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**STATEMENT BY
INDIVIDUAL COMMITTEE MEMBER
JAY KATZ**

We were assigned two tasks: to examine the past and to examine the present. Telling the full story of government sponsored Cold War human radiation experiments serves many important purposes--remembrance, warning, healing. Ultimately, however, the value of knowing the past resides in the lessons it can teach us for the present and future. Thus, the central question is this: Do current regulations of human experimentation adequately protect patient-subjects? Here I have the most serious reservations about our Report.

In summary, my conclusions are these: (1) In the quest to advance medical science, too many citizen-patients continue to serve, as they did during the Cold War period, as means for the sake of others. (2) The length to which physician-investigators must go to seek "informed consent" remains sufficiently ambiguous so that patient-subjects' understanding of the consequences of their participation in research is all too often compromised. (3) The resolution of the tensions inherent in the conduct of research--i.e., respect for citizen-patients' rights to, and interest in, self-determination on the one hand and the imperative to advance medical science, on the other--confronts government officials with policy choices that they were unwilling to address in any depth during the Cold War or for that matter in today's world. (4) Our Recommendations only touch on these problems and at times make too much of the safeguards that have been introduced since 1974. The present regulatory process is flawed. It invites in subtle, but real, ways repetitions of the dignitary insults which unconsenting citizen-patients suffered during the Cold War.

Medical research is a vital part of American life. The Federal government allocates billions of dollars to human research, and the pharmaceutical industry spends many more billions to develop new drugs and medical devices. And research is by and large conducted with patients. Since all of us at one time or another will be patients, we are readily available subjects for research. Thus, the protection of the rights and interests of citizen-research subjects in a democratic society is a major societal concern.

Let me introduce my Reservations by offering some preliminary remarks about the current regulatory scheme and the history of consent. The contemporary regulatory scheme provides insufficient guidance for addressing one basic question: When, if ever, should conflicts between advancing medical knowledge for our benefit and protecting the inviolability of citizen-subjects of research be resolved in favor of the former? Inviolability, unless patient-subjects agree to invasions of mind and body, requires punctilious attention to disclosure and consent and, in turn, imposes considerable burdens on physician-investigators--be it taking the necessary time to converse with patient-subjects or, if necessary, making discomforting disclosures. Moreover,

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taking informed consent seriously may slow the rate of medical progress with painful consequences to investigators' work and to society. These dilemmas must be resolved forthrightly, instead of allowing them to be "resolved" by discretionary subterfuge.

Neither the drafters of the 1974 Federal Regulations nor the members of the research community were willing to respond to the reality that taking informed consent seriously in this new age of informed consent confronted them with problems that required sustained and thoughtful exploration. Implementation would also turn out to be a most formidable task because of physicians' low regard for patient consent throughout medical history. The Committee's analysis of the informed consent requirements in existence during the Cold War and earlier in the 20th century acknowledges, but not sufficiently so, that the millennia-long history of medical custom casts a dark shadow over what transpired during the Cold War.

Patient consent, until most recently, has not been enshrined in the ethos of Hippocratic medicine. As I once put it, the idea of patient autonomy is not to be found in the lexicon of medicine. It is important to be aware of this history; for it explains why our Findings on contemporary research practices, which time constraints prevented us from probing in sufficient depth, revealed deficiencies in the informed consent process, both at the levels of physician-investigator interactions with their patient-subjects and of IRB review. This is not surprising; for not only does it take time to change historical practices, it also requires more thoughtful rules and procedures than currently exist.

My reading of the Cold War record suggests that governmental officials in concert with their medical advisers at best paid lip service to consent. Whenever they considered it, they worried mostly about legal liability and embarrassment. They were not worried or embarrassed about their willingness to conscript unconsenting patient-subjects to serve as means in plutonium and whole body radiation experiments. All this is a frightening example of how thoughtlessly human beings, including physicians, can treat human beings for "noble" purposes. Most references to consent (with rare exceptions) that we uncovered in governmental documents or in exchanges between officials and their medical consultants were meaningless words, which conveyed no appreciation of the nature and quality of disclosure that must be provided if patient-subjects were truly to be given a choice to accept or decline participation in research. Form, not substance, punctuated most of the policies on consent during the Cold War period. The drafters of the Federal Regulations would eventually build their rules on this shaky historical foundation, disregarding in the process that the imprecision of their policies invited physician-investigators not to alter decisively customary Hippocratic practices.

The long established tradition of obtaining consent from healthy subjects is a separate story; for this tradition did not extend to patients or patient-subjects. Put another way, the latter were quarantined from disclosure and consent. In our Finding 10, this was clearly stated: "[D]uring the 1944-1974 period . . . physicians engaged in clinical research generally did not obtain consent from patient-subjects for whom the research was intended to offer a prospect of medical benefit." Therefore, it should come as no surprise, as noted in our Report, that when a decision was reached in 1951 not to pursue radiation research with prisoners or healthy subjects in connection with an important defense project, "the military immediately contracted with a private

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hospital to study patients being irradiated for cancer treatment." Patients have always been the most vulnerable group for purposes of research.

From the perspective of history no significant conclusions can be drawn about ethical consent standards that "should" have existed for research with *patients* by drawing attention to consent requirements that existed for *healthy volunteers*. When persons became patients, the rules of consent changed. This observation also has relevance for the impact of the Nuremberg Code on the conduct of research. The Code emerged from contexts not only of research with non-patients but also of sadistic and brutal disregard for the sanctity of human life, unparalleled in the annals of Western research. American physician-investigators, therefore, found it doubly easy to consider the pronouncements of the Allied Military Tribunal irrelevant to their practices.

Let me interject here a few brief remarks about risks: Taking risks is inevitable in research. After all, research is by its nature a voyage into the unknown. To pierce uncertainty, to gain scientific knowledge requires risk taking. And, as our Report makes clear, physician-investigators and government officials as well have generally been attentive, whenever physical risks needed to be taken, to minimize them. But such care notwithstanding, research requires taking risks; for example, research with highly toxic agents affects the quality and extent of remaining life. In our review of contemporary research we identified many instances where patient-subjects were unknowingly exposed to such risks, which have both physical and emotional dimensions.

Scientific studies in today's world often involve patient-subjects whose prognosis is dire--the most vulnerable of all disadvantaged groups--and for whom no effective or curative treatments exist. In these situations hope can readily be exploited by intimating that research interventions *may* also benefit patient-subjects, even though the experiment's objectives are in the service of gaining scientific knowledge. Embarking on this slippery slope begins with investigators' rationalizations which justify experimental interventions on grounds of "possible" therapeutic benefits; it continues with apprising patient-subjects insufficiently of the slings and arrows of the experimental component; and it ends with feeding into patient-subjects' own dispositions to deny the truth. In sum, by obliterating vital distinctions between therapy and research, investigators invite subjects to collude with them in the hazy promise of therapeutic benefits. Put another way, the "therapeutic illusion," as one commentator felicitously called it, can lead physician-investigators to emphasize the possible (though unproven) therapeutic benefits of the intervention and, in turn, to minimize its risks, particularly to the quality of (remaining) life. Such considerations played a role in the total body radiation experiments discussed in our Report.

In my Reservations I want to emphasize, however, the centrality of dignitary, not physical, injuries in any appraisal of the ethics of research. This is the uncompromising message of the Nuremberg Code's first principle on voluntary consent, a message which during the Cold War period physician-investigators found impossible to accept. But the problem goes deeper than that. The Code, without extensive exegesis, could not serve as a viable guide for the conduct of medical research. This made its disregard easy and in the process, the central message which the judges tried to convey in their majestic first principle was also lost. Thus too much can be made, as our Report does, of Secretary of Defense Wilson's memorandum endorsing the Nuremberg

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Code. To hold him culpable for not *implementing* the Code makes little sense. If he is culpable of anything, it is for *promulgating* it without first having sought thoughtful advice about what needed to be explicated to make it a viable statement for research practices. Merely embracing the Code invited, indeed guaranteed, neglect.

Finally, from the perspective of history I want to note that only since the early 1960's was the importance of consent given greater attention. Among the social forces that contributed to this development two stand out: Judges' promulgation of a new legal doctrine of informed consent, based on the Anglo-American premise of "thoroughgoing self-determination." And the explorations by a new breed of bioethicists, recruited from philosophy and theology, of the relevance of such principles as autonomy, self-determination, beneficence, and justice to medical decision-making. Their novel and powerful arguments, so alien to the medical mind, disturbed the sleep of the medical community. Physicians had a particularly hard time in coming to terms with the idea of patient autonomy. To this day, I believe, this principle has only gained a foothold in the ethos of medical practice and research.

In our Report we emphasize the primacy of patient-subject autonomy in research. It led us to conclude in our Interim Report that "[a] cornerstone of modern research ethics [is] informed consent." I agree with this statement of principle. From the 1963 beginnings of my work in human experimentation, I have championed the idea of respect for autonomy and self-determination in all interactions between physician-investigators and patient-subjects. But I introduced one major qualification when I wrote that only when the Nuremberg Code's first principle on voluntary consent

is firmly put into practice can one address the claims of science and society to benefit from science. Only then can one avoid the dangers that accompany a balancing of one principle against the other that assigns equal weight to both; for only if one gives primacy to consent can one exercise the requisite caution in situations where one may wish to make an exception to this principle for *clear and sufficient* reasons.

I mention this here because the final and most far-reaching recommendation for change that I shall soon propose is based on two premises: (1) that any exception to the principle of individual autonomy, since it tampers with fundamental democratic values, must be rigorously justified by clear and sufficient reasons; and (2) that such exception cannot be made by investigators or IRBs but only by an authoritative and highly visible body.

I now turn to our Research Proposal Review Project. The Committee's review of contemporary research reveals that of the greater-than-minimal-risk studies (which are the ones that raise complex informed consent issues) 23% were ethically unacceptable and 23% raise ethical concerns. My own independent review tells a grimmer story: 50% raise serious ethical concerns and an additional 24% raise ethical concerns that cannot be taken lightly. Since I focused exclusively on the informed consent process, the differences in our Findings can perhaps

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in part be explained on that basis. My data, like the Committee's, were the protocols submitted to IRBs and the informed consent forms signed by patient-subjects. I appreciate that the evidence available to us does not reflect what patient-subjects might have been told during oral communications. But if the protocols and patient-subject consent forms are flawed in significant ways, it is likely that the oral interactions are similarly flawed. Moreover, since IRBs are charged to pay particular attention to the informed consent process, I contend that IRBs should not have approved the problematic consent forms in the form they were submitted. The forms often seem to "sell" research rather than to convey a sense of caution that invites reflective thought.

I had expected to discover problems, but I was stunned by their extent. Consider what we observed in Chapter 15 and what is described there in greater detail: The obfuscation of treatment and research, illustrated most strikingly in Phase I studies, but by no means limited to them; the lack of disclosure in randomized clinical trials about the different consequences to patient-subjects' well being if assigned to one research arm or the other; the administration of highly toxic agents, in the "scientific" belief that only the knowledge gained from "total therapy" will eventually lead to cures, but without disclosure of the impact of such radical interventions on quality of life or longevity. I do not wish to minimize the impact of making total disclosure on patient-subjects' and physician-investigators' hopes and fears. Yet, nagging questions remain: What are "clear and sufficient reasons" which permit tampering with disclosure and consent; and, if permissible, who decides?

Our Recommendations do not go far enough in remedying the flawed nature of our current regulations which appear to rely so heavily on informed consent, but which in practice I contend, bypass true informed consent. Here I can only make a few comments about the changes required if we wish to protect adequately the rights and interests of subjects of research:

(1) *Informed consent* is central to such protections. The drafters of the Federal regulations have acknowledged that fact. They have failed, however, to take responsibility for making these requirements meaningful ones. Thus, patient-subjects now all too often give a spurious consent; a "consent" that can readily mislead physician-investigators into believing that they have received the authority to proceed when in fact they have not.

(a) The Federal regulations imply that the principle of respect for patient-subjects' autonomy is central to the regulatory scheme. Leaving it at that is not enough; for the principle requires commentary so that physician-investigators will have a more thoroughgoing appreciation of the moral issues at stake whenever they ask human beings to serve as means for the ends of others. Only then will they learn, for example, that to take informed consent seriously requires them to spend considerable time with prospective patient-subjects and to engage them in searching conversations. In these conversations they must disclose (a) that their subjects are not patients or, to the extent they are patients, that their therapeutic interests will be subordinated in specified ways to scientific interests; (b) that it is problematic (and in what ways) whether their welfare will be better served by placing their medical fate in the hands of a practitioner rather than a physician-investigator; (c) that in opting for the care of a physician they may be better or worse off and for such and such reasons; (d) that research is governed by a research protocol and a research question and therefore patient-subjects' interests and needs have to yield (and to what

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extent) to the claims of science; etc.

Such disclosure obligations are formidable ones. They need to be fulfilled in a manner that will give patient-subjects a clear appreciation of the difference between research and therapy, and in the spirit that disabuses them of the belief, so widely held--as our Subject Interview Study demonstrates-- that everything the investigator proposes serves their best therapeutic interests.

The Cold War experiments teach us that misplaced trust can deceive; that trust must be earned by prior disclosures of what research participation entails. I agree, as our Recommendation 9 proposes, that scientists should be educated "to ensure the centrality of ethics in [their] conduct." To accomplish that educational task, however, requires policies that more clearly delineate the ambit of discretion which investigators can exercise in the conduct of research.

(b) Current criteria for informed consent encourage, perhaps even mandate, overwhelming patient-subjects with information on every conceivable risk and benefit as well as on the scientific purpose of the study. Adherence to these mandates has led, and justifiably so, to concerns about the incomprehensibility of the informed consent forms that patient-subjects must sign. Much thought, and then guidance, has to be given to IRBs and investigators as to the essential information they must provide; e.g., alternatives, uncertainties, essential risks, realistic benefits as well as the impact of participation--known and conjectured--on the quality of future (or remaining) lives. Many of the informed consent forms I have examined fail to emphasize the risks germane to the research protocol; instead they go into numbing detail on risks that can be summarized. To put it bluntly: Informed consent criteria in today's world, at least in the ways they are communicated to patient-subjects, often serve purposes of obscuring rather than clarifying what participation in research entails.

(2) Though IRBs serve important functions, they do not have the capacity, if only by virtue of composition and lack of time, either to modify consent standards (including the ones I have just proposed) or, more generally, to make any other decisions that could affect the fundamental constitutional rights and personal interests of subjects of research. IRBs should not have the authority to decide how to balance competing principles in situations where the competence of subjects' consent is in question, or where consent cannot be obtained because patient-subjects suffer from a life-threatening condition, or where other complex issues need to be resolved, as illustrated in our Chapter on the total body radiation experiments. Such fateful decisions are beyond their competence.

Moreover, IRBs work in a climate of low visibility, another species of secrecy about which we expressed so much concern in Chapter 13. These and other complex ethical problems should only be resolved by an *accountable* and highly *visible* national Body. That Body then can provide IRBs with guidelines that will better inform their deliberations. I would like to note here, but only in passing, that the Body I envision will lighten IRBs' tasks; for example, by fashioning policies for cursory review of the many minimal/no risk studies, or by being available for advisory opinions whenever IRBs are confronted with new ethical problems. (IRBs now spend an inordinate amount of time on such problems which they should not resolve in the first place.) The national Body should not review individual research projects except when investigators and IRBs

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disagree. Finally, a national Body is needed for another reason as well: The considerable pressure for approval of protocols to which IRBs are subjected by the scientists at their institutions.

(3) Already in 1973, when I served on HEW's Tuskegee Syphilis Study Ad Hoc Advisory Panel, we proposed in our Final Report that Congress establish a permanent body--we called it the *National Human Investigation Board*--with the authority to regulate at least all Federally supported research involving human subjects. We recommended that this Board should not only *promulgate* research policies but also *administer* and *review* the human experimentation process. Constant interpretation and review by a Body whose decisions count by virtue of the authority invested in them can protect both the claims of science and society's commitment to the inviolability of subjects of research.

A most important task which such a Board would face in formulating research policies is to delineate exceptions to the informed consent requirement when competing principles require it. For example, when might it be permissible for IRBs to "defer consent" (or more correctly, to allow physician-investigators to proceed without consent) with patient-subjects suffering from acute head trauma? Conscripting citizen-patients to anything they have not consented to is deeply offensive to democratic values and, if necessary, requires public approval. Greater public participation in the formulation of research policies is vital, and the Board must therefore establish procedures for the publication of all its major policy and advisory decisions, particularly those where compromises seem warranted between the advancement of science and the protection of subjects of research. Publication of such decisions would not only permit their intensive study both *inside* and *outside* the medical profession but would also be an important step toward the case-by-case development of policies governing human experimentation. If we are truly concerned about the baneful effects of secrecy on public trust, what I propose here could restore trust.

There is, of course, much more to consider, and I have written about it elsewhere. I hope, however, that I have said enough to suggest that the problems inherent in research with human subjects--advancing science and protecting subjects of research--are complex. Society can no longer afford to leave the balancing of individual rights against scientific progress to the low-visibility decision-making of IRBs with regulations that are porous and invite abuse. The important work that our Committee has done in its evaluation of the radiation experiments conducted by governmental agencies and the medical profession during the Cold War once again confronts us with the human and societal costs of too relentless a pursuit of knowledge. If this is a price worth paying, society should be forced to make these difficult moral choices in bright sunlight and through a regulatory process that constantly strives to articulate, confront, and delimit those costs.

We have judged the past and judgments of the past become most relevant when they teach us lessons for the present and future. Yet, we did not judge the present with sufficient care. If the problem was time, I wanted to take the time to offer my judgments. I also took the time and "took [the road] less traveled by" because much is at stake in the quest for advancing medical science that speaks not only to progress in the conquest of disease but to other moral values as well.