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Governing human subjects research in the USA: individualized ethics and structural inequalities

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The abuse of human subjects has always been, and continues to be, a problem in the United States. In spite of regulation to protect subjects, the exploitation of disenfranchised groups and the reproduction of social inequalities are entrenched in the American research enterprise. This paper argues that current approaches to protecting subjects are insufficient because they prioritize individualized responses to structural problems. What is not often acknowledged or accounted for is that the worst cases of abuse to subjects occur because of unethical treatment of groups, not individuals. Solutions are proposed to make regulation more responsive to these concerns.

HISTORICALLY, SCIENTIFIC research has led to the abuse of human subjects. During the past 60 years, the United States Government has been aware of the need to create and revise federal policies to protect the health and safety of those who are subjects in research. Worldwide attention to this issue emerged after World War II and the subsequent Nuremberg trials at which an American military tribunal adjudicated cases from 1946 to 1949 against physicians in the Nazi party accused of inhumane and unnecessary medical experimentation on humans (Annas and Grodin, 1992; Schmidt, 2004).

At the time, the medical malfeasance that occurred in Nazi Germany was perceived as a symptom of the national depravity of the German people. American science, in contrast, was viewed, and continues to be viewed to a large degree, as immune from such immorality. This was because of the popular belief that American physicians and researchers would never allow or participate in the unethical research practices in which the Nazis had engaged (Faden and Beauchamp, 1986). As a result, the United States did not adopt comprehensive federal regulations governing human subjects research until the 1980s, after decades of ethically problematic research had already been conducted within the country (Mishkin, 2000).

This paper examines the history of human subjects research and questions the adequacy of regulation enacted to protect those subjects from abuse in the United States. In spite of discourses about the ethicality of American science and the presence of regulation, the treatment of human subjects in medical research has been, and persists today as, a problem. Moreover, the exploitation of disenfranchised groups and the reproduction of social inequalities are deeply entrenched in the American research enterprise.

This paper argues that historical and contemporary approaches to protecting human subjects have been, and continue to be, insufficient because they prioritize individualized responses to structural problems. Specifically, both the scientific community and regulatory apparatus largely conceptualize the ethics of human subjects research in individualistic terms. On one hand, scientists' claims to self-regulation focus on individual researchers' adherence to professional norms dictating ethical behavior. On the other hand, US regulation focuses on individual human subjects as autonomous agents and aims to protect their rights to participate in research. What is

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not acknowledged or accounted for in these individualistic approaches is that the worst cases of abuse to human subjects are disturbing not because of the treatment of individuals but because of the treatment of groups.

This paper investigates the mismatch between the unethical treatment of human subjects in the USA and the current solutions to this problem. First, I recount historical examples of experimentation in which the research community systematically exploited disenfranchised groups. Next, I analyze the norms governing ethical scientific behavior to illustrate why researchers were not, in fact, able to govern themselves effectively. From there, I examine the subsequent regulation to illustrate how the policy-making process responded only to specific historical cases, not future contingencies. Finally, I conclude by arguing that the current regulation of human subjects research needs to adopt a structural approach that can take into account profound social inequalities.

A history of bodies as property

Although US researchers and policy-makers conscientiously present a front of responsible medical research and treatment of humans, they have not always been so concerned. Most public attention about research abuses has focused on the human atrocities committed systematically by the Nazis and only peripherally on ethically problematic US medical research such as the well-known Tuskegee syphilis study. Prior to World War II, human subjects used in US medical research were treated and represented as though their bodies were the property of the state, of science, and of 'humanity.' Specifically, slaves in the antebellum USA, rural African–Americans, Native Americans, institutionalized psychiatric patients, and prisoners were deliberately subjected to medical experiments that offered them little or no therapeutic value.

By briefly discussing the history of these cases, I aim to show that the bodies of certain marginalized groups have historically been utilized to serve the needs of 'science' and the state and that current regulation of human subjects research has not altogether eliminated this trend. What is incredible about American medical research is not that it has had high profile cases of abuse of human subjects, but rather that, in spite of its history of systematically exploiting disenfranchised groups for the benefit of 'progress,' the scientific and policy-making communities have treated these as isolated events. These cases were not the result of a few 'bad' researchers; instead, social inequalities and prejudices have catalyzed, or at least allowed, abuse of these groups.

The historical use of African–Americans in biomedical research illustrates hypocrisies that were deeply rooted in American racism. Until the Civil Rights Movement in the 1960s, black bodies were spoken of, in political rhetoric, as biologically different from white bodies (King, 2000). For example, the blood of black individuals was described as distinct from that of whites, justifying separate supplies of blood for soldiers during wartime (Chinn, 2000).

Yet, when it was time to find bodies to autopsy and bodies on which to experiment, the medical establishment had no qualms about assuming that the information gleaned from the bodies of black Americans could, and should, be applied to whites (Savitt, 1982). Most notably, in the antebellum period, it was not uncommon for slaves to be purchased for the sole purpose of being used in medical experimentation (Gamble, 2000). At this time, Southern medical schools boasted "that their cities' large black population provided ample supplies of clinical and anatomical material" (Savitt, 1982: 341). Even free blacks and slaves owned by others were used indiscriminately in medical studies because they were thought of as available bodies on which to experiment, rather than as individuals with free will.

The most well-known example of mistreatment of African–Americans in medical research is the Tuskegee Syphilis Study (Jones, 1981; Reverby, 2000). Funded by the US Public Health Service (PHS), this research, as it is documented, was designed to observe the effects of untreated syphilis in African–American men in one rural community in Alabama. A prior study had been done in Norway to document the effects of untreated syphilis in the early 1920s, and the PHS decided to compare the course of the untreated disease in black Americans.

At the outset of the research in 1932, there were variably effective treatments for syphilis but no cure. The 399 men recruited were told that they had "bad blood," were not told they were part of a research study, and were given placebos as "treatment" for the illness (Brandt, 2000). In exchange for their participation, the men were promised free meals, free medical examinations, and burial insurance. Even after penicillin was discovered to cure syphilis and became widely available in the early 1940s, the men were not treated, nor were they permitted to know about the existence of an effective cure. Recent evidence indicates the men were not treated because their syphilis-infected blood samples contributed to the development of a diagnostic test for syphilis (Roy, 1995). The PHS research continued until 1972 when the study received national media coverage and the project was quickly terminated.

Similarly targeted by researchers as a result of racism, Native Americans and Latinos have been subjected to medical experimentation in the USA. Native Americans have sometimes been referred to as "the Nation's first guinea pigs" because of the exploitative practices of the federal Government in relation to many native tribes (Moreno, 2001; Smith, 2005). One well-documented example of experimenting on Native people occurred during the 1940s and 1950s when Navajos were employed to mine uranium that would be used in military research for bombs. The US Government, particularly the PHS, knew that uranium was highly toxic, but the miners were not provided with any protective clothing or equipment to minimize exposure (Eichstaedt, 1994). The PHS then initiated a ten-year study to document how quickly miners would die after their exposure to uranium dust.

In a similar way, profound prejudice has made Latinos targets of scientific research in the USA and its territories. For example, medical researchers in the 1950s sought Latinos for risky studies as part of the development of female contraceptives (Tone, 2002; Watkins, 2001). American researchers even established a base of operations in Puerto Rico to conduct large-scale clinical trials on oral contraceptives, justified by racist views about 'overpopulation' and Puerto Rican women's sexuality (Briggs, 2002).

State institutions, such as mental institutions, orphanages, and prisons, have also historically been a common locus of medical inquiry because researchers saw their occupants as convenient, captive populations. In the case of mental institutions, the belief within the biomedical community during the first half of the century was that, if a person was unable to give true consent, that person could be used without even being asked (Pappworth, 1967). To some extent, this assumption implied that, if individuals were not able to function 'normally' in American society, their bodies were rendered the property of the state, mental institution, and/or medical research facilities.

The best-known case of medical experimentation within psychiatric facilities occurred during the 1960s at the Willowbrook State School for Retarded Children in New York to test the effectiveness of gamma globulin in treating hepatitis (Rothman and Rothman, 1984). Although hepatitis was extremely prevalent in public institutions at that time, the investigators decided to infect children deliberately with the disease under allegedly carefully controlled research conditions rather than to include children in the study who were already infected with hepatitis.

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Interestingly, the biggest fallout from public attention on Willowbrook had less to do with the study and more to do with the prevalence of hepatitis and the squalid conditions in this type of institution. Rather than leading to any sort of regulation of medical research, the Willowbrook controversy resulted in widespread reforms in the sanitary conditions of psychiatric institutions (Rothman and Rothman, 1984).

Similarly, prisoners were often thought of as a sanctioned group for experimentation because research was seen as a way in which they could repay their debt to society (Harkness, 1996; National Academy of Sciences, 1975). By the 1960s, medical experimentation was deeply integrated into the penitentiary system, such as military research on LSD, radiation studies, and diverse pharmaceutical trials. Unlike the previous example of patients in mental institutions, prisoners were often paid for their participation or were offered a reduction in their prison sentence. For example, wardens and parole boards viewed prisoners' participation in research favorably.

In general, recruitment of prisoners was not viewed as cruel and unusual punishment because participation was technically voluntary and prisoners received monetary compensation in exchange for their involvement. Moreover, prisoners often received some secondary gains, such as better living conditions and better food. Because of these benefits, prisoners actually viewed medical research as a positive means by which to earn some money while serving their sentences. Not unlike Willowbrook, questions about the conditions of prisons and prisoners' need for money resulted in broad reform of the American penitentiary system in the 1970s (Hornblum, 1998).

With media coverage of the Tuskegee syphilis study and the publication of an exposé on the use of prisoners in research (Mitford, 1971), the early 1970s were marked by public alarm about the conduct of US researchers. Policy-makers could no longer ignore the need for regulating research on human subjects. To begin assessing the extent of the problem, the US Congress held hearings on human experimentation beginning in 1973 to investigate different types of ongoing human experimentation in the United States. The hearings challenged both the researchers' 'right' to use institutionalized persons and the specific institutional context that enabled such research practices in the first place.

Ultimately, the testimonies and findings from the Congressional hearings led to the passage of the National Research Act of 1974. At the time, the issue on the table, however, was to determine whether the ethical abuses in the headlines were indicative of a general depravity within the research community or were simply cases of a few immoral researchers whose practices were dominating the headlines.

US ethics and scientific self-regulation

There are two common explanations offered by historians, ethicists, and policy-makers for how and why incidents involving abuses of human subjects could have happened in the decades leading up to the 1970s. First, abuses occurred because there simply was no system of normative ethics guiding research on human subjects (Jones, 1981; Faden and Beauchamp, 1986). Second, abuses occurred because a few unethical researchers did not follow their community's scientific norms (Spitz, 2005). Both explanations imply, in part, that researchers were not regulating themselves.

However, when examining the research practices of scientific and medical communities from the decades preceding World War II, there is ample evidence that there were, in fact, codes of conduct outlining how both humans and animals should be treated as subjects of experiments (Guerrini, 2003; Lederer, 1995) and that practical problems, such as ambiguities in measuring risk, interpreting results, and determining 'lesser harm', determined how well researchers followed these codes of conduct (Halpern, 2004).

Historian Susan E Lederer (1995) has argued that at no time have American investigators been free to do whatever they pleased with human subjects involved in their studies. She found that four conditions governed experimentation on humans from the 19th century onward:

- prior experimentation on animals;
- willingness to self-experiment or to use the new drug/procedure on one's own family;[1]
- therapeutic benefit or at least the absence of injury; and
- consent or at least non-coercion of the subjects involved.

Sociologist Sidney Halpern (2004) describes similar norms in her analysis of the "indigenous moralities" structuring particular research cultures. While these guidelines for conducting research were not often enforced by any organization or body *per se*, the American Medical Association and other groups tacitly endorsed these criteria for research on humans (Dalla-Vorgia *et al*, 2001).

Because there was some anxiety in the USA in the early 20th century surrounding 'medical heroism' and experimental medicine, the revelations of the atrocities committed by Nazi doctors played into the American public's pre-existing fears that research harmed individuals (Lederer, 1995). In response, the American scientific community articulated distinctions between American and Nazi science and research. Bolstered by early work in the sociology of science (for instance, Merton, 1938; 1942), good, legitimate scientific research was framed as free from both politics and national interests (Hess, 1997). The strength of this position is witnessed in its longevity; even in contemporary USA, 'good' science continues to be defined as autonomous and apolitical.

The stance of scientific self-regulation was especially subject to debate in the post-war period. Beginning in the 1960s, the medical community began to experience internal conflict surrounding human subjects research. For example, in 1966 an American physician named Henry Beecher sparked controversy by publishing in the *New England Journal of Medicine* a whistle-blowing article about the abuses of human subjects in the USA (Campbell, forthcoming; Rothman, 1991).

The critique was particularly cutting because Beecher drew from American medical journal publications and the information they provided about human subjects. He argued that extremely prevalent unethical practices were encouraged by the medical community's complacency with regard to regulating itself concerning the treatment of human subjects. Beecher further accused the medical journals of condoning this type of unethical behavior by publishing the findings from these studies. For Beecher, however, it was still an issue of self-regulation; the problem for him was that the medical community was being lax in its responsibility and thereby encouraging investigators to behave irresponsibly toward their subjects.

The controversy that Beecher instigated with his 1966 article and later publications did have policy effects at the national level (Faden and Beauchamp, 1986). Beecher's article made many waves and generated discussion within the Public Health Service (PHS) and the National Institutes of Health (NIH). In response, these organizations decided that some regulation was necessary, particularly because they had directly funded many studies that had exploited human subjects. The directors at NIH worried that the public would lose its trust in the medical establishment and wanted to prevent negative public opinion from having an effect on their budget (Kutcher, 2003). At the same time, PHS and NIH were afraid of making policies that would discourage research.

During the late 1960s and early 1970s, they began to establish systems for institutional review of the ethics of research protocols based on the system of scientific peer review in place at NIH at the time. The changes underway at the federal level did not, however, begin to get teeth until catalyzed by Congressional intervention several years later.

US policy and regulatory environments

Identifying ethical principles

The impetus for regulation in the United States did not come until publicity surrounding the Tuskegee syphilis study and exposure of prison experimentation drew public attention. At that point, there was widespread public concern that the medical community was perhaps not able to regulate itself (Mishkin, 2000). In response to media and public pressure, Congress passed the National Research Act of 1974, thereby creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research ('National Commission'). Charged with identifying ethical principles to govern human subjects research (Faden and Beauchamp, 1986), this group directly shaped federal regulation in the United States through their recommendations documented in the Belmont Report (1979).

In its deliberations, the National Commission drew upon two documents that had preceded it: the Nuremberg Code (1949) and the Declaration of Helsinki (1964). The former consisted of a set of criteria for defining permissible and legitimate conduct in human experimentation. In its prosecution of Nazi doctors, the US military tribunal used this document as a method to assess the guilt or innocence of the physicians who were on trial (Annas and Grodin, 1992). These criteria came to embody what is now known as the 'Nuremberg Code.'[2]

In contrast, the Declaration of Helsinki was developed by the World Medical Association as a code of ethics to be followed by physicians in research settings. The hope was that the Declaration would prevent research atrocities from happening in the future through a system of accountability (Annas, 1992).[3] The Declaration has since served as a model for regulation by many countries, including the USA, as they have struggled to create rules for human subjects research (McNeill, 1993).

What the Nuremberg Code and Declaration of Helsinki provided for the National Commission was the initial delineation of how research subjects should be treated, including voluntary and informed participation, and how the risks of research should be balanced against the benefits to society (Faden and Beauchamp, 1986). The Belmont Report, however, differed significantly in form and structure from its predecessors. Rather than consisting of a list of criteria, it adopted a more philosophical approach from which policy-makers were to base subsequent regulation.

Specifically, the National Commission developed three ethical principles that should be the basis of all human subjects regulation: respect for persons, beneficence, and justice. It gave a complex definition of research to indicate what needed to be regulated and outlined three applications to match the respective ethical components: informed consent, risk/benefit assessment, and selection of research subjects (Emanuel *et al*, 2003).

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In the Belmont Report, the National Commission described the ethical principles and their application in detail and gave each of them specific meaning and purpose. Defining "respect for persons" as the recognition that individuals are autonomous agents, the National Commission asserted that informed consent procedures would maintain and reinforce individuals' autonomy through the three ingredients of information, comprehension, and voluntariness. In other words, the National Commission believed that providing information about risks and benefits, institutionalizing a procedure to assess whether the information was understood, and recruiting research subjects in a non-coercive way would guarantee respect for persons in the research process.

The second ethical principle of beneficence is described in two parts: "do no harm" and maximize possible benefits while minimizing possible harm. Through risk/benefit analysis, the National Commission stressed the importance of measuring the risk of the research to the individual compared to its benefit to the individual and, more broadly, to society.

Finally, the third ethical principle identified by the National Commission is that of justice. They defined it in terms of "fairness of distribution." Concerned with the distribution of the benefits and the burdens of medical research, the Report discussed the need for fairness (but not equality). In this view of justice, participation in research is taken as a right and should, therefore, be available to anyone who would benefit (Weinstein, 2001).[4]

One of the problems with the Belmont Report and the approach taken by the National Commission is that its attention to abstract ethical principles decontextualized the human research enterprise. Whereas the Congressional hearings preceding the National Research Act of 1974 attended to the institutional problems that catalyzed abuses of human subjects, the National Commission was more concerned with identifying 'universal' principles that could apply to human subjects research regardless of its context.

This is not to criticize the desire to have a set of universal principles to guide research. Rather, I am underscoring that universal principles are not

enough in practice. For example, the focus on abstract universal principles in the Belmont Report — however mitigated by their concrete respective applications — resulted in only nominal attention being given to the historical contingencies and structural conditions leading to their charge.[5] Specifically, the problems at institutions such as prisons and state sanitaria were not with the practices of researchers *per se*, but the conditions that made those institutions ideal places for researchers to conduct their studies. The only institutional reform under the purview of the National Commission concerned the research enterprise itself, not the institutions hosting that research.

Federal regulation

The task of transforming the National Commission's recommendations from the Belmont Report (1979) into federal regulation fell to the US Public Health Service – the same agency that funded the Tuskegee syphilis study (Faden and Beauchamp, 1986). First, the PHS defined the scope of the regulation: federal regulation only applies to research projects that are performed or funded by federal departments and agencies. Private research is not required to follow the federal requirements or guidelines.

Next, the PHS mandated the creation of local institutional review boards (IRBs) to ensure that researchers follow a procedure of voluntary informed consent with their research subjects. Finally, the regulation discussed "vulnerable populations" and created additional explicit safeguards for research involving "fetuses, pregnant women, and human in vitro fertilization" (in that order), prisoners, and children (Emanuel *et al*, 2003). These provisions resulted in a dramatic decrease in research involving individuals from these groups, particularly prisoners, labeled as vulnerable populations.[6]

Even though groups such as ethnic minorities, the poor, and the terminally ill were identified as potentially vulnerable groups in the Belmont Report, no special provisions were created within the federal regulation to provide additional protection to these groups. By ignoring other types of vulnerability to research abuses, the regulation effectively cast all other human subjects as equally 'autonomous' and able to protect themselves through the informed consent process.

Thus, in spite of a "vulnerable populations" category, in practice, research ethics is highly individualized, focusing predominantly on human subjects' consent. As a result, those who participate for important structural reasons, such as poverty, lack of health insurance, and/or illness, must protect themselves individually through the informed consent process. Evidence suggests, however, that, because of their personal situations, individuals from these same groups are unlikely to have interest in the details of consent forms, enabling a 'valence' towards participation in research studies (Fisher, 2006).

In 1981, the Department of Health, Education, and Welfare (DHEW) (now Department of Health and Human Services, DHHS) enacted the US federal regulation for human subjects protection (US 45-CFR-46). At that time, however, the regulation applied only to research activities sponsored by DHEW, and the US Government did not enforce this or any regulation for other human subjects research conducted by or funded through other US departments and agencies for another full decade.

In 1991, in response to inquiries into the research practices of the Department of Defense and other agencies, the US Government expanded the jurisdiction of the regulation to all Government bodies engaging in, or funding, research on human subjects. The DHEW regulation became known as the "Common Rule" because it was adopted as the standard for all federal agencies rather than crafting new guidelines or rules specific to each agency (McCarthy, 1998).

Yet, even with its increased reach, the regulation does not apply to all research conducted by US researchers. For example, it still does not directly regulate human subjects research that is conducted in the private sector. Additionally, research that is done overseas by American federally funded researchers is subject to some, but not all, of the regulation compared with those projects completed within the physical territory of the United States (Macklin, 1999). Although the US Food and Drug Administration (FDA) has its own regulations for human subjects research (for protocols seeking approval as part of the drug development and approval process), this only governs research directly leading to the marketing of products (Hilts, 2003).

The distinction between public- and private-sector research made by the PHS and enacted in the regulation sends an important message: the US Government does not want to be implicated in any way for unethical practices concerning human subjects in research settings (Kutcher, 2003). Because the same regulations do not apply to private-sector research, this suggests that the Government is more concerned about protecting itself than it is with protecting individuals who volunteer for research studies (King *et al*, 1999). Upon analysis of the regulation, it is clear that while it imposes some constraints on federally-funded researchers, it also continues to allow them much autonomy in their research practices (Kutcher, 2003; McCarthy, 1996; Weisstub, 1998).

Will regulation discourage research?

At the core of the policy environment is the fear that regulation of human subjects research will discourage or inhibit research, and hence progress, in the public and private sectors (Weisstub, 1998). Indeed, policy-makers have relied heavily on recommendations from the medical and scientific communities to direct policy to ensure that research and medical innovation would not be stifled by regulation (Faden

and Beauchamp, 1986). Physicians, researchers, pharmaceutical companies, and their public and private organizations and lobbying groups have played key roles in the development of regulation (Fletcher and Miller, 1996; Wolf, 1996).

Resulting from their involvement in the policy-making process from Congressional testimony, public comments on draft recommendations, and appointments to federal commissions, physicians and researchers have contributed a number of key distinctions that serve to define what needs to be regulated and what does not (Tong, 1996). One such distinction structuring the regulation of research is the categorization of "risk" versus "minimal risk" (McCarthy, 1998). This distinction is based on the idea that most research involving humans involves little risk to the subjects, so researchers should not be burdened by the same amount of bureaucracy as high-risk research (Nelson, 1998).[7]

This dichotomization often explicitly mobilizes the assumption that Americans are ethical and do not need much federal oversight of research. For example, Bernard Lo, a high-profile American ethicist who was a member of the National Bioethics Advisory Board in the 1990s, has stated in defense of the distinction between risk and minimal risk research, "This is not Nazi Germany. We know what is awful. If it is not scientifically sound, no risks are acceptable ... and the research will not be performed" (Conference presentation, ASLME, 11/9/01). Embedded in the need for a distinction at all among levels of risk to human subjects is a response to the ways in which federal regulation is translated into layers of bureaucracy (Lo and Groman, 2003).

Protecting human subjects

What have been the effects of the Common Rule on protecting human subjects? US federal regulation has been effective at minimizing particular types of abuse of subjects. As a result of its history of human experimentation, the system is specifically designed to eliminate deception and coercion (Howard-Jones, 1982). The solution to these unethical practices is epitomized by an overemphasis on informed consent (Cocking and Oakley, 1994). While informed consent has radically transformed the ways in which researchers interact with human subjects, it does not automatically imply that human subjects are protected from harm or exploitation (Corrigan, 2003; Fisher, forthcoming). The view of informed consent as a panacea obscures the inherent risks of any participation and ignores structural reasons compelling some groups to participate more than others (Sherwin, 1996; Nelson and Nelson, 1996).

Because the approach to defining US regulation was influenced by philosophical thought, policy-making was seen by Government officials as a finite process to solve human-subject abuses through the application of universal ethical principles. The translation of these principles into practice has emphasized the autonomy of individuals involved (that is, both the researchers and human subjects) at the expense of the bigger picture of scientific research.

Thus, the impact of scientific communities on groups of human subjects is obscured. As a result, the attitude towards regulation during the past 25 years has generally been that any problems associated with human subjects research have already been solved and there is little need for further regulation. Within this regulatory environment, policy-makers, and frequently bioethicists, do not identify or anticipate new types of abuse that can, and do, occur. As a result, the regulation fails to protect human subjects from harm in current and future research (Mahowald, 1996).

Contemporary research and policy climates

The research landscape in the United States has shifted significantly since the regulation to protect human subjects was enacted in 1981 and extended in 1991 by the Common Rule. In response to the regulation, particularly the restrictions placed on experimentation using prison populations, researchers needed to seek out new populations to recruit into medical studies (Campbell, forthcoming; Harkness, 1996). The pharmaceutical industry, in particular, slowly began to privatize and globalize its clinical research.

The pace of outsourcing to private-sector (that is, non-academic) clinics accelerated in the 1990s as did many other industries during the same time period (Rainville, 2002; Sox, 2001). The difference between the pharmaceutical industry and other sectors is that this form of outsourcing did not have the purpose of seeking out cheaper labor, but of taking clinical trials to populations that would be willing to enroll in clinical studies (Fisher, 2005; Petryna, 2006).

Within the USA, neoliberal economic policies stemming from the Reagan administration have enabled the pharmaceutical industry to conduct thousands of studies each year using American populations (Evans *et al*, 2005). With the profound changes in employment patterns, welfare, and healthcare delivery, many Americans find themselves without access to healthcare or in dire financial situations (Light, 2004; Quadagno, 2005). Clinical trials have increasingly been marketed to these Americans as a way of addressing their needs (Fisher, forthcoming).

As a result, pharmaceutical studies in the USA are overwhelmingly conducted on uninsured and impoverished citizens (Fisher, 2005). Because of the limited definition of who is vulnerable in the context of human subjects research, nothing in the current regulation proscribes or restricts such research on economically disenfranchised groups, nor is the uninsured understood to be a potentially vulnerable population.

Because of the limited definition of who is vulnerable in human subjects research, nothing currently proscribes or restricts such research on economically disenfranchised groups, nor is the uninsured understood to be a potentially vulnerable population

Although the Common Rule has been updated and revised since the original regulation was issued in 1981, little has actually changed in terms of the protection it affords human subjects (Beauchamp and Childress, 1993). To assess whether such change is needed, during the last decade policy-makers in the executive and legislative branches of Government have appointed *ad hoc* committees and have created agencies within the Department of Health and Human Services to investigate the ethics of current human subjects research and to provide recommendations for new policy and regulation. Where these committees and agencies have been successful in effecting change has been in creating federal guidance regarding subjects' privacy, financial conflicts of interest for researchers and institutions, and centralized reporting of clinical trial results (Spicer, 2000).

There are profound limitations and problems with current federal policies governing human subjects research. In spite of formal discussions in Washington about better protecting human subjects, there has been little explicit examination to date of how the pharmaceutical industry takes advantage of political and economic conditions in the USA that disenfranchise its citizens (Fisher, 2005).[8] In the context of current modes of pharmaceutical drug development, the existing regulation is impotent to protect new and different forms of misuses, if not abuses, of human subjects. This is in part because of the regulation's individualistic approach to protecting such subjects. Rather than tracking the groups being targeted to take part in the research, an individualistic orientation focuses on whether informed consent can be documented. If informed consent is given, the research is perceived as ethical (Cocking and Oakley, 1994; Sherwin, 1996; Nelson and Nelson, 1996).

There are two approaches that can, and should, be taken to attenuate US regulatory reliance on individualistic models of research ethics. One involves the broader social, economic, and political context, and the other targets the research enterprise itself. First, what is missing from the regulatory picture of human subjects research are the structural reasons that draw individuals from marginalized groups to the research. Like the reforms following Willowbrook in the 1960s and the hearings on prison research in the 1970s (see above), efforts must be made to change the conditions that allow researchers to profit from, and reproduce, social inequalities.

This would include significant increases in the minimum wage to mitigate the economic reasons propelling impoverished citizens to enroll in studies. It would also include providing universal health coverage to all Americans so that lack of health insurance would no longer make clinical research the only mechanism for receiving some type of affordable medical attention. By minimizing existing social inequalities on the broader level, these differences among groups of Americans would not be exacerbated to the same degree or in the same way within the context of human subjects research.

In addition to these higher-level reforms, the research enterprise itself must be made more accountable to the structural problems that lead to the exploitation of disenfranchised Americans. To do so, the regulation must include specific guidelines for research conducted using poor and/or uninsured populations. By classifying these groups as vulnerable, the US Government could change relations among pharmaceutical companies, researchers, and those groups who are currently seen as easy to enroll (Fisher, forthcoming).

For example, in cases of human subjects without insurance, the regulation could require researchers to inform potential subjects not only about the risks of the research but also about any alternative healthcare services available to them at reduced cost or free of charge. Many citizens may not be as aware of available county or state medical services as they are of clinical research, because of the pervasive advertising of the latter.

In addition, by classifying these groups as vulnerable, the regulation could strengthen the existing ethical principle of justice. Because the current framing of justice is concerned with the distribution of risks and benefits of research, explicit attention to the poor and uninsured as vulnerable groups would emphasize the need to provide more benefits for their participation. For example, sponsors could be required to provide healthcare to uninsured human subjects for several months up to a year after the conclusion of a research study, to ensure that they have not had any negative consequences from the termination of their participation in a clinical trial. Likewise, human subjects could receive free or discounted access to medication that makes it to the market as a result of their participation in research studies. In these and other ways, the regulation could afford more equitable distribution of the risks and burdens of research, particularly for vulnerable groups.

These proposed solutions are not meant to be a blueprint for change. Rather, they should serve as an indication of how US regulation could be more responsive to structural issues that impact on human subjects' participation in research. What is important

here is that reform of the current regulation is necessary because the system as it stands enables the continued exploitation of disenfranchised groups. Even if reform cannot work to minimize broader social, economic, and political problems, it could adopt a more structural approach to ethics and federal oversight. In short, if the goal is to protect its citizens, the US Government can, and must, ensure that the system of human subjects research does not exacerbate existing social inequalities.

Notes

1. In addition to the researchers themselves, students have played a large role as human subjects in many fields from medicine to psychology. Not only a convenient population, students have been thought to make good study subjects because of their level of education and their presumed familiarity with the areas under investigation (Prescott, 2002).
2. In spite of the intellectual and symbolic value of the Nuremberg Code, it has proven disappointing in its influence on legal and legislative systems around the world (Faden and Beauchamp, 1986). In large part, this is because it was designed to assess scientific practice retrospectively. Because its concern was judging the conduct of completed research, the tribunal gave little guidance for practicing ethical research into the future (Childress, 2000).
3. The World Medical Association has amended the Declaration of Helsinki five times, most recently in 2000. Although the Declaration has been an admirable and interesting document from its inception, it has no particular legal status (Emmanuel *et al*, 2003). As a set of ethical principles alone, it serves as a model for 'good clinical practice' (GCP), rather than a mandate to govern and oversee research enterprises.
4. The principle of justice in the Belmont Report has been mobilized since to advocate for the explicit inclusion of women and minorities in clinical trials (Epstein, 2004; Kass, 1998; King, 1998).
5. The Belmont Report (1979) does not ignore the ethical abuses that occurred in the USA In fact, it reads:

   > Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied.

   The Belmont report even mentions the Tuskegee syphilis study explicitly. The problem is that the report gives no concrete indication how to prevent these types of abuse from continuing to occur or how 'respect for persons' and informed consent could provide solutions.
6. Recently, however, there is increasing interest in relaxing the regulation on use of prisoners in research. In addition, there are now federal incentives, such as extensions of patent protections, for companies to conduct pediatric clinical trials.
7. Within the regulatory system, bureaucratic requirements related to liability concerns often eclipse the proactive protection of human subjects (Kutcher, 2003). For example, paperwork and time delays, not critical thinking about ethics, are the norm when dealing with IRBs (Eckenwiler, 2001).
8. One exception is a DHHS report issued in June 2000. Based on preliminary empirical findings, the report presented critical results of its investigation into the recruitment of subjects in private-sector pharmaceutical research. It identified recruitment practices as a "fundamental concern" because "the consent process may be undermined when, under pressure to recruit quickly ... investigators misrepresent the true nature of the research" (OIG, 2000: 2).

References

Annas, G J 1992. The changing landscape of human experimentation: Nuremberg, Helsinki, and beyond. *Health Matrix Journal of Law and Medicine*, **2**, 119–140.

Annas, G J and M A Grodin eds. 1992. *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation*. New York: Oxford University Press.

Beauchamp, T L and J F Childress 1993. *Principles of Biomedical Ethics*. New York: Oxford University Press.

Belmont Report 1979. Available at: <http://ohsr.od.nih.gov/guidelines/belmont.html>, last accessed 10 December 2006.

Briggs, L 2002. *Reproducing Empire: Race, Sex, Science, and U.S. Imperialism in Puerto Rico*. Berkeley CA: University of California Press.

Brandt, A M 2000. Racism and research: the case of the Tuskegee syphilis experiment. In *Tuskegee's Truths: Rethinking the Tuskegee Syphilis Study*, ed. S Reverby, pp. 15–33. Chapel Hill NC: University of North Carolina Press.

Campbell, N D forthcoming. *Discovering Addiction: the Science and Politics of Substance Abuse Research*. Ann Arbor MI: University of Michigan Press.

Childress, J F 2000. Nuremberg's legacy: some ethical reflections, *Perspectives in Biology and Medicine*, **43**(3), 347–361.

Chinn, S E 2000. *Technology and the Logic of American Racism: a Cultural History of the Body as Evidence*. New York: Continuum.

Cocking, D and J Oakley 1994. Medical experimentation, informed consent, and using people. *Bioethics*, **8**(4), 293–311.

Corrigan, O P 2003. Empty ethics: the problem with informed consent. *Sociology of Health and Illness*, **25**, 768–792.

Dalla-Vorgia, P, J Lascaratos and P Skiadas 2001. Is consent in medicine a concept only of modern times? *Journal of Medical Ethics*, **27**, 59–61.

Declaration of Helsinki 1964. Available at <http://www.wma.net/e/ethicsunit/helsinki.htm>, last accessed 10 December 2006.

Eckenwiler, L 2001. Moral reasoning and the review of research involving human subjects. *Kennedy Institute of Ethics Journal*, **11**(1), 37–69.

Eichstaedt, P H 1994. *If You Poison Us: Uranium and Native Americans*. Santa Fe NM: Red Crane Books.

Emanuel, E J, R A Crouch, J D Arras, J Moreno and C Grady eds. 2003. *Ethical and Regulatory Aspects of Clinical Research: Readings and Commentary*. Baltimore MD: Johns Hopkins University Press.

Epstein, S 2004. Bodily differences and collective identities: the politics of gender and race in biomedical research in the United States. *Body and Society*, **10**, 183–203.

Evans, D, M Smith and L Willen 2005. Big Pharma's shameful secret. *Bloomberg Markets Special Report*, December.

Faden, R R and T L Beauchamp 1986. *A History and Theory of Informed Consent*. New York: Oxford University Press.

Fisher, J A 2005. *Pharmaceutical Paternalism and the Privatization of Clinical Trials*. Troy NY: Rensselaer Polytechnic Institute.

Fisher, J A 2006. Procedural misconceptions and informed consent: insights from empirical research on the clinical trials industry. *Kennedy Institute of Ethics Journal*, **16**, 251–268.

Fisher, J A forthcoming. 'Ready-to-recruit' or 'ready-to-consent' populations?: informed consent and the limits of subject autonomy. *Qualitative Inquiry*, **13**.

Fletcher, J C and F G Miller 1996. The promise and perils of public bioethics. In *The Ethics of Research Involving Human Subjects: Facing the 21st Century*, ed. H Y Vanderpool. Frederick MD: University Publishing Group.

Gamble, V N 2000. Under the shadow of Tuskegee: African–Americans and health care. In *Tuskegee's Truths: Rethinking the Tuskegee Syphilis Study*, ed. S Reverby, pp. 431–442. Chapel Hill NC: University of North Carolina Press.

Guerrini, A 2003. *Experimenting with Humans and Animals: From Galen to Animal Rights*. Baltimore MD: Johns Hopkins University Press.

Halpern, S A 2004. *Lesser Harms: The Morality of Risk in Medical Research*. Chicago IL: University of Chicago Press.

Harkness, J H 1996. *Research behind Bars: a History of Nontherapeutic Research on American Prisoners*. Madison WI: University of Wisconsin.

Hess, D J 1997. *Science Studies: An Advanced Introduction*. New York: New York University Press.

Hilts, P J 2003. *Protecting America's Health: The FDA, Business, and One Hundred Years of Regulation*. New York: Knopf.

Hornblum, A M 1998. *Acres of Skin: Human Experiments at Holmesburg Prison*. New York: Routledge.

Howard-Jones, N 1982. Human experimentation in historical and ethical perspectives. *Social Science and Medicine*, **16**(15), 1429–1448.

Jones, J H 1981. *Bad Blood: The Tuskegee Syphilis Experiment*. New York: Free Press.

Kass, N E 1998. Gender and research. In *Beyond Consent: Seeking Justice in Research*, ed. J P Kahn, A C Mastroianni and J Sugarman. New York: Oxford University Press.

King, N M P, G E Henderson and J Stein eds. 1999. *Beyond Regulations: Ethics in Human Subjects Research*. Chapel Hill NC: University of North Carolina Press.

King, P A 1998. Race, justice, and research. In *Beyond Consent: Seeking Justice in Research*, eds. J P Kahn, A C Mastroianni and J Sugarman. New York: Oxford University Press.

King, PA 2000. The dangers of difference. In *Tuskegee's Truths: Rethinking the Tuskegee Syphilis Study*, ed. S Reverby, pp. 424–430. Chapel Hill NC: University of North Carolina Press.

Kutcher, G 2003. Risk to medicine or the autonomy rights of subjects?: governing American medical research. Paper read at Vital Politics, London, 5–7 September.

Lederer, S E 1995. *Subjected to Science: Human Experimentation in American before the Second World War*. Baltimore MD: Johns Hopkins University Press.

Light, D 2004. Ironies of success: a new history of the American health care 'system'. *Journal of Health and Social Behavior*, **45**(extra issue), 1–24.

Lo, B and M Groman 2003. NBAC recommendations on oversight of human subject research. *Seton Hall Law Review*, **32**(3), 493–512.

Macklin, R 1999. Is ethics universal?: gender, science, and culture in reproductive health research. In *Beyond Regulations: Ethics in Human Subjects Research*, eds. N M P King, G E Henderson and J Stein. Chapel Hill NC: University of North Carolina Press.

Mahowald, M B 1996. On treatment of myopia: feminist standpoint theory and bioethics. In *Feminism and Bioethics: Beyond Reproduction*, ed. S M Wolf. New York: Oxford University Press.

McCarthy, CR 1996. Challenges to IRBs in the coming decades. In *The Ethics of Research Involving Human Subjects: Facing the 21st Century*, ed. H Y Vanderpool. Frederick MD: University Publishing Group.

McCarthy, C R 1998. The evolving story of justice in federal research policy. In *Beyond Consent: Seeking Justice in Research*, ed. J P Kahn, A C Mastroianni and J Sugarman. New York: Oxford University Press.

McNeill, P M 1993. *The Ethics and Politics of Human Experimentation*. New York: Cambridge University Press.

Merton, R K 1938. Science and the social order. In *The Sociology of Science*, pp. 254–266. Chicago IL: University of Chicago Press, 1973.

Merton, RK 1942. The normative structure of science. In *The Sociology of Science*, pp. 267–278. Chicago IL: University of Chicago Press, reprinted 1973.

Mishkin, B 2000. Law and public policy in human studies research. *Perspectives in Biology and Medicine*, **43**(3), 362–372.

Mitford, J 1971. *Kind and Usual Punishment: The Prison Business*. New York: Knopf.

Moreno, J D 2001. *Undue Risk: Secret State Experiments on Humans*. New York: Routledge.

National Academy of Sciences 1975. *Experiments and Research with Humans: Values in Conflict*. Washington DC: National Academy of Sciences.

Nelson, H L and J L Nelson 1996. Justice in the allocation of health care resources: a feminist account. In *Feminism and Bioethics: Beyond Reproduction*, ed. S M Wolf. New York: Oxford University Press.

Nelson, R M 1998. Children as research subjects. In *Beyond Consent: Seeking Justice in Research*, eds. J P Kahn, A C Mastroianni and J Sugarman. New York: Oxford University Press.

Nuremberg Code 1949. Available at <http://www.nihtraining.com/ohsrsite/guidelines/nuremberg.html>, last accessed 10 December 2006.

OIG, Office of the Inspector General 2000. *Recruiting Human Subjects: Pressures in Industry- Sponsored Clinical Research*. Washington DC: Department of Health and Human Services.

Pappworth, M H 1967. *Human Guinea Pigs: Experimentation on Man*. Boston MA: Beacon Press.

Petryna, A 2006. Globalizing human subjects research. In *Global Pharmaceuticals: Ethics, Markets, Practices*, eds. A Petryna, A Lakoff, and A Kleinman, pp. 33–60. Durham NC: Duke University Press.

Prescott, H M 2002. Using the student body: college and university students as research subjects in the United States during the twentieth century. *Journal of the History of Medicine*, **57**, 3–38.

Quadagno, J 2005. *One Nation, Uninsured: Why the U.S. Has No National Health Insurance*. New York: Oxford University Press.

Rainville, B 2002. Strategic outsourcing with contract research organizations: targeting corporate goals, *Drug Information Journal*, **36**(1), 77–81.

Reverby, S ed. 2000. *Tuskegee's Truths: Rethinking the Tuskegee Syphilis Study*. Chapel Hill NC: University of North Carolina Press.

Rothman, D J 1991. *Strangers at the Bedside: A History of How Law and Bioethics Transformed Medical Decision Making*. New York: Basic Books.

Rothman, D J and S M Rothman 1984. *The Willowbrook Wars*. New York: Harper-Collins.

Roy, B 1995. The Tuskegee syphilis experiment: biotechnology and the administrative state. *Journal of the National Medical Association*, **87**, 56–67.

Savitt, T L 1982. The use of blacks for medical experimentation and demonstration in the Old South. *Journal of Southern History*, **48**, 331–348.

Schmidt, U 2004. *Justice at Nuremberg: Leo Alexander and the Nazi Doctors' Trial*. New York: Palgrave Macmillan.

Sherwin, S 1996. Feminism and bioethics. In *Feminism and Bioethics: Beyond Reproduction*, ed. S M Wolf. New York: Oxford University Press.

Smith, A 2005. *Conquest: Sexual Violence and American Indian Genocide*. Cambridge MA: South End Press.

Sox, H 2001. Sponsorship, authorship, and accountability. *Annals of Internal Medicine*, **135**(6), 463–466.

Spicer, C M 2000. Federal oversight and regulation of human subjects research: an update. *Kennedy Institute of Ethics Journal*, **10**(3), 261–264.

Spitz, V 2005. *Doctors from Hell: the Horrific Account of Nazi Experiments on Humans*. Boulder CO: Sentient Publications.

Tone, A 2002. *Devices and Desires: a History of Contraceptives in America*. New York: Hill and Wang.

Tong, R 1996. Feminist approaches to bioethics. In *Feminism and Bioethics: Beyond Reproduction*, ed. S M Wolf. New York: Oxford University Press.

Watkins, E S 2001. *On the Pill: a Social History of Oral Contraceptives, 1950–1970*. Baltimore MD: Johns Hopkins University Press.

Weinstein, M 2001. A public culture for guinea pigs: U.S. human research subjects after the Tuskegee study. *Science as Culture*, **10**(2), 195–223.

Weisstub, D N 1998. *Research on Human Subjects: Ethics, Law, and Social Policy*. Oxford: Pergamon.

Wolf, S M ed. 1996. *Feminism and Bioethics: Beyond Reproduction*. New York: Oxford University Press.