
Legal Regulation of the Use of Race in Medical Research

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We have previously addressed the use of race in health care generally.¹ Subsequent developments have made the issue even more pointed. Given the recent Food and Drug Administration (FDA) approval of BiDil as a result of a clinical trial limited to participants identifying themselves as African-American, this Symposium could not be more timely as an effort to further advance the dialogue on the issue of race in medical research.² While this dialogue has informed our own analysis, we believe our distinctive contribution concerns the extent to which the law does and should constrain such use of race. Even in legal academic circles – somewhat notorious for considering problems of little practical significance – the issue has been given little thought.³ This piece, therefore, attempts to analyze extant legal regimes against the backdrop of medical and scientific developments.

While a number of other commentators have focused on relevant federal policies such as those adopted by the National Institutes for Health (NIH) for research they fund,⁴ there has been little analysis of how current constitutional and statutory regimes structure the debate. We do not attempt to determine why so few have addressed these questions in the past, but the absence of commentary may be related to a sense that the use of race in medicine is permissible because the goals of such use are honorable. If so, that is profoundly mistaken both as a matter of history and as a matter of law.

It is true that no existing federal statutes directly target this issue, but as we will discuss, several laws indirectly restrict the use of race in medical research. And federal regulations on point have generally been aimed at ensuring the *inclusion* of racial and other groups, rather than addressing whether race ought to be used at all.

In this article, we aim to shed further light on the present legal restrictions governing the use of race in medical research. We begin by distinguishing among types of research. We then consider whether the use of race in each type of research is presently permitted under federal law and the federal Constitution. We conclude with some thoughts about whether federal restrictions on the use of race ought to be expanded and whether federal policies that encourage the use of race ought to be abandoned.

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I. Defining “Research”

The term “medical research” actually covers a wide range of disparate activity. It includes case histories of patients, surveys of patients and patient histories, more formal epidemiological studies, “biomedical studies,” and clinical trials. Race can play a role in many of these kinds of research, but that role may vary substantially. For instance, racial data may be collected in a statistical study of the health outcomes of subjects, and may even be the variable of interest. More dramatically, race can also be used as a condition for inclusion in a clinical trial.

For purposes of this article, we distinguish several different kinds of research, roughly following distinctions we have drawn elsewhere.⁵ First, there are *epidemiological studies*, which we define as studies involving record reviews of human subjects,⁶ often, but not always, coupled with surveys or interviews of the subjects.⁷ Such studies can be used for a number of purposes. Sometimes they seek to identify a correlation between disease and potential causes. For instance, one recent study found “[a]n association...between exposure to traffic and the onset of a myocardial infarction within one hour afterwards.”⁸

Second, there is *biomedical and biochemical research*, in which the researcher’s aim is to investigate the biological and chemical mechanisms underlying a disease. This category covers a wide range of fields that we believe can be grouped together for our purposes, including core biochemical research (which explores how molecules interact), developmental biology (which concerns the chemical and biological mechanisms by which humans develop), and microbiology and immunology (the study of the molecular interactions of the immune system), among many others. Sometimes, such research is conducted *in vivo*.⁹ One example of such research involves the use of genetically modified mice to study the effectiveness of certain pharmaceuticals for organisms that are carriers of certain alleles.¹⁰ Such research can also be conducted *in vitro*.¹¹ In pharmacogenomic research, such studies have been described as “typically involv[ing] model cells that have been transfected with cDNAs representing the various polymorphic genes and the wild-type gene.”¹²

Third, modern *genetic research* combines aspects of both biochemical and epidemiological research. Often, such research involves taking DNA from participants and investigating whether particular genetic variants are correlated with particular diseases. One recent example of such research attempted to tie allelic variants in the gene for the prostanoid DP receptor to susceptibility for asthma.¹³

Fourth, once a potential intervention has been identified, researchers frequently engage in *clinical stud-*

ies to test the effectiveness of the treatment.¹⁴ Such treatments often, but not always, are pharmaceutical. Non-pharmaceutical trials include tests of surgical techniques and medical devices.¹⁵

With these definitions in mind, we turn to the role of race in research.

II. The Role of Race in Research

It is, by now, well documented that racial information is frequently produced by medical research. But before discussing the role that race plays in such research, we need to be clear about what we and, more importantly, what *researchers* mean by the term “race.” In most medical research in the United States, racial information is generated through self-reporting: the study participant identifies him- or herself as a member of a racial group.¹⁶ In this setting study subjects are generally believed to use an ancestral notion of race in their reporting.¹⁷ That is to say, subjects generally construct their racial identity based on the place of origin of their ancestors. Thus, subjects who might, say, appear “white” (or “black”), but who believe their ancestors come predominantly from sub-Saharan Africa (or Europe), will report themselves as “black” (or “white”).

When an individual has mixed ancestry, some believe there is a tendency, in America at least, to describe oneself in terms of the minority ancestry.¹⁸ However, if there is such a tendency, it may largely be an artifact of the choices available. For example, the 2000 Census generated a heated debate between those who wanted a mixed race category available – so as to avoid the necessity of choosing an identity ancestry – and civil rights groups who opposed changing the categories then existing.¹⁹ The result for that Census was to allow individuals to mark more than one race on census forms, thus creating a “mixed race” category for the first time; the result was that “almost seven million people, or 2.4 percent of the country, marked two or more races.”²⁰ This new counting technique thus produced a dramatic shift in the racial breakdown of the United States. As applied to the medical context, the clear message is that how the race question is asked will influence how it is answered.²¹ Nevertheless, no matter what range of choices is offered, self-reporting necessarily speaks to identity,²² which means that there will remain a risk that self-reports of race will provide information about *felt* identity rather than ancestry. Of course, this phenomenon may be reduced in the medical context – when life and health are at stake, people may be more inclined to report ancestry – as opposed to the Census context in which people may be inclined to report social identity to make a political statement.

For the purposes of this article, we assume that racial information is self-reported and that it is a rough proxy for information about ancestry (with the accuracy of the reporting on ancestry bearing on the accuracy of the proxy).²³ We do so for two reasons. First, as we have just described, the concept of race is generally used in U.S. medical research to refer to self-reported race, which is generally assumed to correlate with ancestry. Second, as we have discussed elsewhere,²⁴ an ancestry-oriented understanding of the term “race” is

After all, if race is defined based on felt identity, rather than on ancestry, then there is little reason to believe that the distributions in alleles among the various races will differ significantly from one another.

The second, less obvious reason for medical researchers to use race is to identify what we will call social causes of disease. The assumption – valid we think – is that the members of different races may engage (on average) in different health-related behaviors and (perhaps more importantly) are subject to different

physical and social environments. For example, members of racial minorities are generally poorer and more urban-based than whites in the United States. As a result, they may be more prone to contract certain diseases than whites. Further, being African-American may itself result in health

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consistent with American legal definitions. Although the statutes are not always clear, most at least imply that race is based on information about ancestors. And, more importantly for our purposes, Office of Management and Budget (OMB) guidelines explicitly define races in these terms.²⁵

Assuming racial information in medical research is about ancestry, researchers are doing one of two things with that information. First, they use such information to identify potential variation in the distribution of particular alleles. The human species, even today, is not panmictic; that is to say, humans do not randomly mate with one another.²⁶ At a bare minimum, geographic location of potential mates continues to play a large role: people generally tend to mate with those who live near them and often those who grew up close to them. And, of course, historically the geographic location of potential mates tended to be even closer. As a result, the human population has a genetic structure, with different subpopulations exhibiting different variations in allelic frequencies.²⁷ This may be either because the effects of natural selection are stronger in one population, or (more likely in the cases we will be discussing) because of *genetic drift* – the tendency of two groups that are not completely panmictic to evolve different allelic frequencies, simply as a matter of statistical chance.²⁸ But whether it is the result of natural selection or genetic drift, the reality is that human populations tend to have a structure, with variations in allelic frequencies between different parts of the structure. Race, then, is used by researchers as a proxy for identifying the underlying genetic structure of the species. How well it works for this purpose we consider below. Note, though, that to the extent race does work for this purpose, that functionality is premised on an ancestry-based understanding of race.

threats to the extent that remaining racism imposes physical, economic, or psychological injuries.²⁹ This use of race in research does not depend on ancestry. Particularly when researchers are studying the effects of racism on the health of individuals, what matters is the group an individual is perceived to belong to, not where her ancestors actually came from. For instance, a person of Native Australian ancestry in the United States, if perceived as black, would suffer the same racism as people of sub-Saharan African ancestry. What matters, then, is *perception*. Information about the race of a study participant may serve as a proxy for information about how that participant is perceived, assuming that internal and external perceptions of race are usually identical.³⁰

Although these are the two main uses of racial information in medical research, the precise way that race is used as a proxy for ancestry and to identify social causes of disease varies for each type of research that we identified in Part I.

Epidemiology

The broadest use of race is in the context of epidemiology, which is generally understood to be the study of disease in populations, both to determine the occurrence and the causes of the disease.³¹ One reason to collect information about race in epidemiological studies is to see whether there are, in fact, differences in disease occurrence among racial groups.³² Numerous studies have documented such differences, and it would be surprising if there were none. As simply a matter of statistical chance, given an infinite set of diseases, even two randomly-generated populations would no doubt show some differences in disease occurrence. Of course, the occurrence of health disparities between white and non-white groups in the United

States almost assuredly cannot be explained simply by statistical chance. But this, too, is no surprise. The impact of higher poverty, lower socio-economic status, and continuing racism facing minority groups in the United States certainly play a role in the distribution of different diseases among racial groups.³³

The key question for epidemiology is what role, if any, race can play in helping to determine the *causes* of disease.³⁴ This is a decidedly mixed bag. Some researchers have suggested that race is somehow pertinent to etiological studies. For instance, Professor Esteban Gonzalez Burchard and his colleagues have written in the *New England Journal of Medicine* that “in epidemiological...research, racial and ethnic categories are useful for generating and exploring hypotheses about environmental and genetic risk factors, as well as interactions between risk factors, for important medical outcomes.”³⁵ The article itself, however, focuses on how the use of race aids *genetic* research (a subject to which we will turn below) with little discussion of how race aids epidemiological research, beyond identifying racial disparities in health outcome. This is not to deny there is evidence that the use of race in epidemiological studies can be useful. For instance, Burchard and his colleagues note that epidemiological studies focused on race-based differences in treatment may generate information explaining differences in disease outcomes.³⁶ Such research into racial disparities in disease occurrence can then lead to hypotheses that some disparities arise from conscious and unconscious racism, both inside and outside the medical establishment. But note that in this argument made by Burchard and his colleagues, the use of race is very focused: after generating a hypothesis about the causes of racial differences in treatment outcomes, the hypothesis then has to be tested to see whether there really are disparities in the relative rates of usage of procedures.³⁷

Race can also be used as a tool to cast doubt on or even disprove possible causal mechanisms. For instance, Professor Raj Bhopal notes that some researchers had pointed to a possible link between dietary fat and heart disease on the one hand and intestinal and female breast cancer on the other.³⁸ Yet data from the Indian immigrant community in the United Kingdom, which has a high incidence of heart disease but low levels of the two types of cancer, cast doubt on that link.³⁹

Race thus *can* play a role not just in identifying racial differences in the occurrence of various diseases, but also in identifying the underlying causes of disease. It does not necessarily follow, however, that race should be used as frequently as it is now in epidemiological research or that it is in any way essential.

Biomedical and Biochemical Research

The need to use race is comparatively low in what we have termed biomedical and biochemical research. To the extent that researchers are interested in studying the genetic basis of human disease by examining how related genes act in mice or cells, there is no reason to base such research on race. Instead, what is relevant is attempting to match the genes in the cells or the mice to particular alleles in human populations. However, even in this context race might sometimes be useful. For instance, one recent study – a study relied upon in part by the BiDil researchers – compared the release of nitric oxide by endothelial cells from the umbilical vein of white and black females.⁴⁰ The study, although based on a very small sample (the cells of only twelve white and twelve black females were included), demonstrated an appreciable difference in the release of nitric oxide, as well as in the release of superoxide and oxidant peroxynitrite between the white and black study groups. Here, the hypothesis was that observed differences in epidemiological research in the rates of hypertension in blacks in comparison to whites might be the result of differentiated functioning of endothelial cells in white and black subjects. In light of their results, the authors speculated that this was the result of “upregulated gene expression or posttranscriptional upregulation of protein levels” leading to greater amounts of superoxide, oxidant peroxynitrite and basal nitric oxide in black patients.⁴¹ If this study were verified on a larger study group of endothelial cells, it would suggest possible differences in the frequencies of alleles controlling endothelial cell functioning in whites and blacks, or that there are environmental factors that cause differential release of nitric oxide in endothelial cells, and that white and black populations are exposed to these environmental factors at different rates. Of course, in the actual study, given the very small sample size, no one can be sure that either of these relationships exists.

Genetic Research

Researchers also use race in genetic research. Indeed, it is this use of race that has generated the most scholarly attention over the past few years.⁴² We do not wish to rehash that debate here; instead, we simply want to articulate the justifications given for that use. What follows is not our argument, but rather our recapitulation of the arguments in favor of the use of race. We will address our critiques of these arguments in Part IV.

As noted above, race serves as a proxy for underlying human population structure. That population structure is important, because there are alleles that either (1) have a role in causing disease or (2) have a role in affecting treatment of a disease *and* are found either solely or mainly in members of particular subpopula-

tions. For instance, the allele for Tay-Sachs disease is found *mainly* (but not only) in the Ashkenazi Jewish subpopulation.⁴³ If researchers are not going to perform genetic testing on a whole population, they may focus their efforts on those individuals self-identifying as Ashkenazi Jews in the belief that those efforts will capture most individuals with the allele. Thus, identifying the subgroup is used as a proxy for more accurate genetic information about the whole population.⁴⁴

This explanation, however, does not completely explain the need for race in genetic research. If the basis for a disease or treatment difference is genetic (and that, of course, is the underlying assumption of genetic medical research!), it would be helpful to test the entire population and identify all known allelic variants of the gene being tested. Why worry about population structure or race at all? One reason is to ensure that the genetic study picks up as many allelic variants as possible, and, if important allelic variants are mainly confined to particular subpopulations, failing to include members of those subpopulations in the genetic studies will mean that the particular variants will never be uncovered. Race is then used as a proxy for population structure, but only to ensure a wide range of samples.

Another reason to use race is to control for other possible genetic and/or (perhaps) environmental causes of differences. Even most diseases that are caused by genes are not classically Mendelian; they are instead the result of the interactions of multiple genes. As a result, an allelic variant that causes increased disease susceptibility in one population group may have a much more muted effect in another population group, because other alleles are muting the effect.⁴⁵ Information about population structure is necessary to control for such situations, and race, again, is used as a proxy for such structural information.

An example is an article on asthma susceptibility entitled “Role of Prostanoid DP Receptor Variants in Susceptibility to Asthma.” The underlying study identified four common alleles of *PTGDR* (the gene for the prostanoid DP receptor) and showed that specific alleles were associated with asthma in both white and black populations.⁴⁶ Because the first step of the study attempted to identify various alleles for *PTGDR*, racial information was collected to ensure that the sample had both white and black patients, presumably thereby ensuring that all major variants were identified.⁴⁷ Race was then reported on the linkage between the various alleles and asthma. The purpose was, presumably, to show that the linkage is *not* the result of other genetic or environmental factors. Unfortunately, however, the study also indicates the problems with the use of race, since the authors never tell us that the purpose of reporting racial data was to eliminate these other possi-

ble factors, and therefore the reader is never quite sure why the authors have racialized their work. While we are not convinced that race, as used in this study, *effectively* performs even the tasks we have suggested,⁴⁸ the study does illustrate how race *could* be used in genetic studies to control for differences in allelic frequencies between groups, particularly when the purpose is laid out explicitly.

Clinical Research

Finally, there is the use of race in clinical research. Conceptually, these studies are much like epidemiological studies in that the researchers are trying to see if a particular variable – giving or withholding a particular treatment – can be correlated with disease outcomes. And once again, researchers presumably use race as a possible proxy for other hidden environmental or genetic causes that might explain differences in treatment outcomes. In many cases, it appears that racial information is collected from subjects just to ensure that the patient and control groups are similar. As a simple example, in a recent study focusing on treatments for early pregnancy failure, the researchers were interested in the effectiveness of treatment with the drug misoprostol as compared with vacuum aspiration.⁴⁹ The researchers reported the racial make-up of both the misoprostol and the vacuum aspiration groups as part of a determination that “[t]here were no significant differences in demographic characteristics at enrollment between the two groups,” but they otherwise provided no racial data.⁵⁰ Because the researchers in this study made no other use of the information, it appears that they were interested in showing only that any differences in the treatment outcomes for the two groups were *not* the result of genetic or environmental differences between the two groups, and race was used as a proxy for these possible effects.

There is at least one other way to use race in clinical trials, and it is this use that has generated much of the controversy to date. At times, researchers actually use racial information to examine whether the effectiveness for a particular treatment varies according to racial group. This can be done in retrospective analysis of data that were originally analyzed without regard to race. In the case of BiDil, for instance, a reanalysis of the data from the Vasodilator Heart Failure Trial (V-HeFT I & II) suggested that BiDil was effective for black patients, but not for white patients.⁵¹ Alternatively, a trial can be consciously designed to test whether there are racial differences in treatment outcomes, although the difficulties here are muted since, to provide valid racial information, one would anticipate adequate representation of all races. Finally, there are studies, such as the African-American Heart Failure Trial (A-HeFT) to test

BiDiI's effectiveness in African-Americans, in which racial group membership is a criterion for inclusion in the trial.⁵²

III. Existing Legal Restriction on the Use of Race in Research

Our goal in this section is to describe the existing legal constraints on the use of race in research. In the next section, we will discuss the normative desirability of such constraints. Here we offer guidance on whether researchers' current uses of race are permissible under now-existing laws.

The legal constraints on the use of race in research are more limited than might be expected given the strong ethical consensus against harmful use of racial categories. The three major sources of federal regulation, the Equal Protection Clause and two federal statutory schemes, together leave large areas untouched.⁵³ Nevertheless, what might seem the distinguishing feature of research – an assumed benign purpose in drawing racial distinctions – is not reflected in the law.⁵⁴ Where legal regimes bear on race-related research, they do not provide a free pass to researchers merely because the researchers are seeking scientific insight in the quest to alleviate human suffering.

A. The Applicable Legal Regimes

The narrowest prohibition, both in terms of reach and in substantive restrictions, is the Equal Protection Clause of the U.S. Constitution. The clause limits discrimination by the government and therefore covers actions by the Food and Drug Administration (FDA) and by public research facilities, including state universities. It does not reach private facilities, even if the research is government-funded.⁵⁵ Suits are limited to intentional race discrimination, usually called "disparate treatment." When disparate treatment occurs, the Equal Protection Clause subjects it to "strict scrutiny,"⁵⁶ that is, such treatment is permissible only if it is "narrowly tailored" to achieve a "compelling governmental interest." In an often forgotten passage of *Regents of University of California v. Bakke*,⁵⁷ Justice Powell considered the defendants' claim that a racial preference was justified as part of the University's attempt to "improve the delivery of health-care services to communities currently under-served." Justice Powell wrote:

It may be assumed that in some situations a State's interest in facilitating the health care of its citizens is sufficiently compelling to support the use of a suspect classification. But there is virtually no evidence in the record indicating that petitioner's special admissions program is either needed or geared to promote that goal.⁵⁸

As applied to research, grouping individuals by racial categories might be permissible, but only if the extant evidence of racial differences is sufficiently strong to justify further study and the categories used are properly tailored to study those differences.

There are two major statutory schemes that expand the protection against racial discrimination beyond the relatively limited constraints of the Equal Protection Clause, Title VI of the Civil Rights Act of 1964 and 42 U.S.C. § 1981.⁵⁹ Title VI prohibits race discrimination in federally funded programs,⁶⁰ and § 1981 prohibits denying the right of individuals to contract on the basis of race.⁶¹

Title VI would seem to apply to most colleges and universities – certainly the major research universities likely to be conducting research with federal funding. Title VI has been held largely to track the Equal Protection Clause in its substantive protections,⁶² although it also reaches private institutions that accept federal funds.⁶³ Further, private institutions are subject to Title VI even if the research in question is not directly supported by federal grants.⁶⁴

As for § 1981, it has been read to reach any contractual relationship in either the public or private sectors, although it bars only intentional disparate treatment. Importantly, § 1981 contains no justification for racial discrimination in contracting; in that sense, § 1981 is more stringent than the Equal Protection Clause because nothing comparable to a compelling state interest justification has been recognized. Admittedly, there have been few instances in which such a defense might have been attempted, but it has been rejected whenever raised.⁶⁵ Indeed, the only recognized exception to the ban on race discrimination is the judicially created one of valid affirmative action plans, which also operates for Title VI.⁶⁶

In considering the reach of Title VI and § 1981, First Amendment constraints may sometimes restrict what would otherwise be the sweep of the statute.⁶⁷ Speech relating to racial differences or racially-differentiated treatment would be protected under the First Amendment as scientific discussion or policy debate. But limitations on research policies by § 1981 with which we are concerned will rarely trigger First Amendment protection. Although some have seen free speech problems in federal regulation of research by institutions receiving federal assistance,⁶⁸ § 1981 by its terms controls not speech but conduct – the act of contracting – and First Amendment concerns are at their weakest here.⁶⁹

B. Application of the Legal Regimes to Various Kinds of Research

In statistical and epidemiological studies, whether involving merely medical record reviews or including

surveys or interviews of the subjects, race is often employed, but the law imposes few restrictions. Although such studies commonly use racial classifications, these are not the kind of classifications prohibited by the Equal Protection Clause since they do not allocate either societal benefits or burdens by race.⁷⁰ Government involvement in generating such data, therefore, is not problematic under the Constitution unless the data are likely to be put to some questionable use.⁷¹ Since Title VI largely tracks the commands of the Equal Protection Clause, these classifications also pass muster under that statute. The prohibitions of § 1981 seem completely inapposite⁷² to statistical and epidemiological studies.

In contrast, the use of race in biomedical and biochemical research and in genetic research poses significant legal issues. In such research, samples may be drawn from different populations, which may be defined by race. And, as we have seen, in genetic research race may be used as a proxy for underlying human population structure or as a control for other possible genetic and/or environmental causes of differences. Some uses of race in both contexts are essentially identical to those in statistical studies and therefore are not legally problematic: researchers merely report and analyze racial data about samples they would otherwise examine, but do not otherwise select by race.

Other studies in both the biomedical and biochemical and genetic testing contexts, however, may be structured to affirmatively seek samples from different races. For example, we discussed above a very small study using samples from twelve black and twelve white females to determine the release of nitric oxide. The genetic study of asthma referred to above may have used both epidemiological and recruitment techniques. That study genotyped “fresh whole blood collected from 518 white and eighty black patients with mild to moderate asthma.”⁷³ Apparently, these samples were drawn from existing patients at U.S. centers for drug treatment trials, who may or may not have been racially selected. But a “racially-matched” control group of 175 whites and forty-five blacks without a history of asthma was also created; this group was drawn from a U.S. Army population,⁷⁴ and it seems likely that it was “matched” to provide control in racial terms.

The legality of this kind of research is more questionable. On the one hand, finding something to be a racial “classification” for equal protection purposes is likely to turn not on whether results are formally classified by race but rather on whether individuals are subjected to burdens or denied benefits on the basis of their race. Under this approach, such a test would not violate the Equal Protection Clause or Title VI since the subjects of the research are asked to undergo a

minimal burden and there is no benefit denied to them. Similarly, it is hard to view any excluded individual as having a claim under § 1981 because it is likely that no subject was denied the opportunity to contract with the researchers on the basis of race, especially since the blood samples provided were almost certainly donated, thus taking the transaction entirely out of traditional contract analysis.⁷⁵

On the other hand, there is something problematic about the research design insofar as it excludes Asians and, therefore, any potential race-correlated results have uncertain applicability to that large racial group. There may also be concerns about the expressive effects of including only two racial groups in dealing with a disease as serious and wide-spread as asthma.⁷⁶ If the action were viewed as a racial classification in the first place, it would seem hard to defend: while collecting and analyzing data by race may be justified by race as a proxy for population groups or social/environmental factors, it is hard to see what justification exists for limiting the sample set to exclude racial groups that might also be relevant to the study.

The response, of course, is that the lack of justification is irrelevant if the classification is not cognizable to begin with because it does not allocate benefits and burdens by race. Nevertheless, in deciding whether to treat a racial distinction as a racial classification within the meaning of the Equal Protection Clause, the apparent basis for drawing the distinction might be important. In the few cases involving racial record keeping, the courts have seemed inclined to permit such data to be collected as long as no purpose to use it invidiously was apparent *and* legitimate purposes could be imagined (such as enforcing civil rights laws).⁷⁷ Finally, to the extent an expressive theory of the Equal Protection Clause gains any traction, there seems to be a clear risk of expressive harm in the exclusion of a racial group from such a study, if only from the message that Asians are not an important enough group in America to warrant inclusion.⁷⁸

The last type of study, clinical trials, is the most difficult to square with current legal regimes. This is no longer merely an academic problem in light of the recent completion of the BiDil clinical trial, which was limited to African-Americans⁷⁹ and which resulted in approval of BiDil to treat heart disease in African-Americans.⁸⁰ In terms of the law, clinical trials clearly implicate Equal Protection concerns (at least when the government itself conducts or permits as part of a drug trial a racially-exclusionary study such as BiDil)⁸¹ or Title VI (when federally-funded research is at issue), and § 1981 (when researchers refuse to enter into contracts for participation depending on the race of the subject).⁸²

Where the Equal Protection Clause (and therefore Title VI) is concerned, use of a racial classification in a clinical trial would trigger strict scrutiny, but not necessarily a finding of invalidity since the classification could be justified by a compelling governmental interest: remedying of health disparities between various groups. Demonstrating that such classifications are narrowly tailored will be more difficult. Race-based limitations on who can participate in a trial exclude persons in the absence of *existing* evidence of racial distinctions in the safety or efficacy of the intervention. In some cases the very point of a race-based clinical trial is to demonstrate such differences. However, focusing a trial on one group does not appear likely to

the Equal Protection Clause, there is no acknowledged justification for such a refusal. Thus, even when the research is performed by corporations or by research institutions that receive no federal funds, the research remains illegal because all excluded individuals potentially have a claim against the researchers.⁸⁷

The legality of efforts to *include* racial groups is more uncertain. For example, NIH rules presumptively require the inclusion of minority groups in all NIH-funded clinical research;⁸⁸ that is, despite exceptions, the policy appears to generally require the inclusion of such groups at some unspecified level, an action that may border on creating quotas for representation in clinical trials. This policy may, in limited circum-

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give us much information about the underlying *causes* of racial differences in the response to treatment regimens. Thus, the trial of the efficacy of BiDil generated data suggesting that BiDil is more effective in African-Americans than whites,⁸³ but the reasons for any such differences remain unclear. The researchers' hypothesis for the difference – that African-Americans “have a greater deficiency of nitric oxide generation that is restored by” BiDil⁸⁴ – does not preclude a number of white patients, as well as Asian patients, from sharing the deficiency that BiDil restores.⁸⁵ Even if such deficiencies are less frequent among white (or perhaps Asian) patients, they almost assuredly *do* exist, just at lower frequencies. Furthermore, unlike pure research, race-based clinical trials cannot be justified solely as increasing our knowledge and lending valuable clues to disease causes and the source of treatment response variations. Instead, race-based clinical trials may lead to denial of potentially life-saving treatment to individuals on the basis of race. Accordingly, we believe that such research by institutions covered by either the Equal Protection Clause or Title VI – which includes almost all universities, public and private – is illegal.

From the perspective of § 1981, the result is even clearer. While particular individuals may not care about being excluded from a particular trial, and therefore may never bring suit, the refusal to enroll a subject on racial grounds seems like a classic refusal to contract since the arrangement has all the elements of a contract, albeit a unilateral one.⁸⁶ And, unlike under

stances, violate the Equal Protection Clause because it clearly involves a racial classification. Once again the ultimate answer turns on whether the NIH can satisfy the strict scrutiny standard. In cases involving drugs already shown to have differential effects on racial groups, there is a compelling state interest, and requiring the collection of additional data is probably narrowly tailored to that interest. In cases in which no prior racial effect has been shown, NIH policy does not require the inclusion of racial groups, thereby avoiding any constitutional difficulties. The most difficult cases are those involving drugs for which prior trials have neither shown nor negated the possibility of significant differences between races. Here, NIH policy requires the inclusion of minority groups, albeit at a lower level than for drugs where an actual effect has been shown.⁸⁹ Such cases might involve a compelling state interest. The lack of evidence that this drug is not effective, plus the reality that some other drugs do show such an effect, may be sufficient to justify some racial disparity. The close question for courts will be whether these rules are narrowly tailored. NIH's willingness to weaken the requirement for racial inclusion in such cases most likely would satisfy this standard.

IV. A Normative Perspective on How Law Should Approach the Use of Race in Research

In this section, we recommend the appropriate legal regime to govern the use of race in medicine. In doing so, we do not address what ought to be *ethically* permitted,

a topic that others have addressed.⁹⁰ Instead, we ask what the *law* ought to proscribe.⁹¹ To set the context, we first consider the active steps that the law presently takes to *encourage* the use of race in research. We then discuss in more detail what steps the law should take to require, support, discourage, or prohibit the use of race in various forms of research.

A. Legal Encouragement of the Use of Race in Medicine

A number of scholars, including Professor Dorothy Roberts in her contribution to this Symposium,⁹² have noted that the law frequently does more than simply permit the use of race in research; the law frequently encourages or even requires such use.⁹³ Perhaps the most innocuous of these practices is the requirement of various federal agencies that racial data be collected. As we have seen, NIH insists that all researchers “address” the inclusion of minority groups in NIH-funded research by describing the study population’s racial and ethnic make-up, and also “provide a rationale for selection of such subjects.”⁹⁴ Similarly, the Department of Health and Human Services (DHHS) requires the collection of data on race and ethnicity in most data collection and reporting undertaken by that department,⁹⁵ and the FDA requires that the race of research subjects be reported in the annual report of trials conducted under an Investigational New Drug Application (IND).⁹⁶ Professor Roberts argues that such uses of race – to the extent that they categorize race as a genetic or biological category – should be discouraged or prohibited by the government because “they reinforce ideologies of racial subordination.”⁹⁷

Potentially more pernicious than these requirements that racial data be collected are government actions that either directly or indirectly encourage research on differences between races. For instance, the government has funded research on differences between whites and blacks, thereby giving an incentive to researchers to undertake such studies.⁹⁸ Here, the difficulties posed by the research may turn on precisely what is being studied. In a number of cases, federal funding has been used to investigate differences in the use of various treatments for members of different racial groups, a classic form of epidemiological study.⁹⁹ More controversial are situations in which the federal government funds research of genetic studies involving race,¹⁰⁰ or when the government funds clinical trials involving race.¹⁰¹

The government can also encourage the use of race through less direct means. The most pertinent examples are the actions of the Patent and Trademark Office (PTO) and the FDA approving applications for patents and INDs that phrase their claims in explicitly racial

terms. As Professor Jonathan Kahn has noted, the research into BiDil by NitroMed, Inc. was encouraged by the willingness of the PTO to grant NitroMed patents on the use of BiDil in African-Americans.¹⁰² Without such patents, the intellectual property rights in BiDil would have expired in the near future, giving NitroMed little incentive to fund the research. Similarly, the FDA has promoted the use of race in research by approving an application for a use of BiDil as “indicated for the treatment of heart failure in black patients.”¹⁰³ A prior application without such a designation had been rejected by the FDA because there was not sufficient evidence of effectiveness.¹⁰⁴ The availability of both intellectual property rights and FDA-approved indications based on explicitly racial criteria now provides a powerful incentive for researchers to undertake such research.

B. Should the Law Encourage or Even Permit Use of Race in Research?

We now turn to the fundamental policy question: should the law encourage or even permit the use of race in research? As our discussion up to this point suggests, we believe a great deal turns on two factors: first, the type of research involved, and second, the nature of governmental involvement. The law should be least restrictive of the use of race in epidemiological studies, and most restrictive in clinical trials. In addition, we are far more supportive of governmental actions that seek to ensure *inclusion* of racial groups should be permitted, when government actions that lead to the *exclusion* of particular groups are not. We proceed by taking up each type of research in turn.

Epidemiological Studies

Some scholars have criticized the use of race in epidemiological research.¹⁰⁵ There are at least two components to such objections: first, research on subject populations divided by race does not provide particularly useful information, and second, regardless of what information is provided by the research, the harms that arise from such research outweigh any benefits.

We agree with the critics that epidemiological research that includes race as a variable has the potential to promote racism. Even when the research is designed to uncover racial differences in the treatment received from physicians by members of different racial groups – an effort to fight persisting racism in medicine – the research, particularly when it uncovers differences, tends to reinforce the notion that races are real biological categories. Because such ideas have been used to reinforce racism in the past, even research into racial differences in treatment runs some risk of increasing racism.

The key question, as we see it, is whether the benefits of such research nonetheless outweigh the drawbacks. We believe that, at least at this point in time, the answer is probably yes. When such research is designed to measure the differences in disease occurrence and differences in treatments among different groups, most commentators conclude that such research has benefits that outweigh the potential costs.¹⁰⁶ Furthermore, given the racial disparities that exist in the United States, we see no reason to bar such research and believe that such research also ought to be encouraged, both directly and indirectly, by the government.¹⁰⁷

A slightly more difficult question is posed by epidemiological research that seeks to use race in finding the cause of disease (or the effectiveness of a treatment), which we refer to as etiologic research. As Professors Jay Kaufman and Richard Cooper have pointed out, even when researchers attempt to control for socioeconomic status, etiologic research runs the serious risk of falsely indicating that race acts as an independent cause of disease.¹⁰⁸ In particular, they criticize the use of race in etiologic studies that seek to determine the relative contributions of genetic and social components of race because of the difficulties in specifying the appropriate social and other non-genetic components; there is a risk of suggesting independent effects that do not, in fact, exist.¹⁰⁹

This does not mean, though, that all uses of race in etiologic research should be abandoned. For instance, even Kaufman and Cooper agree that it is appropriate to study race in situations where we are seeking to determine whether medical professionals are reacting to the patient's race and prescribing different treatments on that basis.¹¹⁰ In addition, as Dr. Camara Phyllis Jones has noted, race can be used as a marker to search for other potential "real" causes of differences, through statistical analysis.¹¹¹ For example, upon discovering that there is a difference in the rate of occurrence of a particular disease (coronary heart disease, for example) between two races, epidemiologists can try to control for race and see if the racial disparity can be explained by another variable, which may then lead researchers to the true root cause.¹¹²

Some, perhaps even much, epidemiologic research that uses race may be misguided. But such research can also be done properly; even Kaufman and Cooper note that race can be used to study the effect of racism on referral rates and also to make statistical adjustments when attempting to estimate the causal effect of some other variable.¹¹³ Thus, the use of race in epidemiologic research ought not to be prohibited, and government should continue to fund such research. Nonetheless, we agree with those who call for more precision in the use of race by researchers.¹¹⁴ Particularly in the context

of epidemiologic studies, there is a danger of conflating the two possible uses of race we noted previously: as a proxy for the subject's ancestry, and as an indicator or proxy for how one is identified by society.¹¹⁵ Accordingly, while the government should continue to fund such research, it should also spend its money wisely, by requiring researchers using government funds to articulate exactly how they are collecting information about race and why.

Genetic Studies

Genetic studies provide a harder case. A large literature has developed over the past few years debating the validity and ethics of such research.¹¹⁶ Despite extensive dispute, there is some agreement. There is little doubt that there is structure to the distribution of alleles in human populations. Additionally, there is no real debate that there are a number of disease-causing or disease-influencing alleles that are more common among certain racial groups.¹¹⁷

The debate tends instead to focus on a number of other links in the chain of inference that support the argument for the use of race. First, race may be correlated with ancestry, which in turn is correlated with geography¹¹⁸ (and we have explicitly defined race in those terms in this article), but there is a great deal of disagreement over the extent to which race tells us something *useful* about ancestry. In the United States, this problem tends to be minimized by some researchers because, historically, members of particular races came from different geographical locations that were relatively isolated from one another until at least the fifteenth century: African-Americans predominately from West Africa; whites from Europe, (perhaps mostly from Western and Central Europe); and Asians from East Asia.¹¹⁹ As a result, it has been relatively safe, at least in the United States, to assume that race correlated with ancestry, although even in the United States the admixture of races is significant.¹²⁰

There are good reasons, however, to be increasingly dubious about the strength of this correlation. The correlation has never been exact, and as more people from East Africa, the Middle East, and South Asia – all areas with more admixed populations – come to the United States, the genetic distinctiveness of "black," "white," and "Asian" groups will lessen. Furthermore, the African-American population already has a significant admixture of European ancestry (~20%), and the white population has a significant ancestry outside of Europe.¹²¹

Second, there is profound disagreement about how useful genetic research is likely to be without regard to its race connection. To conclude that such research has value, one has to believe that genes play a signifi-

cant role in causing disease and/or affecting treatment outcomes, *and* one has to also believe that to the extent that genes do play a role, there is a significant difference in the distribution of the relevant alleles among different population groups. In a few diseases genes play an important role and the responsible allele is far more concentrated in one population group than another.¹²² But disorders caused by a single gene are rare. The vast majority of diseases result from a complex interaction of environment and multiple genes. Researchers are currently unsure of the extent to which research into genetics will provide useful information about such diseases.¹²³

Despite uncertainty over the long-term value of such research, we are opposed to prohibiting such research. We acknowledge that such research poses a serious risk of being misinterpreted as validating racism in American society. Indeed, the risk here is greater than with epidemiological research, precisely because so often in the past racism has been tied to genetics.¹²⁴ There are, however, two countervailing factors. First, even though First Amendment law probably does not *require* that such research be permitted, we believe that the underlying importance of freedom of research is significant. There is little doubt that past researchers have at times pursued lines of inquiry that seemed fruitless or even dangerous or heretical, but nonetheless led to important discoveries. Indeed, it is this very rationale that gives rise to notions of academic freedom. Cutting off such research may well be harmful, and in unexpected ways.

Second, while there are theoretically better ways to undertake research based on ancestry, we are not convinced that those options are currently feasible in most cases. One possibility is to group people not by race, but by “explicit genetic data (such as genome-wide SNPs, AIMS).”¹²⁵ The difficulty is that such a research protocol at the present time would add large costs. A more practical possibility would be instead to require that researchers acquire self-report information not about race, but instead ancestry, which would at least have the advantage of reporting directly the information of interest.¹²⁶ We would support this in light of the experience with the 2000 Census, which suggests that “race” is becoming an increasingly confused concept for individuals of mixed ancestry.¹²⁷ Inquiry into ancestry might focus the subject’s attention on the variable of interest. However, it should not be used to replace race over the wishes of researchers. A major problem is that categorization of ancestry data may be difficult. Although no doubt many subjects will continue to report themselves as white, black, etc., others will give themselves labels that are more difficult to use: should Germans be grouped with those who call themselves Cen-

tral Europeans or Eastern Europeans? Should people who describe themselves as Burmese be included with East or South Asians? This problem, we fear, will be magnified in smaller studies. While we nevertheless believe such research would be better than research that uses race, the problems lead us to reject a complete prohibition on the use of race in genetic research.

Government encouragement of genetic research using race, however, is more problematic. Commentators have suggested, for instance, that the NIH ought not to sponsor the publication of research that makes “claims about genetics associated with variables of race, ethnicity, nationality, or any other category of populations that is observed or is imagined as heritable” unless “these will yield clear benefits of public health.”¹²⁸ We both agree and disagree. Research that seeks to tie *ancestry* to disparate distributions of alleles that may cause or influence the occurrence of disease is sufficiently promising at this stage that it should not be abandoned by federal funding sources. Professor Mike Bamshad has recently noted that there are proliferating examples of situations in which the risk created by a particular allele will itself differ depending upon the ancestry of the individual.¹²⁹ For instance, in one study protection against malaria from variants of *TNFD* varied depending upon whether the individual was from West or East Africa.¹³⁰ Here, focusing on ancestry may allow researchers to undercover other genes that themselves affect how great an influence the *TNFD* alleles have on malarial resistance.

In addition, being aware of ancestry allows researchers to understand the breadth and depth of the sample with which they are working. Samples that include individuals of only a few ancestry groups may fail to uncover disease-causing alleles that are common in other populations. Another problem is that a sample containing a small number of individuals from many populations may fail to uncover alleles that occur only in a single, small population group. As an example, consider cystic fibrosis, a disease that is caused by carrying two mutant alleles of the *CFTR* gene.¹³¹ Cystic fibrosis occurs more frequently among whites than other groups.¹³² Despite this, the incidence of the various alleles that cause cystic fibrosis varies widely among different European populations.¹³³ Thus, a genetic sample that did not include people of Scandinavian descent might not pick up the 394delTT allele, which constitutes thirty percent of the *CFTR* mutations in Finland but is generally not found outside Scandinavia and Russia.¹³⁴ At the same time, a sample that only included people of Scandinavian ancestry would fail to pick up many mutations not present in that region.

Accordingly, we do not support efforts to stop funding genetic studies that use *ancestry* as a variable. Using

race as a proxy for ancestry, though, is far less justified. As we have already noted, race is at best an imprecise proxy. Furthermore, its use in genetic studies increases the risk of supporting racism (even if inadvertently), and that risk is magnified by having the government fund such research. Therefore, genetic research that uses race as a variable ought not to receive government funding, with two exceptions. First, funding should not be cut off when researchers refrain from using race as an actual variable, but simply report the demographics of their sample by race. Of course, reporting the demographics by ancestral group would be more helpful, but the harm of this use of race is not great enough to bar funding.

Second, we believe that race can still be used when there are important reasons for doing so. Kahn, for instance, has suggested that applicants to federal agencies – which we assume includes those individuals seeking federal funding of research – should be required to justify any use of race by an application of the strict scrutiny test arising out of constitutional law (which we discussed in the previous section). This involves showing that the use of race will serve a “compelling interest” and that the use of race “is narrowly tailored to serving that interest.”¹³⁵ Testing for alleles for diseases known to occur disparately in various races would usually pass the compelling interest test, as remedying those health differences ought to be a compelling interest for the government.¹³⁶ Meeting the “narrowly tailored” requirement would be harder; researchers would have to articulate why the use of race was the best way to study those differences. In particular, they would have to show why self-report of ancestry or use of genetic markers would not be a superior method.

Finally, we think that the application of Kahn’s test should turn at least somewhat on how race is used in the study.¹³⁷ As other commentators have noted, genetic studies of disease in non-white populations have been limited to date.¹³⁸ To the extent that race is used to collect data about the prevalence of alleles in understudied populations, the “narrowly tailored” requirement should be easier to meet. For instance, to the extent that researchers wish to focus on cystic fibrosis alleles in Asian or African populations, given the large literature available on their prevalence in white populations, we believe that the standard would be met.

Biomedical and Biochemical Research

Biomedical and biochemical research involving race appears to be far less common. To the extent that race is used in this context, however, the same considerations apply as with genetic research. Presumably, the reason for using race in a biomedical and biochemical study is the hypothesis that there is a relevant physiological

difference between racial populations, and in general we assume that such a physiological difference would be seen as genetic in origin.¹³⁹ Thus, the use of race in research that is government-sponsored should be forbidden, at least to the extent that race is a variable of interest. Again, we would not bar the simple reporting of racial demographics, and we would remain open to the use of race when there has been a showing of both a compelling interest and that the use is narrowly tailored to that interest.

Clinical Research

Clinical trials present the strongest case for a prohibition on the use of race, at least in one context. As we noted in Part II, researchers use race in clinical trials for two separate reasons: first, to attempt to ensure that the control and subject groups are demographically equivalent, and, second, to see if there are differences in treatment outcomes for different racial groups.

Using race simply to ensure equivalence between the control group and the treatment study group may very well be misguided, but it is not particularly harmful. The only reason to ask about race in this context is to uncover allelic distributional differences or socioeconomic or cultural differences. As for the socioeconomic and cultural differences, all-white and all-black groups, at least in the United States, will tend to have such differences. But it is misguided to rely on race as a proxy to uncover such possible differences. A far better approach is to attempt to monitor such variables directly, as by taking a thorough history of the patient at the outset of the study.¹⁴⁰ For possible genetic differences, we return to our observations above that race is at best an imprecise proxy for ancestry, which is the variable of actual interest. As with other research, we nonetheless do not support prohibiting such use of race, because we believe that the dangers of this particular use are sufficiently small.

Testing to find different treatment outcomes based on *race*, however, should be banned. More than in any other context, we believe that the use of race in clinical research runs the risk of reinforcing racism in the United States, because it is particularly likely to reinforce false beliefs about the genetic distinctiveness of races.¹⁴¹ Most clinical trials require FDA approval; running a trial on racial differences essentially gives governmental imprimatur to the existence of differences between racial groups.¹⁴² Furthermore, the message is likely to be that the reason for racial differences in the effectiveness of pharmaceuticals is that there are *genetic* differences that affect the biochemical mechanisms that process and interact with the pharmaceutical agents.¹⁴³ Of course, environmental influences alter the effects of pharmaceuticals.¹⁴⁴ But environmental ef-

fects on drug responses are likely to be seen as less important than genetic effects on drug responses, as the rise of the field of pharmacogenetics demonstrates.

Kahn has suggested that in order to protect against these problems, the FDA ought not to permit an applicant to use race as a biologic or genetic category unless the strict scrutiny test is met.¹⁴⁵ However, his proposal, at least in the context of clinical research, does not go far enough to prevent the use of race. Clinical research is usually explicitly designed to be used by the FDA in approving the use of a drug or to aid medical practitioners in treating patients. Using race as a proxy here is potentially even more harmful than its use in other forms of research because it will mask important differences that exist within races and potentially overstate the differences that exist between races.

For instance, the percentage of individuals classified as poor metabolizers of drugs using the enzyme CYP2D6 varies from one percent in Asians to ten percent in whites and nineteen percent in African-Americans.¹⁴⁶ This might suggest that there should be more caution in using such drugs in African-Americans than in whites or Asians. But these data may overstate the differences. For instance, whites are at much higher risk of being extremely slow metabolizers, while Asians may be slower metabolizers within the normal group. And there is also within-race variation; for example, there are important distinctions between the metabolism of Chinese subjects, on the one hand, and Japanese and Korean subjects, on the other.¹⁴⁷

Furthermore, as we have noted, there are alternatives to the use of race: using genetic data to group individuals or relying on self-reports of ancestry. As we noted previously, both of these alternatives have their problems.¹⁴⁸ In the context of genetic studies, we therefore oppose proposals to prohibit the use of race and instead support proposals to eliminate government funding for such research. In clinical research, though, we take a more restrictive view. Such research, unlike genetic research, directly affects patients. This creates additional potential harms from the misuse of race. For instance, the failure to enroll patients who were not African-American in the A-HeFT may have harmed a large number of non-African-American patients who would have benefited from BiDil.¹⁴⁹ Clinical research is also more closely connected with the potential marketing of a product to the public. Because of the profit-making possibilities of such research, allowing the use of race here only gives incentives to pharmaceutical companies and others to continue engaging in such research, to the exclusion of follow-up research on the underlying causes of the differences.¹⁵⁰ Creating such incentives seems misguided to us. Indeed, given the potential harm from such research and the

availability of alternatives, we believe that it is unlikely that anyone would ever be able to satisfy the “narrowly tailored” prong of Kahn’s strict scrutiny test, at least as to clinical research.

At the same time, we should be clear that we are not arguing for the elimination of the use of *ancestry* in such research. As in genetic studies and biomedical and biochemical research, ancestry categories may help researchers understand variability in the effectiveness of treatments. But collection of such data should be *explicitly* ancestry-based, and should not simply rely on self-reporting of race as a “good-enough” proxy for ancestry. Furthermore, explicitly using ancestry, rather than race, will help signal that the information is only relevant to signaling *genetic* differences, rather than social and/or environmental differences. Hopefully, emphasis on ancestry will also lead to the collection of more information on social and environmental variables.

Finally, requiring clinical research to be based on ancestry, rather than race, will (we believe) have a long-term educational effect on practitioners. As doctors and other health professionals increasingly see research reported based on ancestry, rather than race, hopefully these professionals will begin to internalize that it is ancestry and/or environment that truly matters in medicine, *not* race.

Conclusion

Our analysis suggests a nuanced approach to the use of race in research, perhaps too nuanced for easy assimilation. Nevertheless, our recommendations yield a few straightforward points:

- Information about ancestry and social and environmental influences should always be preferred to race in research; information about ancestry and social and environmental influences should be collected instead of race when possible.
- Race may be tolerated as a proxy for ancestry or social and environmental factors when racial data is all that is available (as is often the case in epidemiological studies) and social causes are the primary variable of interest.
- Government authorization and funding raises significantly different concerns than government simply not prohibiting the research in question.
- We would not bar race-based research, except in clinical trials; current law already bars this use of race.
- We would bar both government authorization of race-based clinical trials and government funding of studies in which race is the variable of interest, except when a compelling interest can be

identified (such as testing for alleles for diseases known to occur disparately in different races) and researchers can show why they need to use race instead of using genetic markers.

Acknowledgements

We would like to thank our research assistants Jessica Brennan, Lauren DeWitt, Rawan Hmoud and Randall Samson and the Dean's Summer Grant fund for providing financial support.

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- See, e.g., A. J. J. Wood, "Racial Differences in the Response to Drugs - Pointers to Genetic Differences," *New England Journal of Medicine* 344 (2001): 1393-96; R. S. Schwartz, "Racial Profiling in Medical Research," *New England Journal of Medicine* 344 (2001): 1392-93; E. G. Burchard, et al., "The Importance of Race and Ethnic Background in Biomedical Research and Clinical Practice," *New England Journal of Medicine* 348 (2003): 1170-71; R. S. Cooper, et al., "Race and Genomics," *New England Journal of Medicine* 348 (2003): 1166-67; N. Risch, et al., "Categorization of Humans in Biomedical Research: Genes, Race and Disease," *Genome Biology* 3 (2002): 1-12.
- But, see Lillquist and Sullivan, *supra* note 1.
- B. Noah, "Racial Disparities in the Delivery of Health Care," *San Diego Law Review* 39 (1998): 135-178.
- See Lillquist and Sullivan, *supra* note 1, at 398.
- There is a debate over whether the term "subject" or "participant" is more appropriate. C. Coleman, "Duties to Subjects in Clinical Research," *Vanderbilt Law Review* 58 (2005): 387-449, at 387, n. 1.
- For a similar definition, see Office of Human Research Protections, Department of Health and Human Services, *Institutional Review Board Guidebook*, Chapter IV, available at <http://www.hhs.gov/ohrp/irb/irb_chapter4.htm#f3> (last visited June 14, 2006).
- A. Peters, et al., "Exposure to Traffic and the Onset of Myocardial Infarction," *New England Journal of Medicine* 351 (2004): 1721-30.
- That is, research done in a living organism. See *The American Heritage Dictionary* (New York: Dell Publishing, 4th ed., 2001): at 449.
- For a discussion of the use of such mice research, see S. B. Liggett, "Genetically Modified Mouse Models for Pharmacogenomic Research," *Nature Reviews Genetics* 5 (2004): 657-63.
- That is, research done outside a living organism. See *The American Heritage Dictionary*, *supra* note 9, at 449.
- Liggett, *supra* note 10, at 657.
- T. Oguma, et al., "Role of Prostanoid DP Receptor Variants in Susceptibility to Asthma," *New England Journal of Medicine* 351 (2004): 1752-63.
- See *Institutional Review Board Guidebook*, *supra* note 7.
- Lillquist and Sullivan, *supra* note 1, at 461-62.
- See, e.g., Oguma, et al., *supra* note 13, at 1753 ("Ancestral origin was determined by self-report"). Interestingly, researchers outside the United States often do not seem inclined to collect such information. See, e.g., Peters, et al., *supra* note 8 (no report of race in study performed in Germany); G. E. Thwaites, et al., "Dexamethasone for the Treatment of Tuberculous Meningitis in Adolescents and Adults," *New England Journal of Medicine* 351 (2004): 1741-51 (no report on race in study performed in Vietnam).
- See Risch, et al., *supra* note 2, at 6.
- This was in part the basis of opposition to a mixed race category in the Census: some black political leaders believed that, if forced to choose, individuals of mixed race would choose to be identified as black, thus increasing the numbers and power of that group. See K. L. Karst, "Myths of Identity: Individual and Group Portraits of Race and Sexual Orientation," *University of California Los Angeles Law Review* 43 (1995): 263-369, at 330.
- See N. Mezey, "Erasure and Recognition: The Census, Race and the National Imagination," *Northwestern University Law Review* 97 (2003): 1701-68, at 1752 ("Traditional civil rights groups who testified before Congress on the issue uniformly opposed a single multiracial category. Their motivation appeared to be twofold. First and foremost, they sought to protect the fragile advances that anti-discrimination laws have made toward racial equality, and this entailed protecting the prevailing race categories and the number of minorities who identified with them. A related but distinct strategy also becomes evident in their testimony: they sought to police the boundaries of racial identity in effort to keep those who might identify themselves as multiracial from defecting.") The history of the racial categories in the Census is a fascinating study of the social construction of race in the most literal sense. See generally, C. B. Hickman, "The Devil and the One Drop Rule: Racial Categories, African-Americans, and the U.S. Census," *Michigan Law Review* 95 (1997): 1161-1265.
- Mezey, *supra* note 19, at 1760.
- Whether race should be inquired into by a check-the-box approach (with the concomitant question of which boxes are available to check) or by a more open-ended question is worthy of considerable attention. The use of a Hispanic or Latino category is particularly troubling from an ancestry perspective. The appropriate approach might be that of the Census, which "presently categorizes Hispanics as an ethnic group, as opposed to a racial group, and defines Hispanics as 'persons of Mexican, Puerto Rican, Cuban, Central or Southern American or other Spanish culture or origin, regardless of race.' Because the Hispanic category is not a racial category, persons who identify with the Hispanic ethnicity must also identify with one of the five racial categories." J. A. Powell, "A Minority-Majority Nation: Racing the Population in the Twenty-First Century," *Fordham Urban Law Journal* 29 (2002): 1395-1415, at 1407.
- C. Ford, "The Determination of 'Race' in Race-Conscious Law," *California Law Review* 82 (1994): 1231-1285.
- Burchard, *supra* note 2, at 1173-74. "Accuracy," of course, merely means that the individual's genetic heritage is from ancestors who predominately came from a particular geographic location; it does not suggest genetic "purity."
- Lillquist and Sullivan, *supra* note 1, at 407-08.
- Id.* As we note there, American law tends to be ambiguous about how broadly or narrowly a race should be defined; what tends to be consistent is the emphasis on ancestry over physical traits, although there are exceptions.
- P. Kitcher, *In Mendel's Mirror: Philosophical Reflections on Biology* (New York: Oxford University Press, 2003): 239-45.
- Race, Ethnicity, and Genetics Working Group, "The Use of Racial, Ethnic, and Ancestral Categories in Human Genetics Research," *American Journal of Human Genetics* 77 (2005): 519-32.
- Lillquist and Sullivan, *supra* note 1, at 430-36.
- A. L. Whaley, "Ethnicity/Race, Ethics, and Epidemiology," *JAMA* 95 (2003): 736-42.
- This assumption may or may not be true. If the assumption is wrong, then this particular use of race is unjustified.
- For similar definitions, see B. B. Gerstman, *Epidemiology Kept Simple*, 2nd ed. (Hoboken, NJ: Wiley-Liss, 2003): at 2.
- At least initially, it may be more important to determine occurrence rather than causation. Thus, race may be useful whether the goal is to identify allele variances or social causes of disease. When the inquiry shifts to causation, however, it will typically be critical to distinguish between genetic and other factors.
- Whaley, *supra* note 29.
- Cf.* R. Bhopal, "Is Research Into Ethnicity and Health Racist, Unsound, or Important Science?" *British Medical Journal* 314 (1997): 1751-56, at 1753 [hereinafter Bhopal, *Research into Ethnicity*] (noting the need for epidemiology to cease simply demonstrating racial differences and to instead focus on causal mechanisms). There is an alternative way to justify the use of race in epidemiological research, which is the provision of services. Once we know that one racial group has an increased incidence

- of a disease, we can target treatment efforts at that group. See R. Bhopal, "Ethnicity as a Variable in Epidemiological Research," *British Medical Journal* 309 (1994): 327-20, at 327-28 [hereinafter Bhopal, *Ethnicity as a Variable*] (noting use of ethnicity in the provision of services). Elsewhere, we have addressed the use of race in the provision of services to racial groups. See Lillquist and Sullivan, *supra* note 1, at 469-74. There, we argued against the use of race in the provision of screening tests and against outreach efforts that are targeted only at a particular racial group. We also noted that race-based screening appears to violate existing legal restrictions, see *id.*, at 457-59, but that race-based outreach efforts, even when targeted only at a particular racial group, may indeed pass legal muster, see *id.*, at 455-56. For purposes of this article, we will deem these uses generally impermissible, and therefore not a way in which the use of race in epidemiology can be justified.
35. Burchard, et al., *supra* note 2, at 1171.
 36. *Id.*, noting that certain "black Americans" are referred for renal transplantation and cardiac catheterization at lower rates than "white Americans".
 37. We, of course, are not trying to say that all differences are the result of treatment usage rates. As Burchard and his colleagues note, there are cases where, even controlling for many possible treatment variables, differences in disease occurrence persist. *Id.*
 38. See Bhopal, *Research into Ethnicity*, *supra* note 34, at 1753.
 39. *Id.*
 40. L. Kalinowski, et al., "Race-Specific Differences in Endothelial Function: Predisposition of African-Americans to Vascular Disease," *Circulation* 109 (2004): 2511-17, at 2512.
 41. *Id.*, at 2515.
 42. See generally, *supra* note 2.
 43. N. Risch, et al., "Geographic Distributions of Disease Mutations in Ashkenazi Jewish Population Supports Genetic Drift Over Selection," *American Journal of Human Genetics* 72 (2003): 812-22.
 44. See generally, M. Bamshad, et al., "Deconstructing the Relationship Between Genetics and Race," *Nature Reviews Genetics* 5 (2004): 598-609.
 45. M. Bamshad, "Genetic Influences on Health: Does Race Matter?" *JAMA* 294 (2005): 937-46, at 944.
 46. See Oguma, *supra* note 13, at 1752.
 47. The limitation of the study to white and black patients also ensured that large population groups were excluded.
 48. See Oguma, *supra* note 13, at 1752.
 49. See J. Zhang, et al., "A Comparison of Medical Management with Misoprostol and Surgical Management for Early Pregnancy Failure," *New England Journal of Medicine* 353 (2005): 761-69.
 50. See *id.*, at 763, 765, table 1.
 51. P. Carson, et al., "Racial Differences in Response to Therapy for Heart Failure: Analysis of the Vasodilator Heart Failure Trials," *Journal of Cardiac Failure* 5 (1999): 178-87.
 52. See A. L. Taylor, et al., "Combination of Isosorbide Dinitrate and Hydralazine in Blacks with Heart Failure," *New England Journal of Medicine* 351 (2004): 2049-57, at 2050.
 53. We have discussed elsewhere a third federal statutory scheme, Title II of the Civil Rights Act of 1964. Lillquist and Sullivan, *supra* note 1, at 446. Because for our purposes Title II generally overlaps with Title VI and the Equal Protection Clause, which we will discuss below, we ignore it in this piece.
 54. For example, *Adarand Constructors v. Peña*, 515 U.S. 200 (1995) (benign purpose does not avoid strict scrutiny of racial classification).
 55. *Rendell-Baker v. Kohn*, 457 U.S. 830 (1982); *Davis v. Regis College*, 830 P.2d 1098, 1101 (Colo. Ct. App. 1992) ("Regis' receipt of federal funds for research and energy assistance grants...without other indicators of government involvement, is insufficient to establish state action."). See generally, J. P. Byrne, "Academic Freedom: A Special Concern of the First Amendment," *Yale Law Journal* 99 (1989): 251-340, at 301. ("Thus, the state action doctrine mandates judicial enforcement of constitutional liberties against institutional infringements for half the nation's academi-
 - ics and denies it to the other half for reasons which, if desirable at all, are very far removed from the realities of academic life.")
 56. See, e.g., *Shaw v. Hunt*, 517 U.S. 899 (1996); *Miller v. Johnson*, 515 U.S. 900 (1995); *Korematsu v. United States*, 323 U.S. 214 (1944).
 57. 438 U.S. 265, 310 (1978).
 58. *Id.*
 59. See 42 U.S.C. § 2000a (2000).
 60. See 42 U.S.C. § 2000d (2000).
 61. For example, *Johnson v. Ry. Express Agency*, 421 U.S. 454, 459-60 (1975) ("It is well settled among the federal Courts of Appeals – and we now join them – that § 1981 affords a federal remedy against discrimination in private employment on the basis of race." [footnote omitted]).
 62. *Grutter v. Bollinger*, 539 U.S. 306, 343 (2003) (because its Equal Protection Clause claims fail, "petitioner's statutory claims based on Title VI...fail," quoting the opinion of Justice Powell in *Regents of Univ. of Cal. v. Bakke*, 438, U.S. 265, 287 (1978) that "Title VI...proscribes only those racial classifications that would violate the Equal Protection Clause of the Fifth Amendment").
 63. Title VI provides: "No person in the United States shall, on the ground of race, color, or national origin, be excluded from participation in, be denied the benefits of, or be subjected to discrimination under any program or activity receiving Federal financial assistance." 42 U.S.C. § 2000d.
 64. This is because "program" is defined to include "all of the operations of" a number of entities, including "a college, university, or other postsecondary institution." 42 U.S.C. § 2000d-4a.
 65. See, e.g., *Ferrill v. Parker Group*, 168 F.3d 468, 473 (11th Cir. 1999). ("Because § 1981 proscribes discrimination solely on the basis of race, and the BFOQ [bona fide occupational qualification] defense [in Title VII] does not apply to racial discrimination, the BFOQ defense is never available to the § 1981 defendant" [emphasis added].)
 66. The Supreme Court's approval of affirmative action plans under Title VII (see, e.g., *Johnson v. Transp. Agency*, 480 U.S. 616, 641-42 (1987); *United Steelworkers v. Weber*, 443 U.S. 193, 209 (1979)), has been carried over into § 1981. See, e.g., *Schurr v. Resorts Int'l Hotel*, 196 F.3d 486, 498-99 (3d Cir. 1999). ("While a valid affirmative action plan serves as a defense to an action under section 1981, the standard for evaluating the validity of a plan is identical to the standard developed in Title VII cases.")
 67. For example, *Boy Scouts of America v. Dale* 530 U.S. 640 (2000), invalidated a state public accommodation law to the extent it would require a nonprofit organization to admit individuals whose presence would affect in a significant way the organization's ability to advocate its viewpoint.
 68. P. Hamburger, "The New Censorship: Institutional Review Boards," *University of Chicago, Public Law Working Paper No. 95* (May 2005) (arguing that institutional review boards are the equivalent of licensing publications).
 69. *United States v. O'Brien*, 391 U.S. 367 (1968). See generally, B. McDonald, "Government Regulation or Other Abridgements' of Scientific Research: The Proper Scope of Judicial Review Under the First Amendment," *Emory Law Journal* 54 (2005): 979-1091. In contrast, Professor Hamburger argues that courts will find governmental regulations that facially control conduct to constitute regulations of speech when they discriminate against certain content and, more generally, when they fail a balancing test.
 70. *Nordlinger v. Hahn*, 505 U.S. 1, 10 (1992). ("The Equal Protection Clause does not forbid classifications. It simply keeps governmental decision makers from treating differently persons who are in all relevant respects alike.") See also, M. L. Saunders, "Equal Protection, Class Legislation, and Colorblindness," *Michigan Law Review* 96 (1997): 245-337, at 314-16 ("a state can classify persons in the lay sense – that is, divide, sort, or arrange them into classes – without subjecting those classes to differing benefits or burdens. For example, it can sort persons into classes for informational purposes, as it does when it gathers and organizes census or other demographic data. Such a classification does not, in and of itself, implicate the Equal Protection Clause,

- for it does not single out any class of persons for special benefits or burdens”).
71. If such research were directly linked to a questionable use, the research itself might be more problematic. A handful of cases invalidate racial data-keeping by the government. For example, *Anderson v. Martin*, 375 U.S. 399 (1964) invalidated racial designations in elections, and, in a case closer to the medical data context, *Hamm v. Virginia State Board of Elections*, 230 F. Supp. 156 (E.D. Va. 1964), *aff'd sub nom. Tancil v. Woolls*, 379 U.S. 19 (1964) (mem.) struck down a Virginia law that required public records regarding voting and property taxes be maintained with racial designations, although the plaintiffs were not discriminated against in any way. The same court, however, upheld racial designations in divorce records. Other courts have struck down racial collection of information, but usually in the context of a threatened or intended use against one race. See, e.g., *Hall v. Pa. State Police*, 570 F.2d 86 (3d Cir. 1978) (finding that a police photography program targeted at black bank customers was impermissible). Generally speaking, when the data collection has not been viewed as likely to be used in impermissible ways, racial collection and retention of data has been permitted, at least when a legitimate use can be envisioned. See *Caulfield v. Bd. of Educ.*, 583 F.2d 605 (2d Cir. 1978) (affirming the denial of a preliminary injunction to prevent collection of racial data in connection with federal enforcement of Title VI against a school district); *United States v. New Hampshire*, 539 F.2d 277 (1st Cir. 1976) (noting that hypothetical misuse of racial data collected by the federal government did not justify finding unconstitutional a statute requiring such data to be provided).
 72. Even the Racial Privacy Initiative in California, which failed, would have exempted “otherwise lawful classification of medical research subjects and patients” from its general proscription of race classifications in government record keeping. See California Secretary of State, *Official Voter Information Guide* 45, § 32(a) (2003); see also Proposition 54 to amend Cal. Const. art. I (2003), available at <<http://vote2003.ss.ca.gov/voterguide/english.pdf>> (last visited June 15, 2006).
 73. Oguma, et al., *supra* note 13, at 1753.
 74. *Id.*
 75. “Consideration” is normally required to make a promise enforceable, i.e., to make a contract. See §§ 17, 71, Restatement (Second) of Contracts (St. Paul, MN: American Law Institute Publishers, 1981).
 76. The notion that the Equal Protection Clause should be applied from an expressivist perspective is far more supported by commentators than by cases. See Lillquist and Sullivan, *supra* note 1, at 398-99; see generally R. Bowser, “Racial Profiling in Health Care: An Institutional Analysis of Medical Treatment Disparities,” *Michigan Journal of Race and the Law* 7 (2001): 79-133. However, government or government-sponsored research that suggests that one race is less important than others is very problematic.
 77. See *supra* note 70.
 78. Lillquist and Sullivan, *supra* note 1, at 474, n.450.
 79. S. Stolberg, “Shouldn’t a Pill Be Colorblind?” *New York Times*, May 13, 2001, section 4, at 1. The exclusion of non-minorities from BiDil trials would be especially ironic in light of the history of BiDil’s development. Jonathan D. Kahn argues that BiDil is an “ethnic drug” today because of the interventions of law and commerce rather than because of any biomedical considerations; he concludes that the story implicates federal agencies in inappropriately giving the state’s imprimatur to using race as a biological category. J. Kahn, “How a Drug Becomes ‘Ethnic’: Law, Commerce, and the Production of Racial Categories in Medicine,” *Yale Journal of Health Policy, Law & Ethics* 4 (2004): 1-46. He traces the development from “a drug for everyone, with no ethnic marketing,” *id.*, at 4, to its present focus on African-Americans as stemming from a re-analysis of the trial data after the FDA had disapproved the drug’s use in the general population. *Id.*, at 15-16.
 80. S. Saul, “FDA Approves a Heart Drug for African-Americans,” *New York Times*, June 24, 2005, Late Edition-Final, section C, column 1.
 81. See *supra* text accompanying notes 51-52.
 82. One could argue that there is no consideration where participants are not paid for their services, but the opportunity to participate may itself be of value to at least some subjects and the free medication provided may operate as consideration in any event.
 83. See Carson, et al., *supra* note 51.
 84. *Id.*, at 186.
 85. See Kahn, *supra* note 79, at 481.
 86. Presumably, the terms of the contract are the subject’s participation in return for whatever medications (including the possibility of a placebo) and consideration for time spent.
 87. As with every other suit under § 1981, the plaintiff would seek either damages for refusal of the other party to enter into a contract or damages for the expectation interest denied. Admittedly, quantifying the expectation interest might be difficult in these cases.
 88. NIH requires that researchers “address” the inclusion of such groups by describing the composition of the proposed study population in terms of “racial/ethnic group,” and it directs researchers to “provide a rationale for selection of such subjects.” National Institutes of Health, “Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research,” last modified October 11, 2001, available at <http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm> (last visited June 15, 2006). The most detailed guidance is given in connection with Phase III drug studies, where inclusion is generally presumed, but not required when no significant differences between races have been demonstrated in prior studies. *Id.*
 89. *Id.* “If the data from prior studies strongly support no significant differences of clinical or public health importance in intervention effect based on sex/gender, racial/ethnic and/or relevant subpopulation comparisons, then sex/gender and race/ethnicity will not be required as subject selection criteria. However, the inclusion and analysis of sex/gender and/or racial/ethnic subgroups is still strongly encouraged.”
 90. See generally, *supra* note 2.
 91. For one of many discussions justifying the difference between moral and legal prohibitions, see H. L. A. Hart, *The Concept of Law* (New York: Oxford University Press, 1961): at 181.
 92. D. E. Roberts, “Legal Constraints on the Use of Race and Ethnicity in Biomedical Research,” *Journal of Law, Medicine & Ethics* 34, no. 3 (2006): 526-534.
 93. See, e.g., J. Stevens, “Racial Meanings and Scientific Methods: Changing Policies for NIH-Sponsored Publications Reporting Human Variation,” *Journal of Health Politics, Policy and Law* 28 (2003): 1033-87 (calling for an end to NIH funding for genetic studies of associations of traits with race or ethnicity); Kahn, *supra* note 79 (calling for restrictions on when federal agencies permit use of race as a biological or genetic category).
 94. National Institutes of Health, Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research, available at <http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm> (last visited June 15, 2006).
 95. U.S. Department of Health and Human Services, Office of Information Resource Management, HHS Policy for Improving Race and Ethnicity Data, available at <<http://www.hhs.gov/oirm/infocollect/nclusion.html>> (last visited June 15, 2006).
 96. 21 CFR §312.33(a)(2)(2006).
 97. Roberts, *supra* note 92.
 98. See, e.g., V. Vaccarino, et al., “Sex and Race Differences in the Management of Acute Myocardial Infarction, 1994 through 2002,” *New England Journal of Medicine* 353 (2005): 671-82, at 681 (noting partial funding through grants by NIH).
 99. See, e.g., *id.*; A. K. Jha, “Racial Trends in the Use of Major Procedures Among the Elderly,” *New England Journal of Medicine* 353 (2005): 683-91, at 691 (funded in part by National Institute of Aging); A. N. Trivedi, “Trends in the Quality of Care and Racial

- Disparities in Medicare Managed Care,” *New England Journal of Medicine* 353 (2005): 692-700, at 700 (funded in part by the Health Resources and Services Administration and the Agency for Healthcare Research and Quality).
100. See, e.g., Stevens, *supra* note 93 (arguing against such funding).
101. We are not aware of a situation in which the government has done this yet. The best example of such a trial of which we are aware is, of course, the A-HeFT, but that trial appears to have operated without any governmental financing. See Taylor, et al., *supra* note 52, at 2055.
102. See Kahn, *supra* note 79, at 31-32; see also U.S. Patent Nos. 6,784,177 (issued Aug. 31, 2004) & 6,465,463 (issued October 15, 2002).
103. NitroMed application, page 12.
104. See Kahn, *supra* note 79, at 14.
105. See, e.g., J. S. Kaufman and R. S. Cooper, “Commentary: Consideration for Use of Racial/Ethnic Classification in Etiologic Research,” *American Journal of Epidemiology* 154 (2001): 291-98 (suggesting limitation on usefulness).
106. See, e.g., *id.*, at 296 (recommending the continuation of both “surveillance” research and research into the interaction between patients and health care providers).
107. It is possible that some might disagree with this conclusion. Given that the existence of racial disparities has been well documented (see N. Lurie, “Editorial: Health Disparities – Less Talk, More Action,” *New England Journal of Medicine* 353 (2005): 727-29, at 727), there is a non-trivial argument that the investment of more resources into such research is misplaced. This would then suggest that, at a minimum, the federal government ought to cease funding such research. We believe, however, that such a move would be short-sighted. Continuing to monitor the existence of racial differences is necessary in order to determine whether efforts to eradicate such differences are successful and to help choose among potential strategies. See *id.*, at 728-29.
108. See Kaufman and Cooper, *supra* note 105, at 294-95.
109. *Id.*
110. *Id.*
111. C. P. Jones, “Invited Commentary: ‘Race,’ Racism and the Practice of Epidemiology,” *American Journal of Epidemiology* 154 (2001): 299-304.
112. *Id.*, at 302-03.
113. Kaufman and Cooper, *supra* note 105, at 296, table 3.
114. See, e.g., Bhopal, *Research into Ethnicity*, *supra* note 34, at 1755.
115. See *supra* text accompanying notes 26-30.
116. See *supra* note 2.
117. For a recent cataloging of such alleles, see Bamshad, *supra* note 45.
118. The correlation between geography and ancestry is not perfect because people sharing a similar ancestry may find themselves in quite distinct geographic locations.
119. See *id.*, at 939.
120. Lillquist and Sullivan, *supra* note 1, at 434.
121. See *id.*, at 940 (noting that 30% of European Americans have less than 90% European ancestry).
122. The common examples are sickle-cell anemia and Tay-Sachs, but there are others.
123. Cooper, et al., *supra* note 2.
124. Lillquist and Sullivan, *supra* note 1, at 408-09.
125. See Bamshad, et al., *supra* note 44, at 607.
126. Bamshad, *supra* note 45, at 944-45.
127. See *supra* text accompanying, at note 18.
128. Stevens, *supra* note 93, at 1075.
129. Bamshad, *supra* note 45, at 944.
130. *Id.* (citing J. C. Knight, et al., “A Polymorphism that Affects OCT-1 Binding to the TNF Promoter Region Is Associated with Severe Malaria,” *Nature Genetics* 22 (1999): 145-50).
131. B. Mercier, et al., “Complete Detection of Mutations in Cystic Fibrosis Patients of Native American Origin,” *Human Genetics* 94 (1994): 629-32.
132. See Lillquist and Sullivan, *supra* note 1, at 431, n. 236.
133. See X. Estivil, et al., “Geographic Distribution and Regional Origin of 272 Cystic Fibrosis Mutations in European Populations,” *Human Mutation* 10 (1997): 135-54.
134. *Id.*, at 136-37, table 1; J. Kere, et al., “Cystic Fibrosis in a Low-Incidence Population: Two Major Mutations in Finland,” *Human Genetics* 93 (1994): 162-66.
135. Kahn, *supra* note 79, at 44.
136. *Cf. id.* (suggesting that “[p]roviding an effective therapy for heart failure in African-Americans would likely be a compelling interest”).
137. Professor Kahn, we believe, agrees with us on this score. E-mail from Jonathan D. Kahn to Erik Lillquist (Jan. 17, 2006) (copy on file with authors).
138. Bamshad, *supra* note 45, at 944.
139. If the hypothesis instead is that the biochemistry has been affected not by genetics but by the environment, then it would be improper to use race as a proxy for ancestry. Instead, researchers in such a case should be focused on the social construction of the subject’s race – both how the person identifies herself and how she is perceived – in order to draw any conclusions about the effect of environmental factors through the use of race. Here again, we would suggest that the government should only fund such research where it meets the strict scrutiny test, and we believe that this would rarely occur; just as ancestry can generally be directly ascertained without the use of race, in most cases, environmental factors can be discussed without resort to race.
140. The sole exception to this is where the hypothesis is that the difference is caused by racism. In the context of clinical research, however, we generally believe that, at least with pharmaceuticals, it is highly unlikely that a drug will or will not work for an individual because of racism. Of course, research has already shown that members of some groups appear to receive less or different treatments as a result of racism. See *supra* note 99. But uncovering such differences is mainly the work of what we have referred to as epidemiological research, not clinical research.
141. For a similar view, see Kahn, *supra* note 79, at 42.
142. Lillquist and Sullivan, *supra* note 1, at 399-400.
143. A whole field, pharmacogenomics, has arisen to account for “the effects of genetic variability on drug toxicity and efficacy.” Homepage of the Pharmacogenomics Journal website, *available at* <<http://www.nature.com/tpj/index.html>> (last visited June 15, 2006).
144. See Lillquist and Sullivan, *supra* note 1, at 461-62.
145. Kahn, *supra* note 79, at 44.
146. Lillquist and Sullivan, *supra* note 1, at 475.
147. *Id.*, at 475-76; see also M. K. Cho, “Racial and Ethnic Categories in Biomedical Research: There’s No Baby in the Bathwater,” *Journal of Law, Medicine & Ethics* 34, no. 3 (2006):497-499 (also noting variations in CYP2D6 allelic frequencies).
148. See *supra* text accompanying notes 125-126.
149. See Lillquist and Sullivan, *supra* note 1, at 478.
150. See M. G. Bloche, “Race-Based Therapeutics,” *New England Journal of Medicine* 351 (2004): 2035-37, at 2036-37.