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**Herein of Scandal and Advancement:
A Chronicle of Human Experimentation in the United States**

Whitney Lee Aidenbaum
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This paper is submitted in satisfaction of the course requirement.

Abstract

An account of the history of human experimentation in the United States necessarily involves a recounting of scandals and the research policies that developed in response. This paper aims to provide a review of this history, along with observations about recurring themes that pervade the narrative. In so doing, this author hopes to provide a useful reference, and also to reveal the inherent tensions and difficult problems posed by the conduct of research using human subjects.

In June 1769, 29-year-old physician William Stark began a new diet. For 12 weeks he lived on bread and water with little sugar. William became “dull and listless,” and his gums were swollen and bled easily. In the following three weeks he “quite recovered” by varying his diet. Then he returned to a diet of bread or flour, with various supplements such as olive oil, butter, suet, a little cooked lean meat, and honey. By the end of December, his gums again became purple and swollen. On February 23, William died.¹ Most likely, William Stark died of scurvy. In fact, his diet was an experiment to test the effects of simplified diets on health, for it was surmised that a deficiency of vitamin C could explain the onset of scurvy.²

In October 1939, John Crandon, a resident surgeon at Harvard Medical School, used himself as an experimental subject to research scurvy. He placed himself on a diet of bread, crackers, cheese, eggs, beer, pure chocolate, and sugar with supplements of yeast and all the known vitamins other than vitamin C. Crandon continued his surgical work throughout the experiment. After twelve weeks, he felt fatigued. After nineteen, his skin became dry and rough and hair follicles on his buttocks and the back of his calves began to develop hard lumps or “plugs” at the base.³ After twenty-three weeks – that was seventeen weeks with no detectable vitamin C in his blood plasma – Crandon began to develop hemorrhages on his lower legs. At thirteen weeks, he had a wound deliberately inflicted on his back, and showed normal healing after ten days. After twenty-six weeks, he again had a wound inflicted, and showed no healing after ten days. He was given a fatigue test, and he found that he could run at seven miles per

¹ See KENNETH J. CARPENTER, *THE HISTORY OF SCURVY AND VITAMIN C* 200–01 (Cambridge University Press 1986).

² *See id.*

³ This “hyperkeratosis” had previously been regarded as a sign of vitamin A deficiency, but Crandon tested for a normal level of vitamin A in his blood.

hour for only sixteen seconds, and showed rapid exhaustion in other tests. He was then given 1,000 mg of ascorbic acid (vitamin C) each day for a week. He noticed a subjective improvement in the first twenty-four hours, and the second wound healed rapidly in the following ten days.

Separated by nearly two centuries, these two physicians engaged in the same line of research, and engaged themselves as human subjects.⁴ That they performed these experiments as medical scientists, rather than physicians, seems evident. The protocol had no therapeutic value to Stark and Crandon – both undertook the research to advance what was known about scurvy. Crandon, for one, continued his work as a physician as the experiment went on; the experiment was a separate endeavor.

While the accounts of these endeavors in self-experimentation might be unsavory or even shocking to some, likely far fewer would find them unethical. Each man assumed the risks of his experiment knowing the protocol, and knowing the “knowns” and “unknowns” about what might occur as a result. Each man had control over the administration of the experiment and could, presumably, stop it at any time. The experiment was a personal undertaking that did not affect the wellbeing of any other individual – except perhaps the physicians’ patients. At least in this author’s judgment, the enterprise seems honorable. Moreover, Stark and Crandon likely found several advantages to self-testing in terms of collecting experimental data. Using himself as subject, each man had a constant ability to control and observe his subject.

All this changes, however, when medical scientist uses not himself, but another human being, as subject.

⁴ The next experiment of this kind was carried out in England during World War II, and was performed on volunteers who were conscientious objectors to military service. *See id.* at 202.

Walter Reed's yellow fever research in 1900 was oft-cited before and during World War II as a precedent to justify military-medical human experimentation,⁵ perhaps because he was widely thought to have volunteered himself as one of the subjects.⁶ Reed was assigned as an Army scientist to Cuba, where yellow fever had killed thousands more American soldiers than had the Spanish army in the recent war. Most who caught the disease suffered a terrible fate. The skin would first begin to yellow. Next would follow violent hiccupping and uncontrollable, persistent retching and black vomit, and death.⁷ Reed hypothesized that mosquitoes carried the disease.⁸

At first, Reed carried out his experiment in secret. He had no permission from the high military authorities when he subjected the first volunteers, members of his commission, to the mosquito bite. Only after Yellow Fever Commissioner Jesse Lazear became ill and died did Reed report to his commanding general.⁹ He informed him of Lazear's death, and requested permission to use himself and other men as subjects, which was granted.¹⁰ More men were recruited from among the soldiers stationed in Cuba.¹¹

⁵ JONATHAN D. MORENO, *UNDUE RISK: SECRET STATE EXPERIMENTS ON HUMANS* 16 (W.H. Freeman 2000).

⁶ JONATHAN D. MORENO, *IS THERE AN ETHICIST IN THE HOUSE?: ON THE CUTTING EDGE OF BIOETHICS* 112 (Indiana University Press 2005).

⁷ See MORENO, *supra* note 5, at 16.

⁸ *Id.* at 17.

⁹ Lazear was 34-years-old when he died. He was a successful microbiologist trained in Europe, appointed as the first chief of clinical laboratories at Johns Hopkins Medical School. He left behind a widow and two children. *Id.*

¹⁰ Although the military medical folklore is that Reed subjected himself to the bite, he actually left Cuba before the appointed day on which he was going to do so. *Id.*

¹¹ *Id.* at 19.

The secretive nature of the experiment's beginnings seem to indicate that there was at least an informal army policy prohibiting human experimentation.¹² Reed devised and presented the new volunteering soldiers with a contract, which warned them that they might die in the experiment (and also suggested that they might die outside of it). The exact terms are unknown, but the volunteers were also offered some kind of financial reward. Some Spanish immigrant workers were recruited and received money for their participation, but it has been claimed that the Americans declined the offer of compensation out of patriotism.¹³

This initial modern American example of human testing exemplified several important themes that would emerge repeatedly in the subsequent history of human testing in America. First, that military emergency provided the impetus for the testing. Reed was driven to, and perhaps felt justified in, his experiments because of the need to discover a remedy for a disease that had cost many American lives and compromised the robustness of American military operations. Second, that the experiments proceeded in secrecy. Although Reed was prepared to conduct his experiments, evidently he was not necessarily prepared to make others aware of his project, at least until he had achieved some progress. Third, that the experiments took place in an environment in some manner isolated from the general American public, or at least the American public eye. Reed's experiments took place not on American soil, but in a military-base environment in Cuba, apart from the awareness of the American layman. Fourth, that consent was sought from the subjects. Finally, that the ensuing perception of the experiment was affected by an understanding of the experimenter as a patriot or even a martyr. The folklore that Reed subjected himself to the bite of the mosquito, alongside his subjects, seemed to have the effect of curing any ethical shortcomings of the experiment in the eyes of his successors.

¹² *Id.* at 19.

¹³ *Id.*

In 1941, President Roosevelt created a Committee on Medical Research (CMR) to coordinate America's medical research needs, should the U.S. enter the European war. In the tradition of Walter Reed, the committee sponsored dozens of projects involving human subjects. Civilian and military officials struggled with the issue of whom to use in these experiments, but they had little time to deliberate and little guidance from existing codes or conventions.¹⁴ In 1942 a University of Rochester researcher, looking to research the prevention of gonorrhea using human subjects, asked CMR for "an opinion that such human experimentation is desirable."¹⁵ In response, the CMR chairman, in a statement endorsed by the full committee, wrote:

[H]uman experimentation is not only desirable, but necessary in the study of many of the problems of war medicine which confront us. When any risks are involved, volunteers only should be utilized as subjects, and these only after the risks have been fully explained and after signed statements have been obtained which shall prove that the volunteer offered his services with full knowledge and that claims for damage will be waived. An accurate record should be kept of the terms in which the risks involved were described.¹⁶

After the war, CMR's work was summarized in a report called *Advances in Military Medicine*. The report contained little information regarding attitudes about human testing, the method utilized to recruit subjects, or any applicable rules and policies. It was, however, filled with tributes to the volunteer subjects. For instance, in records of experiments regarding the effects of mustard gas, there were expressions of patriotic camaraderie with the subjects. Yet there was no explanation of how the subjects had been recruited.¹⁷

¹⁴ *Id.* at 15.

¹⁵ ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT pt. I, ch. 1, § 3 (1995) available at <http://www.hss.energy.gov/HealthSafety/ohre/roadmap/achre/index.html>.

¹⁶ *Id.*

¹⁷ MORENO, *supra* note 5, at 25–26.

One Army project in the early 1940s clearly failed to meet the asserted CMR standard. At the Manhattan Project Army Hospital, studies of plutonium began in light of concern about the risks to laboratory workers, who were exposed to the substance on a daily basis. Eighteen patients were injected with plutonium as part of the study.¹⁸ All but the last of the patients was injected without having knowledge of the experiment or giving consent. Three patients were told that the substance would “not necessarily” help them, but might help others.¹⁹ The first seventeen injections took place during a time of war, and while it appears that there was no explicit permission to use some individuals as unwitting experimental subjects, it seems it was assumed that it could be done because of necessity for the war effort. Yet, a U.S. Atomic Energy Commission (AEC) declassification officer wrote of a 1947 memorandum regarding the experiment:

The document appears to be the most dangerous since it describes experiments performed on human subjects... Unless, of course, the legal aspects were covered by the necessary documents, the experimenters and the employing agencies, including the U.S., have been laid open to a devastating lawsuit which would, through its attendant publicity, have far reaching results.²⁰

There was no evidence that consent had been obtained from the first seventeen subjects, and it was decided that the project should remain secret.²¹

In 1947, the AEC was looking to confront its experiences with secret human experiments of this kind and set new rules for the future, according to which the AEC would fund researchers. In April and November of 1947, Carroll Wilson, the general manager of the AEC, wrote letters to Stafford Warren and Robert Stone, who were important players in the wartime Manhattan

¹⁸ *Id.* at 120.

¹⁹ *Id.* at 126.

²⁰ *Id.* at 136.

²¹ *See id.* at 137. There was no sign of injury to the subjects, but ultimately President Clinton compensated them because of the failure of the experimenters to inform them and the subsequent cover-up. *Id.* at 120.

Project medical research. Wilson wrote to them that clinical testing with patients could occur only where there was a prospect that the patient could benefit medically and only after the patient had been informed about the testing and there was documentation of consent by the patient.²²

Wilson's April letter was ostensibly given little distribution or effect. The one known instance of observance of the letter was, in fact, with regard to the eighteenth subject of the aforementioned Manhattan Project plutonium experiment, who was injected at the University of California at San Francisco. There is indirect evidence that someone at the university had been informed of Wilson's letter, and in the eighteenth patient's medical chart, there is documentation of knowledge and consent. Yet Wilson's prescription was not observed in its entirety, for there was no real expectation that the injection would have therapeutic effect for the subject.²³

In his second letter of November, Wilson again instructed upon the AEC's requirements for human testing. He described the conclusions of the AEC's Medical Board of Review, a group appointed to review the AEC's medical program by the AEC chairman, David Lilienthal. In the letter, Wilson referred to the Board of Review's June meeting, and quoted from a draft of the Board's report to the Commissioners:

The atmosphere of secrecy and suppression makes one aspect of the medical work of the Commission especially vulnerable to criticism. We therefore wish to record our approval of the position taken by the medical staff of the AEC in point of their studies of the substances dangerous to human life. We [the Medical Board of Review] believe that no substances known to be, or suspected of being, poisonous or harmful should be given to human beings unless all of the following conditions are fully met: (a) that a reasonable hope exists that the administration of such a substance will improve the condition of the patient, (b) that the patient give his complete and informed consent in writing, and (c) that the responsible next of kin give in writing a similarly complete and informed consent, revocable at any time during the course of such treatment.²⁴

²² ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 1, § 2.

²³ *Id.*

²⁴ *Id.*

The Advisory Committee on Human Radiation Experiments (ACHRE), in a 1995 report, stated that it found little evidence of efforts to communicate or implement the rules stated by Wilson in this 1947 letters, despite that they were developed in response to a demand for clarity about the rules for the conduct of human research.²⁵ AEC's Division of Biology and Medicine (DBM), which directed the AEC's medical research program, did not routinely communicate Wilson's statements in response to requests for guidance from non-AEC researchers. For example, in April 1948 a university researcher wrote to DBM and inquired as to what should be done about "medical-legal aspects" and "permission forms" for a human experiment using phosphorous 32 for purely investigational, non-therapeutic purposes. DBM did not reply with a statement of Wilson's rules, but rather referred the researcher to the Isotopes Division at AEC-sponsored Oak Ridge Institute for Nuclear Studies, a research hospital. The Isotopes Division told the researcher that it could be "of little assistance," but "understood that most hospitals do require patients to sign general releases before entering into treatment."²⁶

There is some indication that views on the matter remained unsettled within the AEC. For instance, the ACHRE found some evidence, in a document dated March 29, 1948, that the AEC's Subcommittee on Human Applications recommended human radiation experiments not only when they would offer diagnostic and therapeutic value to their human subjects, but also when they would advance knowledge about radiation protection generally. This stance would have changed the AEC's policy as explicated in Wilson's 1947 letters, which prohibited experimentation that was without any expectation of therapeutic benefit to the subject himself.²⁷

²⁵ *Id.*

²⁶ *Id.*

²⁷ *Id.*

CMR's work exhibited again, like Reed's work, the force of military concern and necessity in driving human experimentation, even in spite of uncertainty about the propriety of certain methods. Again, an existing or impending military emergency left government officials and medical researchers with a feeling that there was little time for philosophizing about medical research ethics, and again much of CMR's work proceeded in secrecy. Moreover, again, consent was emphasized as a requirement to protect the rights of subjects, legitimize human experimentation, and guard against liability.

Furthermore, another theme emerged: that the question of the propriety of human experimentation is often framed in terms of whether the protocol of the experiment provides the human subject with any therapeutic benefit. Unlike the early scurvy experimenters, who very clearly performed their scurvy research wearing a "medical researcher hat" rather than a "medical caregiver hat," physicians who use other individuals to advance their research persistently operate within an ambiguous realm. To a sick individual, a physician is a caregiver. To a physician, however, a sick individual might be both a patient with therapeutic needs as well as a source of research data. As this theme begins to emerge, the "therapeutic value" ideal seems to be a compromise between the dual roles of a physician, by which a medical researcher who performs human experimentation within this ambiguous realm can justify his work.

After the war, the Nuremberg trials put American defense planners on the defensive about the American use of human subjects for the war effort. The Nazi defense team managed to turn the tables on the Allies during the course of the trial, by comparing Nazi practices of human experimentation to the human experiments that were performed in the U.S.²⁸ In anticipation of

²⁸ MORENO, *supra* note 5, at 54.

this tactic, Dr. Andrew C. Ivy, the American Medical Association's official consultant to the Nuremberg prosecutors, drafted several principles of medical research, which would ultimately serve as the basis for some of the 10 Nuremberg Code principles. It seems Ivy was chosen for his consultant position because, for one, some of his wartime research interests had corresponded in topic to some of the experiments that the Nazis had undertaken, with shocking methods, on the prisoners of the concentration camps. Moreover, Ivy was known as a defender of animal experimentation against American antivivisectionists.²⁹

In July or early August of 1946, Ivy went to Germany to meet with the Nuremberg prosecution team. While there to assist them with understanding the technical details of some of the experiments, he recognized that the prosecutors “appeared somewhat confused regarding the ethical and legal aspects” of human experimentation. After his visit, upon the request of the Board of Trustees of the American Medical Association, Ivy penned a 22-page report. In the report, Ivy laid out the “the rules” of human experimentation, which he stated were standards “well established by custom, social usage and the ethics of medical conduct.” He wrote:

1. Consent of the human subject must be obtained. All subjects must have been volunteers in the absence of coercion in any form. Before volunteering the subjects have been informed of the hazards, if any...
2. The experiment to be performed must be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease under study that the anticipated results will justify the performance of the experiment. That is, the experiment must be such as to yield results for the good of society unprocurable by other methods of study and must not be random and unnecessary in nature.
3. The experiment must be conducted

²⁹ ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 2, § 2. Ivy was later a proponent of the quack cancer drug Krebiozen. FDA found that Krebiozen contained nothing but creatine monohydrate, a common body chemical of no medicinal value. See *Cancer: The Krebiozen Verdict*, Feb. 11 1966, <http://www.time.com/time/magazine/article/0,9171,842474-2,00.html>.

- (a) only by scientifically qualified persons, and
- (b) so as to avoid all unnecessary physical and mental suffering and injury, and
- (c) so, that, on the basis of the results of previous adequate animal experimentation, there is no *a priori* reason to believe that death or disabling injury will occur, except in such experiments as those on Yellow Fever where the experimenters serve as subjects along with non-scientific personnel.³⁰

Ivy also delivered a copy of his report to the Nuremberg prosecution team. It is not certain that the judges on the Nuremberg Tribunal actually saw Ivy's report; however, comparing Ivy's rules with the Nuremberg Code as issued by the Tribunal in August 1947, it is clear that the judges borrowed important elements of Ivy's formulation, including voluntary consent, prior animal experimentation, avoidance of undue risk to subjects, and the right of the subject to bring the experiment to an end at any time. Some of this was almost verbatim. The judges also reiterated Ivy's claim that his rules were already widely understood and followed by medical researchers in the U.S.³¹

Historian David Rothman has explained that even medical researchers in the U.S. who would have been aware of the events at Nuremberg did not seem to perceive the implications it might have for their own work as medical researchers.³² Rothman explains, "the prevailing view was that [the Nuremberg medical defendants] were Nazis first and last; by definition nothing they did, and no code drawn up in response to them, was relevant to the United States."³³ As one medical school professor put it, it was perceived as "a good code for barbarians but an unnecessary code for ordinary physicians."³⁴

³⁰ *Id.*

³¹ *Id.*

³² *Id.* at pt. I, ch. 2, § 5.

³³ *Id.*, citing DAVID J. ROTHMAN, STRANGERS AT THE BEDSIDE: A HISTORY OF HOW LAW AND BIOETHICS TRANSFORMED MEDICAL DECISION MAKING 62 (Basic Books 1994).

³⁴ MORENO, *supra* note 5, at 80.

Moreover, it appears that the aforementioned distinction between medical researcher and medical practitioner was, in the postwar period, unclear and elusive to the medical research community.³⁵ As explained by the 1995 report of the ACHRE, this was a period of great change in American medical science.³⁶ Many young clinical researchers at this time would have been trained under a paradigm of paternalism in medical practice, which encouraged physicians to take responsibility for determining what was in the best interest of their patients and to act accordingly. Patients trusted their physicians with great authority and discretion, and doctors did not shy from creative treatment that could be called experimentation if it helped a patient. The postwar period, however, brought with it significant advances in medical research practice as well as unprecedented expansion of universities and research institutes.³⁷ The ACHRE Report describes:

Many more physicians than ever before were no longer solely concerned, or even primarily concerned, with aiding *individual* patients. These medical scientists instead set their sights on goals they deemed more important: expanding basic knowledge of the natural world, curing a dread disease (for the benefit of many, not one), and in some cases, helping to defend the nation against foreign aggressors. At the same time, this new breed of clinical researchers was motivated by more pragmatic concerns, such as getting published and moving up the academic career ladder. But these differences between medical practice and medical science, which seem relatively clear in retrospect, were not necessarily easy to recognize at the time. And coming to terms with these differences was not especially convenient for researchers; using readily available patients as “clinical material” was an expedient solution to a need for human subjects.³⁸

The Nuremberg Code, as a watershed development in human experimentation policy, illustrates the most prominent manner by which such policy has developed in America. Namely, policy in the field of human research has persistently evolved in response to scandal. Ivy’s

³⁵ See ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 2, § 3.

³⁶ *Id.*

³⁷ *Id.*

³⁸ *Id.*

principals were manifestly drafted in order to manage a scandal of American research ethics, which would have had enormous public relations implications. The American experience at Nuremberg also reveals another recurring theme: the tension between secrecy and the evolution of policy. Namely, while scandal drives policy, secrecy obstructs the revelation of scandal to the public, thus impeding the evolution of policy. Much World War II-era human research was kept out of the public eye until the Nuremberg trials, and thus it was not until then that the government and medical research community was forced to respond by formulating and articulating ethical standards.

Soon after Nuremberg engendered this hour of doubt and reflection on the ethics of medical research in the United States, the pressures of a new postwar world pushed medical researchers even further, as part of the U.S. effort to seek scientific advantages over its potential new enemies.³⁹ In 1952, a funding proposal was submitted to the director of the CIA for a project “[t]o develop an offensive capability in the covert use of biological and chemical materials, including the production of various psychological conditions which could support clandestine operations,” and “[t]o develop a comprehensive capability in the field of covert chemical and biological warfare that would give us knowledge of the enemy’s theoretical potential, thus enabling us to defend ourselves against a foe who might not be as restrained in the use of these techniques as we are.”⁴⁰

This proposal became the basis for the MKULTRA project, established in April 1953. Its purpose was to research and develop chemical, biological, and radiological materials for clandestine operations, capable of controlling or modifying human behavior. As described by

³⁹ MORENO, *supra* note 5, at 89.

⁴⁰ ANDREW GOLISZEK, *IN THE NAME OF SCIENCE: A HISTORY OF SECRET PROGRAMS, MEDICAL RESEARCH, AND HUMAN EXPERIMENTATION* 154 (St. Martins Press 2003).

Richard Helms, the assistant deputy director for plans and the author of the 1952 proposal, MKULTRA sought to investigate “the development of a chemical material which causes a reversible, nontoxic, aberrant mental state, the specific nature of which can be reasonably well predicted for each individual.”⁴¹ Such a material, he said, could “aid in discrediting individuals, eliciting information, implanting suggestions and other forms of mind control.”⁴² The project lasted for 10 years, and although many of the records were ordered destroyed by the Chief of the Technical Services Division, Dr. Sidney Gottlieb, enough documentation was inadvertently saved to expose the program.⁴³

There were 149 MKULTRA subprojects, many of them involved with research into behavior modification, hypnosis, drug effects, psychotherapy, polygraph studies, truth serums, pathogens and toxins in human tissue, knockout drops, and testing or administering drugs surreptitiously.⁴⁴ One of the first MKULTRA studies was conducted at the National Institute of Mental Health Addiction Research Center in Lexington, Kentucky, which was working with the CIA to develop new, mind-altering drugs. In exchange for volunteering to participate in experiments, young patients, usually drug addicts serving various sentences for drug violations, were offered the drug of their addiction. Some payments consisted of heroin and morphine.⁴⁵

MKULTRA also included research projects regarding the administration of LSD, many of which were conducted at the Army Chemical Warfare Laboratories in Edgewood, Maryland. The program included ninety-five human subjects. For one experiment, researchers created a simulated social reception where they surreptitiously administered doses of LSD to volunteers.

⁴¹ *Id.* at 155.

⁴² *Id.*

⁴³ *Id.*

⁴⁴ *Id.* at 156.

⁴⁵ *Id.* at 158.

The volunteers were not aware of the nature or purpose of the experiment in which they were participating. After the administration, some were polygraphed, and others were confined to “isolation chambers.”⁴⁶ In collaboration with the Federal Bureau of Narcotics, the CIA also covertly tested LSD on patrons of San Francisco and New York bars in a project dubbed Operation Midnight Climax. The CIA had hired drug-addicted prostitutes to pick up men and bring them back to CIA bordellos, where they would be enticed to drink alcohol laced with LSD. CIA researchers watched through two-way mirrors.⁴⁷

A most infamous incident of the LSD experiments occurred on November 18, 1953, when ten scientists from the CIA and Fort Detrick, including Dr. Gottlieb, gathered for a conference at a secluded cabin in Deep Creek Lake, Maryland. The scientists agreed that they would require unsuspecting human subjects in order to verify the effects and potency of LSD. One of the officers, Dr. Robert Lashbrook, poured seventy micrograms of LSD into a bottle of Cointreau to be served after dinner the following evening. Several conference participants partook in the laced Cointreau, and twenty minutes later – once odd and boisterous behavior commenced – Dr. Gottlieb told the group what they had done. One subject, a civilian employee of the army named Dr. Frank Olson, had taken a drink of the Cointreau and felt especially edgy that night. He was unable to sleep, and the following morning he was completely fatigued and unable to concentrate. Shortly thereafter he became paranoid, and within days sank into a depression so severe that Dr. Lashbrook recommended immediate medical treatment. Olson flew home to Washington to spend Thanksgiving with his family. Once he reached the airport, however, he was too fearful to face his family – knowing his mind had changed – and had to be

⁴⁶ *Id.*

⁴⁷ *Id.* at 160.

returned to New York for more psychiatric consultations. Ultimately, Olson jumped out the window of his Manhattan hotel room, to his death.⁴⁸

For the ten years of its execution, MKULTRA was kept absolutely secret. In 1963 an inspector general survey of the Technical Services Division led to a revelation about the projects, including the surreptitious administration of LSD to unwitting, nonvoluntary human subjects. This spurred an investigation that put a stop to the research. Following a report by the inspector general, MKULTRA was terminated in 1964.

MKULTRA was yet another example of the force of national security-related concerns in driving medical experimentation. It also, of course, was another example of experimentation proceeding in secret. In the MKULTRA case, secrecy had dual significance. Namely, secrecy was crucial to protecting military intelligence and preventing a public relations crisis. The function of secrecy in preventing public outrage, however, has the coincident function of insulating medical research, at least temporarily, from the moral judgment and ethical evaluation of the public – another recurring theme. Thus, secrecy impedes the evolution of policy not only by slowing the rate at which officials are forced to deal with scandal, but also by keeping the ethics of the general community, rather than the medical research community, from informing policymaking.

Along with the CIA's interest in human experimentation, the military's interest intensified during this period, especially as the Korean War began in mid-1950. There was no Department of Defense (DOD) policy, however, to permit or guide researchers in performing human experimentation to study the topics of the military's interest – chemical, biological,

⁴⁸ *Id.* at 159.

atomic, and radiation warfare. From 1950 to 1953, discussions about human experimentation policy were held in several high-level DOD panels headed by civilian researchers, including the Armed Forces Medical Policy Council (AFMPC), the Committee on Medical Sciences (CMS), and the Joint Panel on the Medical Aspects of Atomic Warfare. A DOD attorney, Stephen S. Jackson, suggested to the AFMPC that their proposal for a human experimentation policy be modeled after the Nuremberg principles, with an additional rule barring experiments with prisoners of war and an additional requirement that consent be expressed in writing, before at least one witness. It appears that the AFMPC proposal was unpopular among other DOD committees, but it had the support of President Truman's Secretary of Defense, Robert A. Lovett. The AFMPC strongly recommended the Nuremberg Policy to the incoming Eisenhower administration's Secretary of Defense, Charles Wilson.⁴⁹

On February 26, 1953, Secretary Wilson issued a Top Secret memorandum to the secretaries of the Army, Navy, and Air Force, approving of the AFMPC's proposed Nuremberg policy, with the modifications suggested by Jackson. The policy of the Wilson memorandum would "govern the use of human volunteers by the Department of Defense in experimental research in the fields of atomic, biological, and/or chemical warfare for defensive purposes."⁵⁰ It stipulates that any proposed experiment of this kind, along with the name of the person who will conduct the experiment, be submitted for written approval by the secretary of the department in which the experiment will be conducted, and that the Secretary of Defense be informed.⁵¹

⁴⁹ ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 1, § 3.

⁵⁰ Memorandum from Secretary of Defense Charles Wilson to the Secretary of the Army, Secretary of the Navy, Secretary of the Air Force, "Use of Human Volunteers in Experimental Research" (Feb. 26, 1953).

⁵¹ *Id.*

The 1995 ACHRE report, however, indicates that there were problems with the dissemination and communication of Wilson's secret memorandum. Within a year of the memorandum's issuance, it reports, officials of the Armed Forces Special Weapons Project (AFSWP) solicited guidance from DOD regarding the use of human subjects in experimentation. This inquiry was precipitated by a routine review of reports, upon which an AFSWP reviewer found that some volunteers had been injured in a flashblindness experiment at an atomic bomb test site, which had been conducted prior to the issuance of the Wilson memorandum. The AFSWP reviewer discovered the Wilson memorandum policy upon further inquiry, but found that "no serious attempt [had] been made to disseminate the information to those experimenters who [had] a definite need-to-know."⁵² Thus, it seems the effect of secrecy again exerted itself to the detriment of human research policy. Namely, beyond creating tension with the development of policy, secrecy creates a tension with the effective communication of policy once it is promulgated.

Roughly a decade later, Congress acknowledged similar problems to those of DOD with the lack of policy regarding human experimentation, in private civilian industry. A Senate subcommittee chaired by Senator Estes Kefauver of Tennessee had begun in 1959 to investigate the conduct of pharmaceutical companies, and found that it was common practice for these companies to provide samples of experimental drugs to physicians. The drug companies would then pay the physicians to collect data on their patients taking the drugs. Physicians would prescribe the drugs, which had not been proven safe and effective, to patients without their

⁵² ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 1, § 3, *citing* Irving L. Branch, Colonel, USAF, Acting Chief of Staff, to the Assistant Secretary of Defense (Health and Medicine), "Status of Human Volunteers in Bio-medical Experimentation" 3 (Mar. 3, 1954).

knowledge or consent.⁵³ In 1962, Congress passed the Kefauver-Harris amendments, which amended the Federal Food, Drug, and Cosmetic Act of 1938 to require pharmaceutical companies to obtain informed consent from patients in the testing of investigational drugs. Consent was not required when, “according to the best judgment of the doctors involved,” it was “not feasible” or was not in the best interests of the patient.⁵⁴ In 1963, FDA promulgated regulations echoing the informed consent requirements of the amendments.⁵⁵

The passage of the amendments came on the heels of the thalidomide disaster in Europe, Canada, and to a very small degree, the United States.⁵⁶ Starting in late 1957, the sedative thalidomide was given to pregnant women, thereby causing thousands of birth defects in newborn infants. The tragedy was widely covered by the television networks, stunning Americans who saw images of the affected infants. A prominent defect was in the upper-limbs, often including the absence of both arms or phocomelia. In some cases, the newborns virtually

⁵³ ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 3, § 2.

⁵⁴ *Id.*, quoting *Congressional Record*, 87th Cong, 2d Sess., 22042, as cited in an attached memorandum, C. Joseph Stetler, Pharmaceutical Manufacturers Association, to James L. Goddard, M.D., Commissioner of Food and Drugs, DHEW, "Regarding Statement Appearing in August 30, 1966 Federal Register Concerning Clinical Investigation of Drugs" (Oct. 11, 1966).

⁵⁵ See Frances O. Kelsey, *FDA's Enforcement of IRBs and Patient Informed Consent*, 44 FOOD DRUG COSM. L.J. 13, 13 (1989).

⁵⁶ Dr. Frances Kelsey, on her first assignment at FDA, withheld approval of thalidomide in the U.S, despite pressure from manufacturers. She was concerned by some data from Europe – where the drug was already used widely – suggesting dangerous side effects in patients who took the drug repeatedly. For her judgment in this case, President John F. Kennedy awarded her the President's Award for Distinguished Federal Civilian Service in 1962. Biography of Dr. Frances Kathleen Oldham Kelsey, http://www.nlm.nih.gov/changingthefaceofmedicine/physicians/biography_182.html. Few American women were affected. Most of them had taken thalidomide while participating in investigational studies or had obtained it while living abroad. Rachel Spiege, *Thalidomide Gets a Second Chance*, <http://science.education.nih.gov/Home2.nsf/Educational+Resources/Resource+Formats/Online+Resources/+High+School/544E6D04B78B8E9E85256CCD0063E875>.

lacked all four limbs.⁵⁷ The Kefauver-Harris amendments thus responded to scandal; namely, the public's anxiety about the protections, or lack thereof, of patients who might receive experimental drugs from their physicians.

During the 1960s, Dr. Henry Beecher, a Harvard professor of anesthesiology and well-known researcher, became a hero in medical ethics for his exposure of numerous human experiments. In 1959, he published an article in the *Journal of the American Medical Association* called "Experimentation in Man." He wrote that it is "unethical and immoral to carry out potentially dangerous experiments without the subject's knowledge and consent."⁵⁸ He was, however, a severe critic of the Nuremberg code.⁵⁹ Beecher criticized the Code's requirement that experimental subjects ought to have sufficient knowledge of the proposed experiment before they agree to be subjects, inasmuch as very few people, he asserted, have the expertise to truly understand the hazards of an experiment. Even the scientists themselves might not fully comprehend the mysteries involved, especially in advance, he wrote. Beecher also objected to the Code's assertion that human experiments should not be "random." Many medical breakthroughs, he said, had occurred by accident, including the discovery of X-rays and penicillin, as well as anesthetic agents. Beecher wrote: "It is not my view that many rules can be laid down to govern experimentation in man. In most cases, these are more likely to do harm than good."⁶⁰

⁵⁷ See A. White Franklin, *Thalidomide Babies Memorandum From The British Paediatric Association*, 2 THE BRITISH MEDICAL JOURNAL 522, 523 (Aug. 25, 1962).

⁵⁸ GOLISZEK, *supra* note 40, at 240.

⁵⁹ *Id.*

⁶⁰ *Id.*

In 1966, Beecher published a controversial paper entitled “Ethics and Clinical Research” in the *New England Journal of Medicine*. In the article, Beecher identified twenty-two cases of published medical research utilizing human subjects that he found unethical.⁶¹ This was an unprecedented act of whistle-blowing, and was regarded as scurrilous by many of his former colleagues.⁶² Beecher claimed in his paper that it was not a willful disregard of patients’ rights but rather thoughtlessness and carelessness that accounted for most of the abuses he discovered. Emphasis on human experimentation, Beecher found, was sound. The trouble, however, was that the vast resources available for such experimentation surpassed the supply of responsible investigators.⁶³ For moral and legal reasons, Beecher wrote, “consent” should be the goal emphasized in all cases; but often consent in any fully informed sense would not be attainable.⁶⁴ The more reliable safeguard, he found, was “the presence of an intelligent, informed, conscientious, compassionate, responsible investigator.”⁶⁵

Beecher’s paper reflected again the way in which the concealment of human experimentation from the public eye impedes the development of ethical standards that are in tune with the conscience of the general community. Beecher’s view that many of the abuses he discovered were products of “thoughtlessness” and “carelessness” suggests that medical researchers struggle to conceptualize the ethics of their experimental protocols with the morals of the community in mind. It is perhaps not until their experiments are subjected to the scrutiny of the public eye, or at least some outside opinion, that some medical researchers can see the ethical issues that inhere in their experiments.

⁶¹ *Id.* at 242.

⁶² *Id.*

⁶³ Henry K. Beecher, *Experimentation in Man*, 264 *NEW ENGLAND J. OF MED.* 367 (June 16, 1966).

⁶⁴ *Id.* at 368.

⁶⁵ *Id.* at 372.

Among the instances of unethical published research that Dr. Beecher identified was an infamous cancer experiment performed at the Jewish Chronic Disease Hospital in 1963. With funds from the U.S. Public Health Service and the American Cancer Society, researchers at the hospital aimed to determine if foreign cancer cells would live longer in debilitated non-cancer patients than in patients with cancer, and also if cancer could actually be induced by injection of live cancer cells. The researchers did not tell their subjects, patients with and without cancer, that the injections contained cancer cells, and later explained that they “did not wish to stir up any unnecessary anxieties in the patients who had phobia and ignorance against cancer.” Still, the doctors claimed that oral consent had been obtained.⁶⁶

Some younger doctors who had patients at the hospital heard about the experiments and complained to a hospital board member who was also a lawyer, William Hyman. He sued to obtain records of the experiment. Three years later, in 1966, the case consummated with the New York Board of Regents taking the virtually unprecedented step of censuring the doctor who had performed the research, along with the director of the hospital who had agreed to the research, placing them on one year of probation.⁶⁷

The Jewish Chronic Disease Hospital case has been cited as the first incident since the Nuremberg trials themselves to draw widespread attention to issues of research ethics.⁶⁸

“Homegrown” scandals, it is said – unlike the Nazi experiments, which seemed so extreme and distant – truly began to change attitudes about the rights of research subjects in the 1960s.⁶⁹

Included in the many disturbed by the Jewish Chronic Disease Hospital incident was James

⁶⁶ GOLISZEK, *supra* note 40, at 227–28.

⁶⁷ MORENO, *supra* note 5, at 246.

⁶⁸ *Id.* at 247.

⁶⁹ *Id.*

Shannon, the director of the National Institutes of Health (NIH) in Bethesda, Maryland. The NIH started as a government-sponsored cancer research laboratory and grew into a vast enterprise, including a number of institutes specialized in research on various diseases, as well as a pioneering research hospital called the Clinical Center. Using federal funds, the NIH is able to pursue scientific inquiry that might not be profitable, and thus unattractive to private industry. Some NIH work is done by its own scientists, but it is performed in great measure by experts throughout the country who receive NIH funding.⁷⁰ Shannon understood the vulnerability of a growing federal agency such as the NIH, and that its moral integrity would be the key to its continuing to receive public support.⁷¹

In the same year of the Jewish Chronic Disease Hospital Case, 1963, a researcher who was partially funded by the NIH transplanted a chimpanzee kidney into a human. The patient had consented, but there was no reason to believe that the transplant would work, or that the performance of the procedure would provide enough new information about animal-to-human transplants to justify the risk to the patient. Though Shannon was at the helm of the NIH, he heard about the incident in the newspapers.

Disquieted by these disturbing cases and concerned by the growing attention paid to research ethics, Shannon created a committee in late 1963 under the direction of the NIH associate chief for program development, Robert B. Livingston, whose office supported centers at which NIH-funded research took place.⁷² The committee was charged with studying problems of inadequate consent and the standards of self-scrutiny involving research protocols and procedures, and also with recommending controls for the protection of human subjects in NIH-

⁷⁰ *Id.*

⁷¹ *Id.*

⁷² ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 3, § 2.

sponsored research. The committee recognized unethical research like that of the Jewish Disease Hospital cancer experiments could wreak havoc on public perception, increase the likelihood of liability, and inhibit research.⁷³ Yet, it was concerned about the NIH “taking too authoritarian a posture toward research oversight.”⁷⁴ Thus, in its report to Shannon in 1964, the committee did not recommend any changes in NIH policy. It urged deference to physician autonomy and the traditional regard for the sanctity of the doctor-patient relationship and, moreover, warned that, “whatever NIH might do by way of designating a code or stipulating standards for acceptable clinical research would be likely to inhibit, delay, or distort the carrying out of clinical research.”⁷⁵

Shannon was disappointed with the Livingston Committee’s report.⁷⁶ He felt that the NIH should take increased responsibility for research ethics, especially in light of the Jewish Chronic Disease Hospital case.⁷⁷ Still, he used the report as the basis of discussions with the U.S. Surgeon General, Luther Terry, in 1965.⁷⁸ Together, Shannon and Terry proposed to the National Advisory Health Council (NAHC), an advisory committee to the surgeon general of the Public Health Service, which includes the NIH, that the NIH should assume responsibility for formal controls on individual investigators. Shannon argued for impartial prior peer review of the risks research posed to subjects and questioned the adequacy of the current protections for

⁷³ *Id.*

⁷⁴ *Id.*

⁷⁵ *Id.*, quoting Robert B. Livingston, Associate Chief for Program Development, Memorandum to the Director, NIH, "Progress Report on Survey of Moral and Ethical Aspects of Clinical Investigation" [the Livingston report] 7 (Nov. 4 1964).

⁷⁶ MORENO, *supra* note 5, at 248.

⁷⁷ ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 3, § 2.

⁷⁸ MORENO, *supra* note 5, at 248.

human subjects.⁷⁹ In 1966, the Public Health Service ordered that anyone who wanted to perform human experiments using its funds must meet certain standards, including informed consent and review of the experiment in advance by a committee composed of professional and public members.⁸⁰ This peer review requirement was a significant acknowledgment of the aforementioned problem, demonstrated by the examples in Henry Beecher's paper, that medical researchers may have difficulty seeing the ethical issues involved in their experiments.

In the same year that the Public Health Service ordered these new safeguards for human experimentation, another scandal of human experimentation came into the public eye, involving a New York State institute for the mentally ill called Willowbrook, located on Staten Island. Like many other institutions of its kind, Willowbrook was experiencing great demand and overcrowding. By the mid-1960s, it was filled to more than twice its intended capacity.⁸¹ After it had officially closed its doors to patients, Willowbrook offered admission to retarded children if their parents would agree to allow them to be part of a hepatitis study. With few other options available to them, parents agreed. The consent forms the parents signed stated that their children were to receive a vaccine against hepatitis, instead of accurately indicating that they would be infected with the disease.⁸²

The research team was led by Saul Krugman of New York University, and before beginning the work, Krugman had discussed it with many colleagues, and gotten approval from the New York University School of Medicine and the Armed Forces Epidemiological Board,

⁷⁹ ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 3, § 2.

⁸⁰ MORENO, *supra* note 5, at 248.

⁸¹ *Remembering an Infamous New York Institution*, NPR (Mar. 7, 2008), <http://www.npr.org/templates/story/story.php?storyId=87975196>.

⁸² GOLISZEK, *supra* note 40, at 250.

which also provided funding for the research.⁸³ When a review committee for human experimentation was formed in 1955, it too approved the research.⁸⁴ As the experiment began, the researchers took stools from hepatitis-infected individuals and used them to make extracts, which were then fed to healthy subjects.⁸⁵ The experiment lasted from the mid-1950s to the early 1970s and was well known in the medical research community, inasmuch as Krugman's team had published many articles fully describing the experiment and its protocol.⁸⁶ Later confronted about the experiment, the researchers justified their work, saying the children would have gotten hepatitis within six months at Willowbrook regardless of the experiment, so that it was better to have them participate in a controlled study, because of which they would be monitored and given treatment.⁸⁷ Moreover, Krugman claimed that the parents of each subject had received detailed information about the research prior to signing a consent form, without any pressure to enroll their child.⁸⁸

The Tuskegee syphilis study, brought into the public eye by a journalist in 1972, shared with the Willowbrook study that insiders – here, public health officials at all levels of government and researchers – knew of the research, but it was shocking news to the general public.⁸⁹ In 1932, the venereal disease division of the U.S. Public Health Service (USPHS) began a study in Macon County, Alabama, to follow the effects of untreated syphilis in some 400

⁸³ ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 3, § 2.

⁸⁴ *Id.*

⁸⁵ David J. Rothman, *Were Tuskegee & Willowbrook 'Studies in Nature'?*, 12 THE HASTINGS CTR. REPORT 5, 6 (Apr. 1982); GOLISZEK, *supra* note 40, at 251.

⁸⁶ ROTHMAN, *supra* note 83.

⁸⁷ GOLISZEK, *supra* note 40, at 251.

⁸⁸ ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 3, § 2, *quoting* S. Krugman, "Ethical Practices in Human Experimentation," text of lecture presented at the Fifth Annual Midwest Student Medical Research Forum 3–4 (Mar. 1 1974).

⁸⁹ *Cf.* MORENO, *supra* note 5, at 248.

African-American men (along with a control group of 200 non-infected African-American men).⁹⁰ The subjects were recruited to the study with offers of free medical examinations, and once selected to be subjects, they were not informed as to the nature of their disease or of the fact that they would derive no therapeutic benefit from participating.⁹¹ The study was not intentionally secret, but neither was it widely announced or subjected to review by an independent advisory group.⁹² The study went on for forty years. As described by David J. Rothman,

The study continued through World War II, when a number of the men were called up for the draft and, had they not be research subjects, would have receive medical attention for their infection. It continued through the 1950s, after the efficacy penicillin treatment was established, and after the Nuremberg trials produced a code of ethics for biomedical research. It lasted through the 1960s, untouched by the civil rights agitation, and unaffected by the code of research ethics adopted by the USPHS itself. It ended only in 1972, when an account of the experiment in the *Washington Star* sparked a furor.⁹³

Furthermore, over the course of the forty years of the experiment, at least 28 participants died and approximately 100 more suffered blindness and insanity from untreated syphilis.⁹⁴

The Willowbrook and Tuskegee cases demonstrate the recurring disconnect between the ethical conscience of the general public and medical researchers' conceptions of their own experiments. It is certainly charitable to attribute the ethical shortcomings of these experiments to failure of perception, but if Beecher's assertions are to be taken seriously, this does often play a significant role in human experimentation abuses.

⁹⁰ ROTHMAN, *supra* note 83 at 5; ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 3, § 2.

⁹¹ *Id.*

⁹² MORENO, *supra* note 5, at 249.

⁹³ ROTHMAN, *supra* note 83 at 5.

⁹⁴ ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 3, § 2.

In 1972, the Tuskegee study made the front page of the *New York Times*.⁹⁵ In response, the Department of Health Education and Welfare (DHEW) appointed the Tuskegee Syphilis Study Ad Hoc Panel to review the Tuskegee study as well as the department's policies and procedures for the protection of human subjects. The ad hoc panel found, despite the existence of the 1966 PHS rules, that neither DHEW nor any other agency in the government had adequate policies for oversight of human subjects research. The panel recommended that the Tuskegee study be stopped immediately and that remaining subjects be given necessary medical care resulting from their participation, and also that Congress establish “a permanent body with the authority to regulate at least all federally supported research involving human subjects.”⁹⁶

In 1973, Senator Edward Kennedy introduced a bill to create a National Human Experimentation Board, as recommended by the Tuskegee Panel. It became clear, however, that the bill, which would have created a national regulatory body to oversee all federally funded research, would not succeed. Senator Kennedy, thus, introduced a bill that would become the National Research Act, which created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, and approved of soon-to-be promulgated regulations of DHEW, in return for DHEW issuing human subject research regulations.⁹⁷ As a result, the agency responsible for the greatest proportion of human subject research would promulgate regulations for the protection of subjects, but oversight in general was left to each agency instead of one independent regulatory body.⁹⁸ In May 1974, DHEW published its new regulations, which notably required that each grantee institution form a committee to approve all

⁹⁵ *Id.*, citing Jean Heller, *Syphilis Victims in U.S. Study Went Untreated for 40 Years*, N. Y. TIMES, Jul. 26 1972, at 1, 8.

⁹⁶ ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 3, § 2.

⁹⁷ *Id.*

⁹⁸ *Id.*

research proposals before they were passed to DHEW for consideration. Such a committee became known as an institutional review board (IRB). The regulations also defined the procedure and substantive criteria for obtaining informed consent. In June, the National Research Act was passed.⁹⁹

With the passage of the National Research Act, the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research was formed.¹⁰⁰ The report of the commission, the Belmont Report of April 1979, states three basic ethical principles and guidelines for research involving human subjects:

1. *Respect for Persons.* Respect for persons incorporates at least two ethical convictions; first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection.... In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information....
2. *Beneficence.* Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well being.... The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not harm and (2) maximize possible benefits and minimize possible harms....
3. *Justice.* Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved." ...[T]he selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied....¹⁰¹

⁹⁹ *Id.*

¹⁰⁰ *Id.*

¹⁰¹ THE NATIONAL COMMISSION FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, THE BELMONT REPORT: ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH (Apr. 18, 1979).

Applications of the three principles were given as “informed consent,” “assessment of risks and benefits,” and “selection of subjects.”¹⁰²

The Belmont Report dealt only with research conducted or sponsored by DHEW (which was succeeded by the Department of Health and Human Services), but it was eventually recommended as the policy for all federal agencies.¹⁰³ In 1981, the Department of Health and Human Services (HHS) and the Food and Drug Administration (FDA) revised their respective human subjects regulations to be as compatible as possible with the Belmont Report.¹⁰⁴ Most significantly, in 1991, the Belmont Report became the basis of the Federal Policy for the Protection of Human Subjects, or the “Common Rule,” when 15 federal departments and agencies published and codified the language of the HHS regulations, 45 CFR, part 46, in their own chapter of the Code of Federal Regulations.¹⁰⁵ Under the Common Rule, an IRB has the authority to approve, require modifications to, or disprove of a research activity covered by the policy. The Rule prescribes requirements for the membership of an IRB along with the criteria an IRB must follow in reviewing proposed research activity, and performing continuing review of research.¹⁰⁶ The criteria for approval of proposed research, all of which the IRB must determine to be satisfied, are laid out in §46.111 of the Rule:

- (1) Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- (2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In

¹⁰² *Id.*

¹⁰³ PAUL F. BASCH, *VACCINES AND WORLD HEALTH: SCIENCE, POLICY, AND PRACTICE* 87 (Oxford University Press 1994).

¹⁰⁴ *Federal Policy for the Protection of Human Subjects ('Common Rule')*, U.S. Department of Health and Human Services, <http://www.hhs.gov/ohrp/humansubjects/commonrule/>.

¹⁰⁵ *Id.*

¹⁰⁶ *See* 45 C.F.R. § 46.109 (2009).

evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research...as among those research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative...

(5) Informed consent will be appropriately documented...

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

These IRB requirements, a further evolution of earlier peer review requirements, have the virtue of dealing with another recurring issue in ethical evaluation of experiments. Namely, while peer review addresses the difficulties that medical researchers face in seeing the ethical problems with their own experiments, it does not necessarily go so far as to subject medical experiments to the moral judgment of the general public. After all, peer review consists of the judgment of colleagues within the medical profession, who may also be entrenched in the mindset of the medical research community, and thus limited in their ability to see ethical problems in experiments. The criteria in the Common Rule have the virtue of specifically iterating issues that would be relevant to the moral judgment of an American layman, such as whether the subjects are a part of a vulnerable population.

In December 1974, the *New York Times* reported that the CIA had conducted illegal domestic activities, including experiments on U.S. citizens, during the 1960s.¹⁰⁷ Prompted by these claims, a presidential commission under Vice President Nelson Rockefeller and congressional committee under Senator Frank Church of Idaho were established to investigate the domestic activities of the CIA, FBI, and intelligence-related agencies of the military.¹⁰⁸

In the forthcoming summer of 1975, the Rockefeller Commission held hearings and issued a report that revealed the CIA's MKULTRA project. The report disclosed that the CIA had tested behavior-influencing drugs, such as LSD, on unwitting human subjects in the United States, for the purpose of countering the clandestine use of such drugs by the then enemies of the U.S., namely the Soviet Union and North Korea.¹⁰⁹ The Commission declared that testing potentially dangerous drugs on unsuspecting U.S. citizens was clearly illegal.¹¹⁰ The report noted that following the Inspector General's discovery of the testing, new stringent criteria were issued prohibiting drug testing by the CIA on unknowing persons. Between 1963 and 1967, it indicated, the testing of drugs continued on voluntary subjects, primarily inmate volunteers at various correctional facilities, and all drug testing programs were ended in 1967.¹¹¹

In April of 1976, the Church Committee issued its report, which also described the CIA's experimental programs on unwitting human subjects. The report stated that the continuation of the studies, for years after the danger to the subjects was known, demonstrated a fundamental disregard for the value of human life, and that the Committee's investigation had raised serious

¹⁰⁷ ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 3, § 4.

¹⁰⁸ *Id.*

¹⁰⁹ COMMISSION TO INVESTIGATE CIA ACTIVITIES WITHIN THE UNITED STATES, REPORT TO THE PRESIDENT ("ROCKEFELLER REPORT") 226 (June 1975), *available at* http://www.history-matters.com/archive/contents/church/contents_church_reports_rockcomm.htm.

¹¹⁰ *Id.* at 228.

¹¹¹ *Id.*

questions about the adequacy of command and control procedures within the CIA and military intelligence.¹¹² For instance, the report described that the CIA's normal administrative controls were waived for programs involving chemical and biological agents to protect their security, and that this had produced "the paradoxical effect of providing less restrictive administrative controls and less effective internal review for controversial and highly sensitive projects...."¹¹³ The report also explained that because the testing programs were considered so sensitive by the agencies administering them, few people, even within the agencies, knew of the programs.¹¹⁴ The report quotes the CIA Inspector General: "the knowledge that the Agency is engaging in unethical and illicit activities would have serious repercussions in political and diplomatic circles and would be detrimental to the accomplishment of its missions."¹¹⁵

On August 3, 1977, the U.S. Senate Committee on Human Resources held a Joint Hearing before the Select Committee on Intelligence and the Subcommittee on Health and Scientific Research to discuss MKULTRA.¹¹⁶ Senator Kennedy of Massachusetts expressed outrage at the project, and stated that the CIA itself acknowledged that the LSD tests on unwitting human subjects, for one, made little scientific sense – that the agents doing the monitoring were not qualified scientific observers and, moreover, the subjects were rarely accessible for follow-up beyond the first hours of the test.¹¹⁷ Admiral Stansfield Turner, Director of Central Intelligence, testified before the Joint Hearing, presenting newly discovered findings

¹¹² SELECT COMMITTEE TO STUDY GOVERNMENTAL OPERATIONS WITH RESPECT TO INTELLIGENCE ACTIVITIES, UNITED STATES SENATE, FINAL REPORT ("CHURCH COMMITTEE REPORT") 386 (Apr. 26, 1976), *available at*

http://www.aarclibrary.org/publib/contents/church/contents_church_reports_book1.htm.

¹¹³ *Id.*

¹¹⁴ *Id.* at 385.

¹¹⁵ *Id.* at 386.

¹¹⁶ S. REP. NO. 96-406, at 7 (1977).

¹¹⁷ *Id.*

about MKULTRA since the Church and Rockefeller reports.¹¹⁸ After his testimony, Senator Kennedy addressed the Admiral, stating, “I did not get much of a feeling in reviewing your statement here this morning of the kind of abhorrence to this type of past activity which I think the American people would certainly deplore and much I believe that you do.” In response, Admiral Turner stated:

Senator Kennedy, it is totally abhorrent to me to think of using a human being as a guinea pig and in any way jeopardizing his life and his health, no matter how great the cause. I am not here to pass judgment on my predecessors, but I can assure that this is totally beyond the pale of my contemplation of activities that the CIA or any other of our intelligence agencies should undertake. I am taking and have taken what I believe are adequate steps to insure that such things are not continuing today.¹¹⁹

Asked to describe these steps, Admiral Turner explained that he had asked for a special report assuring him that there were no extant drug activities involving experimentation conducted by the CIA, and that he had ordered a special check of storage places for certification that there were no unauthorized chemical or biological materials in the CIA’s possession. Beyond that, he stated: “...I have to rely in large measure on my sense of command and direction of the people and their knowledge of the attitude I have just expressed...in this regard.”¹²⁰

With the airing of the CIA experiments, similar stories about Army experiments emerged. In 1975, the secretary of the Army responded by ordering the Army inspector general to conduct an investigation. In the course of the investigation, the still-classified 1953 Wilson Memorandum was discovered, and consequently declassified in 1975.¹²¹ The inspector general found that the Army had, in accordance with the Wilson Memorandum, largely used only

¹¹⁸ *Id.* at 8.

¹¹⁹ *Id.* at 16.

¹²⁰ *Id.*

¹²¹ ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 3, § 4, *citing* U.S. Army Inspector General, *Use of Volunteers in Chemical Agent Research* [Army IG report] 2 (1975).

volunteers for its drug testing. The inspector general also found, however, that the volunteers were not fully informed, and that the methods used to recruit them were, in many cases, contrary to the intent of the Army policies governing the use of volunteers for research.¹²²

Exemplary of the Army's practice was the case of James B. Stanley. In February of 1958, Stanley was stationed with his wife and children at Fort Knox, Kentucky. Responding to a posted notice, he volunteered to be a subject in a study advertised as developing and testing measures against chemical weapons. Stanley was transferred, along with thousands of other men who volunteered, to Edgewood Arsenal in Aberdeen, Maryland, where he was a subject in the Army's LSD experiments.¹²³ Stanley claimed that he was never told that he was given a psychoactive drug for the experiment, and that he was not debriefed or monitored for hallucination, which he thereafter experienced. He discovered that he had been given LSD in 1975, when he received a letter from the Army asking him to come to the Walter Reed Army Medical Center in Washington for a follow-up study of the LSD subjects. In the meantime, he had suffered emotional problems.¹²⁴

Like many others subjects and their survivors did during this period, as revelations about the CIA and Army experiments came out, Stanley brought a suit against the federal government for conducting the experiments. Some of the plaintiffs managed to receive compensation through court order, out-of-court settlement, or acts of Congress. Stanley's case, however, was dismissed by the Supreme Court in 1987.¹²⁵ A divided court, 5-4, found that, like all other

¹²² ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 3, § 4, *citing* U.S. Army Inspector General, *Use of Volunteers in Chemical Agent Research* [Army IG report] 87 (1975).

¹²³ MORENO, *supra* note 5, at 251.

¹²⁴ *Id.* at 252.

¹²⁵ ADVISORY COMMITTEE ON HUMAN RADIATION EXPERIMENTS, FINAL REPORT, *supra* note 15, at pt. I, ch. 3, § 4.

current or former members of the Armed Forces, Stanley was barred from suing the United States for injuries incurred “incident to service,” a legal rule known as the *Feres* Doctrine.¹²⁶ By the majority’s account, departing from the *Feres* Doctrine would lead to a judicial encroachment upon the province of the military. The majority opinion states, “a test for liability dependent on the extent to which particular suits would call into question military discipline and decision making would itself require judicial inquiry into, and hence intrusion upon, military matters.”¹²⁷ In his dissenting opinion, Justice Brennan invoked the Nuremberg Code, and stated that military officials had acted in defiance of its principles.¹²⁸ Finally, Justice O’Connor, dissenting separately, wrote that no judicially crafted rule should insulate the government from liability for the experimentation it conducted in contravention to the Nuremberg principles.¹²⁹

On the one hand, Stanley’s defeat showed how toothless the Nuremberg-based Wilson Memorandum was, inasmuch as it was in effect during Stanley’s participation in the LSD experiments, but could not be used as an avenue of recovery when that policy was violated and caused him harm.¹³⁰ On the other hand, however, the case’s dissenting opinions put the Army and the rest of the government on notice that the use of individuals for experimentation without obtaining informed consent was unlawful.¹³¹

In the fall of 1990, as the Pentagon made its preparations for the invasion of Kuwait, intelligence reports about Saddam Hussein’s chemical and biological warfare capacity prompted inquiries about medical protections for the troops. There was concern that service-members

¹²⁶ MORENO, *supra* note 5, at 252; *Feres v. United States*, 340 U.S. 146 (1950).

¹²⁷ *United States v. Stanley*, 483 U.S. 669, 682 (1987).

¹²⁸ *See id.* at 687–88.

¹²⁹ *See id.* at 709–10.

¹³⁰ MORENO, *supra* note 5, at 253.

¹³¹ http://www.hss.energy.gov/HealthSafety/ohre/roadmap/achre/chap3_4.html at 93.

might face nerve gas, anthrax bacteria, and botulinum toxin, all of which can cause death within days.¹³² Each of these agents could in theory be countered with protective medications.¹³³ During the buildup of forces, the Pentagon approached the new FDA commissioner, Dr. David Kessler, requesting a waiver of the FDA's normal informed-consent requirement for "investigational drugs." The request was based on the need to protect combat troops with methods thought to provide a reasonable prospect of defense against the threats. It was claimed that it was an extreme measure, demanded by the circumstances.¹³⁴

In response, the FDA adopted Rule 23(d), which created an exception to its regulations, allowing the commissioner to waive the consent requirement for those combat situations in which consent is "not feasible." The rule requires the commissioner to consider whatever evidence there is about the safety and effectiveness of the drug, the context in which it is to be used, the type of condition it is intended to treat or prevent, and the nature of information to be provided the recipients concerning the risks and benefits of taking the drugs.¹³⁵

Thus, the Pentagon's request was granted. During the Gulf War, all of the troops were given pyridostigmine bromide (PB) pills, which may enhance nerve gas antidotes like atropine if taken before exposure. About 250,000 of the troops elected to take them. About 150,000 troops received at least one anthrax vaccine, and about 8,000 received at least one dose of botulinum toxin vaccine. The botulinum toxin vaccine was considered to be "investigational" by the FDA, and PB had not been approved for use in the military against chemical weapons.¹³⁶ The FDA's relative lack of experience with the medicines, and the fact that it gave the Pentagon special

¹³² MORENO, *supra* note 5, at 269.

¹³³ *Id.* at 270.

¹³⁴ *Id.* 21 C.F.R. § 50.23(d).

¹³⁵ *Id.* at 271.

¹³⁶ *Id.* at 270.

permission to use the “unapproved drugs” on service-members without their informed consent, made it appear that the soldiers had been used as guinea pigs. Yet, even if there were something to learn from the incident as an experiment, few records were kept, beyond the rough numbers of how many took the drugs. Moreover, when veterans started to have medical problems, there were no records to identify who actually took the drugs and under what conditions.¹³⁷

In September 1999, President Clinton answered these concerns with Executive Order 13139, “Improving Health Protection of Military Personnel Participating in Particular Military Operations.”¹³⁸ Regarding the administration of investigational new drugs to members of the armed forces, it says that although it is the expectation that the U.S. Government will administer products approved for their intended use by FDA, in some cases a product that has not yet been approved by FDA might be administered to deployed military personnel, under certain circumstances and strict controls.¹³⁹ Namely, a product not approved for its intended use by FDA might be administered when the Secretary of Defense “considers a product to represent the most appropriate countermeasure for diseases endemic to the area of operations or to protect against possible chemical, biological, or radiological weapons....”¹⁴⁰

The Order also provides for a procedure whereby the President may waive the informed consent requirement when “absolutely necessary.” Specifically, it provides that DOD must obtain informed consent from each individual unless the Secretary can justify the need for a waiver. To waive informed consent, the President must then make a written determination that obtaining informed consent is not feasible, is contrary to the best interests of the member, or is not in the interest of national security. In making this determination the President must apply the

¹³⁷ *Id.*

¹³⁸ GOLISZEK, *supra* note 40, at 388.

¹³⁹ *Id.* at 389.

¹⁴⁰ *Id.*

standards and criteria set out in FDA regulations.¹⁴¹ The Secretary may also request that the President waive informed consent with respect to the administration of an investigational drug, and the Order sets out several requirements for this process, which includes consultation with the FDA.

The Executive Order also acknowledges and addresses problems with the Gulf War administration of investigational drugs by requiring DOD to provide, to all military personnel, ongoing training and health risk communication on the requirements of using an investigational new drug in support of a military operation to all military personnel. Under the Executive Order, such training and health risk communication must include, at a minimum, the basis for any determination by the President that informed consent is or may not be feasible, the means for tracking use and adverse effects of the investigational drug, the benefits and risks of using the investigational drug, and a statement that the drug is not approved (or not approved for the intended use).¹⁴² Thus, once more, controversy led to further, and detailed, policy regarding experimental measures on human subjects.

By way of conclusion, it may be apropos to note that “...the axiom that history repeats itself was never truer than in the case of human experimentation.”¹⁴³ Indeed, as this paper has aimed to illustrate, the history of research using human subjects has demonstrated persistently recurring themes. To recapitulate several of these, from Reed’s yellow fever experiments to the Gulf War vaccinations, research using human subjects has often been propelled by military necessity and national security concerns. Part and parcel to the both nature of military and

¹⁴¹ 21 C.F.R. § 50.23(d).

¹⁴² GOLISZEK, *supra* note 40, at 389.

¹⁴³ *Id.* at xii.

national security intelligence, as well as the difficult ethical issues that inhere in medical research, much of this research has proceeded in secrecy. As a result, several implications of secrecy in research have pervaded the history, such as the tension between secrecy and the development of policy, the tension between secrecy and the effective communication of policy, and the tension between secrecy and the ability of the moral conscience of the general public to inform human research policies. Similarly, a recounting of this history repeatedly demonstrates that medical scientists have at least two distinct difficulties that pose recurring problems in human experimentation; namely, the difficulty of operating within an ambiguous realm between medical practice and medical research, and the difficulty of seeing ethical problems that inhere in one's own medical research. Finally, perhaps most prominently, the history makes evident that scandal has driven the evolution of human research policy in the United States. There is little doubt in this author's view that this history will continue to repeat itself. Still, the evolution of policy herein described has come quite far in establishing important ethical standards and safeguards in human research, and this, too, is a trajectory on which the United States is likely to continue.