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NOTE: At the time of publication, author Jonathan D. Moreno was affiliated with the University of Virginia. Currently March 2007, he is a faculty member in the Department of Bioengineering at the University of Pennsylvania.

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Abstract
In the ethics of human subjects research, protectionism is the doctrine that human beings should be protected from the risks of participation in research. Evidently, unless one believes that scientific progress always trumps the interests of human subjects, protectionism per se is hardly a controversial view. Controversy enters mainly when several nuanced interpretations of the doctrine are distinguished with an eye toward its application to actual research projects.

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Ethical and Policy Issues in Research Involving Human Participants

Volume II

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August 2001

PROTECTIONISM IN RESEARCH INVOLVING HUMAN SUBJECTS

Commissioned Paper
Jonathan D. Moreno
University of Virginia

> "We can never rest comfortably in the belief that the soil from which our satisfactions sprout is not watered with the blood of martyrs. But a troubled conscience compels us, the undeserving beneficiaries, to ask: Who is to be martyred? in the service of what cause? and by whose choice?"
>
> Hans Jonas[1]

In the ethics of human subjects research, protectionism is the doctrine that human beings should be protected from the risks of participation in research. Evidently, unless one believes that scientific progress always trumps the interests of human subjects, protectionism per se is hardly a controversial view. Controversy enters mainly when several nuanced interpretations of the doctrine are distinguished with an eye toward its application to actual research projects.

There are alternative perspectives to protectionism, from the standpoint of subjects and of investigators. From the subjects' point of view, a philosophy that calls for ease of access to clinical research emerged in the 1980s, and I will allude to it later in this paper. But enthusiasm for research participation as an alternative "back door" to medical care has waned in recent years.

From the standpoint of investigators an alternative to protectionism is reliance on their moral virtue, thus emphasizing the high degree of discretion over the management of human subjects that has traditionally been accorded scientists. On closer inspection, however, a position that favors investigator discretion is not an *alternative* to protectionism but a particular *version* of it, one that places the onus for protecting subjects on the researcher.

In this paper I shall analyze the historical origins of protectionism as a philosophical position in the ethics of human subjects research. I shall also distinguish three versions of protectionism that have emerged in this history: moderate, strong, and weak versions, framed in terms of how much discretion investigators should be allowed concerning the management of human subjects. Weak protectionism entails reliance on the discretion of the investigator with modest constraints understood as guidelines. Moderate protectionism makes room for investigator discretion but within a framework of rules. Strong protectionism involves greatly reduced investigator discretion in a context of direct intervention by a third party, perhaps in the form of monitoring of actual research activities.

There are several critical issues for a protectionist policy in human subjects research. The first is the relationship between the interests of the subject and those of science and "future patients." The second is whether and in what manner the conduct of the investigator may be monitored or controlled by third parties. A corollary of these issues is the question of special arrangements for subject populations that are vulnerable by virtue of age, medical condition, or social status. All of these topics will be recurrent themes in this paper.

Individuality and Society

No endeavor presents more strikingly the tension between individual and social interests than does medical research involving human subjects. Although the origins of the contemporary idea of individuality with its associated rights and interests are complex, largely Western, and relatively recent, the originality of the idea of individuality should not be exaggerated. What seems to have emerged since the Enlightenment is not so much the notion of the individual, which was surely available to ancient thinkers who meditated on the meaning of human subjectivity, as it is the inferences (moral and otherwise) drawn from that notion. Eastern and traditional cultures, too, are hardly ignorant of the idea of individuality, though again they may attribute different implications to it.

The fundamental ideas behind our contemporary understanding of society are arguably more continuous with the ancient world than that of individuality. From the Greeks we inherited the ideal of social solidarity and the conception of social roles that entail role-related duties, as well as a general sense of public responsibility. Enlightenment thinkers, the founders of our Western political framework, reached back to classical sources for their inspiration but also developed medieval notions of consent as the basis for governmental legitimacy. It is perhaps in that ambiguity, deep in the Enlightenment tradition, that we may locate the tension between individual and societal interests.

Yet in another sense individual and society are complementary rather than conflicting ideas. Few thinkers (apart from the most extreme libertarians and "objectivists" on the one hand and radical collectivists and "pan-psychists" on the other), have found it acceptable to treat matters concerning human nature as reducible to one or the other. Most have presupposed an anthropology of "social individuals," with the true battleground mainly a matter of line-drawing. Even our current preoccupation with genetics tends to accept this presupposition, couched in terms of genomic background and phenomic expression.

It is also useful to recall that the same period that gave rise to modern experimental method also refined ideas about personal dignity that we today take for granted. That scientific progress is finally in the service of improving opportunities for human beings to express their best and most humane selves is today hardly questionable. In that sense scientific activity that undermined human dignity would be a cultural contradiction. It is this sensibility that underlies the nearly universal condemnation of the use of human beings as mere means to scientific ends.

Traditional medical ethics embodies a resolution of the tension between individual and societal interests. Hippocratic tradition favors care for the individual patient but also emphasizes the continuous learning or "practice" that must take place, clearly with an eye toward benefiting future patients and thereby society in general. Experimentation in an emergency is authorized though care must be taken to avoid engendering more harm than good. Presumably the learning that takes place through experimental results can be applied to future practice and passed on to one's apprentices in the fraternity. All this is in the spirit of the Hippocratic tradition and survives in modern medical values.

Clearly the modern experimental environment creates vast new complications for application of the Hippocratic "harm" principle, but the principle itself rests on a presumption of protection of the immediate patient. Vulnerable persons, exemplified as slaves in the versions of the Oath that antiquity has bequeathed to us, must be specifically included in this protectionist attitude. How, then, to effect the resolution called for by the Hippocratic tradition in the modern experimental environment? Because protectionism is a doctrine that is rooted in experience, an understanding and justification of the ways it has been implemented require an historic approach.

From Havana to Nuremberg

Concerns about the involvement of human beings in research are at least a century old. Many institutionalized children were subjects in vaccine experiments in the nineteenth century, in Europe and the United States, and by the 1890s anti-vivesectionists were calling for laws to protect children. At the turn of the century the Prussian state imposed research rules and Congress considered banning medical experiments for certain populations, such as pregnant women, in the District of Columbia. In the ensuing decades there were occasional well-publicized scandals, mostly involving child subjects, and the first attempt to test a polio vaccine was stopped after the American Public Health Association censured the program.[2]

Prior to World War II, however, medical researchers were largely inoculated against regulation by the nearly legendary status of the self-experimentation by members of U.S. Army physician Walter Reed's Yellow Fever

Commission in Cuba. One of the commissioners, Dr. Jesse Lezear, died after subjecting himself to the mosquito's bite, helping to confirm the hypothesis of the disease's spread. A less celebrated but equally notable element of the Reed story is his use of an early written contract for the Spanish workers who were among the commission's other subjects, which itself appears to have followed a controversy involving yellow fever research subjects.[3]

For some reason Reed himself was widely thought to have been one of the volunteer subjects, perhaps due to his untimely death only a few years later that resulted from a colleague's error. This misconception added to the legend and to the model of medical researchers as of exceptional moral character, even to the point of martyrdom. The Reed mythology became a singular reference point and justification for the self-regulation of medical science. During the 1960s, when physician researchers were coming under new levels of scrutiny, the distinguished physician-scientist Walsh McDermott referred to the Reed story to demonstrate the social importance of medical research, with the high moral standing that went with it.[4]

An occasion for the significant revision of this picture became available at the end of the Second World War, when 23 Nazi doctors and medical bureaucrats were tried for crimes associated with vicious medical experiments on concentration camp prisoners. The defendants were selected from about 350 candidates. Although only 1,750 victims were named in the indictment, they were a handful of the thousands of prisoners used in a wide variety of vicious experiments, many in connection with the Nazi war effort. Some involved the treatment of battlefield injuries or in preventing the noxious effects of high altitude flight. Others, such as the sterilization experiments, were undertaken in the service of Nazi racial ideology, and still another category had to do with developing efficient methods of killing.

A strong defense mounted by the defendants' lawyers pointed to the fact that the Allies, too, had engaged in medical experiments in the service of the war effort. As the prosecution's attempt to demonstrate that there were clear international rules governing human experimentation faltered, the judges decided to create their own set of rules, known to posterity as the Nuremberg Code, the first line of which is "The voluntary consent of the human subject is absolutely essential." Although the court seemed to believe that protections were needed, it is not clear how intrusive they wished these protections to be in the operations of medical science. The judges declined, for example, to identify persons with mental disorders as in need of special provisions, although urged to do so by their medical expert. The very requirement of voluntary consent for all undermined the relevance of their code to experiments involving persons with diminished or limited competence, and the extreme circumstances that gave rise to the trial itself seemed quite distant from normal medical research.[5]

Discovering Informed Consent

Unlike the medical profession as a whole, in 1947 the new Atomic Energy Commission apparently took note of the Nazi doctors' trial and attempted to impose what it termed "informed consent" on its contractors as a condition for receiving radioisotopes for research purposes. It also established—or attempted to establish—a requirement of potential benefit for the subject. Both of these conditions were to apply to nonclassified research. This relatively protectionist attitude may not have been adopted with a great deal of appreciation of its implications. In any case, the AEC's position met with resistance among some of its physician contractors, but not its physician advisors. The AEC's early protectionist stance finally did not become institutionalized, and the letters setting out the requirements seem to have soon been forgotten. (The potential benefit requirement seems itself to have been incompatible with all the trace-level radiation research the AEC sponsored shortly thereafter.) Similarly, in the early 1950s the Department of Defense adopted the Nuremberg Code, along with written and signed consent, as its policy for defensive research on atomic, biological, and chemical weapons, but a 1975 Army Inspector General report pronounced that initiative a failure.[6]

Thus by the early 1950s although there were gestures in the direction of a protectionist attitude toward human subjects, even these expressions were in a fairly abstract philosophical vein rather than in a robust set

of institutionalized policies and procedures. An example is the Army's failure to implement a compensation program for prisoners injured in malaria or hepatitis studies when it was contemplated in the late 1940s.[7] The essential feature of the weak form of protectionism that prevailed at that time was its nearly wholesale reliance on the judgment and virtue of the individual researcher. Deliberations on the World Medical Association's Helsinki Declaration of 1964 (Helsinki I) began in 1953. Informed consent was a far less prominent feature of the first Helsinki Declaration than of the Nuremberg Code. Further, Helsinki introduced the notion of surrogate consent, permitting research when individuals are no longer competent to consent themselves. These moves place a substantial burden on the self-control of the individual researcher, a point to which I shall return later.[8]

To be sure, until the middle and later 1960s, and with the significant exception of the Nazi experience, to many there did not seem to be good reason for worries about human protections. The development of penicillin, the conquest of polio, and the emergence of new medical devices and procedures apparently unmarked by inappropriate conduct, all bolstered the public prestige of biomedical research. Nevertheless, there were some inklings of a continuing, albeit low-intensity, concern about the concentrated power of medical researchers even in the 1950s, exemplified perhaps in the gradual disappearance from professional discussions of the term "human experiment" and its replacement with the more detached and comforting "research."

On the whole, then, the world of clinical studies from the late 1940s up through the mid-1960s was one in which a weak form of protectionism prevailed, one defined by the placement of responsibility upon the individual researcher. Written informed consent (through forms generally labeled "permits," "releases," or "waivers"), though apparently well established in surgery and radiology, was not a common practice in clinical research and in any case cannot be said to provide more than a modicum of increased protection to human subjects. For example, whether a medical intervention was an "experiment" or not, and therefore whether it fell into a specific moral category that required an enhanced consent process, was a judgment largely left up to the researcher. Partly that judgment depended on whether the individual was a sick patient or a healthy volunteer. The former were as likely as not to be judged as wholly under the supervision of the treating doctor even when the intervention was quite novel and unlikely to be of direct benefit. Therefore an individual might be asked to consent to surgery but not be informed beyond some generalities about its experimental aspect.

There were, however, some important exceptions. For example, the Atomic Energy Commission established a set of conditions for the distribution of radioisotopes to be used with human subjects, including the creation of local committees to review proposals for radiation-related projects. Early Institutional Review Boards (IRBs) were established in several hospitals (including early ones at Beth Israel in Boston and the City of Hope in California), in order to provide prior group review for a variety of clinical studies. Another exception seems to have been the Clinical Center of the National Institutes of Health in Bethesda, Maryland, which opened in 1953. A government-supported research hospital, the Clinical Center appears to have been one of a handful of hospitals that required prospective review of clinical research proposals by a group of colleagues.

As advanced as the Clinical Center might have been in this respect, the prior group review process it established seems, at least at first, to have been confined to healthy, normal volunteers. The moral equivalence of at least some sick patients who would probably not be helped by study participation to normal subjects who would not be benefited (with the possible exception of vaccine studies) was apparently not appreciated in policy. These subtleties were largely lost in a period in which medical discretion and societal benefit weighed heavily.

In Search of the Best Approach

Prior group review is essential to the transition beyond weak protectionism and was not common before the 1970s. Yet decades earlier there was a keen awareness of the psychological vulnerability inherent in the patient role, a vulnerability that could have argued for independent review of a research project. An extensive psychological literature, founded mainly on psychoanalytic theory, propounded a skeptical view of the underlying motivations of experiment volunteers as early as 1954. That year, Louis Lasagna and John M. Von Felsinger reported in *Science* on the results of Rorschack studies and psychological interviews of 56 healthy young male volunteers in drug research. The authors concluded that the subjects exhibited "an unusually high incidence of severe psychological maladjustment." "There is little question," they wrote, "that most of the subjects...would qualify as deviant, regardless of the diagnostic label affixed to them by examining psychiatrists or clinical psychologists." The authors theorized that this group may not have been representative of the population from which it was drawn (college students), and that they might have been attracted to the study for various reasons having to do with their deviance, beyond financial reward.[9]

I describe this study at length not to endorse its psychology or its conclusions, nor to imply that neurotic tendencies are either typical of research volunteers or *a priori* disqualifying conditions for decisionmaking capacity. The point is, rather, that thought was being given as early as 1954 to the question of the recruitment of subjects who may be vulnerable despite their healthy and normal appearance. The article was published in a major scientific journal. It would have been natural to ask further questions about the vulnerability of potential research subjects who are known to be seriously ill. Yet despite this psychological theorizing, which could be viewed as quite damning to the moral basis of the human research enterprise, protectionism was at best a weak force for years to come.

Historians of research ethics generally date the increasing vigor of protectionist sentiment among high-level research administrators, as well as the general public, to the series of events that began with the Thalidomide tragedy and continued with scandals such as the Brooklyn Jewish Chronic Disease Hospital Case and, later, the Willowbrook hepatitis research. These cases cast doubt on the wisdom of leaving judgments about research participation to the researchers' discretion. The Jewish Chronic Disease Hospital Case, in which elderly debilitated patients were injected with cancer cells, apparently without their knowledge or consent, was one of those that attracted the attention and concern of the NIH director, James S. Shannon. Shannon's intervention, and the resistance from within his own staff, was an important and revealing moment in the history of human subjects protections.

In late 1963 Shannon appointed his associate chief for program development, Robert B. Livingston, as chair of a committee to review the standards for consent and requirements of NIH-funded centers concerning their procedures. The Livingston Committee affirmed the risks to public confidence in research that would result from more cases like that of the Jewish Chronic Disease Hospital. Nonetheless, in its 1964 report to Shannon the committee declined to recommend a code of standards for acceptable research at the NIH, on the grounds that such measures would "inhibit, delay, or distort the carrying out of clinical research...." Deferring to investigator discretion, the Livingston Committee concluded that NIH was "not in a position to shape the educational foundations of medical ethics...."[10]

Disappointed but undeterred by the response of his committee, Shannon and Surgeon General Luther Terry proposed to the National Advisory Health Council (NAHC) that the NIH should take responsibility for formal controls on investigators. The NAHC essentially endorsed this view and resolved that human subjects research should only by supported by the Public Health Service if "the judgment of the investigator is subject to prior review by his institutional associates to assure an independent determination of the protection of the rights and welfare of the individual or individuals involved, of the appropriateness of the methods used to secure informed consent, and of the risks and potential medical benefits of the investigation."[11] The following year

Surgeon General Terry issued the first federal policy statement that required PHS-grantee research institutions to establish what were subsequently called Research Ethics Committees.[12] The seemingly innocent endorsement of "prior review by institutional associates" was the most significant single departure from the weakly protectionist tradition to a process that finally yielded the moderately protectionist system we have today.

The surgeon general's policy was, however, hardly typical of contemporary attitudes, and the practice it sought to implement is one we are still trying to effect. To appreciate the weakness of the form of protectionism that prevailed through the 1960s, it is useful to recall the dominant role that prison research once had in drug development in the United States. By 1974 the Pharmaceutical Manufacturers Association estimated that about 70 percent of approved drugs had been through prison research. Pharmaceutical companies literally built research clinics on prison grounds. Although in retrospect we may think of modern limits on prison research as a triumph of protectionism (on the grounds that prisoners cannot give free consent), at the time it was a confluence of political and cultural forces that had little to do with actual abuses (though there certainly were some), and was resisted by prison advocates. Perhaps the most important public event that signaled the inevitable end of widespread prison research was the 1973 publication of "Experiments Behind Bars" by Jessica Mitford in the *Atlantic Monthly.*[13]

Within the medical profession itself, then, weak protectionism remained the presumptive moral position well into the 1970s, if not later. Neither of the most important formal statements of research ethics, the Nuremberg Code and the Helsinki Declaration, had nearly as much effect on the profession as a 1966 *New England Journal of Medicine* paper by Harvard anesthesiologist Dr. Henry Beecher. The importance of timing is evident in the fact that Beecher had been calling attention to research ethics abuses since at least 1959, when he published a paper entitled "Experimentation in Man,"[14] but his 1966 publication "Ethics and Clinical Research"[15] attracted far more attention. One important distinguishing feature of the latter work was Beecher's allusion to nearly two dozen cases of studies alleged to be unethical that had appeared in the published literature. By "naming names" Beecher had dramatically raised the stakes.

It would, however, be an error to conclude that Beecher himself favored external review of clinical trials that would remove them from medical discretion. To the contrary, Beecher was one among a large number of commentators who favored (and in some instances continue to favor) reliance primarily upon the virtue of the investigator. Although he strongly defended the subject's right to voluntary consent, he argued in his 1959 paper that "an understanding of the various aspects of the problem" being studied was the best protection for the human subject, and was quite critical of the Nuremberg Code's dictum that the subjects themselves should have sufficient knowledge of the experiment before agreeing to participate.

Beecher's attitude toward the Code's provisions was hardly limited to philosophical musings. In 1961 the Army attached a new provision to its standard research contract, rules that were essentially a restatement of the Nuremberg Code. Along with other members of Harvard Medical School's Administrative Board, Beecher protested and persuaded the Army Surgeon General to insert into Harvard's research contracts that its Article 51 were "guidelines" rather than "rigid rules."[16]

Beecher's attitude was shared by many other distinguished commentators on research practices through the 1960s and 1970s. In 1967 Walsh McDermott expressed grave doubt that the "irreconcilable conflict" between the "individual good" and the "social good" to be derived from medical research could be resolved, and certainly not by "institutional forms" and "group effort"—apparently references to ethics codes and peer review. McDermott's comments were by way of introduction to a colloquium at the annual meetings of the American College of Physicians on "The Changing Mores of Biomedical Research." In his remarks McDermott alluded to the growing contribution of research to the control of disease, beginning with Walter Reed's yellow fever studies. Thus, he continued, "medicine has given to society the case for its rights in the continuation of clinical investigation," and "playing God" is an unavoidable responsibility, presumably one to be shouldered by clinical investigators.[17]

Another distinguished scientist who made no secret of his skepticism toward the notion that the investigator's discretion could be supplemented by third parties was Louis Lasagna. In 1971 Lasagna wondered "how many of medicines greatest advances might have been delayed or prevented by the rigid application of some currently proposed principles to research at large."[18] Rather, "for the ethical, experienced investigator no laws are needed and for the unscrupulous incompetent no laws will help...."[19] When the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research proposed a moratorium on prison research in 1977, Lasagna editorialized that the recommendations "illustrate beautifully how well-intentioned desires to protect prisoners can lead otherwise intelligent people to destroy properly performed research that scrupulously involves informed consent and full explanation and avoid coercion to the satisfaction of all but the most tunnel-visioned doctrinaire."[20]

It is perhaps worth noting that both Beecher and Lasagna had good reason to reflect on the problem of research ethics, stemming from some work they did together. Between 1952 and 1954 Louis Lasagna had been a research assistant in an Army-sponsored project, directed by Beecher, in which hallucinogens were administered to healthy volunteers without their full knowledge or consent. Recalling the episode for the President's Advisory Committee on Human Radiation Experiments in 1994 interview, Lasagna reflected "not with pride" on the study.[21]

Tuskegee Changes All

Among those who developed an interest in research ethics during the 1960s was Princeton theologian Paul Ramsey. Although Ramsey is today remembered as one who took a relatively hard line on research protections, and he did in fact significantly advance the intellectual respectability of a protectionist stance, in retrospect his position seems remarkably modest. In his landmark 1970 work, *The Patient as Person*, Ramsey declared that "No man is good enough to experiment upon another without his consent."[22] In order to avoid the morally untenable treatment of the person as a mere means, the human subject must be a partner in the research enterprise. However, Ramsey was prepared to accept unconsented treatment in an emergency, including experimental treatment that might save life or limb. He also acceded to the view that children who cannot be helped by standard treatment may be experimental subjects if the research is related to their treatment and if the parent consents.

By 1970 the notion that consent was ethically required was well-established in principle (including surrogate consent for children and incompetents), however poorly executed in practice. Ramsey's contribution was in calling attention to the problem of nonbeneficial research participation, a decision that required at a minimum the human subject's active participation. As though to underline the point, only two years after Ramsey's book was published the Tuskegee Syphilis Study scandal broke into the open, a case in which the subjects were clearly not informed participants in the research. The subsequent federal review panel appointed to review the study, the Tuskegee Syphilis Study Ad Hoc Panel, concluded that penicillin therapy should have been made available to the participants by 1953. The panel also recommended that Congress create a federal panel to regulate federally sponsored research on human subjects, a recommendation that foreshadowed and helped define the later transition from weak to moderate protectionism.

A casualty of the syphilis study was the attitude exemplified in the 1967 essay of Walsh McDermott and the 1969 paper by Louis Lasagna. In the years immediately following Beecher's 1966 article it was still possible to argue that scientists should take responsibility to make what McDermott regarded as appropriately paternalistic decisions for the public good, decisions that recognize that societal interests sometimes take precedence over those of the individual. Although there clearly are instances in which this general proposition is unobjectionable, following the syphilis study such an argument became much harder to endorse in the case of human experiments.

As the implications of the Tuskegee revelations became apparent, philosopher Alan Donagan published an essay on informed consent in 1977 that symbolized the altered attitude. In Donagan's essay the invigorated informed consent requirement is taken as nearly a self-evident moral obligation in clinical medicine. In his discussion of informed consent in experimentation, Donagan explicitly compared the arguments of a Nazi defense attorney with those of McDermott and Lasagna, concluding that they are both versions of a familiar and (one infers), a rather primitive form of utilitarianism. Donagan concluded that, by the lights of the medical profession itself, the utilitarian attitudes instanced in the Nazi experiments and the Brooklyn Jewish Chronic Diseases Hospital case, cannot be justified. Perhaps still more telling about the evolution of the moral consensus concerning research ethics is the mere fact that Donagan, a highly respected moral philosopher and not an easily marginalized "zealot," could associate the arguments of Nazis with those of some of America's most highly regarded physicians. Donagan's essay underlined a leap in the evolution of protectionism through the Tuskegee experience, especially on the question of the balance between the subject's interests and those of science and the public, and on the subsequent discretion to be granted the lone investigator.[23]

Social Science Research

Less scholarly and regulatory attention has been given to protecting subjects in social science research than in clinical trials, and it might well be said that the emphases of this paper reflect that deficit. Nevertheless, there have been some spectacular instances in which social science research issues erupted into public debate, though the regulatory response has, again, been modest. Perhaps the most intense reaction in this area was generated by Stanley Milgram's research on obedience to authority.[24] Milgram purported to show that normal subjects could be induced to cause pain to others, or to think that they were, simply by being asked to do so by an individual perceived to be in authority, in this case an experimenter. Although there were criticisms of Milgram's methodology, much of the reaction focused on the harm the study design may have caused the deceived subjects. Also in the early 1970s Philip G. Zimbardo conducted a study of male volunteers' reactions to a mock prison environment in which some of them were assigned roles as prisoners, others as guards.[25] The experiment elicited such strong reactions from the participants, including abuse of the "prisoners" by the "guards," that Zimbardo halted the study. Milgram's study design is more typical than Zimbardo's, in which deception was not an element. Still, both of these cases raise important questions about the relationship between consent and risk.

Deception is an important element of much social psychological research, and is still largely permissible within the framework of a broad consent process. The Ethics Code of the American Psychological Association (APA) requires psychologists to attend to the potential participant's capacity to consent, and to provide sufficient information about the nature of the research. The code bars excessive financial or other inducements, and mandates an explanation of the voluntary nature of research participation. The APA code permits deception only if its use is justified by prospective scientific benefits and alternatives are not feasible. The deception may not pertain to experiences that would affect prospective subjects' willingness to participate.[26] A new subsection, currently under consideration, would allow participants to withdraw their data once debriefed.[27]

Although many of the elements of the APA code reflect the standard protectionist model, in context the code also exhibits familiar tensions between scientific progress and individual interests. The mere fact that deception is permitted, albeit carefully hedged with protections, exemplifies the view that research may often justificably violate the usual moral rule that prohibits lying, and to do so in a highly sophisticated and systematic fashion.

There have also been well publicized cases of important social science research that appear to go beyond deception to outright invasions of privacy. In the course of preparing his landmark (and sympathetic) study *Tearoom Trade*,[28] about homosexual behavior among men of high social standing in a large Midwestern city,

sociologist Laud Humphreys observed men entering a public rest room in a city park, confirmed that they engaged in anonymous homosexual acts, recorded their license tag numbers, and obtained their names from a contact in the bureau of motor vehicles. He was then able to confirm their identity and status in the community. About a year later Humphreys disguised himself and interviewed them in their homes about their personal lives.

Defenders of such research practices argue that they are acceptable so long as the researcher does not disclose the identities of the sometimes unwitting participants. A similar argument may be made for survey research that seeks information concerning intimate and sometimes illegal behavior. Yet one may question whether even knowing participation in potentially embarrassing or, at an extreme, surveys that pose some personal risk to the subjects should be required to undergo more intensive review than is currently the case. Under the Common Rule "survey procedures" are generally considered exempt from protections unless the individual subjects could be identified and "disclosure of the subjects' responses *outside the research* could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation (emphasis added)."[29] As they will generally not be trained as lawyers, one wonders how much assurance either the subject or investigator can have that information about criminal behavior will not be subject to subpoena by a court of law.

Injuries to Research Subjects

One dimension of Beecher's attitude toward protectionism expressed a much stronger position than he was prepared to take with regard to investigator discretion. In 1969 Beecher urged that, because damage to subjects may occur even if all appropriate precautions have been taken, "It is unreasonable to expect that the society which profits actually or potentially should not share in the responsibility for what was done."[30] Writing in *Science* in 1970, a year after Beecher, legal scholar Clark Havighurst argued that societal responsibility would help ensure that unjustifiable risks would not be undertaken if a system would "not only compensate the unlucky subject but also place the burden on those best able to evaluate and control the risks attending the experiment." Though Beecher and Havighurst both advocated a compensation scheme, Havighurst seemed more inclined to design it in such a way that researchers and research agencies shoulder the burden and not simply society at large. In 1973, the Commission on Medical Malpractice recommended that some party—the researcher, the research institution, the research sponsor, or the federal government—should be required to insure research subjects against injuries.[31]

Today, however, researchers are only required to disclose on consent forms whether or not they will provide compensation for research risks.[32] With a few exceptions, such as veterans of the armed forces who may be eligible for compensation for injuries sustained as part of a Veterans Administration study, there is normally no insurance provided against injuries incurred in the course of a study. Instead, it is standard for consent forms to include language to the effect that emergency care will be provided, but that the sponsoring institutions have made no provisions to compensate for research-related injuries. Some consent forms go further. In the words of one: "[the research institution] will not provide you with financial compensation or reimbursement for the cost of care provided to treat a research-related injury or for other expenses arising from a research-related injury. The institution or group providing medical treatment will charge your insurance carrier, you, or any other party responsible for your treatment costs." Although this waiver would presumably not apply to injuries flowing from a successful malpractice claim, not all "adverse events" that result in injury to the research subject can be attributed to malpractice. Under those conditions the failure of any involved entity to take financial responsibility for persons who have answered the call to contribute to scientific progress and the public good is hardly the act of a grateful society. In this area the reality of our practice grievously fails to match even the rhetoric of our protectionist philosophy.

Classified Research

Elsewhere I have explored in detail the history of debates about the ethical problems entailed by research undertaken on sensitive matters related to national security.[33] Much of this discussion took place immediately prior to and during the cold war, and relevant documents have only recently become available to scholars. The upshot of this complex story is that government officials did engage in detailed debates about the rules that should apply, and that policies were in fact articulated, though often they were inadequately implemented. Although direct physical injuries to those involved have been difficult to confirm, the experience has indisputably left behind a legacy of distrust that continues to trouble many Americans and depresses the morale of many in the armed forces.

In response to a 1995 recommendation by the Advisory Committee on Human Radiation Experiments (ACHRE), the Clinton administration issued an executive memorandum requiring that all classified research meet the requirement of informed consent and prior group review. Obviously all involved would have to receive appropriate security clearances, including the subjects themselves. Any IRB member who disagreed with the majority concerning a classified study would have the right to appeal to the head of the sponsoring agency or the President's science advisor. The 17 agencies that have signed onto the Common Rule are now developing an amendment to the regulations that would regularize the requirements set forth in the President's memorandum.

Protectionism Today: An Assessment

On the account I have presented, protectionism is the view that a duty is owed those who participate as subjects in medical research. The underlying problem is how to resolve the tension between individual interests and scientific progress, where the latter is justified in terms of benefits to future individuals. Weak protectionism is the view that this problem is best resolved through the judgment of virtuous scientists. Moderate protectionism accepts the importance of personal virtue but does not find it sufficient. Strong protectionism is disinclined to rely on the virtue of scientific investigators for purposes of subject protection to any substantial degree.

The Common Rule largely relies on a moderately protectionist approach to subject protection. In so doing, it deploys two principle techniques to constrain investigator discretion: informed consent and prior group review. More strongly protectionist approaches, such as monitoring procedures, would gradually impose more direct controls over the actual consent process and the study activities themselves. Data safety and monitoring boards provide some precedent for such intervention, but their primary rationale is as compensation for the methodological necessity of double-blind study design.

In many respects our contemporary system of human subjects protections is a triumph of moderate protectionism. Consider for example the position exemplified in a recent essay on ethics in psychiatric research, in which the authors state that "the justification for research on human subjects is that society's benefit from the research sufficiently exceeds the risks to study participants." But then the authors continue, "potential risks and benefits must be effectively communicated so that potential subjects can make informed decisions about participation."[34] The current battleground, then, is not whether the subjects should in theory be full participants, or whether prior review of experiment proposals should be required, but whether, or to what extent, subjects can take an active role in the clinical trials process. The extent to which such active participation is possible may help to forestall the introduction of more strongly protectionist requirements.

The tone for the current debate was established by the late 1970s and embodied in the work of the National Commission. With the storm of the syphilis study at their backs, the members of the National Commission could go further in specifying protections for research subjects than would have been possible only a few years before. The National Commission made three critical contributions to the protectionist movement:

the establishment of principles underlying human subjects protections; the identification of populations that needed to be singled out for special protections (fetuses, prisoners, children, and the mentally infirm); and the distinction between research and medical practice. The distinction between research and practice is especially important because it goes to the question that I have argued is critical in the emergence of stronger forms of protectionism: the scope of the physician-investigator's discretion. One National Commission recommendation that would have substantially modified the scope of discretion for some investigators was that of the "consent auditor" who, "where appropriate," would be charged by the IRB to observe and verify the adequacy of the consent process for persons institutionalized as mentally infirm.[35]

Nonetheless, the story I have to tell is not one of an inexorable march toward a stronger form of protectionism, even in the past 20 years. Although the tendency since the advent of the Nuremberg Code—greatly strengthened in the United States by the "Belmont Report"—has been to limit the scope of investigator discretion, there have been countervailing forces. One of these has been the Declaration of Helsinki, which uses the concepts of therapeutic and nontherapeutic research, defining the former as "Medical Research Combined with Professional Care." According to Helsinki IV (1989), "If the physician considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee." Thus Helsinki continues to contemplate a relatively permissive attitude toward investigator discretion, as it has since the first version in 1954. Notably, Henry Beecher preferred Helsinki to Nuremberg precisely because the former is a "set of guides" while the latter "presents a set of legalistic demands."[36]

Another force counteracting the tendency to limit investigator discretion has been movements on behalf of greater access to clinical trials. The most pronounced expression of this effort has occurred among AIDS activists, who successfully insisted upon the creation of alternative pathways for anti-AIDS drugs in the late 1980s. In the face of a disease that resisted treatment and struck down people just entering the prime of life, the determination to find solutions was understandable. The slogan of ACT-UP (AIDS Coalition to Unleash Power) that "A Drug Trial is Health Care Too," was a political expression of confidence in the power of science. As well, the slogan betrayed assumptions about the benefits of research participation and the self-discipline of the medical research community, as well as relying on the very protections it sought to undermine. It should be said that activist organizations have largely revised their attitude toward alternative pathways of access to nonvalidated medications.

Other developments at the federal level in the 1980s and 1990s have been more consistent with the trend toward strengthened protections. The President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research made recommendations on the evaluation and monitoring of IRB performance,[37] and also endorsed the proposition that research-related injuries should be compensated.[38] Among the recommendations of the Advisory Committee on Human Radiation Experiments in 1995 were several that addressed improved human subject protections. For example, the ACHRE urged that regulations be established to cover the conduct of research with institutionalized children and that guidelines be developed to cover research involving adults with questionable competence. The ACHRE also recommended steps to improve existing protections for military personnel concerning human subject research. Substantial improvements were urged in the federal oversight of research involving human subjects: that outcomes and performance should be evaluated beyond audits for cause and paperwork review; that sanctions for violations of human subjects protections be reviewed for their appropriateness in light of the seriousness with which the nation takes failures to respect the rights and welfare of human subjects; and human subjects protections be extended to nonfederally funded research. The ACHRE also recommended that a mechanism be created for compensating those injured in the course of participation as subjects of federally funded research.[39]

On May 17, 1997, the National Bioethics Advisory Commission (NBAC) unanimously adopted a resolution that "No person in the United States should be enrolled in research without the twin protections of informed

consent by an authorized person and independent review of the risks and benefits of the research."[40] That same month President Clinton stated that "[w]e must never allow our citizens to be unwitting guinea pigs in scientific experiments that put them at risk without their consent and full knowledge."[41]

Federal Rules and Reports: In Pursuit of Protections

The contemporary presumption that protectionism is and ought to be the governing philosophy of modern human subjects research has been reflected in several federal reports on the efficacy of prevailing research rules in protecting human subjects, especially the adequacy of the IRB system. The IRB concept is predicated on the protectionist assumption that, contrary to the views of Beecher and other earlier commentators, physician authority concerning the appropriateness of research participation must be subject to the formal constraints of a third party, in this case, a committee of peers and laypersons. It may be useful to review the provenance of the IRB system.

Since the passage of the 1974 National Research Act (Public Law 94-348), universities and other research centers have been required to use what it called Institutional Review Boards to protect the rights and welfare of human subjects. Research institutions provide the Department of Health and Human Services with single- or multi-project assurances that their IRBs will apply the federal rules to all federally funded research conducted at the institution or by its employees; many assurances encompass all research with human subjects regardless of sponsorship.

The National Research Act also transferred oversight of research involving human subjects to a new organization within the National Institutes of Health, the Office for Protection from Research Risks (OPRR). In 1974 the Department of Health, Education, and Welfare (DHEW, now DHHS), also adopted regulations (45 CFR 46 under Section 491 of the Public Health Service Act) that made IRBs responsible for determining whether potential subjects are "at risk" in proposed research, and if so, whether the risks outweigh the possible benefits to them and the importance of the knowledge to be gained.

In 1991 a single set of regulatory protections governing human subjects research was adopted by sixteen federal departments and through an executive order, applied to the Central Intelligence Agency as well. These general provisions are known as the Common Rule, and are identical to the basic DHHS policy for the protection of research subjects, 45 CFR 46, subpart A. Subsequently, the Food and Drug Administration (FDA) changes in its informed consent and institutional review regulations to bring them into general conformity with the Common Rule.

However, in March 1996 the United States General Accounting Office (GAO) published "Scientific Research: Continued Vigilance Critical to Protecting Human Subjects."[42] Conceding a lack of systematic studies of government efforts to ensure compliance with human protections standards, the report found that the current activities generally work to prevent harm to research participants. Through interviews with individuals familiar with the system, the GAO report anticipated a number of themes that resurfaced in subsequent studies. It stated that the oversight system is "impaired by IRBs' heavy workloads and competing demands, limited funds for on-site inspections, the complexity and volume of research under review, and reliance on researchers' self-assurances that they are complying with requirements."

In the same spirit as the GAO report, in June 1998 the Department of Health and Human Services Inspector General (IG) published, "Institutional Review Boards: A Time for Reform." The IG report was organized in four separate documents, one an "Overview and Recommendations," and the others on different aspects of the current status of IRBs: "Their Role in Overseeing Approved Research," "The Emergence of Independent Boards," and "Promising Approaches."[43] The IG recommendations included several that would reform federal IRB requirements so that they would have more flexibility but also more accountability. To strengthen IRB

oversight the IG suggested mandating Data Safety Monitoring Boards (DSMBs) for multi-site trials. It would also require the FDA to inform IRBs about sanctions against investigators, and sponsors and investigators to inform them about prior IRB review of a research plan. The report recommended that IRBs increase their awareness of actual research practices by visiting study sites. Although the authors noted that such observations would represent a departure from the historic relationship between IRBs and investigators, in fact IRBs already have the authority to conduct active monitoring, though this is rarely done.

The report also recommended that both investigators and IRB members receive training in research ethics. To this end, it urged that the Public Health Service require that all its grantee institutions have a program to train investigators in human subject protections, similar to the current NIH requirement for trainees. Investigators should be required to sign a written attestation that they are familiar with and will uphold federal subject protection policies, and institutions should certify that there is a continuing education program for IRB members. There were also recommendations concerning conflicts of interest, workload pressures on IRBs, and strengthening the federal capacity to deal with IRB performance problems as they arise.

The Inspector General noted the increase in independent or private IRBs, which are created outside of organizations that conduct research in order to satisfy federal requirements for board review of clinical research proposals. Although these boards are more efficient than traditional research center-based IRBs, they are not the sort of local review bodies envisioned in previous understanding of human subjects protections. They are also alleged to contribute to conflict of interest concerns and worries about the potential for "IRB shopping," in which sponsors go from one board to the next until they find one that approves their study.

The Inspector General concluded that the IRB system is in jeopardy because the local boards are overworked, they fail to oversee approved studies, their members lack sufficient training, and they face inherent conflicts of interest. These problems persist, the IG report continued, because the Office for Protection from Research Risks and its counterparts in other departments have neither the resources nor the independence to provide adequate guidance to IRBs, much less to monitor their activities. Two years after the 1998 report, in April 2000, the Inspector General expressed her concern that in the intervening years there had been "minimal progress in strengthening continuing protections for human subjects participating in research." Some "promising steps" have been taken by NIH, however, including a new requirement that DSMBs share information with IRBs, new initiatives for IRB member and investigator education, and a website of bioethics resources.[44]

Although I am largely in agreement with the Inspector General's continuing criticisms of the current system—especially with regard to the lack of fit between the current research environment and the decades-old IRB arrangement, the need for IRB member and investigator education, and increased study monitoring—the extent of the problem should not be exaggerated. It is worth recalling some of the conclusions of the only comprehensive empirical study of the IRB system, the 1998 report of the NIH Office of Extramural Research, which found that about 10 percent of IRBs review nearly 40 percent of the protocols, indicating that the large academic research centers are especially hard pressed. This result is somewhat reassuring insofar as it suggests that the problems are mostly manageable and found at institutions that have considerable stocks of human (if not financial) resources to deal with them.[45]

One population that the National Bioethics Advisory Commission itself singled out for special protection is that of persons with mental disorders that may affect decisionmaking capacity. In its December 1998 report the NBAC issued a number of recommendations concerning IRB approval of research proposals involving this population. The report recommended that IRBs reviewing such proposals have two members familiar with the concerns of persons with mental disorders in research, and that protocols should not include persons from this population in research if the research can be done with others. It would also have IRBs look for specific elements of protocols before granting approval to clinical studies with this population, for example, that the capacity assessment of potential subjects is conducted by a psychiatrist not involved in the research, and that investigators specify methods for minimizing risk and evaluate risks and benefits.

The NBAC report also recommended the creation by the DHHS Secretary of a Special Standing Panel (SSP) on research involving persons with mental disorders that may affect decisionmaking capacity. The SSP would review research that could not otherwise be approved with this population under the NBAC recommendations and promulgate guidelines for local IRBs that may reduce the need for SSP approval. The SSP thus has some characteristics that may apply to a national human subjects office, although the report did not address the broader role of such an entity.

Confidentiality

Considering that patient confidentiality is perhaps the most ancient and deeply held moral value in medicine, it may be surprising that modern protectionism, at least as expressed in the bioethical literature, has had relatively little to say about this topic. A classic paper by Siegler in 1982 depreciated confidentiality as a realistic attribute of modern medical institutions and may have served to dampen interest in the topic. In support of his suggestion that confidentiality may be a "decrepit" concept in practice, Siegler found that at least 75 individuals in one academic medical center had legitimate access to a patient's chart.[46]

At the policy level, some protection of medical information is afforded by the 1974 Federal Privacy Act (P.L. 93-579), and the National Privacy Commission filed a report in 1976, but there is still no comprehensive federal legislation to protect medical information. The protection of sensitive information stemming from clinical research is to some degree covered by the Public Health Service Act. The Act "provides for 'certificates of confidentiality' which offer a legal basis for protection against civil, criminal, administrative, legislative, or other proceedings to force disclosure of personally identificable data."[47] However, the certificate system places a higher burden on the claim of confidentiality than is usually thought to be required in physician-patient relations.

Several factors have motivated a renewed concern about confidentiality protections, including utilization review as part of "gatekeeping" strategies in the proliferating managed care marketplace, the increasing use of electronic records, and the foreseen integration of genetic data into patient histories. Specifically with regard to clinical trials, the need to recruit larger numbers of subjects for more complex studies makes access to patient records an attractive opportunity to identify medically appropriate potential subjects. Individuals sought for studies that attempt to measure the prevalence of genetic alterations in a population may also feel themselves to be at risk if positive test results become known.

In spite of longstanding expressions of concern about the privacy of electronic records and genetic information in particular, it has been difficult to achieve agreement on confidentiality standards. The continuing confusion about medical records and confidentiality protections is reflected in the current debate about rules currently proposed by the Department of Health and Human Services. In 1996, Congress passed a law that required DHHS to issues rules protecting medical records that were transmitted through computers if Congress itself failed to pass legislation on medical privacy with a certain period. As the self-imposed deadline came and went last year with a new law, the rule-making process was triggered.

The proposed rules would give patients the right to view and amend their medical records, and require physicians and health care institutions to give notice of their intent to use medical information and track that which is disclosed. They would also make health plans and insurers responsible for monitoring the activities of outside contractors who have access to patient data. However, some critics charge that there would be no informed consent for access to records if they are being used for treatment, to obtain payment for health care services, or for what the proposed rules call "health care operations." In some cases the rules would also enable health care providers to release medical information to policy, employers, government data banks, and researchers without consent.[48]

Apart from the limits of the currently proposed rules, a comprehensive approach to the problem of confidentiality of data gathered in the course of research probably cannot avoid confronting the problem posed by

the Common Rule's narrow definition of research: "a systematic investigation designed to develop or contribute to generalizable knowledge." Under this definition there are numerous "nonresearch" projects that systematically collect and utilize data from medical records, including program evaluations in public health and utilization review in health services management.[49] Semantic niceties should not be allowed to circumvent the legitimate public policy goal of maintaining the confidentiality of medical information.

Summary and Recommendations

The current system of human subjects protections in the United States, formally embodied in the Common Rule, is expressive of a moderately protectionistic philosophy of research ethics. For example, I have asserted that the first critical issue in a system that regulates human subjects research is the relationship between the interests of the subject and those of science and "future patients." The common rule permits legally competent individuals to consent to research participation even though it is not designed to benefit them, but the risks must fall within an acceptable range as determined by an IRB. A weakly protectionist philosophy could dispense with IRB approval, while a strongly protectionistic approach might not find informed consent for certain kinds of research acceptable, even with IRB approval (owing, perhaps, to institutional or other pressures that are substantial but may not rise to the level of coercion or manipulation).

The second critical issue that determines the level of protectionism in a human subjects research regulatory system is whether and in what manner the conduct of the investigator may be monitored or controlled by third parties. The current system in the United States is again moderately protectionistic in this respect because it requires prior review of protocols by an IRB and permits the IRB to engage in concurrent monitoring of the study itself. Thus it provides more protection than a system that places a greater burden on the virtue of the individual investigator, as advocated by Beecher and other early commentators. But the common rule currently provides less protection than a system that requires external assessment of the consent process. A step in this direction is exemplified in NBAC's recommendation that an independent assessment should be sought for a potential subject's capacity to consent to research protocols involving greater than minimal risk, in cases when that subject has a mental disorder that may affect decision making capacity.[50] However, institutional resistance to the National Commission's related proposal for consent auditing for those institutionalized as mentally infirm in 1978 suggests that more protectionist proposals have long been against the grain of our system and does not augur well for NBAC's recommendation.

A system that attempts to balance scientific advancement with the interests of individuals (while holding the latter as ultimately constraining the former) is bound to require continuous reinterpretation and "tuning up." The following recommendations are therefore made in an evolutionary spirit and presume that our society is, in its collective judgment, currently moving toward a more vigorously interventionist interpretation of what remains at bottom a moderately protectionist attitude toward the regulation of clinical trials. At the same time, they do not presuppose significant changes in the attitudes of the clinical research community, which can be relied upon to continue to resist, not wholly without merit, regulation that it perceives as creating bureaucratic obstacles rather than genuine protections.

Informed Consent

NBAC should reaffirm its 1997 resolution that "No person in the United States should be enrolled in research without the twin protections of informed consent by an authorized person and independent review of the risks and benefits of the research,"[51] and should further resolve that this standard become federal law.

There is no good reason—moral, constitutional, or financial—to do without a federal law that guarantees these protections regardless of the source of funding or sponsorship. The Common Rule already serves as a

virtual common law standard and scientific researchers who work with human subjects would be foolish indeed to ignore informed consent, no matter who is supporting their projects. Specific provision should be made for a requirement of informed consent for classified research.

Financial Conflict of Interest

Investigators should be required to disclose to potential subjects any financial interests in the research.

The disclosure of financial interests that could reasonably be construed as presenting conflicts is a well-recognized duty in other professions. Considering the growing proportion of research that is privately funded and the commercial nature of much of this research, the exceptionalism traditionally granted to physicians with respect to financial disclosure is hard to justify. Possible delays in recruiting subjects for promising research and embarrassment on the part of investigators are not acceptable reasons for failure to bring this information to light. In fact, subjects themselves will likely find this information less interesting than IRBs, who will have to face the problem of determining whether certain financial arrangements should be modified.

Decisionmaking Capacity

Investigators should be required to explain to IRBs how they will assess decisionmaking capacity on a continuing basis for persons known to have a history of diminished capacity or are likely to lose capacity for a significant period during a study.

Capacity assessments should not be a windowless box within which investigators have unlimited discretion, particularly considering that important human rights are engaged when persons are exposed to circumstances (regardless of level of risk or theorized benefit) to which they might not otherwise agree. Research involving persons with questionable capacity to consent will increase as new experimental medications to treat neurologic and psychiatric disorders become available, and as new treatment for those who are gravely ill is developed. It is not an undue burden to ask investigators to document a procedure that, presumably, must already be part of their ethically conducted research.

Surrogate Consent

States should clarify the circumstances under which a legal authorized representative (LAR) may give permission for research involving a person who lacks decisionmaking capacity, and whether individuals may give advance authorization for such research if they should lose decisionmaking capacity.

Currently there is often uncertainty about who can function as a LAR under state law and about the scope of their decisionmaking authority. As a result, many clinicians are operating in legally and morally ambiguous territory. In particular, states should clarify whether a LAR has the authority to authorize important research that poses some risk to the subject without the prospect of direct benefit to that person. States should also consider whether individuals should be able to express their wishes concerning such research participation while they still have the capacity to express themselves.

Research Risks

The NBAC or another appropriate federal panel should design and recommend an indemnification system for persons injured in the course of participation as subjects in clinical trials.

Consent forms commonly warn that the sponsoring institution cannot be responsible for injuries incurred as a result of the study. Whatever their legal status, from a moral standpoint these warnings have a distinctly hollow ring, and leave the impression that our society places little value in the willingness to be part of the research enterprise. The recommendations of the 1973 Commission on Medical Malpractice should be revisited and a scheme for insuring persons against the risk of injuries sustained due to research participation should be devised.

Confidentiality

Federal research regulations should provide for clear and unambiguous limitations to access to medical records linked to individuals.

Those who agree to be subjects in medical research should not have to be concerned about the disposition of data with implications about their health status that may be obtained in the course of a study. Regulations should clearly prohibit unconsented access and release of medical records, including those accumulated in a research context, that can be associated with identified individuals. Activities that skirt the definition of research, such as "program evaluations" in public health and "quality assurance" in managed care, should be subject to scrutiny. Effective action in this area may require that the statutory definition of research, couched in terms of "generalizable knowledge," be revisited.

IRB Activities

IRBs should be required to register with the Office for Protection from Research Risks, to compile annual data on the number of research proposals reviewed and the number approved, and the number of subjects in research that has been approved.

Many have commented on the peculiarity that more is known about Animal Care and Use Committee activities than is known about IRB activities. These modest requirements would help to correct that imbalance.

Education

All IRB members should receive initial and continuing education in the history and philosophy of human subjects research, in the current regulations governing such research, and in current issues in the field. Familiarity with federal human subjects protections should also be required of researchers who function as principle investigators.

Many observers have noted wide disparities in the familiarity of IRB members with the regulations they are responsible for interpreting and enforcing. Similarly, investigators should be aware of the rules that condition their work. Current initiatives to create accreditation programs for institutions and their research review system should serve as an impetus on the IRB side. Further measures may be required to help ensure investigator familiarity with the regulations, such as a signed attestation as part of the material submitted for IRB review.

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