuticals industry, has provided the most detailed analysis of community interests in pharmacogenetic research.²⁹ The Pharmacogenetics Consortium acknowledges that, at least in certain cases, pharmacogenetic and pharmacogenomic research may lead to group-based harms. By this they mean 'harms that individuals suffer as a result of being perceived to be members of ethnic or racial groups' (Buchanan A *et al*, p. 13).²⁹ Both community consent and community consultation have been proposed as protections for communities in research. The Pharmacogenetics Consortium rejects community consent, deeming it 'unacceptable, because it wholly subordinates individual autonomy to group preference' (Buchanan A *et al*, p. 13).²⁹ They also see problems with community consultation, pointing out that it may be unclear just who is an authentic representative of a community, and that consultation processes may result in individual community members being subjected to undue pressure or duress. They conclude that

From the standpoint of public policy and regulation, it would be inappropriate to mandate group consultation, much less group consent, as a general requirement for genetic research, including PGx [pharmacogenetic] research. However, in particular circumstances, for especially sensitive research with historically vulnerable groups, responsible researchers will seek to incorporate group input into the research design and informed consent process (Buchanan A *et al*, p. 15).²⁹

It seems, although it is less than transparent, that by 'particular circumstances,' they mean that additional research has demonstrated that group-based harms are likely to occur.

Regrettably, the Pharmacogenetics Consortium's treatment of communities is deficient in a number of respects. First, harms to communities are not merely 'harms that individuals suffer.' While it is true that individual community members suffer the harm, what distinguishes group-based harms from individual harms is that they are suffered by all or a considerable portion of community members by virtue of community membership. The harm is diffuse, resting with the community, and affecting all or most who belong to it. Furthermore, the harms that may be suffered by community members go beyond those resulting from the perceptions or attitudes of others. Research that challenges shared beliefs, origin myths, and so on may alter community members' sense of identity and belonging. The community may be harmed, even destroyed, by such internal disruption.

Second, the Pharmacogenetics Consortium makes the erroneous suggestion that the argument for recognition of community interests depends on the existence of group-based harms. On the contrary, the argument is based on the recognition that community interests are separable from those of individuals, and that the importance of communities to overall social well-being is such that these interests should be recognized. The purpose of a policy that mandates and facilitates recognition of community interests is to accord respect and encourage the empowerment of the community in question. Protection from harm is indeed an important end of these policies, but the protective ends are to be achieved through the establishment of an ongoing partnership of mutual respect between communities and the researchers.

Third, and finally, the Consortium wrongly suggests that one of us (CW) has advanced the view that, in moving beyond individualistic moral principles and policy protections, we need to 'confer a right on the group or its putative representatives to veto an individual member's consent to participation in research' (Buchanan *A et al*, p. 14).²⁹ They misconstrue ours as an approach that 'wholly subordinates individual autonomy to group preference' (Buchanan *A et al*)²⁹ While the Pharmacogenetics Consortium considers the recognition of community interests a zero sum policy exercise—either accord communities powers of consent equal to or greater than those enjoyed by individuals, or do nothing—we do not. In fact, as elaborated below, we argue that the interests of communities are worthy of respect, and that these interests warrant recognition through a framework that allows for variable imposition of a wide range of policy protections. The framework takes into account the central moral fact of human communities, namely, that communities are fundamentally heterogeneous human associations. For some communities, community consent and consultation is appropriate, for others community consultation alone is required, and for yet others no added protections are needed. We believe that this framework can be employed to protect and empower racial and ethnic communities in pharmacogenetic and pharmacogenomic research.

A FRAMEWORK FOR PROTECTING COMMUNITIES IN RESEARCH

One of us (CW), in a paper prepared for the US National Bioethics Advisory Commission, has argued that traditional moral principles for research need to be supplemented by a novel principle of respect for communities.³⁰ The principle is reasonably interpreted as conferring upon the researcher an obligation to take seriously the values and choices of the community and, where possible, to protect the community from harm.³⁰ The principle acknowledges that the community is more than the sum of individual interests; the community has separable interests. Thus, it is appropriate that the community be accorded respect separate from that accorded individual community members. The bases for recognizing the independent standing of the community

are several. First, people generally do not view themselves atomistically; rather they see themselves as members of one or more communities that constitute their values and self-understanding. Second, some communities already possess the authority to make binding decisions on behalf of individual members. Thus, the state may levy taxes, the municipality may decide which school a child may attend, and an American Indian band council may decline research participation on behalf of its community. The autonomy of individual community members is surely curtailed by such decisions, but this curtailment of individual liberty is legitimate. Third, the presumption of the primacy of the individual vs the community varies from one community and culture to the next. It may be that the individual is prime in western liberal states, but in certain communities even within these states, such as American Indian communities, this is not the case.

Early attempts at formulating research policy based on the principle of respect for communities were flawed by the presumption that all communities are sufficiently similar as to be extended a static set of policy protections. Thus, the 1996 draft of Canada's *Tri-Council Policy Statement* extends protections afforded to aboriginal communities, including community consent, to other communities, including racial and ethnic communities, persons with HIV, and women with breast cancer.³¹ Foster *et al*³² propose a model of community consensus and agreement, that is, community consent, for genetic research involving 'socially identifiable populations'. The legitimacy of community consent requirements rests on the presumption that the community in question has a legitimate political authority empowered to make binding decisions on behalf of its members. Many racial and ethnic communities and certainly most 'socially identifiable populations' possess no such legitimate political authority. Accordingly, the proposal to extend community consent protections to these communities generally is unfounded. The early history of policy in this area highlights the need to build policy upon a foundation that acknowledges the heterogeneity of communities.

Our schema for devising protections for communities in research is premised on the fact that communities vary in the degree to which they possess morally relevant characteristics required for particular communal protections. These characteristics include a legitimate political authority, representative group, common economy, and communication network. Particular protections presuppose the existence of one or more characteristics. Thus, community consent is only possible and appropriate if a legitimate political authority runs the community. Community consultation is only possible if the community has one or more representative groups or individuals. Community reimbursement for research costs is only possible if the community uses a common economy. Providing draft research reports to community members for comment is only possible if the community has a communications network. By matching the characteristics of a particular community with attendant protections, protections may be tailor-made for individual

Table 1 Three policy regimes for the protection of communities in research

<i>Proposed community protections</i>	<i>Community consent and consultation</i>	<i>Community consultation alone</i>	<i>No added protections</i>
A. Consultation in protocol development			
1. Respect for culture	✓		✓
2. Input on protocol	✓		✓
3. Research useful	✓		✓
4. Respect for knowledge and experience	✓		✓
B. Process of providing information and obtaining informed consent			
1. Nontechnical and appropriate disclosure	✓		✓
2. Face-to-face meetings	✓		✓
3. Adequate time for review	✓		✓
4. Consent	✓		
5. Consent required for protocol changes	✓		
6. May withdraw consent	✓		
C. Involvement in research conduct			
1. Transfer of skills and expertise	✓		
2. Employment	✓		
3. Reimbursement for research costs	✓		
4. Informed about research progress	✓		✓
D. Access to data and samples			
1. Consent for future use of samples	✓		
2. Storage of data negotiated	✓		✓
E. Dissemination and publication			
1. Involvement in manuscript preparation	✓		✓
2. Draft report for comment	✓		✓
3. Acknowledgment	✓		✓
4. Consent to identify	✓		
5. Report compliance with guidelines	✓		✓
6. Final Report	✓		✓
7. Consent for researcher media interview	✓		

Adapted from Weijer and Emanuel.³³

communities in research. This method is described in detail in an earlier publication.³³

In general when this method is applied, three regimes emerge for the protection of communities in research (Table 1). Community consent and consultation represents the most extensive set of protections and is reserved for highly cohesive communities with a legitimate political authority, such as American Indian or Amish communities (Table 1). A review described 23 individual protections for American Indian communities, including requirements that researchers seek community input on protocol development, engage in a process to provide the community with information about the study and seek its consent, involve community members in the conduct of research, seek community consent for future use of data and samples, and obtain community consent to identify the community in publications.³⁴ Relatively few other racial and ethnic communities, however, are sufficiently cohesive to require such extensive protections.

More commonly, racial and ethnic communities do not possess a legitimate political authority, and therefore

community consent is impossible and inappropriate. When a community, such as the African-American, Hispanic, or Ashkenazi community, has one or more representative groups or individuals, such as church or synagogue groups, community centers, or activist organizations, it is appropriate for researchers to engage these groups in community consultation (Table 1). Typically, consultation will be restricted to representative groups or individuals in the geographic locale where the research is to be conducted. Dialogue might include discussion about protocol development, details of the finalized study, information about study progress, plans for data storage, and provision of a draft report to the community for comment. These discussions will allow community representatives to help researchers identify risks to the community and to develop strategies to minimize them collaboratively, where possible. In some cases, a particular community, due to a lengthy history of oppression, may not have developed representative groups. In these cases, researchers may have an obligation to facilitate the development of such structures, for instance, by creating a community advisory group for the study.³⁵

Some communities are so dispersed and unstructured as to require no special protections (Table 1). Many of the 'socially identifiable populations' identified by Foster and co-workers will fall into this category. Bald men, asthmatics, and apartment dwellers are all 'socially identifiable populations.' Of course, all research subjects are afforded the protections conferred to individuals found in the federal *Common Rule*. However, do they deserve additional protections as communities? We think not. Part of the purpose of establishing policy regimes for communities in research is to protect social structures built up in the community. These groups lack all or most of the requisite characteristics of communities and hence there are no or few social structures in need of protection. Another purpose of policies for communities in research is the empowerment of communities who have long been victims of social oppression. Thus, one might reasonably conclude that African-American communities both require and are deserving of community consultation, while North American communities of European ancestry, together constituting the dominant culture, generally are not.

The Pharmacogenetics Consortium, in its general rejection of protections for communities in research, argues that '...the case for group participation in the informed consent process for PGx [pharmacogenetic] testing appears to be an instance of genetic exceptionalism. Many types of research, including nongenetic and even nonmedical research, have the potential for group based harms' (Buchanan *et al*, p. 14).²⁹ It should be clear that none of the claims in this section with respect to the protection of communities in research are specific to genetic research in general or pharmacogenetic research in particular. The notion of community consent and consultation was first developed in the context of research involving aboriginal communities and is widely understood to apply in differing forms across the spectrum of human subjects research.³⁶ The notion of community consultation was refined by work with the HIV community.³⁷ Thus, protections for communities in research are plainly not an instance of genetic exceptionalism. As we have described them, protections for communities in research allow us to recognize the importance of community interests without advancing sweeping, unsupportable claims about the characteristics of communities, and the protections to which they are entitled.

APPLYING THE FRAMEWORK TO PHARMACOGENETIC AND PHARMACOGENOMIC RESEARCH

Protections for communities in research are premised on the assumption that a particular study significantly impacts the interests of a particular racial or ethnic community. The potential for significant impact is present when the primary study hypothesis in a pharmacogenetic study addresses one, or perhaps more, racial or ethnic communities. Examples of such hypotheses include: to what extent is genetic variation A, known to be significantly correlated with response to drug B, present in persons of Hispanic descent? Is the observed difference in the metabolism of drug C between

persons of Han and European ancestry due to differences in genetic variation between these two communities? In these two examples, study subjects are enrolled because of their membership in the Hispanic and Han communities, respectively, and the study results may have direct and immediate impact upon the interests of these communities. Thus, researchers in these two studies should engage in consultation (Table 1) with the Hispanic and Han communities before initiating the studies. Since neither the Hispanic nor the Han communities have a legitimate political authority, the more expansive regime of protections (community consent and consultation; Table 1) would be inappropriate. As discussed above, because persons of European descent are dispersed in heterogeneous communities constituting the dominant culture in North America, consultation with this group is probably not required.

Race and ethnicity commonly, however, play a less central role in particular pharmacogenetic studies. Investigation of the correlation between race and ethnicity and genetic variation in drug response commonly constitutes a secondary research objective or hypothesis. Accordingly, the study population may be selected so as to be heterogeneous with respect to race and ethnicity. In such studies, the explanatory power of race and ethnicity on the observed variation is relegated to secondary analyses. The results of such analyses, however intriguing they may be, are best thought of as hypothesis generating and as requiring further study. Such studies do not target a single community, and the results of the study have no direct and immediate impact for a community. Thus, no community consultation is required for studies in which race and ethnicity are relegated to secondary hypotheses and subgroup analysis.

Pharmacogenomic research will, at least in some cases and to varying degrees, use samples identified with regard to race and ethnicity. Rather than collect samples directly, researchers typically rely on existing DNA databanks that make samples available to researchers in accord with their own policies. For instance, the NIGMS Human Genetic Cell Repository contains collections of DNA samples from Caucasians, Han Chinese, and Mexican-Americans, and provides these samples to researchers for a fee, under restrictive conditions.³⁸ It would be both repetitive and unduly burdensome to place the responsibility for community consultation on researchers using established collections of DNA samples identified by race and ethnicity. Rather, the responsibility properly rests with DNA databanks and those who collect the samples initially for them. This allows the DNA databank, and its collectors, to work with the community in question upfront to establish the scope of future use of samples collected from the community, and a mechanism for ongoing communication between the DNA databank and community. Established DNA databanks that have not worked closely with communities in the collection of samples should seek to establish ties with relevant communities in order to develop policies and procedures for future use of samples. Fees charged to researchers for the use of DNA samples ought to be used, in part, to support the costs associated with ongoing community consultation.

There is a substantial ethics literature on the collection of DNA for banking purposes.^{39–42} While policy in this area will need to take account of the purposes of particular DNA databanks, the ‘Policy for the responsible collection, storage, and research use of samples from identified populations for the NIGMS Human Genetic Cell Repository’ (hereafter, ‘HGCR policy’) is an instructive exemplar.⁴³ The HGCR policy is a comprehensive document that defines distinct sets of responsibilities for investigators who collect samples, Repository staff, NIGMS project officers, and the investigators who subsequently obtain the samples for their research. The policy requires that community consultation be conducted prior to the collection of samples. Who speaks for a community is a contentious issue—perhaps irreducibly so. The HGCR policy sets out a stepwise approach for identifying appropriate representative groups within the community: consult with overarching political organization for the community; if none is available, consult with political organizations representing segments of the community; if none are available, consult with cultural or social organizations; if none are available, identify other effective ways to consult the community. The HGCR policy notes that consultation may take place in a variety of forms. It may involve interviews, discussions, or public group meetings. Helpfully, the HGCR policy provides guidance on the contents of disclosure to the community.

Once initial community consultation has occurred and samples have been collected, the HGCR policy provides a mechanism for ongoing consultation through a community advisory group. Regular contact will occur between the Repository and the community advisory group, and the group will be consulted on any changes in policy or research goals involving the samples. The policy also recognizes the importance of apprising institutional review boards (IRBs) of the policy protections afforded communities. Documentation of initial and ongoing community consultation will be provided to the Repository’s IRB. Both the Repository IRB and investigator’s local IRB must approve research proposals for the use of samples. A key responsibility of the IRB is to ensure that the proposed use of samples is consistent with the community’s views as documented in initial and ongoing consultations. The scope of the policy extends to the conduct of investigators subsequent to the completion of the study. It requires investigators to provide a copy of research results to both the Repository and the community. This requirement allows the community and the Repository to ensure that the research results are presented in conformity with the researchers’ initial and ongoing representations, and provides a final opportunity for the community to voice concerns and work towards their resolution with the research team.

The HGCR policy represents a thoughtful and instructive instance of the implementation of our framework for pharmacogenomic studies. It requires initial and ongoing consultation with racial and ethnic communities from whom samples for research are obtained. The difficult question of what constitutes a representative group is answered in a manner sensitive to the features of particular

communities. The establishment of a community advisory group facilitates an ongoing and productive dialogue between the Repository and community.

There are a number of shortcomings of the HGCR policy. The HGCR policy does not clearly take into account the fact that a minority of communities, such as American Indian communities, are entitled to community consent as well as consultation. Also, we are not told whether community consultation itself requires IRB approval, an open issue under current federal regulations. Additionally, the policy only requires the collector to document community consultation for the IRB. Since differing views of the consultation process may exist, the IRB should also have access to documentation provided by community representatives. Further, the meaning of providing a copy of research results prior to publication to the community needs to be agreed upon upfront, and a mechanism ought to exist to deal with persistent disagreement on the interpretation of results between the researcher and the community. Finally, the consequences of violating the policy are not clearly set out. Nonetheless, other DNA databanks ought to consider carefully the HGCR policy when creating their policies and procedures.

CONCLUSIONS

The existing EELS literature has usefully identified the scope of ethical issues posed by pharmacogenetic and pharmacogenomic research. The time has come for an in-depth examination of particular ethical issues. The involvement of racial and ethnic communities in pharmacogenetic and pharmacogenomic research is contentious precisely because it touches upon the science and politics of studying racial and ethnic difference. To date, the ethics literature has not seriously taken account of the fact that such research impinges upon the interests of communities, and that taking such interests seriously requires that we both protect and empower communities in research. We propose a framework that rests upon the recognition that communities are heterogeneous human associations and differing policies are appropriate for differing communities. Community consent and consultation and community consultation alone are neither appropriate nor required for all pharmacogenetic and pharmacogenomic research. Rather, these policy protections must take into account particulars of both planned research and the communities involved.

The implementation of protections for communities in pharmacogenetic and pharmacogenomic research is in need of further reflection, innovation, and wide-ranging discussion. There is a paucity of literature detailing the working relationship of researchers with particular communities. Published description of these partnerships will greatly assist others planning studies involving communities. Particularly contentious are agreements with respect to the disposition of study data and samples. Publication of model agreements is a high priority. While the HGCR policy is a highly instructive document, other DNA databanks should be encouraged to publish their policies on the protection of communities in research. Descriptions of the challenges

faced by DNA databanks and communities, and solutions realized, will be instructive to other researchers. As experience is gained, shared, and assimilated into practice, we will come closer to realizing the dual goals of respecting communities and ensuring important scientific progress.

DUALITY OF INTEREST

Charles Weijer is Associate Professor in the Departments of Bioethics and Surgery at Dalhousie University. A Canadian Institutes of Health Research Investigator Award and Operating Grant support his work in research ethics. He is a Fellow of the Hastings Center and a Fellow of the Royal College of Physicians and Surgeons of Canada.

Paul B Miller is a student in law and philosophy at the University of Toronto, a Junior Fellow of Massey College in Toronto, and a research assistant at the University of Toronto and Dalhousie University. He is supported by a doctoral fellowship from the Social Sciences and Humanities Research Council of Canada.

REFERENCES

- Alcade MG, Rothstein MA. Pharmacogenomics: ethical concerns for research and pharmacy practice. *Am J Health-Syst Pharmacol* 2002; **59**: 2239–2240.
- Rothstein MA, Epps PG. Ethical and legal implications of pharmacogenomics. *Nat Rev Genet* 2001; **2**: 228–231.
- Issa AM. Ethical considerations in clinical pharmacogenomics research. *TIPS* 2000; **21**: 247–249.
- Buchanan A, Califano A, Kahn J, McPherson E, Robertson J, Brody B. Pharmacogenetics: ethical issues and policy options. *Kennedy Inst Ethics J* 2002; **12**: 1–15.
- Lipton P. Pharmacogenetics: the ethical issues. *Pharmacogenomics J* 2003; **3**: 14–16.
- Carlini EJ, Raftogianis RB, Wood TC, Jin F, Zheng W, Rebbeck TR, Weinshilboum RM. Sulfation pharmacogenetics: SULT1A1 and SULT1A2 allele frequencies in Caucasian, Chinese and African American subjects. *Pharmacogenetics* 2001; **11**: 57–68.
- Yu MC, Skipper PL, Taghizadeh K, Tannenbaum SR, Chan KK, Henderson BE, Ross RK. Acetylator phenotype, aminobiphenyl-hemoglobin adduct levels, and bladder cancer risk in White, Black, and Asian men in Los Angeles, California. *J Natl Cancer Inst* 1994; **86**: 712–716.
- Ameyaw MM, Regatero F, Li T, Liu X, Tariq M, Mobarek A, Thornton N, Folayan GO, Githang'a J, Indala A, Ofori-Adjei D, Price-Evans DA, McLeod HL. MDR1 pharmacogenetics: frequency of the C3435T mutation in exon 26 is significantly influenced by ethnicity. *Pharmacogenetics* 2001; **11**: 217–221.
- Wood AJ. Racial differences in the response to drugs—pointers to genetic differences. *N Engl J Med* 2001; **344**: 1394–1396.
- Schwartz RS. Racial profiling in medical research. *N Engl J Med* 2001; **344**: 1392–1393.
- Rothstein MA, Epps PG. Pharmacogenomics and the (ir)relevance of race. *Pharmacogenomics J* 2001; **1**: 104–108.
- Burchard EG, Ziv E, Coyle N, Gomez SL, Tang H, Karter AJ, Mountain JL, Perez-Stable EJ, Sheppard D, Risch N. The importance of race and ethnic background in biomedical research and clinical practice. *N Engl J Med* 2003; **348**: 1170–1175.
- Foster MW, Sharp RR, Mulvihill JJ. Pharmacogenetics, race, and ethnicity: social identities and individualized medical care. *Ther Drug Mon* 2001; **23**: 232–238.
- Foster MW, Sharp RR. Race, ethnicity, and genomics: social classifications as proxies of biological heterogeneity. *Genome Res* 2002; **12**: 844–850.
- NIGMS Human Genetic Cell Repository. Website: <http://locus.umd-nj.edu/nigms/> date accessed: September 21 2003.
- Pharmacogenetics Research Network. Research funding. Website: http://www.nigms.nih.gov/pharmacogenetics/prnsupp_abstracts.html date accessed: September 21 2003.
- Goldstein A, Weiss R, Howard U. Plans genetic database: school says data on African Americans could lead to better medical care. *Washington Post* 2003; May 28: A6.
- Roses AD. Pharmacogenetics and the future of drug development and delivery. *Lancet* 2000; **355**: 1358–1361.
- Lindpaintner K. Pharmacogenetics and the future of medical practice. *Br J Clin Pharmacol* 2002; **54**: 221–230.
- Goldstein DB. Pharmacogenetics in the laboratory and the clinic. *N Engl J Med* 2003; **348**: 553–556.
- Tsai YJ, Hoyme HE. Pharmacogenomics: the future of drug therapy. *Clin Genet* 2002; **62**: 257–264, at 262.
- Noah L. The coming pharmacogenomics revolution: tailoring drugs to fit patients' genetic profiles. *Jurimetrics* 2002; **43**: 1–28, at 2.
- Robertson JA. Consent and privacy in pharmacogenetic testing. *Nat Genet* 2001; **28**: 207–209.
- Robertson JA, Brody B, Buchanan A, Kahn J, McPherson E. Pharmacogenetic challenges for the health care system. *Health Aff* 2002; **21**: 155–167.
- Beskow LM, Burke W, Merz JF, Barr PA, Terry S, Penchaszadeh VB, Gostin LO, Gwinn M, Khoury MJ. Informed consent for population-based research involving genetics. *JAMA* 2001; **286**: 2315–2321.
- Struewing JP, Hartge P, Wacholder S, Baker SM, Berlin M, McAdams M, Timmerman MM, Brody LC, Tucker MA. The risk of cancer associated with specific mutations of BRCA1 and BRCA2 among Ashkenazi Jews. *N Engl J Med* 1997; **336**: 1401–1408.
- Lehrman S. Jewish leaders seek genetic guidelines. *Nature* 1997; **389**: 322.
- Nuffield Council on Bioethics. *Pharmacogenetics: Ethical Issues—Consultation Paper*. Nuffield Council on Bioethics: London 2002.
- Consortium on Pharmacogenetics (Buchanan A, McPherson E, Brody BA, Califano A, Kahn J, McCullough N, Robertson JA). *Pharmacogenetics: Ethical and Regulatory Issues in Research and Clinical Practice*, Consortium on Pharmacogenetics; 2002. Online: www.bioethics.umn.edu/News/pharm_report.pdf Date accessed: September 21 2003.
- Weijer C. Protecting communities in research: philosophical and pragmatic challenges. *Cambridge Q Healthcare Ethics* 1999; **8**: 501–513.
- Canada Tri-Council Working Group on Ethics. *Code of Conduct for Research Involving Humans (draft)*. Minister of Supply and Services: Ottawa 1996.
- Foster MW, Bernsten D, Carter TH. A model agreement for genetic research in socially identifiable populations. *Am J Hum Genet* 1998; **63**: 696–702.
- Weijer C, Emanuel EJ. Protecting communities in biomedical research. *Science* 2000; **289**: 1142–1144.
- Weijer C, Goldsand G, Emanuel EJ. Protecting communities in research: current guidelines and limits of extrapolation. *Nat Genet* 1999; **23**: 275–280.
- Levine C, Dubler NN, Levine RJ. Building a new consensus: ethical principles and policies for clinical research on HIV/AIDS. *IRB: Rev Hum Subjects Res* 1991; **13**: 1–17.
- Macaulay AC, Delormier T, McComber AM, Cross EJ, Potvin LP, Paradis G, Kirby RL, Saad-Haddad C, Desrosiers S. Participatory research with native community of Kahnawake creates innovative code of research ethics. *Can J Public Health* 1998; **89**: 105–108.
- Spiers HR. Community consultation and AIDS clinical trials, part I. *IRB: Rev Hum Subjects Res* 1991; **13**: 7–10.
- NIGMS Human Genetic Cell Repository. Website: <http://locus.umd-nj.edu/nigms/> Date accessed: September 21 2003.
- Weir RF, Horton JR. DNA banking and informed consent—part 1. *IRB: Rev Hum Subjects Res* 1995; **17**: 1–4.
- Weir RF, Horton JR. DNA banking and informed consent—part 2. *IRB: Rev Hum Subjects Res* 1995; **17**: 1–8.
- O'Neill O. Medical and scientific uses of human tissue. *J Med Ethics* 1996; **22**: 5.
- National Bioethics Advisory Commission. *Research Involving Human Biological Materials: Ethical Issues and Policy Guidance: Report and Recommendations*, National Bioethics Advisory Commission: Rockville, MD; 1999. Website: <http://www.georgetown.edu/research/nrcbl/nbac/hbm.pdf> Date accessed: September 21 2003.
- Policy for the responsible collection, storage, and research use of samples from identified populations for the NIGMS Human Genetic Cell Repository. Website: <http://locus.umd-nj.edu/nigms/comm/submit/collpolicy.html> Date accessed: September 21 2003.