THE IMPACT OF REGULATING SOCIAL SCIENCE RESEARCH WITH BIOMEDICAL REGULATIONS

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Abstract

The Impact of Regulating Social Science Research with Biomedical Regulations: A Qualitative Study

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Since 1974 Federal regulations have governed the use of human subjects in biomedical and social science research. The regulations are known as the Federal Policy for the Protection of Human Subjects, and often referred to as the "Common Rule" because 18 Federal agencies follow some form of the policy. The Common Rule defines basic policies for conducting biomedical and social science research. Almost from the inception of the Common Rule social scientists have expressed concerns of the policy's medical framework of regulations having its applicability also to human research in the social sciences. The purpose of this dissertation was to investigate the impact of regulating social science research with the framework of biomedical research regulatory standards.

Qualitative methodology is used to analyze the Office of Human Research Protection's Determination Letters, to facilitate in-depth interviews of human research protection program administrators, and to evaluate the Common Rule policy.

The researcher reviewed 763 letters with 43 letters determined to be associated with social science research projects. The 763 determination letters represented a time span of 10 years, from 2000 to 2010. The letters were reviewed for indications of noncompliance or deficiencies to regulations specified in the Federal Regulations 45 CFR 46, Subpart A, (the Common Rule). Noncompliance or deficiencies by the IRB and HRPP support staff represented the majority of determination letter findings.

In-depth interviews were conducted with HRPP administrators. The lack of flexibility of the Common Rule in its application to social science disciplines was a common theme in the responses of HRPP administrators. Evaluation of the Common Rule suggested the policy was effective and efficient for the IRB and its administrative support staff, but was less effective and not efficient for social science research projects.

The assessment of the impact of regulating social science with biomedical regulations highlights the need for additional education and training of IRBs and their administrative support staff to more effectively apply a biomedical model of research regulation to the review and approval of social science research activity. The assessment additionally suggests the need for an “update” of the Common Rule to address the specificity of new areas of social science research in which IRBs deliberate scrupulously with no regulatory guidance.

Dedication

In Memory

of

my father

Manuel L. Braxton, Sr.

and

my brothers

Manuel L. Braxton, Jr. & Michael S. Braxton

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Chapter 1

Introduction

Human research can be traced as far back as the sixth century B.C. Sharav (n. d.) details in *A Chronology of Human Research* (see Appendix A) vegetable and meat experimentation with young Jewish prisoners.[1,2] As research continued during the Age of Enlightenment, medical human experimentation sought prisoners as research subjects with routine frequency (Jones, 1993). Eighteenth century research procedures included offers of free pardon to inmates who agreed to be inoculated with infectious small pox in variolation experimentation [3] (Lederer, 1995; Sharav, n.d.). Variolation experimentation resulted in disease and death for many of those inoculated with small pox. (Moreno, 2000; Faden & Beauchamp, 1986; Gibelman & Gelman, 2005).[4] In most, if not all cases, prisoners were subjected to variolation experimentation without their consent or offer of free pardon. Vollman & Winau (1996) puts forward that human research should not put subjects at risk to benefit others. They further suggest human subjects should receive a quotient of benefit from their participation in research.

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[1] No date is mentioned for the compilation of Human Experiments: A Chronology of Human Research by Vera Hassner Sharav

[2] Katz (2008) suggests Sharav is referring to the Book of Daniel, 1:3-5, 8, 11-13 in which the king requests the presence of some of the Israelites of royal blood and nobility. The king allotted them a daily portion of food and wine from the royal table…But, Daniel was resolved not to defile himself with the kings food or wine…Then Daniel said …"Please test your servants for ten days. Give us vegetables to eat and water to drink…Then see how we look in comparison with the other young men who ate from the royal table."

[3] Variolation is an obsolete method of immunizing humans against smallpox by infecting them with the pustules of infected humans. The method was popularized in England in 1721-1722. In America, Cotton Mather (1663-1728) used the method on slaves. During that time variolation continued to be opposed by religious groups and most physicians, who were not convinced of the safety of the method. It was replaced by vaccination in 1799. In 1842 an act of Parliament in England made the practice of variolation a felony in that country.

[4] Philip S. Hench Walter Reed Yellow Fever Collection details historical accounts of Walter Reeds experimentation with small pox research. See: http://yellowfever.lib.virginia.edu/reed/commission.html.

Vollman & Winau (1996) suggest that in 1900, as scientific information expanded so too did questions of unethical medical research practices. In Berlin, prostitutes were subjected to syphilis serum treatment without their knowledge or consent. The serum from patients recovering from syphilis was administered to the prostitutes by way of injection. The procedure was administered with the belief that the practice was a discovery in the cure for syphilis. An immeasurable epidemic among prostitutes and their customers resulted from the experimental procedures. The epidemic laid grounds for public outrage (Vollman & Winau, 1996). The authors suggest that the outraged public demanded action to be taken to halt unethical experimentation.

Early Human Research Regulatory Codes

Berlin Code

As a result of public outrage for unethical medical syphilis experiments, the Berlin Code of 1900 (the Code) was developed (see Appendix B). The Berlin Code was the first and strongest Code of that time to specify the conditions of ethical experimental procedures while conducting medical research with human subjects (Vollman & Winau, 1996). The Code required:

- unambiguous consent, after thorough explanation of possible negative consequences of participation in study;
- the study be conducted or directed by the institute's medical administrator;
- of minors or incompetent subjects be excluded;

- documentation of fulfillment of the Code requirements in subjects medical records; and that
- the research not interfere with standard diagnostics, care and prophylaxis.

Accounts of unethical human medical experimentation by world famous and revered doctors continued throughout the 1920s and beyond, forcing the medical community, courts, and the public to consider additional protections for human research subjects in addition to those protections stated in the Berlin Code of 1900. Examples of continued unethical treatment of human research subjects are documented in the historical events of medical experimentation by the Nazi regime.[5] Nazi regime doctors performed many series of unethical medical experiments on hundreds of prisoners held in concentration camps[6] during World War II (1939-1945).

Annas & Grodin (1992) suggests that camp prisoners were coerced and forced into participating in the medical research experiments. The experiments conducted resulted in harmful and often deadly consequences for the subjects (see Appendix C, Appendix D; Appendix E; Appendix F; and Appendix G). The harmful and deadly medical experiments were never accompanied by informed

[5] The National Socialist German Workers' Party, known in German as the Nationalsozialistische Deutsche Arbeiterpartei and commonly known in English as the Nazi Party, was a political party in Germany between 1919 and 1945. The party's last leader, Adolf Hitler, was appointed Chancellor of Germany in 1933 and established a totalitarian regime known as the Third Reich. Nazi ideology stressed the failures of communism, liberalism, and democracy. They supported the "racial purity of the German people" and that of other Northwestern Europeans. The Nazis persecuted those they perceived as either race enemies or those with "life unworthy of living". This included Jews, Slavs, Communists, homosexuals, the mentally and physically disabled, and others. Source: http://en.wikipedia.org/wiki/Nazi_human_experimentation.

[6] The Oxford English Dictionary, 2nd ed. defines concentration camp as: a camp where non-combatants of a district are accommodated, such as those instituted by Lord Kitchener during the South African war of 1899-1902; one for the internment of political prisoners, foreign nationals, etc., especially as organized by the Nazi regime in Germany before and during the war of 1939-45.

consent.[7] Public awareness of the medical research atrocities being performed in the camps surfaced. Doctors and scientists that had engaged in the human experiments were put on trial for war crimes, including "violations of the laws or customs of war" (Annas & Grodin, 1992, p. 95).

Nuremberg Code

In 1946 Nazi doctors and scientists that conducted harmful and fatal experiments were indicted for war crimes before the International Military Tribunal in Nuremberg, Germany. Shelton and Cengage (2005, para. 1) state that:

> The trial of the Nazi doctors, known as the *United States of America vs. Karl Brandt et al.* the Medical Case, or the Nazi Doctors Case, was based on the Agreement for the Prosecution and Punishment of the Major War Criminals of the European Axis, signed in London on August 8, 1945 by the United States, the United Kingdom, France, and the Soviet Union, which created the International Military Tribunal (IMT). The Nazi doctors were not tried by the IMT, but rather by a U.S. tribunal acting pursuant to Control Council Law No. 10, signed on 20 December 1945.

The U.S. tribunal condemned all such harmful and fatal experiments and classified the experiments as crimes against humanity. These crimes were the result of Nazi doctors and scientists performing vile and potentially lethal medical experiments on concentration camp inmates and other living humans. The trials resulted in the conviction of 16 of the 23 physician defendants. Seven of those indicted were sentenced to death (Selton & Cengage, 2005).

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[7] Informed consent represents giving the research subject a clear appreciation and understanding of the facts of the research, the implications, and any foreseeable future consequences of the research procedures. In order to give informed consent, the individual concerned must have adequate reasoning faculties and have all relevant facts at the time consent is given. 45 CFR 46.116 of the Common Rule addresses informed consent. This term was first used in a 1957 medical malpractice case by Paul G. Gebhard. See Salgo v. Leland Stanford etc. Bd. Trustees, 154 Cal.App.2d 560 [Civ. No. 17045. First Dist., Div. One. Oct. 22, 1957.]

Shelton & Cengage further suggest the tribunal resulted in the judgment of principles that must be observed by medical researchers to satisfy moral, ethical, and legal concepts of research. The principles, as shown in Table 1, are known as the Nuremberg Code (see Appendix H). The tribunal espoused ten principles by which physicians must conform to when carrying out experiments on human subjects. The Nuremberg Code established additional standards of ethical medical behavior for the post-World War II human rights era (Annas & Grodin, 1992)

Grodin (1992) suggests that the Nuremberg Code was the cornerstone of modern human experimentation ethics. Whereas, Rothman (2003) suggest there were little if any impact of the Nuremburg Trials on medical experimentation in the U.S. The harmful scientific research performed on humans in Germany had little, if any, impact on improving medical research practices in the U.S. (Rothman 2003). Rothman acknowledges that although twenty-three medical doctors and scientists were indicted for the atrocities, with seven of them being executed, the majority of American medical researchers did not find the German doctors' engagement in the unethical experimentation of human research subjects to be unscrupulous.

Annas & Grodin (1992) and Rothman (2003) put forward that German scientists and research doctors were trusted and revered scientists. Oakes (2002, p. 444) suggests that:

> Americans believed that its physician-researchers acted in accordance with their Hippocratic ideals and voluntary consent was unnecessary in a society with a long and untarnished history of medical research.

Table 1

Principles of the Nuremberg Code

1.	Voluntary consent of the human subject is absolutely essential
2.	The experiment should be such as to yield fruitful results for the good of society
3.	The experiment should be so designed and based on the results of animal experimentation
4.	The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury
5.	No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur
6.	The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment
7.	Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death
8.	The experiment should be conducted only by scientifically qualified persons
9.	The human subject should be at liberty to bring the experiment to an end
10.	The scientist in charge must be prepared to terminate the experiment at any stage

American ethicists justified human research without the protections of informed consent given to subjects as unnecessary due to the need of experimentation for the persons own therapy; experimentation for the good of humanity in general, and experimentation to advance science (Oakes, 2002; Moreno, 2000; Vollman & Winau, 1996).

Unethical Human Research in the United States

Tuskegee Syphilis Study

Jones (1993), Reverby (2009) and Washington (2006) suggest the forty year Tuskegee Syphilis Study conducted from 1932 until 1972, captures the unethical medical experimentation with humans in the United States after regulatory guidance of the Berlin Code and the aftermath of the Nuremberg Trials and the Nuremberg Code. The authors further suggest that the United States Public Health Service (PHS) continued to conduct unethical medical research.

The Tuskegee Syphilis Study included medical research on 399 indigent men infected with syphilis. The men, black illiterate sharecroppers in Alabama, were never told by the medical researchers what disease they were suffering from or the seriousness of the disease. The research subjects became enrolled in the study without their knowledge or consent (Reverby, 2009; Jones, 1993; Moreno, 2000; Oakes, 2002; Washington 2006). Medical researchers told the men they were suffering from “bad blood” instead of the disease of syphilis. The research doctors had no intention of treating the men for their illnesses (Jones, 1993; Washington, 2006; Oakes, 2002). Jones, Moreno and

Washington suggest that the men were left to expire with their disease in order that data could be collected from autopsies of their diseased bodies. One of the medical research team involved in the study explained, referring to the research subjects, “As I see it we have no further interest in these patients until they die” (Washington, 2006, p. 164).

The men died a slow and painful death without treatment being administered for their disease although penicillin had proven to be an effective treatment for syphilis in 1946 [8] (Jones, 1993; Moreno, 2000). Medical research funding by the U.S. Public Health Office had been greatly increased for human subject research, although increased protections for subjects had not yet had been also put in place (LaFollette, 1994; Dubois, 2008).

Increased Funding for Medical Research

Major Federal government financing of medical research appeared during World War II. Research funding escalated from $4 million to more than $100 million between 1947 and 1957 while the National Institutes of Health (NIH), an agency of the Public Health Service, had grown from a budget of $8 million to over $1 billion by 1966 (Schrag, 2009). Under the same legislation that grew NIH’s budget, the legislation also authorized the opening of a Clinical Center to “specifically provide researchers with people, some of them not even sick, on whom to experiment” (Schrag, 2009, p. 5).

[8] In 1946, extensive trials with penicillin had demonstrated that the antibiotic was successful in curing syphilis. Supervising Physicians of the Tuskegee Study made certain that the experimental group were never to be given penicillin so as not “to contaminate” the study as it was designed to determine the natural evolution of untreated chronic syphilis.

Schrag suggests Institutional Review Boards (IRBs) were formed to respond to the increased amount of medical research taking place in the United States. Although, as Schrag further suggests, the NIH had required their studies, having increased risk to subjects, be approved by their medical review committee with participating patients to be given written consent to participants in the studies. The NIH did not require signed informed consent from subjects participating in minimal risk studies as a condition for research institutions to receive Federal funding for their medical research projects. A comparable system of human research protection was recommended to be applied to all programs financially sponsored by NIH during the 1960s (Schrag, 2009).

In 1966 medical research funded by the Public Health Service was required to undergo “prior review” by institutional associates to insure research participants’ protection of their rights and welfare (Gray, 1978). Pattullo (1985), Schrag (2009), and Oakes (2002) suggest that prior review was the first Federal prerequisite placed on institutions conducting research outside of the Federal government’s agencies. Currently, all institutions receiving Federal funding are now required to have an institutional review committee (IRB) review and approve all medical and social science research projects before implementation of the research.

Research with Vulnerable Populations in the United States

In the United States biomedical researchers believed they were far removed from participating in unethical research atrocities as those perpetuated by Nazi doctors and scientists (Vanderpool, 1996). Vanderpool points out that

between 1946 and 1966 U.S. biomedical researchers “resisted ethical and regulatory oversight” (p. 8). Beecher (1966) brought unprecedented attention to research practices in the United States involving unethical research practices in general and more specifically unethical research on children. Criticisms of unethical medical research practices involving children gained new attention (Vanderpool, 1996). The Willowbrook State Hospital study, as Rothman & Rothman (1984) note, is the most widely known unethical study on children. The Willowbrook Study involved children diagnosed with mental retardation, living at the Willowbrook State Hospital as patients from 1956 to 1971 (Levine, 1988). Researchers infected the otherwise healthy children with hepatitis to gauge its natural history, prevention, and treatment of the disease. A public uncovering of the Willowbrook Study forced researchers to suspend the hepatitis research.

Other fragile populations continued to be enrolled in unethical research studies in the U.S. (Faden & Beauchamp, 1986). The Jewish Chronic Disease Hospital Study, undertaken in 1963 included live cancer cells being injected into 22 senile patients. The purpose of the research was to determine how a weakened immune system influenced the spread of cancer (Jones, 1993; Lederer, 1995). Patients were not informed of the research or asked to give their consent by the researchers about the experimental procedures of receiving live cancer cells. Researchers also neglected to get approval from the hospital’s research committee or the patients’ physicians or patients’ legal guardians.

According to Jones (1993) part of the researchers’ defense was that there was no need to unnecessarily frighten the patient and their family with the details

of the research study. The researchers conducting this study were tried and found guilty of fraud, deceit, and unprofessional conduct (Jones, 1993; Lederer, 1995; Dubois, 2008). Still, unethical medical research practices continued (Dubois, 2008, Vanderpool, 1996).

Congressional hearings produced the Kefauver-Harris Bill of 1962 as a result of pregnant women given birth to deformed infants in the United States, Canada, and Europe after being given the drug thalidomide. The experimental drug was given to women without their knowledge or consent. Originally developed to relieve nausea during pregnancy, the drug's birth defects of the fetus from the drug resulted in more than 12,000 severely deformed infants, many without limbs (National Center for Juvenile Justice [NCJJ]), n.d.). The Kefauver-Harris Bill required researchers to inform all subjects about impending risks and benefits of experimental drugs and to acquire consent from participants prior to taking part in the study (NCJJ, n.d.). NCJJ notes that this bill was the first U.S. statute requiring informed consent.

The NCJJ suggest the requirements of the Kefauver-Harris Bill did not "address the capacity of minors or adults with limited decision-making skills to make an informed decision" (para. 7) to participate in research activity. To address this issue, the World Medical Association issued the Declaration of Helsinki (Appendix 1) in 1964, which required "surrogate consent when the participant is incapable of decision-making (para.7). The Declaration of Helsinki (the Declaration) requires surrogate consent if minors and adults are to be

enrolled in a study and, "lack cognitive ability or emotional maturity to understand potential risk or harm associated with research participation" (para.8).

The 1970s brought about much controversy over unethical medical research practices in general, and specifically the 40 year Tuskegee Syphilis Study (Caplan, 1992; Lederer & Grodin, 1994). Negative publicity of the studies garnered publication in medical journals, major newspapers, and discussions in Congress (Field & Berman, 2004; Goldman, 1973; Faden & Beauchamp, 1986; Lederer & Grodin, 1994).

Human Research Regulatory Statutes in the United States

National Research Act

"While the 1947 Nuremberg Code was the world's reaction to Nazi war crimes, the 1974 National Research Act Public Law 93-348 (see Appendix J) was the response of the United States to the Tuskegee Syphilis Study" (NJCC, para. 8). The National Research Act established the IRB process requiring formal peer review and approval of all Department of Health and Human Services (DHHS) research involving human subjects (NCJJ, National Bioethics Advisory Committee (NBAC), 2001).

NJCC and NBAC suggest that the 1974 National Research Act (Public Law 93-348) legislation also created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (National Commission). The National Institutes of Health

> One of the charges to the Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be

> followed to assure that such research is conducted in accordance with those principles. In carrying out the above, the Commission was directed to consider: (i) the boundaries between biomedical and behavioral research and the accepted and routine practice of medicine, (ii) the role of assessment of risk-benefit criteria in the determination of the appropriateness of research involving human subjects, (iii) appropriate guidelines for the selection of human subjects for participation in such research and (iv) the nature and definition of informed consent in various research settings (http://ohsr.od.nih.gov/guidelines/belmont.html, para. 1).

The Belmont Report

The Belmont Report serves as a statement of basic ethical principles and guidelines to assist in resolving ethical problems related to the conduct of research with human subjects. The basic tenets of the Belmont Report (see Appendix K) include three fundamental principles, respect for persons, beneficence, and justice.

As a result of the 40 year Tuskegee Syphilis Study by the U.S. Public Health Service the Belmont Report was developed. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1974 to 1978 revised and expanded 45 CFR 46 Subpart A (see Appendix L) to include principles of the Belmont Report. The National Commission's Report of ethical principles and guidelines for the protection of human subjects was published and was given the name, the Belmont Report for the Belmont Conference Center where the National Commission met to draft the report. Institutional peer review became a formal process to ensure compliance with the basic principles of the Belmont Report.

However, the Belmont Report did have its critics regarding its applicability to nonmedical research. Schrag (2010) suggests that Albert Reiss, a prominent sociologist who participated in the 1976 conference that resulted in the National Commission's creation of the Belmont Report, ignored objections by social scientists participating in the recommendations to the document. Schrag notes that although the Belmont Report "is a notable achievement in the exploration of the ethical challenges raised by medical research, but which serves as a poor guide to research in the social sciences and humanities …" (para. 2). The impact of the Belmont Report is discussed further in the section, Protecting Human Subjects Using Regulatory Standards.

The Common Rule

The National Commission recognized the need for a common Federal policy by recommending in 1991 that all Federal departments and agencies adopt a common core of regulations governing research with human subjects which was to be issued by the Department of Health and Human Services. NCJJ suggested that the adoption of these "common" regulations by 17 Federal departments and agencies became known as the Common Rule. The Code of Federal Regulations, Title 45 Public Welfare Department of Health and Human Services Part 46, Protection of Human Subjects (45 CFR 46) was adopted by 17 Federal agencies and became known as the Common Rule because the rules are common to many Federal departments and agencies conducting human subjects research. Unethical use of human subjects in biomedical research in the

United States brought intervention from the Federal government that provided better protection for human research subjects (Pattullo, 1985).

Although historical accounts of medical experimentation with human subjects identifies a history embedded in horrific pain, disfigurement, and death,[9] Muller (2007) suggests the literature does not bare the same historical unethical events for human subjects participating in social science research.

Human Research Regulations and the "New Sciences"

Although medical research was the initial focus of human research protection intervention by the Federal government, the "new sciences," anthropology, sociology, economics, and political science were also under scrutiny (Pattullo, p. 527). Tropp (1978) suggests that additional Federal policy to protect human research subjects emerged in the early 1970's regulating not only medical human research but also research activity of the social sciences. Yet, Singer & Levine (2002, p. 18) puts forward:

> Unlike clinical research, which at times involves the risk of physical injury and even death as a direct result of a research intervention, the most severe harms likely to befall subjects in social science research arise from potential breaches of the confidentiality of the data collected. Thus, for example, loss of job, criminal prosecution, and public humiliation are all potential consequences of revealing damaging information that a research subject has disclosed to an investigator.

The authors suggest the kinds of limited harm social science research engenders is far less detrimental than that of biomedical research. Seemingly

[9] Vivien Spitz. (2005). Doctors from Hell: The Horrific Account of Nazi Experiments on Humans. During the Nazi doctors' military tribunals Spitz, then a 22-year-old court reporter recounts the atrocities of 20 doctors and medical assistants' use of prisoners for horrific experimentation in German prisons.

"over-zealous medical scientist" has brought an increased level of scrutiny to social science research evidenced by governmental regulations (Patullo, 1985, p. 524). Among noted social science unethical research includes:

- The Harvard Drug Study (Weil, 1963)
  - Psychedelic drug research with students at Harvard University.
- Tearoom Trade (Humphreys, 1970,)
  - Research to investigate who seeks quick, impersonal sexual gratification and the motives for doing so?
- Stanford Prison Experiment (Zimbardo, 2007)
  - Investigation of the psychological effects of becoming a prisoner or prison guard.
- Stanley Milgram Obedience Study (Milgram, 1974)
  - Research of the effect of authority on obedience

The literature suggests the amount of harm experienced by those participating in social science research has been negligible (Pattullo, 1985, Gunsalus et.al., 2004). Additionally, it is put forward that the fields of anthropology, journalism, oral history, ethnography and other social science fields already had well-established ethical research guidelines for their profession (Gunsalus et.al., 2004; Haggerty, 2004)).

Social Scientists' Concerns of Overregulation

As a result of the 1974 National Research Act, and the establishment of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research both disciplines (biomedical and the social sciences) were subject to increased scrutiny. The Code of Federal Regulations, Title 45 Public Welfare Department of Health and Human Services Part 46, Protection of Human Subjects, the Common Rule[10] (Subpart A of 45 CFR 46) in 1979 formally proposed that all human research including social science research be regulated by the same standards as biomedical research practice (Seiler & Murtha, 1980). The 1979 Federal Register (see Appendix M) proposed guidelines requiring all Federal funded social science research to receive institutional review board (IRB) review comparable to that of biomedical research. The Federal Register suggests that social science be included in the Federal regulations (Oakes 2002, p. 448; 44 FR 47688).

Although the Federal Register includes social science research in the human subject research regulations, a number of social scientists saw the applicability of the federal regulations for the protection of research subjects to social science as "being included by mistake" because there were no social scientist involved in the decision-making process to advocate for less restrictive regulatory standards of minimal and less than minimal research practices of social science researchers (Seiler & Murtha, 1980, p. 47). Seiler & Murtha

[10] The Common Rule which has been adopted by 17 government agencies proposes procedures for Institutional Review Boards, including the kinds of research which is exempt from their purview, and the kinds of research that should receive expedited review given there is minimal risk to participants. Felice Levine of the American Sociological Association pointed out in recent testimony, there are "growing fault lines in the system that protects human participants," and a "gap has developed between law and policy on the books and in action.

suggest that there was ambiguity about how social science research became included for oversight in the federal human subject protection regulations. The authors note that documentation of discussions held did not address issues related to the less than minimal risk projects of social science research, including interviews, surveys, or oral history projects.

The NBAC in 2001 proposed various efforts to strengthen the protection of humans participating in research regulated by the Common Rule, applying the tenets of biomedical human research protection to social science research. Gordon (2003) suggests that while these efforts to provide increased protections for human research participants reflect a laudable goal, the regulations do not necessarily apply or translate well to all disciplines of research, particularly social science research. Gordon further suggests that social science researchers commonly perceive the current and proposed human subjects regulations as obstacles to research for social scientists. Anthropologists and other social scientists typically encounter these obstacles at the point of obtaining IRB review and approval of their research protocol. As an example, IRBs require that human subjects research studies comply with the Common Rule by ensuring primarily that the benefits of participation in research outweigh the risks to subjects, and that subjects are consented by way of written informed consent in most cases prior to participation in the research. For anthropological projects and other social science projects these requirements can present unattainable conditions (White, 2007; Hamberger, 2005).

Seiler & Murtha (1980) suggests that regulations and interpretations of the regulations are modeled heavily in the biomedical standards of research. The authors propose that the biomedical model of human research protection does not necessarily conform to social science approaches toward research. White (2007, p. 548) articulates the concerns of social science researchers in stating:

> The government's continued reliance on monopolistic, one-size-fits-all institutionalized solutions such as the IRB process clearly threatens the future of behavioral science, if not of biomedical science, by overloading the system with paperwork and by wasting the time, effort and resources of everyone involved, including researchers, board members, students, teachers and government officials.

Social scientists puts forward that the Common Rule may not be fully applicable to anthropological and other social science research (Mueller, 2007; De Vries; DeBruin & Goodgame, 2000). They suggest that there is no evidence of enhanced safety for research participants of social science research when the one- size-fits-all regulations of the Common Rule are applied to the review and approval of their research projects.

Mueller (2007) suggests dissatisfaction and frustration with the system of applying biomedical regulations of research to social scientist research projects. Much of the frustration he suggest, centers on describing how risk is interpreted in biomedical terms, thereby making it difficult to apply the Common Rule to social science research. Social science researchers express high levels of concern of overregulation and mission creep as a result of applying biomedical regulations to social science research (White, 2007; Schrag, 2009; Mueller, 2007; De Vries et al., 2004).

Haggerty (2004) suggests that IRBs are the instruments of a system of licensing in which scholars, students and other researchers must get permission to conduct research with human subjects. He suggests that IRBs are far more dangerous than the research they review and they offer little if any protection for human subjects. Rothman (1995) suggests that IRB's and their staff may not have adequate education and training in pertinent regulations; therefore inappropriate burdens may be placed on researchers. Similarly, excessive documentation procedures rather than providing guidance in the interpretation of the regulations amount to the overregulation and less protection for research subjects (Hamilton, 2004; Gunsalus, 2004).

Burris & Welsh (2007) characterize IRBs as a regulatory system that often distracts from rather than focus on key ethical concerns. Zywicki (2007) suggests that "IRBs have become a ubiquitous presence on the landscape of America's higher education system" using a system of review of research projects which suggests a one-size-fits-all approach (p. 861). Zywicki proposes that IRBs have been extensively criticized as inefficient, obstructionist, and indifferent to the researchers' needs. He suggests that IRBs are ineffective at protecting the safety and ethical concerns of research participants because of excessive regulations required in biomedical and behavioral research.

De Vries et al. (2004, October) propose that although the Common Rule at §46.117(c) state that the IRB may waive the requirement for the investigator to obtain a signed informed consent for some or all subjects if it finds that either:

(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach in confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

De Vries; Debruin; & Goodgame propose that although the waiver of signed informed consent included in the regulation is a useful exception, beneficial to carrying out social science research, the institutions' administrative bureaucracy of legal cover insists that documented written consent be obtained from participants, even if they cannot write their names. The authors also suggest that documentation of legal consent is to cover the institution, not to provide additional protection for the research participant. Similarly, White (2007) agrees that the waiver is useful to accommodate minimal risk research projects, as most social behavioral research represent; however, some human research protection programs are reluctant to utilize such provisions as the waiver of signed documentation in the protocol review and approval process.

Agreeing with some of the criticisms of social science researchers, the NBAC in 2001 criticized Institutional Review Boards for being grossly overwhelmed by tremendous workloads, scarce resources, and by a regulatory system that routinely distracts from, rather than focuses on more relevant and

important ethical issues. Criticisms by researchers of the practices of their IRB have appeared repeatedly in the literature for the last four decades as documented by the authors cited. The NBAC (2001) suggest that federal regulators' emphasis on procedure and documentation as contributing factors for the creation of a climate of hostility and noncompliance in which the review of research becomes an exercise in avoiding sanctions and liability rather than in maintaining appropriate ethical standards and protecting human research participants.

De Vries et al. (2004); Gunsalus et al. (2004); and Wax (2000) also suggests that IRBs may be overly zealous in their interpretation and application of federal guidelines for conducting research with human subjects, exacerbating the challenges faced by social science researchers seeking IRB approval for their research projects. Professor of anthropology, Murray Wax, in his testimony before President Clinton's National Bioethics Advisory Commission stated:

> The gravest ethical problem facing the people studied by anthropological research is posed by unknowing and overzealous IRBs and by governmental regulators attempting to force qualitative ethnographic studies into a biomedical mold (NBAC, 2000, p. 95).

White (2007) suggests that patterns of noncompliance and litigation are not seen in social science research as in biomedical or clinical research. He suggests that applying similar rules of biomedical research, with no subject being harmed, amounts to IRB mission creep. White further suggests that mission creep is due to OHRP's oversight based in the need for documented administrative procedures, not explicit unethical researcher implementation of the

research project. Gunsalus et al. (2007) refers to mission creep as detailed in the *Illinois White Paper, Improving the System for Protecting Human Subjects: Counteracting IRB "Mission Creep"* as a crisis being caused by the increased workload for IRBs and HRPP's inability to handle the workload effectively. Therefore, the emphasis is placed on the less difficult path of focusing more on procedures and documentation rather than difficult ethical issues presented in research studies.

Gunsalus et al. suggest that the institutions' efforts to comply with federal requirements, even when research is minimal risk, amounts to exaggerated precautions to protect against program shutdowns, and efforts to protect the institution and institutional review boards against lawsuits. The concerns of social science researchers of overregulation and mission creep, permeates the literature. These concerns have given impetus to investigate the impact of regulating social science research with biomedical regulations.

Research Problem

The literature supports the premise of protecting research participants from the risks and harms of research. Regulatory policy has provided guidelines to ensure research risk is minimized, although it is widely perceived that the system of human research protection needs improvement. The literature has consistently revealed social scientists' concern of regulating social science research using research standards assembled from for biomedical research practices. The Common Rule in its application to social science research, social scientists suggests, result in overregulation and mission creep.

The research problem is to test the critical assessment of the Common Rule's impact of applying biomedical research standards for minimal risk social science research.

Research Questions

The research questions for this study include the following:

1. What are the findings of deficiencies and findings of noncompliance indicated in OHRP determination letters (DL) for social science research projects?
2. What impact does the Common Rule have on social science research protocol review by human research protection programs?
3. Has the Common Rule achieved its intended purpose of protecting human research subjects participating in social science research?

Research Method

Data collection and analysis include three research methods

1. Content analysis of public documents (determination letters) issued by the Office of Human Research Protection;
2. In-depth interviews of human research protection program administrators; and
3. Policy evaluation of Federal Policy 45 CFR 46, Subpart A, the Common Rule.

Content Analysis

Gathering and analyzing documents that are produced in the course of everyday events is what Marshall & Rossman (1999) proposes as unobtrusive research. Babbie (2004) suggests unobtrusive research is a method of studying social behavior without affecting it. Bogden & Biken (2003, p. 128) suggests that external documents like those available to the public are more effective for the researcher if it is known who produced the documents and for what reason they were produced. Having this knowledge can better place documents in social context. Babbie (2004) further suggests that content analysis is used to study human communication that has been recorded. He provides as an example, letters. Letters are documents well suited to content analysis, giving the researcher the ability to answer: "Who says what, to whom, why, how, and with what effect (p. 314).

Qualitative content analysis method is used to analyze OHRP public documents (determination letters). The goal of content analysis is to provide

knowledge and understanding of the phenomenon (Weber, 1990). Weber additionally suggests that qualitative content analysis is one of many research methods used to analyze text data and that it can be used to examine and classify large amounts of text into efficient number of categories. Qualitative content analysis is the study of human communications in the forms art, songs, collections and a host of categories of texts such as newspapers, books, letters, speeches (Weber 1990).

Cavanagh (1997) suggests that researchers find content analysis a flexible method for analyzing text data. Conversely, Tesch (1991) suggests that the flexibility that has made content analysis useful on one hand provides constraints to a firm definition of procedures resulting in limited application of content analysis. Whereas, Weber (1990) suggest, the specific type of content analysis approach used by the researcher depends on the theoretical and substantive interests and the problem being studied by the researcher. Additionally, Holsti (1969, p. 608) legitimizes the methods of content analysis as a “technique for making inferences by systematically and objectively identifying special characteristics of messages." Thus, content analysis is reasonable method for conducting inquiry (Weber, 1990; Babbie, 2004; Holsti, 1969; Lincoln & Guba, 2000).

In-Depth Interviews

In-depth interviewing is a qualitative research technique that involves conducting individual interviews with a small number of respondents to explore their perspectives on a particular idea, program, or situation (Boyce & Neale, 2006). The authors suggest that in-depth interviews are useful when detailed information about a person's experiences and behaviors are sought (p. 3). Additionally, Boyce & Neale (2006) and Patton (2002) suggest that in-depth interviews are used to provide context to other data to assist in providing additional information to complete the picture of what is happening in a particular phenomenon. Marshall & Rossman, 1999 suggest that in-depth interviewing may be the overall research method or one of several methods used in a study and the researcher must understand the advantages as well as disadvantages to in-depth interviewing.

The purpose of the in-depth interviews implemented in this study is to better comprehend HRPP administrators experiences in applying the tenets of the Common Rule to minimal risk social science research. Marshall and Rossman suggest that in-depth interviews are like conversations that "uncover the participants views but otherwise respects how the participant frames and structures the responses" (p. 108). Although some systematization may be necessary to guide the questioning, it is the participant's perspective of the phenomenon of interests that should become apparent as the interview unfolds (Marshall & Rossman, 1999). In-depth interviews allow the researcher to

investigate complex topics and allow for ideas to emerge that have not been predetermined by the researcher (Berg, 2006; Denzin & Lincoln, 2005).

Policy Evaluation

Torgerson (1985) and Shapiro & Schroeder (2008) identify Lasswell as the founder of the policy science field. Lasswell, defined policy science orientation utilizing three characteristics (1) a multi- disciplinary approach, (2) problem oriented focus that is contextual in nature and (3) and explicitly normative orientation. These characteristics provide the additional framework of foundation to utilize Fischer's interrelated discourses for policy evaluation

In Fischer's Four Discourses of Policy Evaluation, Fischer (1995) suggest that regardless if one seeks to document accomplishments of a policy or criticize its failures, policy evaluation has emerged as an important component of the policymaking process in American government. Bryne (1987) and Fischer (1995) suggest that policy analysis asks the question of whether or not a policy accomplishes its stated purposes. Fischer (2003) posits that policy evaluation can also take the form of cost benefit analysis. He suggests that the logic of cost-benefit analysis involves a compilation of costs and benefits of a policy to determine its net value. Although, he suggests that cost-benefit analysis has been the subject of theoretical and practical disagreement because of its difficulty in quantifying policy inputs and policy outputs. Fischer (2003) further suggests that "the technique systematically underplays social objectives that cannot easily be measured in quantitative terms" (p. 116).

Utilizing Fischer's (1995) framework of practical informal logic of policy

deliberation (which he uses synonymously with the 'logic of policy evaluation'), this descriptive study is organized around the basic discursive components of four interrelated discourses being viewed from a qualitative lens.

- Technical/Analytic Discourse (Program Verification): does the program empirically fulfill its stated objectives?
- Contextual Discourse (Situational Validation [Objectives]): are the program objectives relevant to the program situation?
- Systems Discourse (Societal Vindication [Goals]): does the policy goal have instrumental or contributive value for the society as a whole?
- Ideological Discourse (Social Choice [Values]): do the fundamental ideas (or ideology) that organizes the accepted social order provide a basis for a legitimate resolution of conflicting judgments?

Title 45 CFR 46, Subpart A, the Common Rule is the focus of policy evaluation utilizing Fischer's Four Steps of Analysis.

Complementary Analysis Research Method Application (CARMA)

The literature suggest, Putney, Wink & Perkins (2006) originally implemented Critical Action Research Matrix Application also called CARMA as an inquiry tool to assess transparency of practices and the implementation of classroom activities (p. 4). Putney suggest that CARMA can be used to evaluate programs for their effectiveness as shown in Table 2). Jezierska (2009) in collaboration with the principal author, Putney (2008) adapted the Critical Action Research Matrix Application as the Complementary Analysis Research Method

Application (CARMA) for use in policy assessment. It is Jezierska's work in collaboration with Dr. Putney that lays the foundation for using the Complementary Analysis Research Method Application tool to assess the implementation and viability of the qualitative research method of analyzing the Common Rule.

CARMA is a flexible and natural tool to assist in the analysis process of the target populations intended to utilize the Common Rule and to assist the researcher to perceive the tangential impact of the Common Rule on social science and to identify elements of the Common Rule to support the tenets of social science research. Using a four tier matrix including; 1) Policy Expectations; 2) Evident Implementation; 3) Results; 4) Recommendations, information is input into the CARMA Matrix in combination with the framework of Fischer's Four Discourses of Policy Evaluation to be analyzed. Putney (2008) suggests flexibility of CARMA lends its evaluation technique to components of this investigation.

Table 2

Complementary Analysis Research Method Application (CARMA)

1 Determination Letter Expectations NOTE-TAKING	2 Evident Implementation NOTE-TAKING	3 Results NOTE-MAKING	4 Conclusions/ Recommendations NOTE-REMAKING
Initiators	Users/ Participants	Compare/ Contrast expected with evident	Evaluator Interpretations
Who is being served? Who is involved?	Who are evident participants?	Expected vs. Evident	What are the implications? Modify or maintain program?
How are participants to be served?	How are participants using the service?	Expected vs. Evident	What are the implications? Modify or maintain program?
What will be produced by participants in the program?	What was produced by participants in the program?	Expected vs. Evident	What are the implications? Modify or maintain program?

Limitations of the Study

Researcher bias is a threat to the validity of conclusions drawn from the data of this qualitative study. For nearly 10 years the researcher of this study has served in the role of HRPP Administrator of a doctoral granting academic research institution which conducts biomedical and social science research. In addition the researcher has conducted social science research, having the projects reviewed and approved by the IRB at a doctoral granting academic research institution. Miles & Huberman (1994, p. 263) suggests that qualitative data that fit the existing theory and preconception of the data selected and the data that "stand out" to the researcher is a threat to qualitative conclusions.

Although the researcher's theories, beliefs and perceptual lens can never be fully eliminated, it is the explanation of the possible biases and how they will be dealt with nonetheless that should be revealed in the study (Maxwell, 2005). Berg and Smith (1988) puts forward that qualitative researchers have a responsibility to science and their research participants which includes examining and reexamining their studies for their connection with their research as they "formulate ideas, collect and interpret data and build theory" (p. 11). It is with these understandings that the researcher pursues this study.

The additional limitations of this study are presented in a three pronged methodological approach of 1) content analysis of determination letters, 2) in-depth interviews of HRPP Administrators and 3) policy, analysis of the Common Rule.

- Content analysis of determination letters: Tesch (1991) suggests that the flexibility that has made content analysis useful on one hand provides constraints to a firm definition of procedures resulting in limited application of content analysis. Determination letters most often address ethical violations and deficiencies of federal agency funded research projects, whether biomedical or social science research projects. A large portion of social science research is unfunded. As the intent of the qualitative content analysis is to identify determination letters applicable to the social sciences which contain research violations or deficiencies, the sample may be small and not generalizable.
- In-depth Interviews: The limitation created by inclusive bias can impact the analysis of the data. Inclusive bias occurs when samples are selected for convenience. This type of bias is often a result of convenience where samples tend to fit a narrow demographic range. In this study HRPP Administrators are a narrow demographic range. Inclusive bias samples do not present concern, as long as the researcher is aware that the results cannot be extrapolated to fit the entire population of that demographic. Therefore the information extrapolated is not generalizable.
- Evaluation of the Common Rule policy: Fischer (1995) suggests that although the policy evaluation process may be narrowed to

specific facets of the policy no absolute criterion exists to ensure the position of the evaluation method.

The characteristics which limit and delimit the scope of this research project and define its boundaries and serve to enhance the overall quality of the data to be analyzed. These include the practice of OHRP in providing determination letters to institutions and researchers in many disciplines. OHRP regularly corresponds with hospitals, pharmaceuticals, medical teaching institutions, academic institutions and others. Correspondence to academic institutions from January 2000 to June 2010 is a delimitation to the study, I'm ready used to the exclusion of other agencies or institutions OHRP sends determination letters. With the focus of this study concerned with social science research projects, these projects can be found in greater numbers at doctoral, profession dominant institutions (Doc/Prof).

The Carnegie Foundation classifies Doc/Prof institutions as those institutions that award doctoral degrees in a range of fields such as education, public policy, and social work. The institutions may also offer professional education in law, and medicine[11]. Doc/Prof institutions are a delimitation to this study. Therefore, some entities are omitted for the reason that they are not directly relevant to this study. Furthermore, human research administrators are recruited from academic institutions sent determination letters reviewed in this study. An additional administrator is recruited from a DOC/Prof institution.

[11] Carnegie classifications can be found at: (http://classifications.carnegiefoundation.org/descriptions/grad_program.php)

Six HRPP administrators are selected for the study. All HRPP administrators have more than five years training and experience in the human research protections field of work and are considered to have adequate knowledge of the tenets of the Common Rule. Over a five year period knowledge gained from professional conferences and workshops, and day to day duties in the role of HRPP administrator is considered adequate to garner understanding of the Common Rule in its application to social science research.[12] HRPP administrators are selected due to their knowledge of the Common Rule by way of their professional training, their consistent contact with social scientists and social science research projects submitted to their HRPP to be reviewed and approval by the IRB. HRPP administrators are obligated to pursue a course of action in creating a culture of research compliance to assist the IRB by developing institutional human research compliance policies based on the policies of the Common Rule. HRPP administrators using the Common Rule as the basis for their institutional policies, could reasonably be a population in which the results of this study could be generalizable to the specific group.

[12] The IRB Forum (at: http://irbforum.org) routinely post job positions for HRPP Directors/Administrators that require five years or more experience to be considered for the position. prior experience to be success.

Definitions

Assurance: A formal written, binding commitment that is submitted to a federal agency in which an institution agrees to comply with applicable regulations governing research with human subjects and stipulates the procedures through which compliance will be achieved, (Office of Human Research Protection)

Behavioral and social science research: The Office of Behavioral and Social Science Research[13] defines behavioral and social research in part as an assortment of methodological approaches including: surveys and questionnaires, interviews, direct observation, physiological manipulations and recording, descriptive methods, laboratory and field experiments, standardized tests, economic analyses, statistical modeling, ethnography, and evaluation. Social science is used interchangeably with behavioral science.

Belmont Report: A statement of basic ethical principles governing research involving human subjects, issued in 1978 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

Biomedical Science: "the application of the principles of the natural sciences to medicine" (Bankert & Amdur, 2006, p. 87)

Human Subjects: Individuals whose physiologic or behavioral characteristics and responses are the object of study in a research

[13] The Office of Behavioral and Social Sciences Research (OBSSR) established by Congress opened in 1995.

project. The Federal Regulations define human subjects: living individual(s) about whom an investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information.

Informed Consent: A person's voluntary agreement, based on adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence (Amdur & Bankert, 2006).

Institutional Review Board (IRB): A specially constituted, federally mandated review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research (Amdur & Bankert, 2006).

Minimal Risk: The Common Rule describes minimal risk as the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination.

Mission Creep: Defined by Gunsalus et al. (2007) as the result of the workload of IRBs that has expanded "beyond their ability to handle effectively." Mission creep they suggest is caused by "rewarding wrong behaviors, such as focusing more on procedures and documentation than difficult ethical questions; unclear definitions, which lead to unclear responsibilities; efforts to comply with unwieldy federal requirements even when research is not federally funded; exaggerated precautions to protect against program shutdowns; and efforts to protect against lawsuits (p. 2).

Protocol: The formal design or plan of an experiment or research activity; specifically, the plan submitted to an IRB for review and to an agency for research support. The protocol includes a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data.

Research: A systematic investigation (i.e., the gathering and analysis of information) designed to develop or contribute to generalizable knowledge (the Common Rule).

Risk: The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal Regulations define only "minimal risk."

Social Science: Branches of social science include anthropology; economics; education; geography; history; law; linguistics; political science; public administration; psychology; sociology (Rule, 1997).

Significance of the Study

The significance of the study is to provide increased knowledge of the impact of the Common Rule for social science research. This study may ground criticisms of a “one-size-fits-all” regulatory policy (the Common Rule) as well as determine the merit to the assertion. This study can provide the basis for additional research to recommend policy changes as a result of the findings of this study for more adaptable regulatory standards for social science research. Additionally, the study can provide a foundation for further research in the area of human research protection policy for federal agencies and academic research institutions. This research is needed to assess public documents held by the regulating authority OHRP and associated with their determination and findings of social science research projects. HRPP Administrative Administrators’ assessment of utilizing a biomedical human research approach to evaluate the ethicality of social science research regulatory standards provide insight to the criticism of overregulation and mission creep. Finally this study can assist in better clarification of the Common Rule's applicability to and impact on social science research.

Summary

The Introduction of this study provides the historical framework of human subject research and human research protections from 6 B.C. to the present. The research problem of the study suggests there is a need to test the critical assessment of the Common Rule in its application to the social science research. The research questions of 1) what are the findings of deficiencies and findings of noncompliance indicated in OHRP determination letters (DL) for social science research projects, 2) what impact does the Common Rule have on social science research protocol review by human research protection programs, and 3) has the Common Rule achieved its intended purpose of protecting human research subjects participating in social science research.

The methods used to address the research questions are, content analysis of public documents, in-depth interviews of human research protection program administrators and policy evaluation of Federal Policy 45 CFR 46, Subpart A using Fischer's (1994) Four Discourses of Public Policy Evaluation, and Putney's (2008) Complementary Analysis Research Method Application.

The study includes a small sample size of HRPP directors which is not generalizable to an entire population but could be generalizable to the specific population of HRPP Directors, and researcher bias. Researchers suggest having social science research viewed through the regulatory eyes of biomedical expectations of risks has implications of unnecessary time barriers and cost to researchers, high workload for IRBs and their administrative support staff, as well as offering little if any additional protection for research subjects of behavioral

research[14]. The significance of the study is to provide increased knowledge of the impact of the Common Rule for social science research. Additionally, the study can provide a foundation for further research in the area of human research protection policy for federal agencies and academic research institutions.

This research is needed to assess public documents held by the regulating authority OHRP, as they are related to the determination and findings of social science research projects. HRPP Administrators' assessments of utilizing a biomedical human research approach to evaluate the ethicality of social science research regulatory standards are assessed. Finally this study can assist in better clarification of the Common Rule's applicability to and impact on social science research.

Although there has been much anecdotal comment in the literature on the topic of the application of a one-size-fits-all approach to regulating social science research with biomedical regulations, it is not apparent in the literature that empirical research has been conducted to substantiate the regulatory premise that social science research participants are better protected as a result of the one- size- fits-all Common Rule.

[14] The Illinois White Paper out of the Center for Advanced Study at the University of Illinois at Urbana-Champaign resulted in much controversy of IRB's and mission creep ,see Gunsalus, 2005.

Chapter 2

Review of Literature

This Chapter presents a review of the literature related to social scientists' concerns of what in the literature is called over-regulation and mission creep in its application to the Common Rule. The Chapter will document the historical perspectives of unethical human experimentation as well as the regulatory standards put in place to protect human subjects. In addition, the Chapter will discuss prior research related to researcher and institutional human research compliance while outlining the necessity to investigate the impact of social science research that is regulated by a medical model of human research protections.

Gunsalus et al. (2007) puts forward that "IRBs blizzard of paperwork is getting in the way of the fundamental mission: to protect the dignity and well-being of human subjects" (p. 4). Institutional Review Board (IRB) workloads have expanded beyond their ability to handle, due to focusing much more on procedures and documentation, unclear definitions, leading to unclear responsibilities and efforts to comply with the standards of human research requirements even when research is not federally funded (Schrag, 2009, Lincoln & Tierney, 2002).

The overzealous responses and exaggerated precautions to protect against program shutdowns and lawsuits is what Gunsalus et al. have referred to as mission creep. Shweder (2006) posits that projects that are not federally funded and "are not mandated for IRB review are under the federal surveillance

system" by IRBs (p. 507). Moreover, the increased scrutiny indirectly "generates a bias favoring overregulation or mission creep" (p. 515).

The concerns of social science researchers reflect the premise of overregulation. Gunsalus et al. suggests that:

> Without any systematic data or evidence of a problem, or even a thoughtful analysis of costs and benefits, the application of the human participant review system within universities is overreaching at the same time that some risky experimentation on humans outside of universities is unregulated… In too many cases, the focus is on form over ethical substance: counting what can be counted, rather than focusing instead on what counts. Some disciplines—oral history and journalism, for example—simply do not belong within the scope of institutional review board jurisdiction. Others, such as survey research, informational interviews, and informal interactions, call for a shift from centralized review to more departmentally based (i.e., rooted in disciplinary ethics) oversight, and clearer guidelines on what requires advance review as opposed to provision of post hoc complaint systems.

Fox (1994), Faden & Beauchamp (1986), and Schrag (2009) concur with Gunsalus (2007) in his interpretation of the concerns related to overregulation. Although substantial social benefits have been produced by scientific research, it has also posed troubling ethical issues of noncompliance and deficiencies (Oakes, 2002; Jones, 1993; Edwards & Mauther, 2002; Dubois, 2008). Medical research has presented an abundance of physical and ethical risks to human subjects (Dubois, 2008; Advisory Committee on Human Radiation Experiments, 1995; Ashcroft & Kirchin, 2004). To address the physical and ethical violations once seen in medical research the regulatory standards by which appointed Institutional Review Boards review, approve and oversee human research is the Common Rule (Alvino, 2003; Schrag, 2009).

Aita & Richer (2005) suggests that the foundations of research ethics has been a result of the biomedical and social sciences fields, saying that the "ethical principles related to human subjects' well-being emerged mostly with biomedical research while issues related to human rights are from the social sciences" (p. 120). Although there is little question that those involved in social science research do not want the human rights of their research participants abdicated and that there must be protections against unethical research, social scientists have found that utilizing the current biomedical system of human research protections result in incongruence of the application of biomedical regulations for social science research projects (Gunsalus et al., 2004; Braxton & Bayer, 1994; De Vries et al., 2004).

Social science researchers characterize their concerns as overregulation and mission creep resulting from the application of a regulatory process created for medical research being applied to non-invasive and minimal risk social science research, that usually is unfunded or privately funded (Oakes, 2002; Gunsalus et al., 2007). The authors suggest the premise of overregulation put forward by social science researchers, lays foundation for inquiry of regulating behavioral science research with biomedical science regulatory standards.

Gunsalus et al. (2007) suggest the result human research overregulation can and do result in unintended consequences for the researcher and their institution's human research protection program (HRPP). Social science researchers express increased concern of overregulation and mission creep, putting forth that increased documentation requirements by HRPPs appears to

have no additional protections for human participants of social science research, but serve to delay and even deny research projects (Gunsalus et al., 2007; White, 2007; Candilis et al., 2006; Coleman, 2004).

To better understand the impetus for the emergence of Federal Regulations to protect human research participants, historical perspectives on human experimentation are presented. The historical accounts of human experimentation provide background for additional perspective of the ethical concerns involved in human experimentation and research regulation in the United States. The majority of social science researchers' concerns focused on overregulation and mission creep suggests the need to evaluate the impact of the Common Rule on social science research. The review of literature applicable to this study include the following topics:

- Historical Perspectives on Unethical Human Experimentation
- Protecting Human Subjects with Regulatory Standards
- Berlin Code
- Nuremberg Code
- Declaration of Helsinki
- Belmont Report
- Common Rule
- National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
- National Bioethics Advisory Commission
- Office of Human Research Protection (OHRP)

Determination Letters

- Human Research Protection Program (HRPP)

  Institutional Review Boards (IRB)

  IRB Administrative IRB Support Staff
- Social Science Research
- Overregulation/ Mission Creep
- Intent and Impact of Policy

Historical Perspectives of Unethical Human Experimentation

Throughout the centuries human experimentation has been constant, as shown in Table 3. Human experimentation in the eighteenth century included regular offers of free pardon to inmates to participate in human experiments (Sade, 2003). One such experiment included the inoculation of prisoners with infectious smallpox in variolation experimentation (Morgan & Parker, 2007). Variolation was a method of immunizing humans against smallpox by infecting them with the pustules of infected human subjects. The method was popularized in England in 1721-1722.

In America, Cotton Mather (1663-1728) used variolation experimental method on slaves (Washington, 2006, p. 72). Selgelid (2003) suggests that in 1900 as scientific information expanded, questions of unethical medical research practices emerged with regularity. In Berlin, Germany, the medical practice of

Table 3
Historical Events in Unethical Human Experimentation

Date	Event
1796	Edward Jenner injects healthy eight-year-old first with cowpox then three months later with smallpox and is hailed as discoverer of smallpox vaccine
1845-1849	J. Marion Sims, "the father of gynecology" performed multiple experimental surgeries on enslaved African women without the benefit of anesthesia. After suffering unimaginable pain, many lost their lives to infection
1900	Walter Reed injects 22 Spanish immigrant workers in Cuba with the agent for yellow fever paying them $100 if they survive and $200 if they contract the disease
1919-1922	Walter Reed injects 22 Spanish immigrant workers in Cuba with the agent for yellow fever paying them $100 if they survive and $200 if they contract the disease
1932-1972	The Tuskegee Syphilis Study, sponsored by the U.S. Department of Health. Studied the effects of untreated syphilis in 400 African American men. Researchers withheld treatment even when penicillin became widely available. Researchers did not tell the subjects that they were in an experiment. Most subjects who attended the Tuskegee clinic thought they were getting treatment for "bad blood."
1939-45	German scientists conduct research on concentration camp prisoners.
1940's	Chicago doctors infect nearly 400 prisoners with Malaria to develop new drugs to fight the disease during World War II. I Inmates given general information that they were helping with the war effort, but not informed about the nature of the experiment. Nazi doctors on trial at Nuremberg cited the Chicago studies as precedents to defend their own research aimed at aiding the German war effort
1944-1980	The U.S. government sponsors secret research on the effects of radiation on human beings. Subjects were not told that they were participated in the experiments. Experiments were conducted on cancer patients, pregnant women, and military personnel
1956-1980	Saul Krugman, Joan Giles and other researchers conduct hepatitis experiments on mentally disabled children at The Willowbrook State School. They intentionally infected subjects with the disease and observed its natural progression. The experiments were approved by the New York Department of Health

Table 3

Historical Events in Unethical Human Experimentation (continued)

1950-1963	The CIA begins a mind control research program, which includes administering LSD to unwitting subjects.
1972	Stanley Milgram conducts his "electric shock" experiments, which proved that many people are willing to do things that they consider to be morally wrong when following the orders of an authority. He publishes Obedience to Authority in 1974
1982	William Broad and Nicholas Wade publish Betrayers of Truth, claiming that there is more misconduct in science than researchers want to admit. Their book helps to launch an era of "fraud busting" in science
1992	National Academy of Science publishes *Responsible Science: Ensuring the Integrity of the Research Process*. The book estimates the incidence of misconduct, discusses some of the causes of misconduct, proposes a definition of misconduct, and recommends some strategies for preventing misconduct
1994	The Clinton Administration declassifies information about secret human radiation experiments conducted from the 1940s-1980s and issues an apology
1999	Jessie Gelsinger dies in a human gene therapy experiment at the University of Pennsylvania. The event triggers heightened scrutiny of conflicts of interest in human subjects research, including institutional conflicts of interest. Penn settles with the Gelsinger family for an undisclosed amount of money
1999	Administrator of National Institute of Mental Health suspends 29 clinical trials that failed to meet either ethical or scientific standards
2001	Ellen Roche, a healthy 27-year old volunteer, dies in study at Johns Hopkins University in Baltimore, Maryland.
2001	Maryland Court of Appeals renders a landmark decision affirming "best interest of the individual child" as a standard for medical research involving children. The Court unequivocally prohibited nontherapeutic experimentation on children. (Higgins and Grimes v. Kennedy Krieger Institute).The case involved exposure of babies and small children to lead poisoning in EPA funded experiment. (http://www.courts.state.md.us/opinions/coa/2001/128a00.pdf)
2004	Liem Scheff authors article on AIDS research project of “Guinea Pig Kids” toxic drugs given to NY Black, Hispanic and poor orphans. The orphan children become subjects of drug trials sponsored by National Institute of Allergies and Infectious Disease, a division of the NIH, the National Institute of Child Health and Human Development in conjunction with some of the world’s largest pharmaceutical companies – GlaxoSmithKline, Pfizer, Genentech, Chiron/Biocine and others.

Sources: Human Experiments: A Chronology of Human Research by Vera Hassner Sharav http://www.ahrp.org/history/chronology.php, Research Ethics Timeline (1932-2004) by David B. Resnik, JD, PhD http://www.niehs.nih.gov/research/resources/bioethics/timeline.cfm. Table does not represent an exhaustive list of unethical human experimentation.

injecting prostitutes with serum from patients recovering from syphilis, with the belief that the protocol was a discovery for the cure of syphilis, laid grounds for public outrage as an immeasurable epidemic among prostitutes and their customers and partners surfaced (Gibelman & Gelman, 2001; Vollman & Winau, 1996).

Despite public concern of unethical research practices questionable research practices continued. The 1920s and 1930s revealed physicians' acts of routinely sterilizing Americans without their consent (Emanuel, 2002). Victoria Nourse's work, *In Reckless Hands* examines the case of *Skinner versus Oklahoma* (2008).[15] Nourse details a history of America's experiment with eugenics[16] resulting in thousands of incarcerated men and women having been sterilized. American ethicists at that time readily justified human research without the protections of informed consent as unnecessary due to the need of experimentation for the persons own therapy, experimentation for the good of humanity in general, and experimentation to advance science (Vollman & Winau, 1996).

American human research practices during the 1920s and 1930s would prove to be ambiguous in the effort to attain ethical research standards arising from the uncertainty of using experimental research methods for providing medical therapy, protecting the rights and welfare of research subjects and furthering scientific knowledge (Vanderpool, 1996; Moreno, 2000). Questionable medical research practices continued to proliferate.

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[15] *Skinner v. State of Oklahoma,*1942, the United States Supreme Court ruling held that compulsory sterilization could not be imposed as a punishment for a crime.

[16] Eugenics is the study and practice of human selective breeding. The aim is to improve the species.

The Willowbrook hepatitis studies and the Tuskegee Syphilis study remain two of the United States most noted human research experiments failing to "adequately protect human research participants" (DuBois, 2008, p. 14). The Willowbrook hepatitis study carried out at the Willowbrook State Mental facility in New York City began in 1963 and was halted in 1966 as a result of public uproar (DuBois, 2008). Although the crowded mental institution had been closed to new patients, parents that agreed to have their child participate in various medical research studies were given placement for their child (Levine, 1988). The experiment, conducted on otherwise healthy children "deliberately infected with the hepatitis virus, fed stool from infected individuals … and received injections from more purified virus preparations" (Levine, p. 70). Researchers defended the studies, suggesting that the children would become infected in the hospital anyway, and by being in the study the children would have better care in "well-staffed" units that would protect the children from more harmful infectious diseases (Beauchamp & Childress, 2001, p. 428).

The 40 year Tuskegee Study of Untreated Syphilis in the Negro Male (1932-1972) is substantiated as the longest nontherapeutic experiment on human beings in history (Heintzelman, 2003; Vanderpool, 1996; Washington, 2006). Jones (1981, p. 179) notes that when John Heller , U.S. Public Health Service Administrator was questioned about the ethical obligation on the part of the Public Health Service toward the participants in the syphilis study he stated that "The men's status did not warrant ethical debate. They were subjects, not patients, clinical material, not sick people."

Washington (2006); Oakes (2002); DuBois (2008); Caplan (1992) suggests the Tuskegee Study is considered by human scientists as one of the pivotal events leading to the regulation of human research in the United States. Emanuel (2002) posits that the Tuskegee Study led directly to the appointment of a National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1974. As a result of the work of the Commission, it was required that all federal funded studies using human subjects to be reviewed by an institutional review board (Jones, 1993; Iltis, Matsuo, & DeVader, 2008).

In 1997 President Clinton encouraged federal human research protections programs to be extended to all Americans. The president stated that "science must respect the dignity of every American. We must never allow our citizens to be unwitting guinea pigs in scientific experiments" (NBAC, 2001, p. 145).

Protecting Human Subjects Using Regulatory Standards

Early human research regulation focused on medical experimentation. The Berlin Code of 1900, one of the earliest documents to address the outrage of medical research and its unethical practices in general and more specifically the outrage of the Berlin prostitute syphilis research (Harnett, 2004; Annas & Grodin, 1992; Vollman & Winau, 1996). Murders, brutalities, tortures, and other inhuman acts were carried out daily as a result of Nazi medical experiments on World War II prisoners, on gypsies, the mentally disabled, and others (Washington, 2006; Jones, 1993; Baumrind, 1971). Although the Code was in place, continued accounts of human experimentation by world famous and revered Nazi doctors forced the medical community, courts, and the public to consider additional

protections for human subjects (Oakes 2002; Harnett & Neuman, 2009).

Nuremberg Trials

After WW II, the Nuremberg Medical Trials *(*October, 1946 until August 1947) resulted in twenty-three German physicians and scientists being convicted of performing vile and potentially lethal medical experiments on concentration camps inmates and other living human subjects between 1933 and 1945. Due to the trials, the Nuremberg Code was established as a set of ethical research principles. The Code includes principles of informed consent and condemns coercion, as well as it promotes that the study must be a properly formulated scientific experiment, and must include beneficence toward experiment participants. The elements of the Nuremberg Code include that: The voluntary consent of the human subject is absolutely essential.

- The experiment should be so designed and based on the results of animal experimentation and knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.
- The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
- The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
- Proper preparations should be made and adequate facilities provided to protect the experimental subject against even

remote possibilities of injury, disability, or death.

- The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment. A complete list of the Code is found at Appendix H

Although the legal force of the Nuremberg Code was not established, and the document was not incorporated directly into either American or German law, the Nuremberg Code and related Declaration of Helsinki are the basis for the Code of Federal Regulations, Title 45 Subpart 46 (45 CFR 46). The Federal Regulations were issued by the United States Department of Health and Human Services which governs federally funded research in the United States.

Oakes (2002) acknowledges, although forty-two doctors were indicted, resulting from the Nuremberg Trials, the majority of American medical researchers did not find the unethical treatment of human subjects appalling (Rothman, 1995). Oakes points out that during that time Americans believed “its physician-researchers acted in accordance with their Hippocratic Oath and that voluntary consent was unnecessary in a society with a long and untarnished history of medical research” (p. 444). The similar contention was pervasive among American physician-researchers.

Declaration of Helsinki

The Declaration of Helsinki (Declaration) of 1964, revised in 1975, was developed by the World Medical Association (WMA), as a set of ethical principles for the medical research community regarding human experimentation. Although the WMA developed the Declaration for the medical community it encourages other researchers conducting medical research to adopt the principles. The Declaration is not a legally binding instrument in international law, instead, draws its authority from the degree to which it has been codified in, or influenced in national or regional legislation and regulations (Dubois, 2008). There have been eight amendments to the Declaration.

Belmont Report: An Ethical Foundation

The National Commission for the Protection of Human Research Subjects task was to consider:

- the boundaries between biomedical and behavioral research and be accepted and routine practice of medicine;
- the role of assessing risks criteria in the determination of the appropriateness of research involving human subjects;
- appropriate guidelines for the selection of human subjects for dissipation in such research;
- the nature and definition of informed consent in various research setting.

The tasks resulted in the Belmont Report. The statement of basic ethical principles and guidelines to assist in resolving ethical problems related to the

conduct of research with human subjects laid another foundation for protection of research subjects. The tenets of the Belmont report include three fundamental principles: respect for persons, beneficence, and justice as shown in Table 4.

The Belmont report is the guiding document of ethical framework for protecting human subjects in the United States (NBAC, 2001).

The Common Rule and Social Science

Williams' (2005) Congress of Research Service Report (CRS) suggests that the Common Rule was designed with a focus on biomedical research, and submits that most social science researchers have questioned whether the Common Rule should apply to social science research. "These regulatory concerns voiced by those in the social science community have focused primarily on the impact of the Common Rule" (p. 24). CRS suggest that social science research researchers "have expressed a desire to have regulations regarding their research carved out from the Common Rule" (p. 24) noting that social science researcher, Joan S. Sieber's presentation "Social and Behavioral Research with Human Subjects: Key Issues for SACHRP[17] and OHRP to Consider"[18] represented the sentiments of an overwhelming number of social science researchers in their concerns of biomedical regulatory standards being applicable to social science research.

[17] In July 2004, *Secretary's Advisory Committee on Human Research Protections* (SACHRP) heard a series of presentations on protecting human subjects in Social Science Research. Presenters raised concerns for having regulations for social science separate from biomedical research regulations. Joan Sieber, an esteemed social science researcher, represented the views of her colleagues.

[18] *Presentation to the U.S. Secretary's Advisory Committee on Human Research Protections,* Washington, D.C., Aug. 8, 2004.

Table 4

Key Concepts of the Belmont Report

Principle	Application
Respect for Persons: Individuals should be treated as autonomous agents • Persons with diminished autonomy are entitled to protection	Informed consent: Subjects, to the degree that they are capable, must be given the opportunity to choose what shall or shall not happen to them. The consent process must include three elements: information, comprehension, and voluntariness
Beneficence: Human subjects should not be harmed. Research should maximize possible benefits and minimize possible harms	Assessment of risks and benefits: The nature and scope of risks and benefits must be assessed in a systematic manner
Justice: The benefits and risks of research must be distributed fairly	Selection of subjects: There must be fair procedures and outcomes in the selection of research subjects

The CRS suggest that IRBs are assembled with biomedical expertise, and a review process focused on that research may not be well suited to review social science research. Social science researchers argue that unnecessary delays in the review and approval of their protocols are due to lack of familiarity with social science research (Oakes, 2002, Gunsalus, 2004). The CSR finds that the IRB review process, in their use of the Common Rule as the standard of regulatory compliance, often does not place protocols in the category acceptable in the Common Rule. As an example, protocols exempt from IRB review are often placed in the expedited category which then does require IRB approval, costing unnecessary time for the researcher and unnecessary documentation for the IRB. The report details that protocols are place in a higher category of risk although the protocol would be "commensurate with the protocols' level" and type of risk described in the Common Rule. Williams (2005) suggest that "risk may be physical in biomedical research but is usually limited to the areas of confidentiality and privacy for social science research" (p. 24).

In concurrence with, the CRS Report (2005); Oakes (2002); Bosk (1998); and Gunsalus (2004) suggest that IRBs' requirements for obtaining informed consent in social science research are overly cumbersome and ineffective due to the consent process required by the Common Rule. The process of consenting as illuminated in the Common Rule focuses on "documenting consent instead of ensuring informed, voluntary decision making" (CRS, p. 24). In spite of long held concerns of the Common Rule, Federal agencies, many which conduct only social science research, have adopted Subpart A (see Appendix L).

The Common Rule, adopted by 16 federal departments and agencies in 1991 is currently the regulatory framework for protecting human subjects for 17 federal agencies. It requires all federally funded research conducted by any of the 17 federal agencies as shown in Table 5 to be reviewed by an institutional review board. Although, the Common Rule is not required to be the regulatory standard of human research protection for nonfederal funded research, human research protection programs at academic institutions have opted to apply the Common Rule also to research that is not federally funded (Oakes, 2004, Gunsalus, 2007, Williams, 2005).

The Common Rule, developed in response to recommendations made by the *President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research in 1981*(Presidents Commission) called for the adoption by all federal agencies of the Department of Health and Human Services. Until 1991, federal departments and agencies that conduct, support, or regulate research used a variety of policies and procedures to protect human research subjects. To promote uniformity of the rules applicable to human research subjects, each of the 17 departments and agencies, as shown in Table 5, adopted as regulation, a common Federal Policy for the protection of human research subjects (NBAC, 2001, p. 5).

Gordon (2003) suggests that significant revisions have been made to the Common Rule. These revisions have been primarily under the supervision of the National Bioethics Advisory Commission (NBAC). Gordon posits that the NBAC (2001) proposed various suggestions to strengthen the protection of humans

Table 5

Federal Agencies Subject to the Common Rule

1. Social Security Administration
2. Central intelligence agency
3. Consumer Product Safety
4. Department of Agriculture
5. Department of Commerce
6. Department of Defense
7. Department of Education
8. Department of Energy
9. Department of Health and Human Services
10. Department of Housing and Urban Development
11. Department of Justice
12. Department of Transportation
13. Department of Veterans Affairs
14. Environmental Protection Agency
15. National Aeronautics and Space Administration
16. National Science Foundation
17. Office of Science and Technology Policy

participating in research but the suggestions did not apply or translate well to social science research. Social science researches commonly perceive the current and proposed human subjects regulations as impediments to research (Gordon, 2003).

The Common Rule's focus on concerns of risk from a biomedical viewpoint makes it difficult to apply the rules to social science research, Gordon suggests. However, the Common Rule does provide revisions for research that poses minimal risk. As such, the Common Rule states that minimal risks are those that are ordinarily encountered in daily life. Gunsalus (2006), and Gordon (2003) are among those who suggest, although minimal risk research is eligible for exemption according to the Common Rule, the general trend for IRBs is to incorporate a level of perceived risk. The perceived risk assessment most often calls for additional explanatory documentation, adding additional time to the review and approval process for the researchers, IRB's and their administrative support staff.

Office of Human Research Protection

The Office for Human Research Protections (OHRP) is an agency of DHHS, that provides leadership and oversight for the protection of the rights, welfare, and wellbeing of subjects involved in research conducted or supported by the United States Department of Health and Human Services (DHHS) (Oakes, 2002, Burris & Welsh, Borror et al., 2003). Prior to 2000 OHRP was called the Office for the Protection of Research Risk (OPRR), at that time an agency under The Office Of Extramural Research in the National Institute of Health (NIH).

In 2000 OHRP was relocated from under NIH to the Office of Public Health and Science within the Office of The Secretary of the Department of Health and Human Services (DHHS). Amdur & Bankert (2002, p. 27) suggest that the administrative location of OHRP was changed to eliminate what could be viewed as a conflict of interest in which the research regulatory office reported to the administrator of an agency having research duties as their primary mission. "The status of the OHRP Administrator was upgraded to the Senior Executives Service, which is the highest level of nonpolitical civil servant" (p. 28). OHRP's mission continues to be toward providing clarification and guidance to institutions and researchers, by maintaining regulatory oversight, providing advice related to ethical and regulatory issues in biomedical and behavioral research and developing educational programs and materials.

The Federalwide Assurance

The OHRP establishes a contract with institutions called Federalwide Assurance (FWA). The FWA (see Appendix N) establishes the standards by which institutions are to conduct research. So that institutions may qualify to receive federal funding for research, the institution must have a Federalwide Assurance on file with the OHRP (45 CFR 46.103). The assurance requires that:

- Each agency provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in the policy,
- The institution must have an approved assurance, and the research must be approved by an IRB provided for in the assurance and the research will be subject to continuing review by the IRB.
- Assurances applicable to federally funded support or conducted research shall at minimum include a statement of principles attesting to be the institutions responsibilities for protecting the rights and welfare of human subjects. Despite whether the research is subject to Federal Regulation designation of one or more IRB's established within the requirements of 45 CFR 46.
- A list of IRB members identified by name, earned degrees, representative capacity, indications of experience such as board certifications and licenses etcetera, sufficient to describe each member's chief anticipated contribution to IRB deliberations.

- Written procedures for which the IRB will follow for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator an institution, for determining which projects require review more often than annually, and for ensuring prompt reporting to the IRB of proposed changes in research activity.
- Written procedures for ensuring prompt reporting to the IRB, the appropriate institutional officials, and the department or agency head of any unanticipated problems involving risk to subjects or others, or any serious or continuing noncompliance, and any suspension or termination of IRB approval.
- Obtain written informed consent from research participants, unless the written informed consent is waived by the IRB.
- The institutional signatory official, the IRB chair, and the human protections administrator must have adequate training.
- Adequate educational and oversight mechanisms must be in place for documenting the training of investigators.
- The IRB must have adequate knowledge of local research regulations.

Although an FWA is not required to conduct research that is not funded by a federal agency, Cohen (2002, p. 313) suggests there are many institutions that have elected to hold all research, even research that is not federally funded, to the same standards of the Common Rule. Many social scientists consider this to

be the impetus for institutional review boards to assert unnecessary regulation of minimal risk research projects (White, 2007). Some institutions are have recently revised their FWA to only include research that is federally funded to be applicable to the Common Rule.

The FWA requires the institution to have a human protections administrator. The administrator is an employee of the institution and serves as an agent of the FWA exercising the day-to-day operations of the human research protections program. In most cases the IRB human protections administrator is also the Director of the institution's human research protection program and supervisor of the HRPP staff. Cohen (2002) suggests that the human protections administrator be extremely knowledgeable of the institutions systematic protections for human subjects. In addition to the human protections administrator, the FWA must also designate an Institutional Signatory Official who has the legal authority to represent the institution named in the FWA. The FWA "formalizes" an institution's commitment to protect human subjects (Cohen, 2002).

The OHRP's Division of Compliance Oversight evaluates all written substantive indications of noncompliance or deficiency of the institution or researcher related to the Common Rule. OHRP requests the institution involved, to investigate the allegations and to provide OHRP with a written report of its investigation. OHRP then determines what, if any, regulatory action needs to be taken to protect human research subjects[19]. However, the NBAC suggests that

[19] OHRP provides information fact sheets to the public relation to their mission, duties and expectations at: http://www.hhs.gov/ohrp/about/ohrpfactsheet.htm.

OHRP takes the lead as a de facto reference point and consensus builder among federal agencies although; it has no congressional or executive authority to do so. Additionally, some agency departments have not established offices comparable to OHRP for interpreting and implementing the regulations. Oversight activities in most of these cases are the responsibility of a single individual, therefore, “the ability to coordinate oversight among the departments is weak, leaving departments and agencies to interpret the Common Rule potentially differently” (NBAC, 2001, p. 9).

Determination Letters

One of the available indicators of accounts of noncompliance and deficiencies resulting in increase of risk to research participants, researcher violation, IRB violations or institution violations is via the publicly available portal maintained by OHRP. OHRP memorializes its findings of noncompliance and deficiencies in determination letters sent to the institution for investigation. The letters outline concerns of OHRP relating to an approved research project. The project can be biomedical or social science research, and are usually federally funded. OHRP does not regulate unfunded research unless the institution’s FWA document indicates that all research conducted at the institution will be under the interpretation of the FWA. Many institutions have opted out of the FWA regulating all research by unchecking the box on the form that previously indicated the FWA would be subject to all research. Only federally funded research is then regulated for those institutions.

The determination letters specifically outline what actions must be taken

by the institution to return to, a compliant state, rectify a deficiency, or resume research activity. The communication from OHRP to the institution is publicly available. The letters have been routinely available to the public since 2000 on the OHRP Internet portal. Sieber (2004) posits that OHRP's publicized determination letters, and the costly sanctions handed down to a few institutions and the negative publicity to the institution makes it understandable that IRBs and research administrators have considered it in their self-interest to enact highly conservative decisions. As an example, IRB's have the authority to waive documentation of informed consent, but often neglect to do so although the Common Rule offers such flexibility (White, 2007).

The Food and Drug administration (FDA) has a similar mechanism in place called Warning Letters. The Warning Letter is issued when the FDA has reason to believe deficiencies and or violations have been committed in an approved research project. The letters are also considered voluntary action letters. The voluntary action letters request voluntary correction of minor issue and deficiencies found by OHRP. The process is usually ended when all concerns raised in the letter has been addressed. Warning letters can and do carry sanctions for the institution and the investigator (Chadwick, 2002). The FDA oversees research involving drugs, biologics, and medical devices and does not oversee social science research, therefore, only OHRP determination letters are the focus of this discussion.

The literature of determination letters studies is scarce, although the literature did reveal three similar research studies, one conducted by Borror et al.

(2003), Burris and Welsh (2007) and Weil et al.(2010). In each case their research revealed the numbers of citations of noncompliance (determination letters) sent to institutions. Borror et al. found 1120 citations of noncompliance and deficiencies and Burris & Welsh found 648 letters of noncompliance and deficiencies were sent from OHRP. The research projects did not investigate which institutions or agencies were involved in the citations of noncompliance nor did the project delineate the numbers of biomedical or social science citations of noncompliance or deficiencies. The authors focused on the kinds and numbers of noncompliance and deficiencies found in determination letters. The focus was not on the discipline in which those noncompliance and deficiencies were found. In the studies conducted by Borror et al. (2003) and Burris & Welsh (2007) they addressed, the percentage of institutions cited by OHRP, problems and remedies based on review of determination letters, and the regulatory requirements of the Common Rule.

Borror et al. (2003) explains that over the last several years OHRP has developed a list of determinations of noncompliance that that include:

- Initial and Continuing Review
- Expedited Review Procedures
- Reporting of Unanticipated Problems
- Noncompliance,
- Suspension of Protocol Changes
- Application Of Exemptions
- Informed Consent

- IRB Membership, Expertise, Staff, Support And Workload
- IRB Documentation, Findings, and Procedures
- Other

Determination letters, also referred to as compliance oversight letters by Borror et al. (2003), are issued by OHRP in response to substantive allegations or indications of noncompliance with the Department of Health and Human Services (DHHS) regulations (45 CFR 46). Borror et al. acknowledges in their research of determination letters that allegations of noncompliance can come from various sources including research subjects, their family members, whistle-blowers, patient/subject advocates, as well as OHRP staff based on the staff's review of data published in professional journals. Borror et al. reports that 269 letters contained 1120 citations of noncompliance and deficiencies. One hundred and forty-two of the 155 institutions in which determination letters were issued had at least one citation of non-compliance.

In a similar study conducted by Burris and Welsh (2007) 271 letters within the timeframe of January 1, 2002, and June 30, 2004, with 5 letters being issued before the study period, were reviewed for their study. Burris and Welsh's data set consisted of 174 letters being studied. Although Borror et al. (2003) and Burris (2007) conducted similar analysis of determination letters, their analysis resulted in divergent interpretation of the findings.

Borror's analysis indicated that institutions did not have adequate IRB policies and procedures and did not maintain records according to regulatory requirements. Borror's findings focused on the gaps in documentation of

researchers' written materials including informed consent documentation and the process of the research project. While Burris & Welsh's qualitative study four years later also reviewed determination letters and focused on the lack of adequate information in consent documents, the level at which consent documents were written and wording issues in the informed consent.

The later study by Weil et al. (2010) reviewed 235 determination letters that the Office of Human Research Protection issued to 146 institutions between August 1, 2002, and August 31, 2007. Weil et al.'s examination of OHRP determination letters revealed 762 citations of noncompliance and deficiencies. However, similar to their first study of determination letters Weil et al. did not focus on the discipline specifically of biomedical or social science research in which the citations of noncompliance and deficiencies represented.

Burris & Welsh's study focused on patterns of noncompliance. They concluded that although there were patterns of noncompliance no subjects were harmed. Burris and Welsh puts forward that their research suggests that documented procedures not explicit researcher unethical implementation of the research projects has been cause for excessive documentation burdens for human research protection programs and researchers. They refer to this process as mission creep as detailed in the *Illinois White Paper, Improving the System for Protecting Human Subjects: Counteracting IRB Mission Creep* (White Paper) by Gunsalus et al. (2005) as a crisis being caused by the increased workload of IRBs and their inability to handle the workload effectively efficiently. Thereby, the focus is placed on the less difficult path of procedures and documentation rather

than identifying difficult ethical issues which may be presented in research studies. The authors of the *White Paper* (Gunsalus et al., 2007) suggest that the institutions' efforts to comply with federal requirements even when research is minimal risk amounts to exaggerated precautions to protect against program shutdowns, and efforts to protect the institution against lawsuits.

Notably, Borror et al.'s findings focused on the gaps in documentation of written materials including informed consent documentation and process. Fifty-two percent of noncompliance or deficiency citations were a result of institutional review board approval of informed consent document/process (27%) or the initial review process (25%). Four percent of overall citations were considered the most serious form of noncompliance putting research subjects at risk if not at serious risk.

Burris and Welsh's study, four years later, focused on what OHRP determination letters consistently detailed. The letters included reference to the lack of adequate information in consent documents, the level at which documents were written and other grammatical misuse of wording in the consent form. Burris and Welsh also suggest:

> Very, very few researchers investigated by OHRP appear to have deliberately broken or disregarded the rules. Very, very few researchers conducted their studies in a way that endangered their subjects. The rate of serious problems—cases in which subjects were put at serious risk or suffered harm—was low, especially when the denominator is not the number of letters, complaints, or audits but the far greater number of studies going on in this period. Most of the violations uncovered involved the failure to document something that may actually have been done, or a failure to do something that, while required by the regulations, does not appear to have

> exposed anyone to any harm or even put anyone at any appreciable risk (p. 671)

The literature has presented the studies of Borror et al., and Burris & Welsh as reviewing the contents of the determination letters but their research nor other research studies in the literature has suggested what portion of the citations can be attributed to social science research. Additional research is warranted to address the gap in the literature of the impact of regulating social science research with biomedical regulations. standards.

Scarce data exists in the literature documenting whether OHRP's citations of noncompliance are the result of biomedical or social science research projects. Knowing if the attributes of noncompliance and deficiencies have its place in biomedical or the social science discipline may assist in better defining the utility of the Common Rule to social science research projects. Additional research in this area will assist in the discourse for continued research of the applicability of IRBs using biomedical standards of research to address social science research. A qualitative content analysis of determination letters will add to the body of literature in this area.

National Bioethics Advisory Commission

The National Bioethics Advisory Committee (NBAC) was established by Executive Order 12975 signed by President Clinton on October 3, 1995. NBAC advises the President on bioethical issues that may emerge from advances in biomedicine and related areas of science and technology. NBAC's functions were defined as follows:

a) NBAC shall provide advice and make recommendations to the national Science and Technology Council and to other appropriate government entities regulating the following matters:
   1. the appropriateness of departmental, agency, and other governmental programs, policies, assignments, missions, guidelines, and regulations related to bioethical issues arising from research on human biology and behavior, and
   2. applications, including the clinical applications, of that research.

b) NBAC shall identify broad principles to govern the ethical conduct of research, citing specific projects only as illustrations of such principles.

c) NBAC shall not be responsible for the review and approval of specific projects.

d) In addition to responding to requests for advice and recommendation from the national science and technology Council, NBAC may also accept suggestions of issues for

consideration from both the Congress and the public. NBAC may also identify bioethical issues for the purpose of providing advice and recommendations, subject to the approval of the national science and technology Council (NBAC, 2001).

By 1997, the NBAC required that no person in the United States should be enrolled in research without the double protections of informed consent by an authorized person and independent for review of the risk and benefits of the research (NBAC, 2001). In 1999 the White House issued orders for the NBAC to compile a report on the concerns related to the human research enterprise. Several areas of concern were indicated to the White House in 1999 that included:

- not all research participants are protected by the federal oversight system,
- several federal departments and agencies that sponsor primarily non-biomedical research or modest amounts of research has failed to implement fully the federal protections available,
- the federal protections do not always include specific provisions for individuals who are especially vulnerable, and
- the federal protections are difficult to enforce and improve effectively across the government, in part, because no single authority or office oversees research protections across all agencies and departments (NBAC, 2001, p. 1).

The NBAC expressed concern stating, "the oversight system for protecting

research participants is losing credibility among some investigators, IRB's, institutions, and, perhaps most important, the public, causing more frustration and less willingness to commit time and resources to the system" (p. 16). The NBAC well aware that the current system for protecting human research subjects in need of reform was in agreement with social science researchers that the system of protection "was often burdened by excessive bureaucracy, confusing or conflicting interpretations of rules and an inability to respond to emerging areas of research" (p. viii).

Human Research Protection Programs

Chodosh (2006) puts forward that human research history has been marred with examples of ethical principles of human research being ignored. Although, most human research scientist have followed the basic tenets of ethical research, those scientists who were the exceptions created a necessity for legal measures formed to avoid future problems. Chodosh proposes that the Western society produced scientists that would not engage or permit the human research atrocities as seen in the World War II Nazi experiments. Although it was factual in most cases that medical researchers would abide by ethical research standards, the western academic world also produced risky biomedical research. The oversight that clinical administrative chiefs provided as guidance to the investigators became much more tenuous as the clinical services expanded and research generated much more operating funding.

Chodosh (2006), Dyer & Dermeritt (2009), Jones (1993) suggests that the Tuskegee Syphilis Study and other unethical research practices brought about a

realization by the scientific community that better means for protecting human research subjects was needed. No longer was just peer review of research protocol enough. Federal agencies now required more intense review of research protocols. Institutional Review Boards now provided the oversight of research projects once held by department supervisors. Edgar & Rothman (1995) suggest that there are two goals which are the focus of IRBs: to determine if the benefits of the project outweigh the risks; and to ensure that all the relevant information is provided in the informed consent document.

The volume and complexity of research protocols increased as did regulatory demands. Chodosh (2006) further suggests that additional resources did not always keep up with the demands. “The IRB's primary role in protecting human subjects often became secondary to meeting regulatory requirements. The institution’s need to meet the conditions of their assurance and continue the income and prestige of the institutions research program became the primary IRB function" (p. 14).

Increased federal funding for research projects increased regulatory demands, and the need to create a culture of research integrity within the campus investigators brought about the need for the three components of the human research protection program that include the investigators; the IRB; and the institution (see Figure 1) to become congruent with protecting human research subjects, Chodosh (2006).

Zywicki (2007) suggests that the size and expense of administrative such as HRPPs have grown substantially in recent decades. He points to the “growing

accumulation of government regulation" which has required the creation of new administrative staff to take care of the regulatory responsibilities. Zywicki suggests, some of the growth of IRBs has been spurred by superfluous governmental regulations (p. 872). In addition, Zywicki proposes that "the preoccupation of IRBs with paperwork and forms has been promoted by a regime of "fear" of governmental oversight, "fear by the institution that it will be 'out of compliance' with one or more aspects of the paperwork, and subject to penalty upon audit, be that by the NIH, the OHRP, the U.S. Department of Agriculture, or whatever other organization is involved" (p. 875).

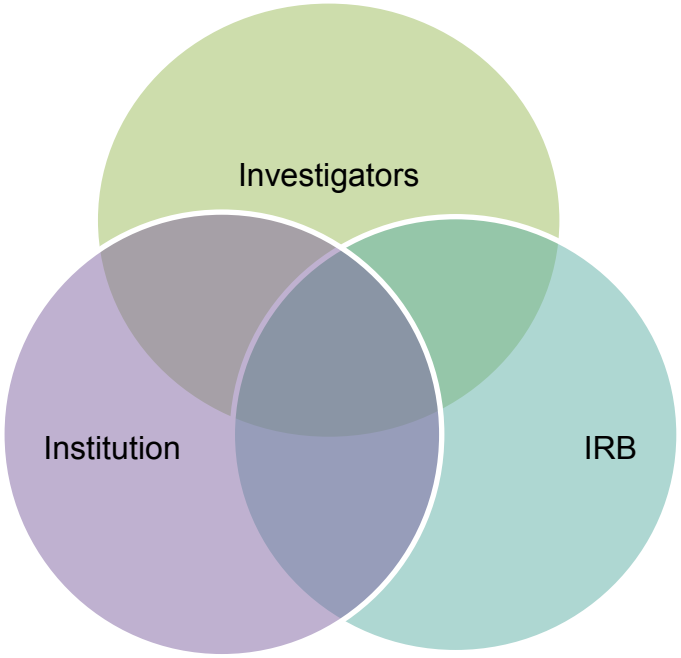


Figure 1. Components of Human Research Protections Program

Institutional Review Board

> Our IRB system is endangered by excessive paperwork and expanding obligations to oversee work that poses little risk to subjects. The result is that we have simultaneous overregulation and under protection" IRBs' burdens have grown to include studies involving interviews, journalism, secondary use of public-use data, and similar activities that others conduct regularly without oversight. Most of these activities involve minimal risks--surely less than those faced during a standard physical or psychological examination, the metric for everyday risk in the federal regulations. And IRBs are pressured to review an expanding range of issues from research design and conflicts of interest to patient privacy. These are beyond the scope of research protection and are best left to others (Gunsalus, 2006, p. 1441).

With the end of WW II bringing large amounts of federal funding for medical research projects, medical research projects escalated substantially. Institutional review boards (IRB) gained a larger role in the review and approval of human research. Haggarty (1966) suggests IRBs were primarily to determine the medical benefits of federally funded research projects. Later some IRBs began reviewing nonmedical research. In the United States, regulations protecting human subjects first became effective on May 30, 1974. The regulations established the IRB as one mechanism through which human research subjects would be protected (Edwards, Ashcroft, & Kirchin, 2004).

The National Research Act passed in July, 1974, established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (the Commission). Peckman (2001) suggests that prior to 1938 the United States placed no restrictions on human experimentation. The Hippocratic Oath of "do no harm," was the guiding principle of research ethics for

experiments on humans, suggests Peckman. Operating in sync with the proponents of “do no harm” was the “cultural bias that relied upon and trusted the expertise of professionals” (Peckman, 2001, p. K-3). However, the acts of unethical experimentation with human subjects lead to the creation of peer review committees (Levine, 1988; Peckman, 2001; Candilis et al., 2006; Advisory Committee on Human Radiation Experiments, 1995). By February, 1966 institutions that received federal funding for biomedical research, were required to create an institutional committee to review their colleagues grant applications including protocol for involvement of human subjects (Peckman, 2001).

By 1974 IRB’s became more formalized (Chadwick, 2000; NBAC, 1999; Edgar & Rothman, 2004). They became committees to oversee the responsible conduct of biomedical and social science research, protect the rights of research participants, reduce their risks, and increase the benefits of the research (Levine, 2001; Gilbert, 2006). The Common Rule provides the structure of institutional review boards in the United States. The Common Rule includes explicit reference to the operations of the institutional review board. IRB operations are found in the following Federal Regulations:

§46.107 IRB membership.

§46.108 IRB functions and operations.

§46.109 IRB review of research.

§46.110 Expedited review procedures for certain kinds of

§46.111 Criteria for IRB approval of research.

§46.112 Review by institution.

§46.113 Suspension or termination of IRB approval of research.

For more than 10 years Institutional Review Boards (IRBs) have been placed under intensive scrutiny as a result of the Office of Inspector General (OIG) of the Department of Health and Human Services report, *Institutional Review Boards: A Time for Reform (1998)*. The report represented a one-year study by OIG. The key findings of the report's concluded that: 1) IRBs face major changes in the research environment as a result of increases in the quantity of research, the commercialization of research, and the number of multicenter trials; 2) IRBs conduct minimum continuing review of approved research; 3) IRBs are overworked; 4) IRBs often lack sufficient scientific expertise to review protocols adequately; 5) IRBs face conflicts of interest that may undermine their independence, and 6) IRBs provide little education or training to members. The report recommended that:

- IRBs should be held more accountable;
- continuing protections for human subjects, such as data safety monitoring boards and adverse event reporting, should be strengthened;
- federal requirements should be enacted to promote education on research ethics for IRB members and investigators;
- steps should be taken to insulate IRBs from conflicts of interest,
- more institutional resources should be devoted to IRBs, and
- the federal oversight process should be revamped.

Extensive criticism has permeated the IRB review and approval process (Dyer & Demeritt, 2009; Gordon, 2003, Oakes, 2004, AAUP, 2000). Dubois (2004) depicts IRBs as the instruments of a system of licensing in which scholars, students and other researchers must get permission to conduct research with human subjects. He suggests that IRBs are far more dangerous than the research they review and they offer little if any protection for human subjects.

Although, IRBs have garnered much of the negative criticism from researchers, the IRB staff has also contributed to the concerns researchers have with human research protection programs. Menikoff (2007) suggests that the "IRB staff may not be adequately educated about applicable regulations, and may be placing inappropriate burdens on researchers, or there may be insufficient staffing leading to inappropriate delays in the review of studies" (p. 798). Rothman (1995) suggests that staff require excessive documentation rather than providing guidance in the interpretation of the regulations.

Burris & Welsh (2007), details IRBs as a regulatory system that often distracts from rather than focus on key ethical issues. The sentiments of DeVries et al. (2004 p. 234) suggests that IRBs have been extensively criticized as inefficient, obstructionist, and indifferent to the researchers needs and ineffective at protecting human research safety and ethical concerns because of excessive regulations required in biomedical research that impacts social science research. Brendel's (2008) writings from the biomedical point of view suggest that there must be a pragmatic approach to IRBs review and approval of clinical research.

The author notes that, the IRB focus should be using case-by-case moral problem solving as “how to balance the drive toward scientific discovery with the need to protect human subjects in clinical research” (p. 25). The sentiments of Zywicki (2007) suggests that “IRBs have become a ubiquitous presence on the landscape of America’s higher education system” using a system of review of research projects which suggests a one-size-fits-all approach (p. 861).

Social scientists routinely encounter impediments to their research when navigating Institutional Review Board (IRB) review process to obtain approval for their research studies. Gordon (2003) suggests that the Common Rule and the interpretation of the Common Rule by the IRB, which is modeled heavily on biomedical research, is not effective for social scientists and especially ineffective in its applicability to anthropological approaches to research (p. 300) concurs with social science scholars having similar concerns of the overregulation in social science research for more than 35 years. Burris, Buehler & Lazzarini (2003); Burris et al. (2003, Winter) propose that good regulations must be effective and efficient. They suggest that the Common Rule may not achieve the “desired behavior among regulated and protected at the lowest possible cost” (Burris, Buehler, & Lazzarini, 2003, p. 650).

Social science researchers point out that research procedures associated with biomedical research cannot be transplanted into the procedures for conducting social science research. Seiler and Murtha (1980) suggested that the federal regulatory efforts censor social research more prominently in federally funded research projects. Seiler and Murtha further argued more than 30 years

ago that the increased documentation and paperwork required by federal oversight agencies and, institutional review boards added no additional protections for human subjects. They proposed that using the biomedical model of protecting research subjects offers no evidence to show that the "swirl of paperwork either protects research participants or substantially changes the quality of social research" (p. 154).

Additionally, Seiler and Murtha put forward that the increase bureaucracy has made for increased delays for researchers, increased workloads and loss of control of even their work situation "leading to a variety of unintended consequences" (p. 154). The consistency of this argument continues to resonate with social science researchers with little if any difference in contention.

In 2001, the National Bioethics Advisory Commission (NBAC) complained that Institutional Review Boards (IRBs) were overwhelmed not only by high workloads generated by the amount of actions to process just one research project (see Figure 2) and limited resources but also by "a regulatory system that often distracts from rather than focuses on key ethical issues" (p. A 14). NBAC attributed "emphasis by regulators on procedure" for contributing to "an atmosphere in which review of research becomes an exercise in avoiding sanctions and liability rather than in maintaining appropriate ethical standards and protecting human participants" (p. 22). The procedure-prone regulator of greatest concern to NBAC was the federal Office for Human Research Protection (NBAC, 2001).

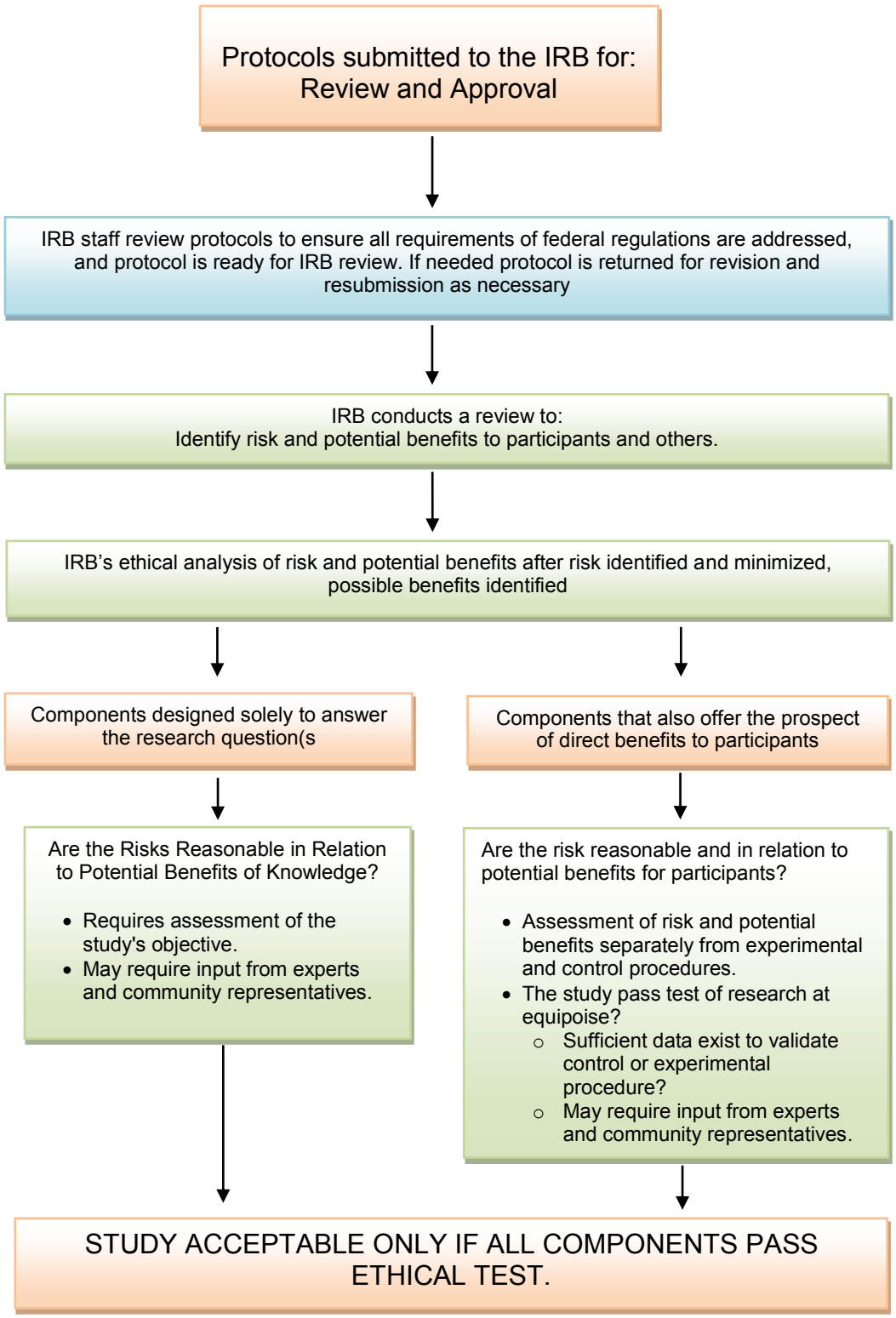


Figure 2. Process of IRB Review including analysis of Risk and Potential

IRB Administrative Support Staff

The IRB Administrative support staff is critical to an institution's human research review system. Although as McGough (2002) points out, the Common Rule at 45 CFR 46.103(b)(2) does not specifically state that staffing is to be hired to support an institutional review board. However, for IRBs to function adequately they must have staff to assist them with administrative duties (Chodosh, 2002). The staff should have appropriate training and expertise and have access to needed resources. McGough (2002) adds that the positions the members serve on the IRB are as volunteers that cannot be expected to provide the administrative work necessary for IRB review of human subject research and daily oversight of the administrative duties required. Additionally, McGough suggests that in order to manage these tasks and many others needed by the IRB, for the mission of protecting those participants in human research, there must be qualified administrative IRB staff support in place with resources provided by the institution to support IRB functions.

The IRB review process can be burdened with excessive paperwork required by Federal Regulations (NBAC, 2001, Gunsalus, 2005, King, 1999; Pattullo, 1985). Although the paperwork fulfills procedural rule requirements of the federal oversight agencies, and is designed to ensure compliance with ethical standards, the paperwork requirements have little relevance to ethical standards or the protection of participants (NBAC, 2001). IRB's also lack the resources suggested by the Office of Human Research Protection, including meeting space, adequate staff and equipment to support IRB functions. They have

increasingly large workloads with inadequate staff and inadequate resources that inhibit the protocol review and approval process (Sugarman, 2000).

Social Science Research Regulation

> Almost no one believes the social sciences should be utterly free from oversight. The history of psychology, for example, is studded with experiments whose designers gave too little thought to the well-being of their subjects.
>
> Shea (2000, p. 4)

Prior to 1974 social science research was unregulated by the federal government (Seiler & Murtha, 1980). The authors suggest that the 1974 National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research would require the social sciences to undergo federal scrutiny for research funded by the federal government. Seiler & Murtha suggests there was no concern of ethical violations reported of social science research during that time, making increased scrutiny of social science research unnecessary. Patullo (1979) agrees, saying that “the record of social scientists is remarkably good” (p. 531).

Although, as with biomedical research, there is always a possibility of harm to those participants of social science research projects through carelessness or ignorance or lack of character or those who abuse the standards, suggests Pattullo. The author further suggests that the possibility of injury in social science research is rare. The concern of social science research harms originated with the Surgeon General's concern at that time for "insuring the integrity of research his agency financed” (p. 533).

Oakes (2002) and Keith-Spiegel & Koocher (2005) suggest that social

scientists are undisturbed by federal regulatory oversight. However, the authors suggest, it is IRB's that have increased their scrutiny of research projects including social science research projects unnecessarily. The increased scrutiny has caused frustration to many social scientists because it results in excessive documentation to address the IRB concerns of perceived risks to research participants (Gunsalus et al., 2004; White, 2007). There is little debate regarding the need to protect volunteers in social science research (Bozeman, 2003; Braxton, 1994; Malone 2003) but social scientists posits that there continues to be a need for improvement of system, improvement that appropriately represents the risks of social science research (Dyer & Demeritt, 2009; Citro et al., 2003; Pittenger, 2003; White, 2007).

Oakes (2002) suggests that as a result of the guidelines proposed by the Department of Health Education and Welfare (DHEW) in August 1979, social research has been made to undergo IRB review despite funding source, and requiring the same rigor as biomedical research. Social scientists, as evidenced by the literature, have argued for decades that the increased scrutiny, identical to that of biomedical research had no foundation of evidence of physical harm occurring in social science research (Pattullo, 1980, Seilar & Murtha, 1980).

Oakes (2002) and Pattullo (1984) puts forward that social scientists were not involved in the development of the Common Rule. Without social scientists involvement in the development process, there was little applicability of the Common Rule to social science research thereby resulting in inappropriate regulations for the social sciences.

However, Amdur & Bankert (2002, p. 105) suggests:

> There is no legal or regulatory basis for making the distinction between social science and biomedical research from the IRB standpoint. Specifically, the U.S. Dept. of Health and Human Services (HHS) regulations that focus on the IRB do not mention the terms social science, behavioral science, or biomedical science. The regulations describe ethical standards for research based on the specific characteristic of the risk to research participants. Not on the academic field into which research may be classified. The fact that the regulations do not distinguish between social science and biomedical science emphasizes the similarities between these two general types of research in terms of ethical standards and research regulation (p. 105).

Amdur and Bankert (2002) suggest that as a result of physical harm imposed on research subjects, ethical codes were developed. The risk of physical harm is not a component of social science research, causing some researchers to not fully understand the applicability of the Common Rule to both biomedical and social science research. The authors point out that social science research does, in fact, have a potential for social harms.

Social harms can include a decrease in quality of life resulting from "information being created or used in a way that is damaging to the individual" causing "loss of employability, loss of insurability and criminal or civil litigation" (p. 106). Often social harm takes the form of disruption of personal relationships, causing embarrassment, humiliation, discrimination or stigmatization. Amdur & Bankert further suggest that social harm is just as much a threat to the rights and welfare of research participants as physical harm (p. 106).

Sieber (2004) suggest that the system of protecting human subjects has been enacted in response to high profile conflicts between the values and

activities of scientists and the values of society as a whole (p. 402). As an example the author also refers to the 40 year of study of untreated syphilis by the U.S. Public Health Service in which informed consent and ethical oversight of research became the requirement. Sieber further suggest that regulations should not be confused with ethics. Ethics have a duty to address the unique characteristics of a circumstance, “regulations are specific requirements, the wording may seem to imply that one size fits all (p. 403).” Although most regulations are written in a way that may be interpreted with some flexibility, the flexibility has not always been extended, causing problems for social scientist, Sieber suggests.

Mission Creep and Overregulation

Marshall (2003) acknowledges that IRBs have had a profound impact on the regulation of research with human participants. The author further acknowledges that the OHRP has shut down research at several United States institutions because of violations of human subjects' protections. Marshall suggests that there is a place for the work of OHRP, although they are overzealous in their approach. The majority of criticisms from researchers concur with Marshall in the observation that regulatory oversight entities are useful and needed, however federal regulatory entities are overzealous in their interpretation and application of federal guidelines, exacerbating the challenges faced by researchers in all fields of human research seeking approval of their research studies (Mosher, 1988).

Kahn, Mastrianni & Sugarman (1998); Emanuel, Wendler & Grady (2000);

and Beyrer & Kass (2002) suggest that in recent years there has been increased debate in both public and professional arenas about a range of ethical concerns involving research with human participants. The authors agree, IRBs play critically important roles in evaluating and managing the risks inherent in research while they protect the rights and welfare of human research participants. Resnick's (2004) concurs with Marshall (2003) and Oakes (2002) in their opinion that IRBs have been placed under intense scrutiny. In 1998, the Office of Inspector General (OIG) of the Department of Health and Human Services issued its report, *Institutional Review Boards: A Time for Reform.* The report suggests that the regulatory system of protecting human subjects has weaknesses that threaten the effectiveness of the system. This, researchers suggest, has been a major factor in the increased documentation called for by IRBs from researchers and performed by human research protection programs. This progression of documentation has had an adverse effect on researchers, while affording little if any additional protections for research subjects.

NBAC (2001) suggests that an IRB's assessment of risks and potential benefits is central to determining that a research study is ethically acceptable and would protect participants of the study. However, with no clear criteria for IRBs to use in judging whether the risks of research are reasonable in relation to what might be gained by the research participant or society, the ambiguity of measuring reasonable risks is left to individual interpretation. The lack of consistency and continuity of the review process is of grave concern to social scientists (Gunsalus, 2006). Zywicki (2007) puts forward that "IRB decisions on a

vague and capacious metric of 'harm' amounts to making decisions according to no predictable rules" (p. 892). Researchers put forward that investigators and IRBs must be more effective and efficient in carrying out their responsibilities, in that way, improving research protections and increasing public trust in research.

Indications of noncompliance resulting in risk of harm to those participating in social science research remains minuscule compared to OHRP findings of noncompliance in biomedical research activity (Braxton, 1994). Although there has been much anecdotal comment in the literature on the topic of the application of a one-size-fits-all approach to regulating social science research with biomedical regulations, there seems to be no abundance of literature of the research to substantiate the assertions that research participants are better protected in social science research studies resulting from the biomedical regulatory model of the Common Rule (Gunsalus, 2007 Mueller, 2007). Similar to others in the literature, Zywicki (2007) states that:

> The requirement of IRB preapproval for research applies only to federally funded research. Nonetheless, universities have extended the mandate to all research involving human subjects, even though the vast majority of social science research is not federally funded. This requirement is typically justified by belief that IRBs are a necessary part of a system of checks and balances to curb the self-interest of researchers, whose natural inclinations may lead them to discount improperly the dangers to human subjects from their research. But the argument that IRBs are necessary to counterbalance the self-interest of researchers is somewhat ironic in that there are no institutional checks to balance the self-interested expansionist tendencies of IRB administrators. Thus, in a classic example of the problem of "who watches the watchers," IRB administrators arrogate to themselves the power to oversee all research involving human subjects, even the vast majority of social science research that is not federally funded (p. 888).

De Vries et al. (2004) suggests social science researcher may be over scrutinized for the harms that may result from their research based on the amount of risk in typical social science research, including surveys, interviews, oral history research and others. The imposed regulations by OHRP on social science research continue to weigh heavily on institutions as they attempt to balance the need for protecting human subjects in research, the need to support their researchers' scholarly efforts and the need to minimize any untoward liability claims on the institution. Gunsalus et al. (2007) suggests that the increased workload burden of the IRB and administrative staff provide a negative impact on high-risk research needing to be reviewed and approved.

The Common Rule - Intent and Impact of Policy

"All compliance systems require the buy-in and collaboration of the regulated, and it will be a sad day if scholars come to see human protection in research as the source of frustrating delays and expensive paperwork" (Gunsalus, 2006, p 26). The literature does not reveal prodigious support for the regulatory system of protecting human subjects in the social sciences with biomedical regulatory standards. Governments translate their political agendas and programs through policymaking to deliver outcomes desired to reflect change (Fischer, 1995). The Common Rule was the United States answer to protecting human subjects in a uniform manner, representing a 10 year collaboration that resulted in 17 federal departments and agencies adopting one set of regulations to include biomedical and social science research (NBAC, 2001). To obtain a more consistent form of protection for research subjects, in

1995 the NBAC surveyed agency's policies and procedures focused on the protection of human subjects research.

The survey instrument was to assess "each department's activities to protect human subjects in research and the structure's, policies, and procedures in place for the review and oversight of human subjects protections" (NBAC, p. J-2). The survey tool was designed to assess department's compliance level with the Common Rule and any difficulties arising from the implementation of the Common Rule. The data collected suggested concerns in the following areas:

- Federal protections for persons serving as subjects in research do not extend to all Americans.
- Despite widespread implementation of Federal Regulations by those departments and agencies sponsoring substantial amounts of biomedical research on a number of departments and agencies that sponsor primarily non-biomedical research or little research over all, have failed to implement fully, the federal protections.
- Many federal agencies find the interpretation and implementation of the Common Rule unnecessarily burdensome.
- Federal protections are difficult to enforce and improve the effect of the lead throughout the federal government, in part because no single authority or office oversees research protections across all government agencies and departments.

- New techniques are needed to ensure implementation at the local level.

Although many federal agencies reported improvement in the way they addressed protecting human research subjects, years later problems still remained. Some problems as noted by the National Bioethics Advisory Commission in 2001 included:

1. Appropriateness of the Common Rule

   Nonclinical nonmedical research communities reported having the greatest difficulty in the interpretation and application of the Common Rule especially as it applies to the finding minimal risks.

   Although the vast majority of agencies support nonclinical research, many of the agencies challenged the biomedical model of the Common Rule for addressing the unique concerns raised by behavioral, social science and educational research (p. J. 14).

2. Lack of a knowledgeable IRB

   Agencies that do not have effective IRBs in place to assess research proposals prior to their funding may not have the appropriate information in place to adequately request revisions or even disapprove greater than minimal risk research, leaving protections for human subjects lacking.

3. Determining exemptions

The interpretations of exemption categories across agencies vary as well as who the designated entity will be to interpret the exemption categories.

4. Adequacy of Administrative Structures

Federal agencies are responsible for communicating policies to relevant research institutions and IRB's, establishing a structure of peer review for scientific merit of research proposals. In addition, negotiating assurances with research institutions verifying that IRB's and researchers comply with Federal Regulations and in investigating and providing follow-up on any complaints of noncompliance

The data suggested that agencies did not devote sufficient resources to administrative structures.

The concerns raised by the NBAC in 2001 reflect many similar concerns of social science researchers recently such as that of Coleman (2009); Kotzer & Milton (2007); Dyer & Dermeritt (2009). In particular, their concerns reflect the findings of the NBAC regarding the interpretation and implementation of the Common Rule as confusing and, or, unnecessarily burdensome. The literature provides a profusion of social science researchers' concern that the Common Rule provides overregulation for social science research. As discussed, social scientists suggest that the biomedical regulatory framework of protecting human research subjects is not congruent with social sciences.

Byrne (1987) suggest that cost-benefit calculations play a role in policy

decisions, although, the value of cost-benefit analysis is in the discipline that brings to the policy process the ability to address social problems in a systematic and efficient manner. Earlier in this discussion details of the basis for federal intervention in unethical research practices funded by the federal government were highlighted detailing Federal intervention, due to unethical research practices, led to the development of Common Rule protection of human research subjects.

The federal policy is a guide for the research practices of biomedical and social science research. The policy is based on a biomedical model of human research protections that also is the basis for protections in social science research. Social Science researchers puts forward that the cost of the federal policy has been in overregulation, human research protection programs deluged in unnecessary paperwork and documentation, having little benefit to research participants and that a reasonable solution has not been achieved for protecting human participants of social science research (Oakes, 2002; White, 2007; Vanderpool, 1996; Pattullo, 1985; Malone, 2003; Marshall, 2003).

Fischer (1987) suggests that cost-benefit analysis in the policy process was institutionalized through the Office of Management and Budget (OMB) during the Reagan administration. Economy and efficiency is the focus of cost-benefit analysis, and "politicians have found cost-benefit analysis to be conveniently compatible with their own biases" (p. 116). Gunsalus (2004), calls for refinements to the regulatory system that will provide a set of policy regulations designed for non-biomedical research. Gunsalus puts forward that

the challenges of the application of the policy (the Common Rule) must be better understood and implemented. Better understanding will assist the IRB and their support staff to "direct attention to the areas of greatest risk, while intentionally scaling back oversight in areas of lesser risk" (Gunsalus, p. 86).

Levine's (2001, January) testimony to *The Committee on Assessing the System for Protecting Human Research Subjects* (see Appendix O) suggested even then that there were "growing fault lines in the system that protects human participants and that a gap has developed between law and policy on the books and in action" in the author's testimony to the American Sociological Association (p. 2). Levine states, "For the social and behavioral sciences, the overall problem with the system is the attempt to fit our research into a framework that was over specified and designed for biomedical-clinical research."

Seiler and Murtha (1980, p 147) suggest that the 1974 National Research Act that was "signed under pressure of Congress to complete the task prior to the next administration coming in". The authors suggest that in the haste for completion of the regulations, there was no mechanism in place to inform the social science community of the new rules that would apply to them or to get their input or feedback (p. 148). The regulations produced were a product of mainly extensive drafting by the NIH staff. Tropp (1978) suggests that:

> Under the gun of imminent congressional passage of the National Research Act, and in order to preempt a possible Senate move to include in it mandatory ethical standards governing federally sponsored research, the secretary of HEW on May 22, 1974, signed a regulation on "Protection of Human Subjects" which essentially transformed the predecessor NIH guidelines into department policy. The regulation was largely a product

> of the “H” part of HEW, drafted without participation by those HEW agencies which customarily commission social science research products and maintain daily conduct with the social science research world. (p. 391)

Having little participation in the construction of development of the policy to regulate human subject research, social scientists need additional mechanisms to address their concerns and to insure that the Common Rule as a tool for protecting human subjects is the most effective and efficient mechanism for doing so (Haggerty, 2004).

The Common Rule, from its inception was formed and charged with the responsibility of insuring research protection for those participating in federally funded research projects, using the Common Rule as the federal regulatory stance for the institution’s human research policy foundation (Aronson, 2008; Payne, 2000; Coleman, 2009). In 1985, Patullo suggests that institutions had adopted policies much more restrictive for protecting human subjects than they need to be, stating that, “outraged by a few excesses we have responded like one who burns down a house to rid the attic of squirrels” (p. 524). Nearly 30 years later social science researchers are still critical of the overregulation of a one-size-fits-all model of applying biomedical standards to social science research.

White (2007) and Bozeman & Hirsch (2005) suggests the negative publicity of institutions appearing in the OHRP database of determination letters has made for increased institutional scrutiny, overregulation and mission creep of human research projects submitted for review and approval. White points out that deficiencies in research protocols recorded by the institution’s HRPP, that

prevents approval of social science projects, mainly represent documentation concerns that have little or nothing to do with the safety and risk to human subjects. Gunsalus et al. (2005) concurs, that HRPPs have increased documentation practices to the extent that researchers see the increased documentation practices as overregulation and mission creep.

The concerns expressed by social scientists about overregulation includes as Wagener et al. (2004, October) points out , HRPPs are requesting much more additional safeguards to be included in minimal risk research projects. Mission creep in Institutional Review Boards permeates the literature of institutional review mission, practice and oversight related to the IRB system of protecting human research subjects. Although, IRBs are a critical safeguard in the system of protecting human research subjects, and social scientists give them credit for such, researchers suggest the system of human research protection is devoid of effective control that does little in protecting human subjects (Coleman, 2004; Resnik, 2004; Oakes, 2002; Burris & Welsh 2007; Marshal, 2003).

Moreno (2000) suggests that IRB members should have more training to understand the regulatory issues that arise in research projects when collaborating with other institutions. The assertion is that research studies are delayed because of the uncertainty of a process to address collaborative projects. Recommendations for increased training and education are also included in the findings of Borror et al. (2003) and Burris & Welsh (2007) along with increased funding for IRB activities. Good practice guidelines for diverse areas of research are highlighted in reports on ethical and policy issues in human

subjects' research published by the Institute of Medicine (2000 & 2001), the National Bioethics Advisory Commission (2001a, 2001b), Similar recommendation, has been proposed by the National Academy of Science's panel on IRBs and social science research. While there is consensus about the general purpose of IRBs, significant problems remain in the applicability of the review process for social science research protocols (Edgar & Rothman, 1995; Ferraro and Orvedal, 1998; Marshall, 1998; Chadwick and Dunn, 2000).

Summary

The history of research violations that brought about the intervention of formal codes and regulations to protect the safety and well-being of human research participants is well documented in the literature. Social science researchers are concerned with the applicability of biomedical research standards to their minimal and less than minimal research. The challenges faced by an oversight system for protecting the rights and welfare of human subjects have resulted in overregulation and under protection of the Common Rule, suggest social scientists. The concerns raised by social scientists mirror similar concerns of the in the NBAC. The over emphasis on procedural requirements has been a major concern of social science researchers as is excessive paperwork requirement of the IRB and its support staff to fulfill the policy requirements of the Common Rule that provides little added protection for human subjects suggest researchers. The quandary of what additional policies need to be put in place continues to be unanswered after more than three decades of contention with utilizing a biomedical model of protecting those human research participants involved in social science research.

Chapter 3

Methods

The Code of Federal Regulations, 45 CFR 46 is not separately distinguished by applicability to the disciplines of biomedical or social science research. The Federal Regulations at 45 CFR 46 contain Subparts A-E (see Figure 3). Subpart A is the basic HHS Policy for the Protection of Human Subjects. Additional protections for vulnerable populations involved in research are included in Subparts B through D. Subpart B provides additional protections for pregnant women, human fetuses and neonates. Subpart C provides additional protections for research involving prisoners, and Subpart D provides additional protections for children. Added to 45 CFR 46 within 2009, Subpart E provides instruction for registration of IRBs. This research study focuses on Subpart A, the Basic HHS Policy for the Protection of Human Research Subjects.

The literature identifies challenges for social science researchers that range from excessive time delays in the implementation of their research projects to disapproval of the projects based on standards applicable to biomedical research projects. Social scientists contend that the current review process applicable to biomedical research may not fit social science methodological research practices. Researchers in the literature provide antidotal experiences that include what they perceive as over-regulatory practices and mission creep. As a result of some over-regulatory practices and mission creep, researchers suggest that some researchers do not seek IRB review and approval for research activity prior to conducting the research study. Although, conducting research

without IRB approval could have an adverse impact on the research subjects depending on the level of risk associated with the project (Dyer & Dermeritt, 2009).

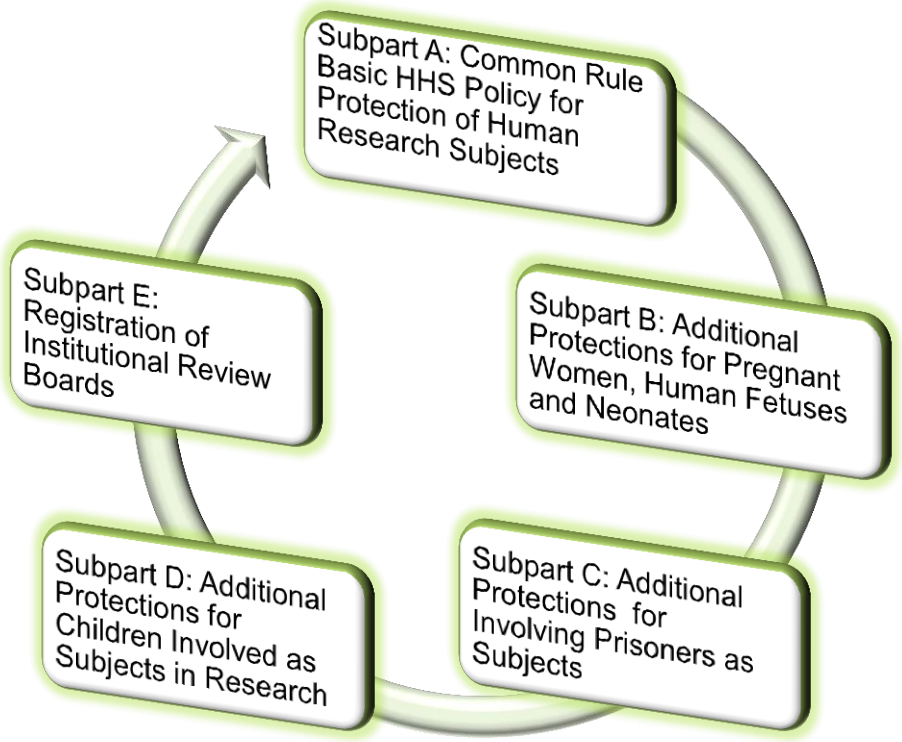


Figure 3. Subparts A - E of HHS Federal Regulation 45 CFR 46.

Gunsalus (2005) suggest the requirement for documentation of social science research projects remains the same as that of biomedical research projects. As a result, the university's human research protection program becomes entangled in a bottleneck of protocols that requires excessive documentation of minimal risk and less than minimal risk research. Imitating the

identical review and approval process for social science research projects as for biomedical research projects may present challenges for all concerned, including the researcher, the human research protection program, as well as the university or college exercising the tenets of their human research protection program to comply with federal agency funding requirements.

To receive federal research funding, universities and colleges must abide by an Assurance from The Office of Human Research Protection (OHRP). The Assurance (see Appendix N) is a document administered by OHRP, signed by an institutional signatory official committing the institution to abide by the regulatory statutes overseeing the conduct of human research as specified in the Common Rule as well as to the Subparts of 45 CFR 46. OHRP requests institutions to investigate concerns of noncompliance or deficiency with the regulatory statutes overseeing human research protection. The institution receives a document called a determination letter detailing issues that must be addressed by the institution.

To provide additional understanding of the impact of regulating social science research with biomedical regulations this qualitative study describes and analyze the contents of OHRP determination letters, analyze in-depth interviews of human research protection program administrators and evaluates the Common Rule policy.

Theoretical Framework

Denzin & Lincoln (2005) suggest that qualitative research can be viewed as “interpretive activities” having “no single methodological practice over another” (p. 6). They suggest that qualitative research is void of a “theory or paradigm that is distinctly its own” and does not belong to a single discipline having its own methods or practices. Merriam (1998) suggests the theoretical framework of a qualitative study is "the structure, the scaffolding, the frame of your study" (p. 5). As suggested by Merriam, the theoretical framework encompasses "concepts, terms, definitions, models and theories of a particular literature or base and disciplinary orientation" (p. 46). The combination of these, she suggests, affects all features of the study including articulating the purpose and problem of the study, to how we interpret the data collected.

Miles & Huberman (1994) are in agreement with Merriam(1998) suggesting, “any researcher, no matter how unstructured or inductive” comes with some orienting ideas (p. 17) being necessitated by the need to structure the process, the gathering of data, interpreting data, and reporting data in ways that is understandable. The authors suggest that the conceptual (theoretical) framework is a combination of theoretical understandings and experiences of the researcher in order to conceptualize the study. Anfara and Mertz (2006) posits that the researchers’ use of any framework or theory is appropriate, considering that it allows the researcher to see and comprehend particular aspects of the phenomenon being studied. The authors suggest that “no theory, or theoretical framework, provides a perfect explanation of what is being studied" (p. 27). With

that said, the theoretical framework to accomplish the goals of this study includes a qualitative methodology of study for content analysis, in-depth interviews and policy analysis.

Research Questions

Based on the statement of the problem as discussed in Chapter 1, the research questions are:

1. What are the findings of deficiencies and findings of noncompliance indicated in OHRP determination letters (DL) for social science research projects?
2. What impact does the Common Rule have on social science research protocol review by human research protection programs?
3. Has the Common Rule achieved its intended purpose of protecting human research subjects participating in social science research?

Research Design

This study encompasses a three prong qualitative methodological approach to answer the research questions above using content analysis, in-depth interviews, and policy evaluation.

Content Analysis of Documents

Determination letters alert the institution and public of any noncompliance or deficiency issues resulting from research conducted by the institutions' faculty, students and staff. Determination letters range from communicating to the

institution that minor deficiencies in a research protocol might have occurred, to notification of shut down of the institutions' research projects. Availability to OHRP determination letters when viewed by the public can result in bad publicity for an institution. The threat of bad publicity for institutions may in turn promote human research protection programs (HRPPs) to surpass the regulatory mandates of the Common Rule and impose extended institutional policies for reviewing and approving research projects, subjecting research protocol to increased institutional policies for protecting human subjects (Gunsalus, 2005). The overly copious policies and regulations can provide additional workload for HRPPs, time delays for the review and approval of research studies, and in many cases, as suggested by the literature, without adding any increased protections for human subjects, but providing better protections for the institution.

Qualitative content analysis of documents encompass a theoretical framework having an approach of empirical, methodological controlled analysis of texts within the context of communication, using systematic content analytical scientific methodology. Krippendorff (1969) suggests that "content analysis is a research technique for making replicable and valid inferences from texts (or other meaningful matter) to the context of their use. The author suggests specialized procedures are used with content analysis that can provide "new insights, increase the researchers understanding of particular phenomena, or informs practical actions" (p. 18). Krippendorff suggests that "content analysis is a scientific tool" (p. 18), as it is "a replicable and valid method for making specific inferences from text to other states or properties of its source" (p. 103)

Marshall and Rossman (1999) suggests that content analysis can be a supplement to additional forms of research including participant observation, interviewing, and analyzing documents used in the course of everyday events as well as those documents specifically constructed for the research at hand. As appropriate for this study, content analysis can render deeper understanding when used with in-depth interviews of human research protection program administrators and evaluation of the Common Rule policy. Qualitative content analysis of documents, being rich in "portraying the values and beliefs of participants in the setting" is an unobtrusive method of compiling information and data (p. 116). In addition, the authors note that content analysis should be linked to research questions in the theoretical framework for the study. Marshall and Rossman note that:

> Although content analysis was once viewed as an objective and natural way of obtaining a detailed description of the contents of various forms of communication, thus counting the mention of specific items was important has evolved, it is viewed more generously as a method for describing and interpreting the artifacts of a society or social group (p. 117).

Content analysis is nonreactive and can be conducted without disturbing the natural setting in any way (Babbie, 2004). It is the researcher that determines where to place the greatest emphases after the data has been compiled (Schutt, 2006; Babbie, 2004; Marshall & Rossman, 1999). However, the researcher can be a potential weakness for the interpretation of the data. Marshall and Rossman suggest that "care should be taken in displaying the logic of interpretation used in inferring meaning from the artifacts" (p. 162)

McBurney & White (2009) credits Lasswell (1951) for formulating the core questions of content analysis: "Who says what, to whom, why, to what extent and with what effect?" Formulating this line of discourse is appropriate when studying the communication of determination letters, because this line of query can supply rich and deep insight. Holsti (1969) offers a broad definition of content analysis as "any technique for making inferences by objectively and systematically identifying specified characteristics of messages" (p. 14) The objective inferences systematically taken from determination letters assists in putting forward a rigorous scientific method for analyzing the texts applicable to the federal regulation of the Common Rule, Subpart A.

Data Collection

The Office Of Human Research Protections (OHRP) is responsible for overseeing compliance with the Department of Health and Human Services (DHHS) regulations governing human subject research. OHRP has made determination letters available to the public via their Internet portal since 2000. These letters detail noncompliance and deficiencies of approved federally funded research studies. Letters were collected from January 2000 until December 2010. Letters are collected that reference academic institutions. The address block in the letters identifies the specific organization. Those organizations that appear to be academic institutions are separated from those organizations and institutions that appear to be by name medical.

The collection phase of data collection identifies in the body of the letter, reference to social science research projects. When a letter determined to

address social science research the letters were separated for further review. When determination letters seeming to reference social science research projects have been separated, they were reviewed for the following:

- Institution name
- Project title
- Reason for correspondents from OHRP
- Response from institution
- Initial finding of OHRP
- Final finding of OHRP

The results of the review of determination letters are compiled using Complementary Analysis Research Method Application (CARMA).

Telephone Interviews

Morgan (1988) suggests that an interview is a purposeful conversation with the purpose to obtain information from the other. Marshall and Rossman (1999) note that in-depth interviews focus on the individual's lived experience. This phase of the study focuses on human research protection program (HRPP) administrators. Marshall and Rossman suggest that in-depth interviews are used as a strategy to capture the deep meaning of the individual's experienced in his or her own words. HRPP Administrators are recruited for this phase of the study.

HRPP Administrators must process specific skills and knowledge of protecting human subjects. Their knowledge includes a high level of proficiency in regulations that oversee ethical standards of human research. In-depth knowledge of the Federal policy (45 CFR 46) which governs human research

protection standards is the paramount expectation for the HRPP Administrator, as the Common Rule (Subpart A) is the basic policy for the protection of human research subjects. Comprehensive knowledge and understanding of the Federal policy is required of the HRPP Administrator to perform adequately in the position (Bankert and Amdur, 2006). The authors suggest the HRPP Administrator has complex responsibilities of understanding, interpreting, and documenting research regulations as well as hold the position of the institution's chief authority on regulations pertinent to the IRB whose primary function is to protect human research subjects.

The HRPP Administrator ensures the IRB is operating in full compliance with Federal and institutional research compliance regulations. The IRB Administrator provides leadership in establishing and modifying IRB policies and procedures including developing ways to improve the IRB functions, policy changes, criteria for classifying projects as research, forms for documentation of IRB activities, as well as develops standard wording in the consent document (Bankert & Amdur, 2004, p. 70). The authors suggest HRPP administrators often are advisers to risk-management and compliance officials for institutional research policies, and advise the institution's teaching professionals on the standards for research compliance for those conducting human research. The HRPP Administrator is also required to develop a structured education program for IRB members and researchers related to human research regulation and the facets of IRB review and approval of research protocols.

Amdur & Bankert further suggest that HRPP Administrators devote "considerable amount of time to continuing education" and their profession because of new regulations being circulated and existing regulations "being interpreted in new ways" (p. 71). The authors additionally put forward that many HRPP Administrators engage in professional organizations specific to their profession, subscribe to professional IRB journals, attend conferences and become members of IRB forums. HRPP administrators are consistently aware of social science research projects submitted and can be in daily contact with the project's investigators. Therefore, HRPP administrators can offer noteworthy insight for this study.

In-depth interviewing is used as a technique to gather descriptive data in the subjects' own words for the purpose of developing insight as to how the HRPP Administrator interprets some portion of their professional world. Bogdan & Biklen (2003) put forward that, although qualitative interviews are relatively open-ended and can vary in the degree to which they are structured, the interviews can be focused on a specific topic and may be guided by general questions. Bogdan & Biklen furthermore, suggest that semi-structured interviews can ensure the researcher of obtaining comparable information across respondents.

Babbie (2004, p. 300) suggests that the qualitative interviewer must be completely familiar with the questions to be asked, allowing the interview to have a natural and smooth progression. The interviewer in this study has more than 10 years' experience in human research protections as a Director and IRB

Administrator. This research project includes a mode of semi-structured questions. Follow-up questions are asked as appropriate to the participants' response.

The qualitative research technique of in-depth interviewing involves individual interviews with a small number of respondents to investigate their perspectives on a particular idea, program, or situation (Creswell, 2007). As noted by Marshall and Rossman (1999) "the participant's perspective on the phenomenon of interest should unfold as the participant views it, not as the researcher views it. Boyce and Neale (2006, p. 3) suggest that "in-depth interviewing is a qualitative research technique that involves conducting intensive individual interviews with a small number of respondents to explore their perspectives on a particular idea, program, or situation." They posit that those associated with the program may be interviewed about their experiences and expectations in regard to the program, including program operations, processes, outcome, and any changes they perceive they have experienced in the program. Six participants were interviewed for this phase of the study.

Boyce and Neale's perspective parallel with the intent of this phase of the research project which involves interviewing HRPP administrators about their experiences in the duties they perform and oversee. The emphasis of the interview questions is to compile data of their experiences, and expectations of their program to protect human research subjects.

The primary advantage of in-depth interviews is that they provide more detailed extensive information than what is available through other data collection

methods, although there can also be disadvantages. Qualitative data from interviews can be ambiguous which may result in a more difficult analysis process. In-depth interviews are useful when detailed information about a person's thoughts and behaviors are to be explored. Interviews are often used to provide context to other data such as the content analysis approach being used in this study for additional understanding of the impact of regulating social science research with biomedical regulations.

However, there are limitations and weaknesses to in-depth interviews. Marshall and Rossman (1999) suggest that interviews involve personal interaction and cooperation is essential. Interviews have particular strengths. According to Marshall and Rossman, in-depth interviews can result in large amounts of data quickly with the possibility of immediate follow-up and clarification. Marshall and Rossman further suggests that there are limitations and weaknesses to the interview process. "Interviews involve personal interaction and cooperation is essential. Interviewees may be unwilling or may be uncomfortable sharing all that the interview hopes to explore, or they may be unaware of recurring patterns in their lives" that may cause the respondent concern (p .110). Although large amounts of data can be acquired through interviewing, the data are very time consuming to analyze.

In-depth interviews are flexible in that they can be presented in a number of ways, having no specific format to follow. In-depth interview data may stand alone or be included in a larger evaluation report (Patton, 2002). The author suggests when presenting results of in-depth interviews, care must be taken in

presenting the data by the use of qualitative descriptors rather than try to quantify the information.

Therefore, with the understanding that in-depth interviews are effective as a tool to use in combination with other research methods, in depth interviews are appropriate for this study. The purpose of the interviews is to explore the HRPP administrators' point of view as it relates to protecting human research subjects, specifically those involved in social science research projects. Using open ended questions in a semi-structured format, the goal of this phase of the project is to interpret what is being said in order to explore the respondent's viewpoint, position and perspectives (Creswell, 1997 and Guion, 2006).

Creswell (1997); Denzin and Lincoln (2005); Kvale (1996); Babbie (2004) posits that there must be a positive rapport with the respondent keeping in mind that the researchers paramount duty is to listen and observe what is being articulated. Guion (2006) and Babbie (2004) suggests strategies to improve the quality of the in-depth interview experience include rephrasing and, allowing the respondent to speak freely as the researcher guides the conversation to ensure issues of interest are covered, to be open to deficiencies from the topic but using care to return the conversation back to the topic (see Figure 4). For increase accuracy and reference, audio record the conversation when possible. In-depth interviewing is used in combination with content analysis and policy evaluation.

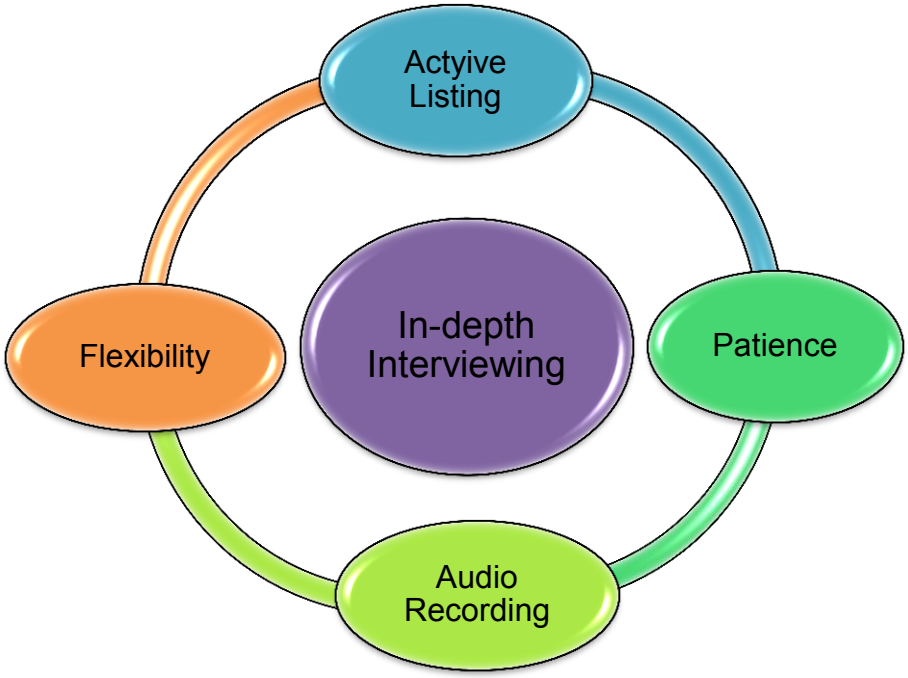


Figure 4. Strategies for In-Depth Interviewing

Telephone Interview Questions

1. What is your role in your institution's human research protection program?

   How long have you worked in this role?
2. What has been the role of the HRPP in protecting human research subjects involved in social science research?
3. If your institution has "un-checked" the box on the Federalwide Assurance, how has un-checking the box affected the review and approval of social science research projects?
4. The Common Rule is based on a biomedical regulatory model of human research protections. How are the components of the

biomedical regulatory model working for social science research projects?

5. What, if any, concerns have social science researchers reported to your HRPP related to the review and approval of their research projects?
    a. How does the Common Rule address some of these concerns?
    b. What do you (if you do) see as the major impediment in applying the Common Rule to social science research project review?
6. How would you characterize the regulation of social science research?
7. If you could modify the Common Rule to be specific to social science research projects, what would the change/s look like?

Policy Evaluation

The system of protecting human participants in social science research studies relies on federal regulatory standards imposed in the policy of the Common Rule. Relying on Fischer's work on policy evaluation method, this phase of the study is focused on the author's four interrelated discourses of policy evaluation including: program verification; situational validation; societal level vindication, and social choice, aligned with CARMA as shown in Table 6.

Jezierska (2009), in collaboration with the author Putney successfully applied CARMA to an evaluation of policy. A similar application of alignment of CARMA with Fischer's' Four Steps of Inquiry is used in this study.

TABLE 6

CARMA Aligned with Fischer's Four Steps of Inquiry/Four Interrelated Discourses

Policy Expectations	Evident Implementation	Results	Conclusions and Recommendations
Initiator's	Users/Participants	Compare/Contrast expected with evident	Evaluate Interpretations
Who is being served? Who is involved?	All are evident participants?	Expected versus evident	What are the implications? Modify or maintain program
How are participants to be served?	How are participants using the service?	Expected versus evident	What are the implications? Modify or maintain program
What will be produced by participants in the program?	What was produced by participants in the program?	Expected versus evident	What are the implications? Modify or maintain program
Step 1	**Step 2**	**Step 3**	**Step 4**
Verification: Intended Outcomes	Validation: Objectives	Societal Vindication: Goals	Social Choice Values
Policy fulfills its stated objective?	Program objective relevant to the problem situation?	Instrumental or contributive value to society?	Provides for a legitimate resolution for conflicting judgments?

Source: Putney (2008) & Jezierska (2009)

Fischer (1995) suggests that policy evaluation is also referred to as policy analysis or policy science. Fischer (2003) indicates that Harold Lasswell's influential approach to policy analysis include assumptions of empiricist and post empiricist thought as a visionary in the evolution of the policy analysis. Quade (1982) denotes that policy analysis is "a form of applied research carried out to acquire a deeper understanding of sociotechnical issues and to bring about better solutions" (p. 5). Yanow (1996, p. 2) suggests that policy analysis is "designed to supply information about complex social and economic problems and to assess how a policy or program is formulated and implemented." Wagener (2003) maintains that policy analysis, as Fischer also suggests, is fundamentally interpretive and reflexive (p. 30). Therefore, to evaluate the Common Rule for better understanding of its effectiveness for the social sciences, policy analysis is appropriate as an investigation technique for this study.

Policy analysis emerged in the 1960s and the 1970s with the practice now being used throughout governmental institutions and political organizations with the emphasis on producing and transforming information and arguments relevant to policy problems. In 1987 Byrne suggested that values are not easily quantified and can often be in conflict, but although a definite solution may not be achieved, a reasonable solution can be achieved, provided there is informed understanding of the general levels of costs and benefits and their distributions (p. 73).

Fischer indicates that the logic of cost-benefit analysis involves a compilation of costs and benefits of a policy to determine its net value. Fischer

further suggests that cost-benefit analysis has been the subject of theoretical and practical disagreement due to its difficulty to quantify “policy inputs” and “policy outputs,” stating “the technique systematically underplays social objectives that cannot easily be measured in quantitative terms." (p. 116). Writing in 1987, John Byrne also suggests that cost benefit analysis was the tool of public policy making and evaluation. Dunn suggests that “policy analysis can be formally defined as an applied social science discipline, which uses multiple methods of inquiry and arguments to produce and transform policy relevant information that may be utilized in political settings to resolve policy problems” (1981, p. 35). As previously discussed, there are many instances in which biomedical research policy has benefited from the Common Rule Policy. Social scientists have concerns that the Common Rule policy does not have similar benefit or have similar impact on research in their disciplines because the policy is geared towards the biomedical model of research.

Lasswell, identified as the founder of the policy field, defined policy science orientation utilizing three characteristics (1) a multidisciplinary approach,(2) problem oriented focus that was contextual in nature and (3) and explicitly normative orientation (Fischer, 2003, p. 3). Yet another way of assessing policy is asking the question, is the policy accomplishing its stated purpose or not (Fischer, 1995)? The question asked by Fischer is also asked in in the analysis using the CARMA methodology.

Validity

Klenke (2008) suggests that the terms of validity in qualitative paradigms are the terms credibility, which parallels internal validity, transferability which parallels external validity, dependability which parallels reliability and confirmability which parallels objectivity. Lincoln and Guba (1985) suggests that trustworthiness of qualitative research methods consist of credibility, dependability, transferability, and confirmability.

Credibility/Internal Validity

Credibility is the extent to which the results as indicated in qualitative research are credible or are believable from the standpoint of the participant. Credibility can be a test when there is the presence of multiple realities to insure the realities are represented adequately. Credibility is seen as the greatest available estimate to the truth of intentions. Internal validity in qualitative research concerns the findings of the research study and its approximate match to the reality espoused (Patton, 1990, Merriam, 2001). It is the degree in which interpretations and concepts share mutual meanings. While, Lincoln and Guba (1985) state that "the determination of such isomorphism is in principle impossible" (p. 294) since “the precise nature of that reality” (p. 295) is not known whereas, Kvale (1996) suggests that validity can apply to qualitative methodology given that, in a broader concept validity can pertain to whether a method of observations reflect the phenomenon or variables of interest, thereby in principle qualitative research can lead to valid scientific knowledge..

Patton (1990) suggests credibility of qualitative data can be enhanced through the use of triangulation of research methods used. As discussed, a three pronged methodological approach consisting of content analysis of documents, in-depth interviews and policy evaluation is used. “Member checks” as posed by Lincoln and Guba (1985, pp. 313-316) can also be used to address credibility. Member checks are used with participants of in-depth interviews along with making the data available for others to analyze.

Transferability/External Validity

Transferability is the extent to which results of the findings can be transferred to additional contexts or settings. In qualitative research although the researcher is unable to specify if the results of the study can be transferred to a larger population ,it can be conceded that the information can be extrapolated to determine if it fits a particular situation (Lincoln and Guba, 1985; Patton, 1990).

Dependability/Reliability

Dependability in qualitative research aligns closely with reliability in quantitative research suggests Lincoln and Guba (1985, p. 300). The authors puts forward that dependability is achieved when independent investigators can obtain similar results of the study. Lincoln and Guba further suggests the use of an “inquiry audit” to enhance dependability of qualitative research (p. 317). The man in his own “inquiry audit” is achieved by reviewers’ examination of the data for consistency of the process and the product of the research study (p. 317). All data from this study will be available for the minimum of three years for reviewers’ to perform an inquiry audit.

Confirmability/Objectivity

Lincoln and Guba (1985) propose that confirmability is the extent to which an audit inquiry of raw data, analysis notes, reconstruction and synthesis products, process notes, personal notes and preliminary development information can be confirmed by another. All data will be made available for confirmation.

Summary

Social science researchers have suggested, the components of their research activity contained much less risk to human research subjects than that of biomedical research. Institutions are required to follow the policies of the Common Rule for federally funded research projects, as they are also required to follow their institutions' policies for human subject research. Social scientist suggest that using the Common Rule to review and approve their research that is minimal and less than minimal risk amounts to overregulation and mission creep by institution's HRPP (Schrag, 2009; Pittenger, 2003; Lincoln, 2005).

To better understand the impact of the Common Rule on social science research activity three methods of inquiry are applied in this qualitative study. Content analysis of OHRP determination letters, in-depth interviews of human research protection program administrators and policy evaluation of the Common Rule will provide a better understanding of the impact of the Common Rule for social science research activity.

Chapter 4

Findings of the Study

The findings of three qualitative research methods are presented in this chapter. Content analysis of OHRP determination letters using CARMA as a tool of analysis, in-depth interviews of human research protection program administrators, and policy evaluation of the Common Rule utilizing CARMA aligned with Fischer's Four Steps of Inquiry were the methods used to address the following research questions:

1. What are the findings of deficiencies and findings of noncompliance indicated in OHRP determination letters (DL) for social science research projects?
2. What impact does the Common Rule have on social science research protocol review by human research protection programs?
3. Has the Common Rule achieved its intended purpose of protecting human research subjects participating in social science research?

Content Analysis of OHRP Determination Letters Using CARMA

CARMA is used as an analysis tool to address Question 1: What are the findings of deficiencies and findings of noncompliance indicated in OHRP determination letters (DL) for social science research projects? Steps in preparation to gather the sample for the analysis of the OHRP determination letters are described below.

Determination letters are publically available and located on the OHRP Internet website at: http://www.hhs.gov/ohrp/compliance/letters/index.html . The public access site contains letters sent to institutions beginning, July 2000. A total of 763 letters (the initial sample) were sent to institutions from OHRP between 2000 and 2010 (see Appendix P). A total of 763 letters were reviewed in Step One of the content analysis of OHRP determination letters.

In Step Two of the content analysis, the researcher further reviewed from the sample letters addressed to colleges and universities within the United States (U.S.). The vast majority of colleges and universities that were sent determination letters fall within the Carnegie Foundation's Classification Description of RU/VH: Research Universities (very high research activity); RU/H: Research Universities (high research activity); and DRU: Doctoral/Research Universities.[20] These research institutions conduct social science, and or biomedical research. However, it was beyond the purview of this research project to definitively calculate which institutions conducted social science research projects, biomedical research projects or both social science and biomedical research projects. RU/VH, RU/H and DRU institutions within the U.S. were included in the sample. Letters sent to what appeared by name to be medical centers, medical companies, hospitals, pharmacies, clinics and other medical facilities were not included in the sample because social science research projects were the focus of this study. There was a high probability that determination letters sent to

[20] The Carnegie Foundation appointed the Carnegie Commission on Higher Education in 1970 to develop a classification of colleges and universities to support its program of research and policy analysis. The classification system was derived from empirical data on colleges and universities. The Carnegie Classification was originally published in 1973, and has been updated in 1976, 1987, 1994, 2000, 2005, and 2010 to reflect changes among colleges and universities.

medical facilities and universities reflected noncompliance or deficiencies in medical research projects. Therefore, in Step Two, the revised sample included 288 determination letters.

In Step Three, the determination letters were reviewed for project information contained in the Reference (RE:) section of the letter. If the determination letters did not reference a Project Title in the “RE:” section of the determination letter, the letter was not included in the sample. Project titles that suggest biomedical research projects were excluded. Samples of biomedical and social science research project titles are shown in Table 7. Two hundred and forty-five determination letters, with what appeared to be biomedical projects were excluded from the sample. Forty-three letters representing social science research projects remain in the new sample.

Table 7

Examples of Social Science and Biomedical Research Project Titles from OHRP determination letters

	Social Science	Biomedical
Examples of Research Project Title	▪ Socio-Cultural Determinants of Utilization of Breast Cancer Awareness and Prevention Services ▪ The Impact of Education in Navajo Nation Border Community Public Schools ▪ Study of HIV/AIDS Perception, Attitudes, and Knowledge Among University Students ▪ Research Investigating How Restaurants Handle Food-Poisoning Complaints	▪ Dynamical Studies in Frontal and Temporal Lobe Epilepsy ▪ A Phase I/II Study of Sequential Vaccinations with ALVAC-CEA with the Addition of IL-2 and GM-CSF in Patients with CEA Expressing Tumors ▪ A Dose Response Study of Inhaled Nitric Oxide in the Treatment of Adult Respiratory Distress Syndrome ▪ Study of 4% Lidocaine Intranasally to Treat Migraine

In Step Four, the contents of the remaining sample of 43 OHRP determination letter were analyzed for noncompliance and deficiency matters related to social science research projects. The sample of 43 documents were analyzed for noncompliance and deficiencies containing reference to the Common Rule, Subpart A, §101-124 using Complementary Analysis Research Method Application (CARMA), as shown in Table 8. A determination letter that appears to be a social science research study (in reviewing the project title) can be found at Appendix Q.

Table 8

Complementary Analysis Research Method Application (CARMA)

1 Determination Letter Expectations NOTE-TAKING	2 Evident Implementation NOTE-TAKING	3 Results NOTE-MAKING	4 Conclusions and Recommendations NOTE-REMAKING
Initiators	Users/Participants	Compare/Contrast expected with evident	Evaluator Interpretations
Who is being served? Who is involved?	Who are evident participants?	Expected vs. evident	What are the implications? Modify or maintain program?
How are participants to be served?	How are participants using the service?	Expected vs. evident	What are the implications? Modify or maintain program?
What will be produced by participants in the program?	What was produced by participants in the program?	Expected vs. evident	What are the implications? Modify or maintain program?

The CARMA process of analysis consists of first, Note-Taking. Note-Taking is used in this study in two ways. First, in Table 9, Column 1, Note-Taking represents the expectations of the program and then compares the expectations of the program with what is evident in how the program functions. The researcher examined what the program initiator (OHRP) expected to accomplish with the determination letter program.

Table 9

Note-Taking Expectations of Initiators and Participants of OHRP Determination Letter Program

1 Determination Letter Expectations Note taking	Note-Taking
Initiators	The Office Of Human research Protection (OHRP) initiates correspondence to institutions that have obtained an FWA from OHRP. Institutions are notified when OHRP finds that there may be a matter of noncompliance or a deficiency with the approved research study. The determination letter details date-specific required action by the institution and responds to the action taken by the institution.
Who is being served? Who is involved?	The institution is ultimately involved as a result of being engaged in research that is covered by the Common Rule and has an approved Federalwide Assurance. Specifically, the institutional review board having approved the research project, human research protection program which provides administrative assistance to the institutional review board, and the social science researcher, who implements the research project are served by the correspondence from OHRP.
How are participants to be served?	OHRP provides leadership in the protection of the rights, welfare, and wellbeing of subjects involved in research by providing oversight and guidance to institutions. OHRP does this in one way by the issuance of determination letters.
What will be produced by participants in the program?	The institutional review boards, human research protection programs, researchers and institutions, as a result of the correspondence from OHRP address concerns of noncompliance and deficiencies stated in the determination letter as applicable to the Common Rule in an attempt to provide protection of the rights, welfare, and wellbeing of subjects involved in the research project.

Second, the researcher then compared the expectations to what is Evident Implementation (how the program is being carried out) of the determination letters being sent by OHRP and received by the participants (the institution) as shown in Table 10.

Table 10

Note-Taking Evident Implementation

2 Evident Implementation	Note-Taking
Users/Participants	Institutions respond to Federal requirements as documented in the determination letters. HRPPs revise and add additional policies and procedures in reference to the findings of the determination letters. IRBs revise their review and approval process to address the determination letters findings of noncompliance and/or deficiencies. Researchers revised their research study to address issues of noncompliance, and or deficiencies.
Who are evident participants?	Same
How are participants using the service?	Institutions implemented additional policies and procedures, increased human research educational programs for researchers, institutional officials, and human research protection program staff. All changes were related to the regulations of the Common Rule as indicated in the findings of noncompliance, and or deficiencies detailed in the determination letter sent to the institution by OHRP.
What was produced by participants in the program?	To ensure that research subjects are fully protected from harm and that research funding is not withdrawn from the institution by Federal agency sponsors, additional policies, and increased procedures, with an increased level of scrutiny in the research protocol review process commenced.

suggests the Note-Taking strategy in this phase is to discern what is evident in the actions of participants. In Table 10 the researcher has described the evident implementation of the program from the researcher's point of view.

Although the entire response from institutions responding to the correspondence from OHRP is not publicly available, the subsequent response from OHRP referencing portions of the institutions response is publicly available. It is the subsequent response information from OHRP that is used for Note-Making as shown in Table 11 to further analyze the reactions to the determination letter by the participants. The Expectations are then compared with the Evident Implementations for interpretation of the data and thereby changing the Note-Taking phase to the Note-Making phase to ascertain whether congruence or divergence exists as shown in Table 11. During the Note-Making stage the researcher sought to determine if the Evident Implementation fit the expectation of response from the institution to OHRP.

Table 11

Note-Making Results of Expectations and Implementations of OHRP Determination Letters

3 Results	Note making
Compare/Contrast expected with evident Modify or maintain?	Institutions respond to Federal requirements as requested by OHRP in the determination letters. Institutions revise and add additional policies and procedures in reference to the findings of the determination letters. IRBs revise their review and approval process to address the determination letter's notation of noncompliance and, or deficiencies. Researchers revised their research protocol to address issues of noncompliance or deficiencies. OHRP's resubmittal of correspondence in reply to the institution's corrective actions taken in the determination letter indicated that the issues of noncompliance and or deficiencies indicated was slated to be addressed by the institution immediately. In all cases the expectation of the correspondence was addressed by the institution. In all cases institutions and their human research protection programs, institutional review boards, and researchers complied with requests in the determination letter made by OHRP. It would appear that OHRP's publicly available determination letters should be maintained.
Expected vs. evident	Same
Expected vs. evident	Social science researchers are expected to safeguard the welfare and rights of those that volunteer in their research projects. From the indications of corrective action requested by OHRP as noted in the determination letters, research subjects were not in imminent danger of being harmed based on the determination letters. It was evident that social science researchers were protecting the welfare and safety of their research subjects since determination letters did

	not indicate that there had been incidents of imminent danger to the research subjects. Administrative procedural deficiencies of the institution were the major focus of determination letters sent to institutions regarding approved social science research projects. Based on the information contained in the determination letters it's supported that institutions needed additional guidance in promulgating the Common Rule. Determination letters served as an educational tool for institutions and should be maintained.
Expected vs. Evident	Institutions and their human research protection program, institutional review boards and researchers provide additional documentation and practices to address the concerns cited in the determination letter. OHRP acknowledged the corrective action that has been addressed. In all cases from the review of each determination letter it was evident that the corrective action was in the process of being addressed, or had been addressed by the institution.

The final stage of the analysis was Note-Remaking as shown in Table 12. The researcher's interpretation from Expectations and Evident Implementation was determined, resulting in the subsequent step, Recommendations. The analysis clearly indicates the evident and expected were aligned.

Forty-three cases of noncompliance and or deficiencies from June 2000 to January 2011 represented social science research projects as determined by the project name listed in the determination letter on the OHRP publicly available Internet portal. In all cases OHRP indicated that institutions were taking corrective action or had taken corrective action to mitigate the concerns of the agency.

Table 12

Note-Remaking Results of Expectations and Implementations of OHRP Determination Letters

4 Results	Note Remaking
Maintain or modify program in terms of who is being served	Of 763 determination letters reviewed from 2000 to 2010 43 letters appear to be related to social science research projects in which OHRP cited issues of noncompliance or deficiencies. Seven hundred and twenty (720) letters were sent to institutions which referenced biomedical research projects. As a result of the corrective actions requested by OHRP, biomedical research projects should be the main focus of the regulatory elements of the Common Rule.
Maintain or modify program in terms of how systems are being served	The number of social science research projects (43) as compared to the number of biomedical projects (720) to receive determination letters may indicate there are far fewer incidents of noncompliance or deficiency in social science research than biomedical research. It may also indicate that biomedical research is funded by federal agencies at much greater rates than social science research. Also the disparity of the disciplines' numbers could suggest that social science has most of its research falling into the exempt or expedited categories of the Common Rule. The program should be modified to address the unique differences of social science research projects due to the level of risk involve in the majority of it research activity. .
Maintain or modify program in terms of outcomes being produced by them	Biomedical research projects in general contain a higher level of risk to the subjects than that of social science research as indicated in a corrective action requests by OHRP. Research implemented at a much lower level of risk to the research subject may not warrant the identical regulatory standards and scrutiny of the institution's IRB as biomedical research projects. The regulatory oversight by OHRP of social science projects should be modified to accommodate research which contains much less risk than that of biomedical research projects.

The concerns of OHRP as documented in determination letters of social science projects were overwhelmingly focused on inadequacies of the review and approval process completed by the IRB, and administrative errors representing noncompliance or deficiencies as shown in Table 13. Based on the specific Federal regulation of the Common Rule, OHRP requested that the institution address findings of noncompliance, and deficiencies involving the particular research study, policies and procedures directly related to the institutional review board, administrative procedures, and institutional human research policies.

The majority of OHRP concerns raised in determination letters were directly related to the functioning of the IRB and their administrative support staff. Very few OHRP concerns raised in the determination letters could be directly attributed social science researchers increasing the risk of harm to subjects participating in their studies. A selection of OHRP's determination letters detailing Required Actions are found in Appendix Q. The database of determination letters can be viewed at http://www.hhs.gov/ohrp/compliance/letters/index.html.

Risk of imminent harm or danger to research subjects did not appear to be the focus of noncompliance or deficiency indicated in the correspondence of the determination letter referencing social science research projects.

Table 13

Noncompliance or Deficiencies Cited In Social Science Determination Letters from 2000-2010

Federal Regulation	OHRP Reference to the Section Of The Common Rule
46.101(b)	IRB has applied an exemption to research activities that exceeded these categories.
46.103(a)	assurance regulations not documented properly in IRB policy
46.103(b)	study conducted without IRB approval
46.103(b)(2)	IRB did not have a duly constituted, functioning IRB and the IRB did not conduct initial or continuing review of the protocol review and recordkeeping duties
46.103(b)(4)	no written procedures conducting initial and continuing review
46.103(b)(4) & (5):	written IRB policies and procedures do not provide specifics of operational details (i.e., initial review, conducting continuing review, etc.)
46.103(b)(4)(iii)	protocol changes were initiated to the approved protocol without further IRB review and approval
46.103(b)(5)	no written policies for unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance
46.103(f)	IRB does not have written procedures adequately describing IRB activities
46.103(f)	IRB did not review grant application referenced in protocol prior to the initiation of research
46.107 (e)	chair and associate chair have conflicting interest – staff of Office of Sponsored Programs
46.107(a)	IRB not sufficiently qualified regarding race, gender, cultural background, and sensitivity to community attitudes
46.109(a)	HRPP sent letter of approval to the investigator prior to getting modifications as requested by IRB move
46.109(e)	regulations make no provision for any grace period extending the conduct of the research beyond the expiration date of IRB approval
46.110(b)	expedited review procedures failed to be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB
46.110(b)(1)	IRB inappropriately compounds the concept of minimal risk and expedited review

Table 13

Noncompliance or Deficiencies Cited In Social Science Determination Letters from 2000-2010 (continued)

46.110(b)(2)	inappropriate use of expedited review procedures
46.110(C)	IRB did not keep all IRB members advised of the approval of expedited protocol
46.111	IRB approval of the proposed research not deferred, pending subsequent review by the convened IRB of responsive material., IRB lacked sufficient information to make determinations required for approval of research
46.111(a)(7)	there are no adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data
46.115(a)(1)	difficult to reconstruct a complete history of all IRB actions related to the protocols, copies of research proposals and backup materials and other documents not available to OHRP
46.115 (a)(2)	IRB meeting minutes not documented
46.115(a)(2)	vote of IRB actions including number of members voting for, against, and abstaining not recorded in the minutes
46.115(b)	signed parental permission forms must be retained for at least three years after completion of the research (no mention of time-frame in protocol)
46.116	IRB failed to require legally effective informed consent or parental permission, and/or document waiver of informed consent Informed consent not presented in language understandable to the subject
46.116(a)	study did not include basic elements of informed consent that was reviewed and approved by the IRB
46.116(a)(1)	IRB did not review adequate explanation of purposes of the research and complete description of procedures to be followed
46.116(a)(2)	adequate description of risk and benefits not described in protocol that was reviewed and approved by the IRB
46.116(b)	informed consent documents and parental permission forms that reviewed and approved by IRB did not include all of the elements outlined in the regulations that was reviewed and approved by the IRB
46.116(d)	no documentation or procedure which alters or waives the requirements for informed consent
46.117(C)	no documentation of IRB waiver of signed informed consent form

Analysis of Determination Letters

To answer the Research Question 1: what are the findings of deficiencies and findings of noncompliance indicated in OHRP determination letters (DL) for social science research projects, a qualitative approach to content analysis of documents (DL) was utilized in this study. Seven hundred and sixty three (763) letters were reviewed by the researcher in order to identify nonmedical academic research institutions that had received a DL from OHRP. Two hundred and eighty-eight (288) DL were identified from the sample of 763 DL as being nonmedical institutions. The 288 DL project title was reviewed for wording that appeared to denote a social science research project.

Forty-three (43) letters were found to have reference to what appeared to be social science research projects. The sample of 43 letters were further reviewed for OHRP reference to the Common Rule, Subpart A, §101-124. Using CARMA to analyze the contents of the sample, Note-Taking (1) (Table 9) identified the expectations of the OHRP DL program. OHRP was identified as the initiator of the DL program, with the institution including the IRB, and the HRPP administrative staff identified as the participants that are being served by the OHRP DL program.

The next stage (2) of Note-Taking in Table 10 identified how the program is implemented and what was produced by the program participants including the institution), the HRPP, the IRB and social science researchers. The next stage (3) Note-Making, in Table 11, was used to determine the expected response from the participants (the institution) versus the evident response related to the

requests of OHRP in the DL. In all cases program participants responded to the requests noted in the DL. The expected and evident response was congruent.

The last stage (4) of CARMA was Note-Remaking. Note-Remaking focuses on assessing whether the program should be maintained or modified. The findings of the Note-Remaking stage suggests the OHRP determination letters program indicate that noncompliance and, or deficiencies to the Common Rule were attributed overwhelmingly to IRBs and their support staff, but not specifically to social scientists' research projects. The concerns of OHRP as documented in the DL of social science projects were overwhelmingly focused on inadequacies of the review and approval process completed by the IRB, and administrative errors of the HRPP. Therefore CARMA suggests that the vast majority of OHRP determination letters were effective in providing guidance and oversight to HRPPs in general, the OHRP determination letter program did not reveal a profusion of non-compliance or deficiencies that could be specifically attributed to social science research projects.

Telephone Interviews of HRPP Administrators

Telephone interviews consisted of identifying and contacting human research protection program administrators (HRPP administrators).HRPP administrators were identified from determination letters sent to the institutions HRPP administrators within the last 7 years. OHRP make determination letters available to the public, thereby publicizing the name and title of the HRPP administrator for the institution notified of non-compliance and or deficiency to the Common Rule. Determination letters (DL) are publically available on the OHRP

internet portal found at: http://www.hhs.gov/ohrp/compliance/letters/index.html. Contact information for the HRPP administrator was available on the institution's employee directory site.

Five HRPP administrators were contacted as a result of the determination letter. One HRPP administrator was chosen at random from the list of universities found on the Carnegie Foundations website at: http://www.carnegiefoundation.org/ . A total of six HRPP administrators were interviewed by telephone. HRPP Administrator's identity remains confidential in this report. Interviewees' names were replaced by identification numbers and their institution is not referred to in this analysis. All participants in the study expressed concern that their institution remain confidential for the purposes of this study. Confidentiality and privacy was maintained in this study. Table 14 shows questions and responses from the interviewees conducted on March 25, and March 28, 2011.

Table 14

Telephone Interviews - Questions and Responses

Question 1: What is your role in your institution's human research protection program? How long have you worked in this role?	
Interviewee 000-050	*IRB Administrator.* *6 years*
Interviewee 052-093	*IRB Director and voting member of the committee.* *23 years*
Interviewee 095-179	*Administrative Director, Social Behavioral IRB.* *8 years*
Interviewee 181- 227	*HRPP Program Director* *11 years*
Interviewee 233-286	*Director, Institutional Research and Effectiveness.* *9 years*
Interviewee 291-342	*Director of Research Compliance.* *8 years*
Question 2: What has been the role of the HRPP in protecting human research subjects involved in social science research	
Interviewee 000-050	*We've done a lot of enhancements in terms of our procedures of our guidance documents and educational outreach to educate our investigators. We now have a stronger program*
Interviewee 052-093	*We protect subjects involved in all types of research*

Table 14

Telephone Interviews - Questions and Responses (continued)

Interviewee 095-179	*The university has worked very hard to be progressive where the federal regulations allow particularly for social and behavioral research. We have unchecked the boxes on our FWA, for research that is federally sponsored that fall under social and behavioral sciences IRB. We have created demonstration projects, we have issued 2 year approval periods, we have created a new exemption category, and we have done a lot of work to try and maintain a superior level of protection for our subjects but also implemented some different procedures that decrease administrative burden while keeping subjects safe.*
Interviewee 181- 227	*As far as social science we have provided some education but not nearly enough for researchers to fully understand the Federal rules and regulations including why what seems to him to be minimal risk research still needing to go through that process. We have done a better job in providing education for the IRB. We constantly try to keep up with the new types of social science research we're seeing. Some of it is now collaborative research with biomedical*
Interviewee 233-286	*We have a lot of workshops with the IRB and researchers. I have a staff person that provides education for researchers and the IRB. This has helped us with the review process to insure research participants are safe and we have a much faster turnaround time for social science protocols since researchers know what the IRB is looking for in providing an ethically sound study.*

Table 14

Telephone Interviews - Questions and Responses (continued)

Interviewee 291-342	*Our role is not unlike that of biomedical. But I think it may be a little more difficult for the IRB to address some of the issues related to social science and the Common Rule. We just had a qualitative study that was very difficult since most of our members do not have experience in qualitative research. The protocol was combined with medical records review and blood draws. So you see how that can be cause for lots of deliberation. Sometimes there is no clear path except common sense. We provided education for the campus and the IRB but we have lots of empty seats.*
Question 3: If your institution has "un-checked" the box on the Federalwide Assurance how has un-checking the box affected the review and approval of social science research projects?	
Interviewee 000-050	*We have unchecked the box. We still review everything the same way but I think the one thing it may have done is given us more flexibility in terms exempt category 1 vs. expedited category 7. So if we're on the fence we can be a little more lenient than we would be otherwise.*
Interviewee 052-093	*No, our committee reviews social science and biomedical research. We treat the review process the same.*
Interviewee 095-179	*By unchecking the box you are able to get flexibility in how you can create equivalent protections for human subjects, so we are trying to take advantage of that by creating different procedures where we are able to, where there is not federal sponsorship or where the research is not held to the Common Rule by contract.*

Table 14

Telephone Interviews - Questions and Responses (continued)

Interviewee 181- 227	*We have just unchecked the box. I think it will mainly help in the review of unfunded research especially student research projects. The expedited reviewer and the IRB will have more flexibility in the approval of minimal risk research.*
Interviewee 233-286	*We unchecked the box two years ago. Review of protocol and now be done much faster. The protocol receives this same amount of scrutiny it did prior to the box being unchecked but the IRB can now use more latitude in the review process.*
Interviewee 291-342	*We have not unchecked the box yet. I expect we will get to it in the next few months. The IO is on board but there are still members of the IRB that believe unchecking the box will have an impact on how we are perceived to our constituents, although we know that the system of review will not change. We will get to it I am sure. It can only help with the speed in getting protocols approved for the researcher*
Question 4: The Common Rule is based on a biomedical regulatory model of human research protections. How are the components of the biomedical regulatory model working for social science research projects?	
Interviewee 000-050	*I think there are some gaps, one is the exempt vs. the expedited particularly in that area with kids and in the other areas some of the regulations need to be updated in regards to what we see in the social sciences in Internet research and newer research areas like that. So we have tried to have templates for each area and we try to use the common sense approach since the Common Rule is written for the biomedical area.*

Table 14

Telephone Interviews - Questions and Responses (continued)

Interviewee 052-093	*I guess I disagree I think the regulations of the Belmont report applies to all research and can be affectively applied to all research*
Interviewee 095-179	*That's a fabulous question. I think social scientists and the IRB have had to work creatively to fit certain social science models into those regulations because as you mentioned they really were contemplated for the biomedical arena so it does take some creativity to do that. I think more recently across three to five years we have noticed a change in the perspective of social science research. For example there is much more bio-specimen and bio-banking collection associated with social science research so, it has more of a biomedical flavor to it than it use to. I also think another emerging research portfolio is research involving the internet research and social networking. That has actually been a challenge to try and find places for that type of research model within the Common Rule because it was clearly not contemplated several decades ago. So on one hand you have a component to social science research getting more of a biomedical flavor on the other hand you have some research diverging even more from those regulations.*
Interviewee 181- 227	*They could be working better for social and behavioral science research projects. With so many different areas that are not addressed (in the Common Rule) it can be difficult for us in the pre-review process and for the IRB*

Table 14

Telephone Interviews - Questions and Responses (continued)

Interviewee 233-286	*I think researchers the IRB and all involved in conducting research want to have to safe studies. The Common Rule does provide components that work for social science research but it is up to the HRPP to provide education for increased understanding of the flexibility within the regulations. The biomedical model used for social science may not accommodate or address the aspects of social science research. The exempt and expedited categories are trying to address some of the aspects but new areas of research including social media, is challenging for the IRB. A revamping of the Common Rule is really needed to support our researchers and the IRB better.*
Interviewee 291-342	*It has worked relatively well here since we began workshops a couple of years ago to address areas of social science research studies with the IRB, staff and our researchers. We are still spending a lot of time on some projects and have no clear guidance like that of biomedical studies. Most of our research here is social and behavioral science.*
Question 5: What, if any, concerns have social science researchers reported to your HRPP related to the review and approval of their research projects.	
Interviewee 000-050	*Of course everyone wants their projects approved yesterday. Chairs and committee members change and the researcher questions why a protocol was approved on day and not approved the next? So I think there are questions about continuity and disapprovals so they get pretty upset with this.*
Interviewee 052-093	*They (social science investigators) felt they had to do it (go through the IRB process) because they are at a medical institution*

Table 14

Telephone Interviews - Questions and Responses (continued)

Interviewee 095-179	*I think savvy researchers realize the Common Rule was not written with social scientists in the forefront of the feel of those regulations, and I think the savvy researchers find the IRBs need to kind of fit a square peg into a round hole troublesome for them because they feel it limits their flexibility, probably the biggest concern for us.*
Interviewee 181- 227	*Investigators frequently remind us that the approval process is too long and that they are required to make revisions to the protocol that protect the institution and not their research participants. Of course we provide training sessions from completing the protocol form to understanding 45 CFR 46 but they still are very frustrated for the most part when the protocol has to conform to the standards of the regulations.*
Interviewee 233-286	*Turn-around time is always a big issue. Exempt protocols are another one. We have an exempt reviewer that turns the study around rather quickly. Most of our researchers don't have a lot of concerns with our office they just want to begin the research as soon as possible.*
Interviewee 291-342	*We have recently had a few calls about additional documentation needed for internet studies. Chat room research has become very popular here. The concern is that we review it mainly as expedited research and there is some concern that it should be an exempt review.*
Question 5a: How does the Common Rule address some of these concerns?	
Interviewee 000-050	*It doesn't.*

Table 14

Telephone Interviews - Questions and Responses (continued)

Interviewee 052-093	*It's pretty clear that it (the regulations) applies to everything, all types of research.*
Interviewee 095-179	*There are so many different models of social science research. I think it (the concerns) is not being addressed. I think the IRB has had to work very hard to make it (the Common Rule) fit the research models. For example some of the issues around waver of documentation of informed consent can be particularly challenging. For example, for more than minimal research you can't always issue a waiver of documentation because that is prohibited by the regulations. That is exactly the time you would want to issue it (the waiver). You don't want the subjects name connected to the research or on a piece of paper of informed consent because it's a risky for the subjects but we are prohibited from waiving that documentation.*
Interviewee 181- 227	*I'm not sure it does. But maybe the key is to understand what is allowable in the regulations during the review process*
Interviewee 233-286	*It doesn't that I am aware of.*
Interviewee 291-342	*There is no mention of Internet research in the regulations. This is one of the concerns we have in applying the regulations to the different kinds of research we have here.*
Question 5b: What do you (if you do) see as the major impediment in applying the Common Rule to social science research project review?	
Interviewee 000-050	*I think it's just keeping up with the times because it (the Common Rule) just has not changed since it was written and there is so much need for its flexibility in terms of some of the investigators with research that just doesn't meet the category of exemption*

Interviewee 052-093	*I don't see an impediment.*
Interviewee 095-179	*Some of the Common Rule elements have too much specificity and not enough flexibility for the IRB to make some of the determinations and that example I gave about when you could issue a waiver of documentation is a perfect one.*
Interviewee 181- 227	*It just not the same fit as it is for biomedical. We spend a lot of time trying to make it fit.*
Interviewee 233-286	*What I see is a lot of busy work that keeps us from doing the essential work of protecting participants.*
Interviewee 291-342	*We have to have some guidelines and right now this is all we have. I don't see so much of an impediment as I see in the need for a specific set of social and behavioral guidelines for human-subject protections.*
Question 6: How would you characterize the regulation of social science research?	
Interviewee 000-050	*They could use some updating. The regulations are just not keeping up with the times, like internet research.*
Interviewee 052-095	*I think the regulations are flexible enough to work for all research*

Table 14

Telephone Interviews - Questions and Responses (continued)

Interviewee 095-179	*It is awkward because the Common Rule has expectations that much of the work will be clinical in nature with the exception of the exemptions which clearly carve out educational research and some other components like that but, strict to Part A, it does not leave enough flexibility with the IRB. It makes it awkward. It makes it a challenge to fit all the different types of social science research models within that. For example, It's quite different when you are being asked to review an ethnography study from a study of children in a behavioral interventional kind of perspective one requires flexibility and the other requires additional protections for the children and neither one of those elements are contemplated well when those Common Rule elements do have such a biomedical focus.*
Interviewee 181- 227	*It can be daunting. On one hand we want to make sure research participants are protected but we don't want to instill unnecessary concern by including everything that might happen to them as a result of the study. The regulations address the necessity to be very specific for biomedical researchers by the very nature of the kinds of research. Many times it's just over kill for social science research. IRBs want to make sure they adhere to their charge and require that which is required for biomedical studies.*
Interviewee 233-286	*We have not had any major incidents so I guess that would speak to the effectiveness of the regulations. IRB deliberations can be very complex and time consuming but they get it right mainly.*
Interviewee 291-342	*The regulations are very useful in protecting human subjects but it needs to be more specific to social and behavioral science projects*

Table 14

Telephone Interviews - Questions and Responses (continued)

Question 7: If you could modify the Common Rule to be specific to social science research projects, what would the change/s look like?	
Interviewee 000-050	*I would give it a facelift especially the exempt categories and also add more flexibility in terms of the continuations and the one-year rule.*
Interviewee 052-093	*I think the regulations are flexible enough to work for all research*
Interviewee 095-179	*As previous in my answer question I would ask that the IRB be given more flexibility to make additional determinations based on the nature of the project particularly if you are not talking about research with vulnerable subjects that would fall under the subparts. That would be really helpful because again I recognize that the government does not want to touch the regulations frequently and change them. Then if that's their model they should either issue guidance more frequently to allow IRB to make certain determinations or expand the determinations possible under the regulations or give the IRB more flexibility to do that themselves with more latitude than the Common Rule currently offers that way we can adapt to new models.*
Interviewee 181- 227	*I would look into disciplines of the social sciences and not group them under the same umbrella of regulation. Research in education may be much different than research in oral history. The humanities are much different than economics. It can be difficult at times for staff and the IRB to reconcile how the regulations best serve a study in these fields. I would just like to make the regulations more in line with social science research.*

Table 14

Telephone Interviews - Questions and Responses (continued)

Interviewee 233-286	*Increase the exempt categories to reflect more of the work that social and behavioral science conducts. I would make specific reference in the regulations to things like Internet research.*
Interviewee 291-342	*Two separate set of regulations would make the process of review and approval so much more efficient and effective for all concerned. We spend so much time in meetings discussing protocols that should be expedited but are not clearly defined as such in the regulations.*

Analysis of Telephone Interviews of HRPP Administrators

Six human research protection program administrators (HRPP administrators) were recruited to be interviewed for this study. HRPP administrators were identified from determination letters that had been sent to their institution by OHRP. Carbon copies of determination letters are sent to the institution's HRPP administrators, thereby publicizing the name and title of the HRPP administrator for that institution. Since determination letters (DL) are publically available on the OHRP internet portal found at: http://www.hhs.gov/ohrp/compliance/letters/index.html the researcher had access to the contact information for the HRPP administrator from the institution's employee directory. Five HRPP administrators were contacted as a result of the determination letter. One HRPP administrator was chosen at random from the list of universities found on the Carnegie Foundations website at: http://www.carnegiefoundation.org/ . A total of six HRPP administrators were interviewed by telephone. HRPP Administrator's identity remains confidential in this report. Interviewees' names were replaced by identification numbers and their institution is not referred to in this analysis. Interviewees were conducted on March 25, and March 28, 2011.

The role of all HRPP administrators suggested the leadership position in the HRPP, although titles were somewhat different. Titles included IRB Administrator, IRB Director, Administrative Director, Program Director, Director, Institutional Research and Effectiveness and Director of Research Compliance. Years of leadership service in the role was from 6-23 years. HRPP administrators

reported enhancing the procedures in their program and documents and revising documents (HRPP policies) for a stronger program of protection for human research subjects.

Interviewee 095-179 reported that the university had worked hard to be progressive especially where the federal regulations allow for social and behavioral research. The administrator had unchecked the boxes on the FWA, to disallow research that is not federal funded from being under the purview of the Common Rule. This being especially beneficial for social science projects that are not federally funded projects. Demonstration projects have been created, and unlike research which falls under the purview of the Common Rule, 2 year approval periods have been issued instead of one year approval periods. Administrator 095-179 also reports that they have "created a new exemption category, and we have done a lot of work to try and maintain a superior level of protection for our subjects but also implemented some different procedures that decrease administrative burden while keeping subjects safe," as shown in Table 14, Question 2.

Administrators report additional human research compliance education for the IRB and researchers as well as the HRPP keeping abreast of new areas of social science research such as social media. Social media is a concern for HRPPs, in that the Common Rule does not directly address this form of research. Interviewees also reported that there are "gaps" in the Common Rule which needs updating to address newer research areas. The lack of flexibility was another concern of administrators. An additional concern as stated by

Interviewee 291-342, in Table 14, Question 2, IRB members “do not have experience in qualitative research” to be efficient in the review and approval process.

Five out of six interviewees expressed concern that the Common Rule did not accommodate social science research practices and that IRB’s struggle in deliberation with the review and approval process for social science projects often this resulted in excessive documentation, revision requests of the researcher to conform to the standards of the Common Rule while creating time delays for the approval of the researcher’s study. Administrators suggest that the concerns of the IRB and researchers related to qualitative research, level of review for social media and other new areas of research studies is not addressed in the Common Rule. The lack of regulatory guidance for social science research projects continue to be a large concern for HRPPs providing regulatory guidance, for IRB’ in their deliberation processes and for the social science researchers needing approval for their research projects while protecting human research subjects and avoiding overregulation and mission creep.

Findings from the phone interviews included comments from HRPP Administrators suggesting the need for additional human research compliance education for the IRB and researchers, as well as for the HRPP staff to keep abreast of new research areas of social science research. Some administrators had already begun additional educational components to their programs but others needed to provide more education. The additional education was useful for HRPP staff and the IRB. The administrators reported that social media is a

concern for HRPPs, in that the Common Rule does not directly address this form of research. Interviewees also reported that there are "gaps" in the Common Rule which needs updating to address newer research areas. The lack of flexibility of the Common Rule was recurring concern reported by administrators. Administrator 291-342, Question 2 in Table 14 reported that IRB members "do not have experience in qualitative research" to be efficient in the review and approval process for social science qualitative research projects.

The finding in the chapter also included interviewees expressed concern that the Common Rule did not accommodate social science research practices and that IRB's struggle in deliberation with the review and approval process for social science projects often resulting in excessive documentation, revision requests of the researcher to conform to the standards of the Common Rule while creating time delays for the approval of the researcher's study. The lack of regulatory guidance for social science research projects was found to be a large concern for HRPPs providing regulatory guidance for IRB' in their deliberation processes and for the social science researchers needing approval for their research projects while protecting human research subjects and avoiding overregulation and mission creep.

Policy Evaluation Using CARMA Aligned with Fischer's Four Steps of Inquiry

This section of the research study addresses the Research Question 3: has the Common Rule achieved its intended purpose of protecting human research subjects participating in social science research? Fischer suggests that

policy related ideas are mainly arguments favoring various ways of looking at the world, which results in resolving the problem and therefore policy should be evaluated in terms of efficiency or effectiveness. In determining efficiency or the effectiveness of a policy, Fischer suggests four interrelated discourses can be used to evaluate the policy: 1) technical analytic discourse or program verification (outcomes), 2) contextual discourse or situational validation systems (objectives), 3) systems discourse or social vindication (goals), and 4) ideological discourse or social choice (values).

Program Verification: The aim of program verification is to understand how the program fulfills its objectives efficiently and effectively. Program verification assesses if the program has fulfilled its objective/objectives, are there secondary or unanticipated effects that offset program objectives and does the program fulfill objectives more efficiently than alternative means available.

Situational Validation: Situational validation focuses on if the program objectives are relevant to situation at hand. Validation has its concern in understanding if the program objective is relevant to the situation, are there circumstances that may require exception to the objectives, and are their two or more conditions that are also relevant to the problem situation.

Societal Vindication: The focus of societal vindication is on the societal system in its entirety, and the consequences of the policy to the societal system. The concerns of societal vindication are deliberated in concerns of instrumental or contributive value for society, and does the policy goal result in unanticipated

problems with important societal consequences, and does the policy goal lead to consequences that are judged to be equitably distributed.

Social Choice: Social choice is discerned by assessing whether the social order is essentially provided with a basis for a legitimate and equitable resolution of judgments that may be in conflict, and is there evident support for an alternative ideology to the policy.

Putney's (2008) qualitative evaluation tool, Complementary Analysis Research Method Application (CARMA) is similarly an evaluation tool to describe and interpret efficiency or effectiveness of a program or in this case, the Common Rule policy. Therefore, to assess efficiency or effectiveness of the Common Rule CARMA was aligned with Fischer's (1999) framework of public policy evaluation. Aligning both qualitative methods assisted in the assurance of credibility of this study.

CARMA and Fischer's framework for public policy evaluation contained four essential steps. Each step of CARMA; (Expectations, Implementation , Results and Conclusions /Recommendations) was aligned with each of the four steps of Fischer's framework for public policy evaluation (Verification, Validation, Vindication, and Social Choice). The alignment of CARMA with Fischer's interrelated discourses produced the following results as shown in Table 15.

Table 15

The Common Rule Policy aligned with CARMA and Fischer's Four Steps of Inquiry

1. Program Expectations Note-Taking	1. Verification Outcomes
Program initiator : Office of Human Research Protections (OHRP) Who is being served? Who is involved? Institutions, HRPPs, IRBs, Researchers are being served and are involved in the program. How are participants to be served? Notified by OHRP of noncompliance or deficiencies in the approved research project of actions and requests that ought to be taken to insure the safety and welfare of research subjects. What will be produced by participants in the program? Requests made by OHRP including revision of institutional human research policies, additional documentation in research protocols, additional education for HRPP staff, IRB, and researchers, additional time investment in the review and approval of research protocols.	Program: Common Rule policy with oversight by OHRP's of institutions having an FWA and conducts human subject research regulated by the Common Rule Does the program empirically fulfill its stated objectives? The Common Rule instructs institutional review boards to ensure that "risks to subjects are minimized" and "risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be reasonably expected to result (45 CFR 46.111(a)(1, 2). Does the empirical analysis uncover secondary or unanticipated effects that offset the program objectives? The regulations of the Common Rule may in some cases increase the risks of those participating in social science research projects (i.e., anthropological studies). The doctrine of signed informed consent may not be applicable to all disciplines within social science. Does the program fulfill the objectives more efficiently than alternative means available?

	Disciplines of social science are guided by their own professional ethics to protect human subjects. However, to qualify for Federal funding for research projects the institution must hold an assurance with OHRP and agree to abide by all regulations of the Common Rule. Therefore it has not been established if the program fulfill the objectives more efficiently than alternative means available seeing that alternative means would not elicit the funding needed to complete the research project. Additionally, most institutions have opted to follow the regulations of the Common Rule and regardless of funding source
2. Evident implementation Note-Taking	2. Situational Validation Objectives
Users/participants. The institution consisting of its HRPP, the IRB, social science researchers. Who are evident participants? Same How are the participants using the service? Required actions by OHRP to fulfill the requirements of the Common Rule result in corrective actions being taken by the institution. What will be produced by participants in the program? Implementation of additional policies and procedures may suggest that risks to subjects are	Is the program objective relevant to the problem situation? The objective of OHRP is to protect the rights, welfare, and wellbeing of subjects involved in research conducted or supported by the U.S. Department of Health and Human Services (DHHS) based on the regulatory provisions of the Common Rule. However, in order to accomplish their objectives OHRP regulators suggest that the institution, its HRPP, the IRB and social science researchers must define their research practices in the Common Rule. Are there circumstances in the situation that require an exception to be made to the objectives? There are no exceptions made to

minimized.	the objectives of the Common Rule in its protection of human research subjects. However, §46.110 espouse expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.
3. Results Note-Making	3. Societal Vindication Goals
Who are the participants? Same How are they working together? Expected vs. evident, alignment or departure? Federal agencies supporting social science research studies, institutions and their researchers work together to provide a culture of research compliance for the safety and welfare of research participants as indication in the determination letters. They appear to be aligned to provide ethical research practices articulated in the Common Rule. Modify or maintain? This practice should be maintained given that it appears from the determination letters that participants are working together to protect human research subjects. What was produced? Additional practices were implemented as detailed in the institution's revised policies and procedures for protecting human subjects. Amended policies and procedures included ethical	Systems discourse: Does the policy goal have instrumental or contributive value for the society as a whole. The Common Rule is comprised of a shared system of responsibility for protecting human research subjects as indicated in corrective action taken by institutions when notified of incidents of noncompliance or deficiencies. The shared system includes the institution, the institutional review board with its administrative support staff (HRPP) and researchers. The Common Rule lays the foundation for ethical research practices contributing to the safety and welfare of research subjects. The policy goal has a contributive value for the society as a whole. Does the policy goal result in unanticipated problems with important societal consequences? OHRP's publicly available information regarding research studies that have issues of noncompliance or deficiencies cause institutions to act swiftly in order to continue with the

research education and training for IRBs, administrative staff and researchers. Expected vs. evident, alignment or departure? These factors are in alignment. The goal of the OHRP program, institutions and their researchers is to protect the safety and welfare of research participants. Modify or maintain? Although the program appears to be working, it is doing so since there are no other alternatives. The institution, HRPPs, the IRB and social scientists have little options to alternative programs.	research, and mitigate bad publicity that can occur to the institution and ensure continued funding for the project. By acting swiftly institutions may only be able to provide the minimum remedy to address the determination letter when remediation in different ways could have additional impact on the system of social science research.
4. Recommendations Note-ReMaking	4. Social Choice Values
Researcher The Common Rule policy of regulating Social science research by the same standards as biomedical research appears on the surface to be working. However, facets of the biomedical model of human research protection cannot always be applicable to social science research. Informed consent is an essential element of the Common Rule. Informed consent can be approved by the IRB as signed informed consent or verbal consent, as in telephone interviews. Social scientists have concerns that the IRB may not utilize the flexibility of the Common Rule in the application of verbal consent,	Do the fundamental ideas (or ideology) that organizes the accepted social order provide a basis for a legitimate resolution of conflicting judgments? The Common Rule provides a medium for shared meanings of the ethical standards by which human research must be guided. The Common Rule effectively provides guidelines in which this can be accomplished. The Common Rule also provides flexibility in the usage of the ethical standards and guidelines applicable to human research. Social scientists contend that flexibility of the Common Rule's usage is not made readily available to them; thereby social scientists see a need for specific regulations to address social science research.

causing cumbersome and time consuming measures for the researcher and the research subjects. Modify or maintain program? The Common Rule should be modified to specifically address new areas of social science research.	

Analysis of Policy Evaluation

To answer Research Question 3: has the Common Rule achieved its intended purpose of protecting human research subjects participating in social science research, Fischer's (1995) four interrelated discourses consisting of: 1) program verification (outcomes), 2) contextual discourse or situational validation systems (objectives), 3) systems discourse or social vindication (goals), and 4) ideological discourse or social choice (values) was aligned with CARMA, Putney (2008). CARMA consists of four areas of evaluation, 1) program expectations, 2) evident implementation, 3) results, and 4) recommendations. The alignment was used to interpret efficiency and effectiveness of the Common Rule policy. Disciplines of social science are guided by their own professional ethics to protect human subjects. However, to qualify for Federal funding for research projects the institution must hold an assurance with OHRP and agree to abide by all regulations of the Common Rule. Therefore it has not been established if the program fulfill the objectives more efficiently than alternative means available seeing that alternative means would not elicit the funding

needed to complete the research project. Additionally, most institutions have opted to follow the regulations of the Common Rule regardless of funding source.

Alignment 1 consists of program expectations (note-taking) with program verification (outcomes). The Office of Human Research Protections (OHRP) oversees the Common Rule policy as operational human research subject policy and guidelines for Institutions, HRPPs, IRBs, and researchers. The Common Rule instructs institutional review boards to ensure that “risks to subjects are minimized” and “risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be reasonably expected to result” (45 CFR 46.111(a)(1, 2). Requests made by OHRP as a result of noncompliance or deficiency to the Common Rule are documented to the institution. Requests can include revision of institutional human research policies, additional documentation in research protocols, additional education for HRPP staff, IRB, and researchers.

Secondary or unanticipated effects that offset the program objectives include, as an example the doctrine of signed informed consent may not be applicable to all disciplines within social science and additional time investment in the review and approval of research protocols are produced by the participants. The regulations of the Common Rule may in some cases increase the risks of those participating in social science research projects (i.e., anthropological studies).

Alignment 2, evident implementation (note-taking) and situational validation (outcomes) suggests the institution consisting of its HRPP, the IRB,

and social science researchers fulfill required actions requested by OHRP consistent with the Common Rule. The objective of OHRP is to protect the rights, welfare, and wellbeing of subjects involved in research conducted or supported by the U.S. Department of Health and Human Services (DHHS) based on the regulatory provisions of the Common Rule. However, in order to accomplish their objectives OHRP regulators suggest that the institution, its HRPP, the IRB and social science researchers must define their research practices with the regulations of the Common Rule, not necessarily by social scientists professional code of ethics. There are no exceptions made to the objectives of the Common Rule in its protection of human research subjects. However, §46.110 espouse expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

Alignment 3 of results (note-making) and societal vindication (goals) suggest Federal agencies supporting social science research studies, institutions and their researchers work together to provide a culture of research compliance for the safety and welfare of research participants as indication in the determination letters appear to be aligned to provide ethical research practices articulated in the Common Rule. The Common Rule is comprised of a shared system of responsibility for protecting human research subjects as indicated in corrective action taken by institutions when notified of incidents of noncompliance or deficiencies. The shared system includes the institution, the institutional review board with its administrative support staff (HRPP) and researchers. The Common Rule lays the foundation for ethical research practices contributing to the safety

and welfare of research subjects. The policy goal has a contributive value for the society as a whole.

OHRP's publicly available information regarding research studies that have issues of noncompliance or deficiencies cause institutions to act swiftly in order to continue with the research, and mitigate bad publicity that can occur to the institution and that may cancel federal funding for the research project. By acting swiftly institutions may only be able to provide the minimum remedy to address the determination letter when remediation in different ways could have additional impact. Based on the analysis of alignment the program should be modified to address additional research areas that impact social science such as social media, qualitative research, anthropological research, and areas specific to social science.

Alignment 4 Recommendations (note-Taking) and social choice (values) The Common Rule policy of regulating Social science research by the same standards as biomedical research appears on the surface to be working. However, facets of the biomedical model of human research protection cannot always be applicable to social science research, especially the new areas of research. Do the fundamental ideas (or ideology) that organizes the accepted social order provide a basis for a legitimate resolution of conflicting judgments?

The Common Rule provides a medium for shared meanings of the ethical standards by which human research must be guided. The Common Rule effectively provides guidelines in which this can be accomplished but may lack the flexibility needed by social scientists to conduct their research in an effective

and efficient manner. Although the Common Rule provides some flexibility in the usage of the ethical standards and guidelines applicable to human research, social scientists contend that flexibility of the Common Rule's usage is not made readily available to them by the IRB, leaving many social scientists to see a need for specific regulations to address social science research (Gunsalus et al., 2006; Schrag, 2009).

The analysis of the alignment of CARMA with Fischer's Four Steps of Inquiry indicates that although the Common Rule is somewhat effective for social science research seeing that it is part of the only federal regulatory tool available, it is not efficient in its use by HRPPs, the IRB and importantly, social science researchers. The inefficiency presents itself in overregulation and mission creep (Gunsalus, 2006; Schrag, 2009). Following, Chapter 5 presents discussion of the findings, recommendations and chapter summaries of this study.

Chapter 5

Discussion, Recommendations and Chapter Summaries

Implications from the Results of Data

Social science researchers suggest the components of their research activity contained much less risk to human research subjects than that of biomedical research. Social scientists conducing human research are required to follow the policies of the Common Rule for federally funded research projects. Using the Common Rule they suggest, to review and approve their research, most of which is minimal and less than minimal risk to research subjects amounts to overregulation and mission creep. To better understand the impact of the Common Rule on social science research, implications from the data of three methods of inquiry in this qualitative study is discussed. Three methods of inquiry include: 1) content analysis of OHRP determination letters, 2) in-depth interviews of human research protection program administrators, and 3) policy evaluation of the Common Rule, Subpart A.

OHRP oversees human research conducted with federal funding. When research projects are found to be in noncompliance to or deficient in the regulations governing human research, OHRP provides a determination letter to the institution. The determination letter contains findings of deficiency or noncompliance based on the regulations of the Common Rule that regulates biomedical and social science research. In an attempt to understand the impact of regulating social science human research with biomedical regulations this study sought to answer the Research Question 1: what are the findings of

deficiencies and findings of noncompliance indicated in OHRP determination letters (DL) for social science research projects? The qualitative approach to content analysis of documents revealed that of the 763 letters 43 were found to reference what appeared to be social science research projects. The sample of 43 letters were further reviewed for OHRP reference to the Common Rule, Subpart A, §101-124. It was determined that deficiencies or noncompliance to the Common Rule was attributed overwhelmingly to IRBs and their support staff, but not specifically to social scientists' research projects.

The implication of the OHRP determination letter content analysis data suggests that participants of social science research activity reviewed by OHRP were not at risk of harm from the research activity. The data did however imply that in many cases the IRBs and their administrative staff did not handle procedural matters of the review and approval process correctly. Implications from the data suggest that additional education and training related to the Common Rule is necessary for the HRPP to develop better institutional human research protection policies and procedures.

Six human research protection program HRPP administrators were recruited for telephone interview for this study to answer the Research Question 2: What impact does the Common Rule have on social science research protocol review by human research protection programs? The role of the HRPP administrators interviewed suggested they held a leadership position in the HRPP, with years of leadership service in the role ranging from 6-23 years. Consistently administrators reported that there was a need for additional human

research compliance education for the IRB and researchers as well as the HRPP staff to keep abreast of new areas of social science research such as social media. New research areas specifically was an expressed concern since Common Rule does not directly address social media as a form of research. Interviewees also reported that there are "gaps" in the Common Rule which needs updating to address newer research areas. The lack of regulatory flexibility of the Common Rule was another consistent concern of administrators, as also was the IRB's lack of experience in qualitative research methods. The administrators also expressed concern that the Common Rule did not fully accommodate social science research practices as it did for biomedical researchers.

Implications from the interview data suggest that IRB's struggle in deliberation with the review and approval process for social science projects, often resulting in excessive documentation, revision requests of the researcher to conform to the standards of the Common Rule while creating time delays for the approval of the researcher's study. Lack of regulatory guidance for social science research can result in inconsistent review of research projects by the IRB during the deliberation process. Requiring additional documentation and revision to protocols when no clear regulatory procedure can be relied upon can contribute to overregulation and mission creep.

The fundamental notion of protecting human subjects whether in biomedical research or social behavioral research is consistent within the disciplines of human research as cited in the literature. However, the quandary of

how best to facilitate the highest levels of human research protection in the social science discipline remains vague. At the core of the issue is the Common Rule and its application to the review and approval process of social science research studies including what the literature suggests is minimal and less than minimal social science research.

The majority of cases of unethical scientific research have focused on biomedical investigations. As a result, federal regulations have provided guidelines to ensure ethical research standards. The Common Rule is the standard by which all federal human research is held, biomedical and social science research. Analysis of the data in this research study indicates the Common Rule does not have the flexibility of regulations to specifically regulate the facets of social science research. IRBs are left to participate in deliberations of social science research areas (with some being new areas of research such as social media) without adequate regulatory guidelines, albeit in an attempt to fit the social science research review and approval process within biomedical regulations of the Common Rule.

The question of, has the Common Rule achieved its intended purpose for social science research was analyzed via policy evaluation, aligning CARMA with Fischer's Four Steps of Inquiry for four interrelated discourses. The analysis indicates that the elements of biomedical research regulations do not translate to the tenets of social science research. Although, the Common Rule is somewhat effective for social science research it is not efficient in its use by researchers, IRBs and the HRPP to address the tenets of social science research.

The implications from the data of this study also suggest that the Common Rule does not fully accommodate social science research practices. Partial accommodation of social science research practices my lead to partial protections for social science research subjects. However, implications of the data also suggest that researchers, IRBs and HRPPs may find flexibility in the Common Rule when the applicability of the Common Rule regulations is fully understood in its application to social science research. As an example, waiver of documentation of informed consent (45 CFR 46.117) may not be used to the extent allowable when there is ambiguity regarding its use. The implication from the data of the need for on-going education is prevalent in the data.

Recommendation for Policy Consideration

Institutional review boards need better regulatory guidelines for the effective and efficient review and approve social science research. A separate regulatory policy applicable to the tenets of social science research should be developed for use by those conducting, reviewing and approving research projects. Definitions must be included in the policy that adopts the language of the disciplines of the social science profession. The policy development should be undertaken by social scientists, vetted in the Federal Register and made applicable to funded as well as unfunded and privately funded research projects. Consistency of the application of the regulations social science research projects should be a priority in the development of the document.

Researchers need to be assured that a policy in whole is applicable to their research discipline. Categories of research applicable to the regulation

should be delineated within the policy as to add consistency throughout the social science research enterprise. The social science research policy should be a document that can be revised and updated as new research areas are identified. The policy should make provisions for all categories of exempt research listed to be reviewed at the department of the primary investigatory. The recommendations should serve as a beginning to removing a one-size-fits-all approach to protecting human research subjects participating in social science research activity.

Recommendation for Further Research

This study has provided a foundation for additional qualitative inquiry to assess the impact of the Common Rule's biomedical standards being applicable to social science research from the lens of the OHRP determination letters, HRPPs and the Common Rule. Further research on IRB social science deliberation strategies applicable to exempt, expedited and full board strategies are needed to build on the foundation of the Common Rule's applicability to social science or the lack thereof. Continued research, from varied social science disciplines qualitatively investigating the impact of a one-size-fits-all regulatory approach to protecting human subjects is needed. This research focused on the basic policy for protection of human subjects, 45 CFR 46 Subpart A, additional Subparts including Subparts B - E should be invested to assess the applicability to social science research. Continued investigation of the current system of human research protections for social science research may warrant an overhaul to influence institutions, and politicians to revise institutional policies and

procedures and federal regulatory mandates that are effective and efficient for the varied disciplines of social science.

Chapter Summaries

Introduction - Chapter 1

In Chapter 1 of this study vegetable and meat experimentation with young Jewish prisoners as early as the sixth century is reported as human research. Prior to and including the 18th, the 19th, 20th centuries and beyond, revealed human experimentation that has resulted in disease and death to some research subjects. This chapter reveals that only since the 20th century has protections for human research subjects been a requirement for ethical human research. Although ethical requirements have been embodied in various professions, a human research protection has taken a longer time frame to be embraced by researchers. As a result of public outrage for unethical medical syphilis experiments, the Berlin Code of 1900 (see Appendix B) was developed. Needing a stronger code of ethical conduct for human subject research, and as a result of the conviction of 16 of the 23 physician defendants, of which seven of those indicted were sentenced to death, the Nuremberg Code was established. The Nuremberg Code established additional standards of ethical medical behavior for the post-World War II human rights era. Although German scientists were found to have committed atrocious research experiments on human research subjects, U.S. medical researchers still considered the research doctors as trusted and revered scientists.

The United States had committed its own unethical medical research for many years without much concern for the human research subjects in their studies. One of the most infamous studies was conducted by the U.S. Public Health Office, was the Tuskegee Syphilis Study, conducted from 1932 until 1972, in which men diagnosed with syphilis were left untreated to study the natural progression of the disease. The Willowbrook State Hospital Study is the most widely known unethical study on children. The study involved children diagnosed with mental retardation, living at the Willowbrook State Hospital as patients from 1956 to 1971. Researchers infected the otherwise healthy children with hepatitis to gauge the disease's natural history, prevention, and treatment.

While the 1947 Nuremberg Code was the world's reaction to Nazi war crimes, the 1974 National Research Act Public Law 93-348 (see Appendix J) was the response of the United States to the Tuskegee Syphilis Study. The National Research Act established the IRB process requiring formal peer review and approval of all DHHS research involving human subjects. The 1974 National Research Act legislation also created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (Commission). Additionally, out of the Commission's Report came what was called the Belmont Report, named for the Belmont Conference Center where the Commission met to draft the report. The Belmont Report summarizes the basic ethical principles identified by the Commission as respect for persons, beneficence and justice in its application to informed consent, assessment to risk and benefits and the selection of subjects. However, the Belmont Report did have its critics regarding

its applicability to nonmedical research. It was noted that although the Belmont Report "is a notable achievement in the exploration of the ethical challenges raised by medical research, but which serves as a poor guide to research in the social sciences and humanities …" Although medical research was the initial focus of human research protection intervention by the Federal government, the "new sciences," anthropology, sociology, economics, and political science also came under scrutiny.

Social scientists voiced concern and suggested that the kinds of limited harm social science research engenders is far less detrimental than that of biomedical research. They put forward that seemingly "over-zealous medical scientist" has brought an increased level of scrutiny to social science research evidenced by governmental regulations. Additionally, it was put forward that the fields of anthropology, journalism, oral history, ethnography and other social science fields already had well-established ethical research guidelines for their profession.

Social scientists suggests that while these efforts to provide increased protections for human research participants reflect a laudable goal, the regulations do not necessarily apply or translate well to all disciplines of research, particularly social science research. Social scientists further suggest that the current human subjects regulations are obstacles to their research studies and view the regulations as overregulation and mission creep because the patterns of noncompliance and litigation are not seen in social science research as in biomedical or clinical research.

Therefore, the research problem of this study suggests there is a need to test the critical assessment of the Common Rule in its application to the social science research. The research questions of, 1) what are the findings of deficiencies and findings of noncompliance indicated in OHRP determination letters (DL) for social science research projects, 2) what impact does the Common Rule have on social science research protocol review by human research protection programs, and 3) has the Common Rule achieved its intended purpose of protecting human research subjects participating in social science research.

Review of Literature – Chapter 2

Chapter 2 presents a review of the literature related to social scientists' concerns of what, in the literature is called, "over-regulation and mission creep". The Chapter documents the historical perspectives of unethical human experimentation as well as the regulatory standards put in place to protect human subjects. In addition, the Chapter discusses prior research related to researcher and institutional human research compliance while outlining the necessity to investigate the impact of social science research that is regulated by a medical model of human research protections.

Chapter 2 details social scientists concerns of the IRBs "blizzard of paperwork getting in the way of the fundamental mission to protect the dignity and well-being of human subjects". Discussed also in this chapter is institutional review board (IRB) workloads expanding beyond their ability to handle, due to focusing much more on procedures and documentation, unclear definitions,

leading to unclear responsibilities and efforts to comply with the standards of human research requirements even when research is not federally funded. Social science researchers characterize their concerns as overregulation and mission creep resulting from the application of a regulatory process created for medical research being applied to non-invasive and minimal risk social science research, that usually is unfunded or privately funded. The chapter details social science researchers increased concerns of the delay and even denial of their research projects.

Historical perspectives of unethical human experimentation is documented in the literature and presented in Chapter 2. Human experimentation in the eighteenth century included regular offers of free pardon to inmates to participate in human experiments. Experiments that included the inoculation of prisoners with infectious small pox in variolation experimentation popularized in England in 1721-1722 is discussed with the same procedures being used in America on slaves. Despite public concern of unethical research practices questionable research practices continued for many years. Victoria Nourse's work, *In Reckless Hands,* examines the case of *Skinner versus Oklahoma* (2008).[21] Nourse details a history of America's experiment with eugenics[22] resulting in thousands of incarcerated men and women having been sterilized. The ambiguity of American human research practices during the 1920s and 1930s to attain ethical research

[21] *Skinner v. State of Oklahoma,*1942, the United States Supreme Court ruling held that compulsory sterilization could not be imposed as a punishment for a crime.

[22] Eugenics is the study and practice of human selective breeding. The aim is to improve the species.

standards arising from the uncertainty of using experimental research methods is expounded.

Research regulation including the Berlin Code of 1900, one of the earliest documents to address the outrage of medical research and its unethical practices, the Nuremberg Code (1947) established as a set of ethical research principles, the Declaration of Helsinki (Declaration) of 1964, revised in 1975, developed by the World Medical Association as a set of ethical principles for the medical research community is discussed.

Chapter 2 discusses the historical factors of the Common Rule having been designed with a focus on biomedical research, with social science researchers questioning whether the Common Rule should apply to social science research. The Chapter presents details of The Office for Human Research Protections (OHRP) as an agency of the Department of Health and Human Services that provides leadership and oversight for the protection of the rights, welfare, and wellbeing of subjects involved in research conducted or supported by HHS agencies. OHRP documentation of the finding of deficiencies and non-compliance in the form of determination letters is discussed. The determination letters specifically outline what actions must be taken by the institution to return to a compliant state, rectify a deficiency, or resume research activity. The communication from OHRP to the institution is publicly available. Research scientists posit that public availability of determination letters force institutions to enact highly conservative in their IRB deliberative decisions.

Previous research relevant to this study is identified and discussed. The

literature of determination letters studies revealed three similar research studies, conducted by Borror et al. (2003), Burris and Welsh (2007) and Weil et al.(2010). In each case their quantitative research revealed the numbers of citations of noncompliance. The research projects did not delineate the numbers of biomedical or social science citations of noncompliance or deficiencies. The authors focused on the categories and numbers of noncompliance and deficiencies found in determination letters. The focus was not on the discipline in which those noncompliance and deficiencies were found.

The chapter expounds on the components of human research protection program consisting of the investigators, the Institutional Review Board (IRB) and its administrative staff as well as the institution. The HRPP of an institution oversees the responsible conduct of biomedical and social science research, protect the rights of research participants, reduce their risks, and increase the benefits of the research. The literature review details concerns of social scientist with their institution's HRPP administrative staff as they routinely encounter impediments to their research when navigating Institutional Review Board (IRB) review process to obtain approval for their research studies.

In 2001, the National Bioethics Advisory Commission (NBAC) complained that Institutional Review Boards (IRBs) were overwhelmed not only by high workloads generated by the amount of actions to process just one research project (see Figure 2) and limited resources but also by a regulatory system that often distracts from rather than focuses on key ethical issues.

Review of the literature in this chapter illustrated that investigators and

IRBs must be more effective and efficient in carrying out their responsibilities, in that way, improving research protections and increasing public trust in research. The literature indications of noncompliance resulting in risk of harm to those participating in social science research remains minuscule compared to OHRP findings of noncompliance in biomedical research activity. Although there has been much anecdotal comment in the literature on the topic of the application of a one-size-fits-all approach to regulating social science research with biomedical regulations, there seems to be no abundance of literature of the research to substantiate the assertions that research participants are better protected in social science research studies resulting from the biomedical regulatory model of the Common Rule. Therefore, leading to the assertion that the social science researcher may be over scrutinized for the harms that may result from their research based on the amount of risk in typical social science research, including surveys, interviews, oral history research and other types of minimal risk research. The chapter discusses the federal regulations in its application to social science research that continue to weigh heavily on institutions as they attempt to balance the need for protecting human subjects in research, the need to support their researchers' scholarly efforts and the need to minimize any untoward liability claims on the institution.

Methods - Chapter 3

Chapter Three discusses the methods used to address three research questions, 1) what are the findings of deficiencies and findings of noncompliance indicated in OHRP determination letters (DL) for social science research projects,

2) what impact does the Common Rule have on social science research protocol review by human research protection programs, and 3) has the Common Rule achieved its intended purpose of protecting human research subjects participating in social science research?

This study encompasses a three prong qualitative methodological approach to answer the research questions above respectively using, content analysis, in-depth interviews, and policy evaluation. To better understand the impact of the Common Rule on social science research activity three methods of inquiry are applied in this qualitative study. Content analysis of OHRP determination letters, in-depth interviews of human research protection program administrators and policy evaluation of the Common Rule is discussed as providing a better understanding of the impact of the Common Rule for social science research activity.

Relying on qualitative content analysis of documents to encompass a theoretical framework having an approach of empirical, methodological controlled analysis of texts within the context of communication and using systematic content analytical scientific methodology is used to study OHRP determination letters. The next phase of the study includes human research protection program (HRPP) administrators. In-depth interviewing is used as a technique to gather descriptive data in the subjects' own words for the purpose of developing insight as to how the HRPP Administrator interprets some portion of their professional world. In-depth interviews are used at this stage of the study as a strategy to capture the deep meaning of the administrators' "lived experience" of the HRPP

administrator in his or her own words. Six HRPP administrators were recruited for this phase of the study due to their high level of knowledge of the Common Rule, are advisers to risk-management and compliance officials for institutional research policies, and advise the institution's teaching professionals on the standards for those conducting human research.

The final method discussed in Chapter 3 is policy evaluation. This phase of the study is focused on the Fischer's Four Steps of Inquiry for four interrelated discourses of policy evaluation including: program verification; situational validation; societal level vindication, and social choice, aligned with Putney's Critical Analysis Research Method Application (CARMA). Policy analysis is used in this study to evaluate the Common Rule for better understanding of its effectiveness for the social sciences.

Findings of the Study Summary - Chapter 4

Chapter 4 details the findings of this study. To answer the Research Question 1: what are the findings of deficiencies and findings of noncompliance indicated in OHRP determination letters (DL) for social science research projects, a qualitative approach to content analysis of documents (DL) was utilized in this study. Seven hundred and sixty three (763) letters were reviewed resulting in two hundred and eighty-eight (288) letters identified as nonmedical institutions. The 288 DL project title was reviewed for wording that appeared to denote a social science research project. Forty-three (43) letters were found to have reference to what appeared to be social science research projects.

The sample of 43 letters were further reviewed for OHRP reference to the Common Rule, Subpart A, §101-124. Using CARMA to analyze the contents of the sample, Note-Taking (1) (Table 9) identified the expectations of the OHRP DL program. The findings suggest OHRP as the initiator of the DL program, with the institution including the IRB, and the HRPP administrative staff identified as the participants being served by the OHRP DL program.

The next stage (2) of Note-Taking in Table 10 found that the OHRP program provided guidance to HRPPs and researchers based on their findings to revise policies and procedures, and revise research protocol. The next stage (3) Note-Making, in Table 11, used to determine the expected response from the participants (the institution) versus the evident response related to the requests of OHRP in the DL found that in all cases program participants responded to the requests noted in the DL. The expected and evident response was congruent.

The last stage (4) of CARMA was Note-Remaking. Note-Remaking focused on assessing whether the program should be maintained or modified. The findings of the Note-Remaking stage suggests the OHRP determination letters program indicate that noncompliance and, or deficiencies to the Common Rule were attributed overwhelmingly to IRBs and their support staff, but not specifically to social scientists' research projects. The concerns of OHRP as documented in the DL of social science projects were overwhelmingly focused on inadequacies of the review and approval process completed by the IRB, and administrative errors of the HRPP. Therefore CARMA suggests that the vast majority of OHRP determination letters were effective in providing guidance and

oversight to HRPPs in general, the OHRP determination letter program did not reveal a profusion of non-compliance or deficiencies that could be specifically attributed to social science research projects.

To answer Research Question 2: what impact does the Common Rule have on social science research protocol review by human research protection programs six human research protection program administrators (HRPP administrators) were recruited and interviewed by phone for this study. Findings from the phone interviews included comments from HRPP Administrators suggesting the need for additional human research compliance education for the IRB and researchers, as well as for the HRPP staff to keep abreast of new research areas of social science research. Some administrators had already begun additional educational components to their programs but others needed to provide more education. The additional education was useful for HRPP staff and the IRB. The administrators reported that social media is a concern for HRPPs, in that the Common Rule does not directly address this form of research. Interviewees also reported that there are "gaps" in the Common Rule which needs updating to address newer research areas. The lack of flexibility of the Common Rule was recurring concern reported by administrators.

The finding in the chapter also included interviewees expressed concern that the Common Rule did not accommodate social science research practices and that IRB's struggle in deliberation with the review and approval process for social science projects, often resulting in excessive documentation, revision requests of the researcher to conform to the standards of the Common Rule

while creating time delays for the approval of the researcher's study. The lack of regulatory guidance for social science research projects was found to be a large concern for HRPPs providing regulatory guidance for IRB' in their deliberation processes and for the social science researchers needing approval for their research projects while protecting human research subjects and avoiding overregulation and mission creep.

To answer Research Question 3: has the Common Rule achieved its intended purpose of protecting human research subjects participating in social science research, Fischer's (1995) four interrelated discourses consisting of: 1) program verification (outcomes), 2) contextual discourse or situational validation systems (objectives), 3) systems discourse or social vindication (goals), and 4) ideological discourse or social choice (values) was aligned with the CARMA, Putney (2008). The alignment was used to interpret efficiency and effectiveness of the Common Rule policy. Disciplines of social science are guided by their own professional ethics to protect human subjects. However, to qualify for Federal funding for research projects the institution must hold an assurance with OHRP and agree to abide by all regulations of the Common Rule. The findings of the alignment of CARMA with Fischer's Four Steps of Inquiry indicates that although the Common Rule is somewhat effective for social science research seeing that it is part of the only federal regulatory tool available, it is not efficient in its use by HRPPs, the IRB and importantly, social science researchers. The inefficiency presents itself in overregulation and mission creep (Gunsalus, 2006; Schrag, 2009).

Discussion, Recommendations and Chapter Summaries - Chapter 5

Chapter 5 discussed the implications of the data that suggests that OHRP determination letters contained findings of deficiencies and noncompliance could be attributed to procedural factors of the IRB and HRPP administration. In most cases determination letters referenced policies that needed to be developed or revision of the institutions existing human research policies, revealing that social science research projects specifically, did not increase risks to human subjects. Telephone interviews of HRPP administrators revealed that excessive documentation, lack of flexibility in the deliberation process and may contribute to overregulation and mission creep.

Recommendations for policy consideration included the need for better regulatory guidelines for effective and efficient review and approval of social science research. The findings of the research suggests that a separate regulatory policy for social science should be considered and undertaken by researchers representing various fields within the social science discipline.

Recommendations for further research included investigating deliberation strategies applicable to exempt, expedited and full board protocol review. Strategies are needed to build on the foundation of the Common Rule's applicability to social science as well as the lack thereof. Chapter 5 included the introduction to this author's research study, history of unethical research practices, a review of the literature applicable to this research study, methods of research to answer the research questions, findings, and finally, discussion of the research.

Epilogue

Research ethics and its impact continue to be a contemporary issue reaching into the past to rectify wrongs created by what could be seen as a lack of Federal oversight. On October 5, 2010 the New York Times reported that from "1946 to 1948 American public health doctors infected nearly 700 Guatemalans" that were comprised of "prison inmates, mental patients and soldiers with venereal diseases in what was meant as an effort to test the effectiveness of penicillin." It is not clear if the penicillin was effective and used to treat those that had been infected by the American medical researchers. Again, financed with American tax dollars the NIH "even paid for syphilis-infected prostitutes to sleep with prisoners", since Guatemalan prisons allowed such visits.

When the prostitutes did not succeed in infecting the men, some prisoners had the bacteria poured onto scrapes made on their penises, faces or arms, and in some cases it was injected by spinal puncture." The Secretary Of State Hillary Clinton and HHS Secretary Kathleen Sebelius "offered an apology to the government and the survivors and descendants of those infected." The complete article is found at:

http://www.nytimes.com/2010/10/02/health/research/02infect.html?_r=2

A recent publicized example of the lack of flexibility in the application of the Common Rule is reported in *Inside Higher Ed* on March 25, 2011 as "IRB Overreach" of social science research:

> An associate professor of education has sued Brown University for barring her from using her own data because she paid her human research subjects different

> amounts of money based on their economic status. The suit raises questions about the role of IRBs in regulating privately funded research, the fairness of their process and the tensions that arise when such boards govern the work of social scientists.

Based on the researchers recommendation discussed above this situation could have been avoided to the satisfaction of the IRB and the researcher using appropriate institutional and regulatory policies. On-going education for IRBs and their support staff lends itself to better understanding of the flexibility available in the Common Rule and regulatory procedures of protecting human subjects. Although the immediate future does not suggest revamping of the Common Rule to separately address social science research projects, the current literature continues to promote that a one-size-fits-all regulatory oversight for social science research and biomedical research may not be as effective or as efficient as it could be otherwise. The article in its entirety can be found at: http://m.insidehighered.com/layout/set/popup/news/2011/03/18/brown_professor_sues_university_for_barring_her_from_using_her_research .

On July, 2011 the U.S. Department of Health and Human Services issued an Advance Notice of Proposed Rulemaking (ANPRM) that proposed changes to the Common Rule as of July 2011. DHHS suggests the proposal entitled: *Human Subject Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators* has been proposed for two reasons, (1) the human subject research landscape has changed dramatically since the early 1980s when the current regulations were first being formulated and (2) in light of that, there is a need to address effectiveness and

the efficiency of the regulations for human subject protections in the current research environment. Proposed changes can be found at: http://www.hhs.gov/ohrp/humansubjects/anprmqanda.html .

This research study also suggested in the analysis of determination letters, interviews with human research protection administrators and analysis of the evaluation of the Common Rule, the need for change to the federal regulations given the identical reasons as indicated above. The most recent article from *Inside Higher Ed* by Doug Lederman on August 3, 2011 further affirms the timeliness of this study. The article suggests that this is "the federal government's first major review of its so-called Common Rule governing the protection of human research subjects and has the potential to ease if not resolve many of the concerns of scholars." The article entitled "Updating the Common Rule" can be found at: http://www.insidehighered.com/news/2011/08/03/u_s_review_of_human_subjects_rules_could_ease_restrictions_on_researchers .

Appendix A

HUMAN EXPERIMENTS: A CHRONOLOGY OF HUMAN RESEARCH

by Vera Hassner Sharav

6th century B.C.: Meat and vegetable experiment on young Jewish prisoners in Book of Daniel.
5th century B.C.: "Primum non nocere" ("First do no harm"), medical ethics standard attributed to Hippocrates. This Oath became obligatory for physicians prior to practicing medicine in the 4th century AD
1st century B.C. Cleopatra devised an experiment to test the accuracy of the theory that it takes 40 days to fashion a male fetus fully and 80 days to fashion a female fetus. When her handmaids were sentenced to death under government order, Cleopatra had them impregnated and subjected them to subsequent operations to open their wombs at specific times of gestation.
[http://www.jlaw.com/Articles/NaziMedExNotes.html#1]
12th century: Rabbi and physician Maimonides' Prayer: "May I never see in the patient anything but a fellow creature in pain."
1796 Edward Jenner injects healthy eight-year-old James Phillips first with cowpox then three months later with smallpox and is hailed as discoverer of smallpox vaccine.
1845-1849: J. Marion Sims, "the father of gynecology" performed multiple experimental surgeries on enslaved African women without the benefit of anesthesia. After suffering unimaginable pain, many lost their lives to infection. One woman was made to endure 34 experimental operations for a prolapsed uterus.
http://www.coax.net/people/lwf/jm_sims.htm
1865: French physiologist Claude Bernard publishes "Introduction to the Study of Human Experimentation," advising: "Never perform an experiment which might be harmful to the patient even though highly advantageous to science or the health of others."
1896: Dr. Arthur Wentworth performed spinal taps on 29 children at Children's Hospital, Boston, to determine if the procedure was harmful. Dr. John Roberts of Philadelphia, noting the non-therapeutic indication, labeled Wentworth's procedures "human vivisection."
1897: Italian bacteriologist Sanarelli injects five subjects with bacillus searching for a causative agent for yellow fever.
1900: Walter Reed injects 22 Spanish immigrant workers in Cuba with the agent for yellow fever paying them $100 if they survive and $200 if they contract the disease.
1900: Berlin Code of Ethics. Royal Prussian Minister of Religion, Education, and Medical Affairs guaranteed that: "all medical interventions for other than diagnostic, healing, and immunization purposes, regardless of other legal or moral authorization are excluded under all circumstances if (1) the human subject is a minor or not competent due to other reasons; (2) the human subject has not given his unambiguous consent; (3) the consent is not preceded by a proper explanation of the possible negative consequences of the intervention."
http://www.geocities.com/artnscience/00berlincode.pdf
1906: Dr. Richard Strong, a professor of tropical medicine at Harvard, experiments with cholera on prisoners in the Philippines killing thirteen.

1913: Pennsylvania House of Representatives recorded that 146 children had been inoculated with syphilis, "through the courtesy of the various hospitals" and that 15 children in St. Vincent's House in Philadelphia had their eyes tested with tuberculin. Several of these children became permanently blind. The experimenters were not punished.

1915: A doctor in Mississippi, working for the U.S. Public Health Office produces Pellagra in twelve Mississippi inmates in an attempt to discover a cure for the disease

1919-1922: Testicular transplant experiments on five hundred prisoners at San Quentin.

1927: Carrie Buck of Charlottesville is legally sterilized against her will at the Virginia Colony Home for the Mentally Infirm. Carrie Buck was the mentally normal daughter of a mentally retarded mother, but under the Virginia law, she was declared potentially capable of having a "less than normal child." By the 1930s, seventeen states in the U.S. have laws permitting forced sterilization

The settlement of Poe v. Lynchburg Training School and Hospital (same institution, different name) in 1981 brought to an end the Virginia law. It is estimated that as many as 10,000 perfectly normal women were forcibly sterilized for "legal" reasons including alcoholism, prostitution, and criminal behavior in general.

1931: Lubeck, Germany, 75 children die in from pediatrician's experiment with tuberculosis vaccine.

1931: Germany adopts "Regulation on New Therapy and Experimentation" requiring all human experiments to be preceded by animal experiments. This law remained in effect during the Nazi regime.

1931: Dr. Cornelius Rhoads, a pathologist, conducted a cancer experiment in Puerto Rico under the auspices of the Rockefeller Institute for Medical Investigations. Dr. Rhoads has been accused of purposely infecting his Puerto Rican subjects with cancer cells. Thirteen of the subjects died. A Puerto Rican physician uncovered the experiment an investigation covered-up the facts. Despite Rhoads' hand written statements that the Puerto Rican population should be eradicated, Rhoads went on to establish U.S. Army Biological Warfare facilities in Maryland, Utah, and Panama, and was later named to the U.S. Atomic Energy Commission. Rhoads was also responsible for the radiation experiments on prisoners, hospital patients, and soldiers. The American Association for Cancer Research honored him by naming its exemplary scientist award the Cornelius Rhoads Award.

1932-1972: U.S. Public Health Service study in Tuskegee, Alabama of more than 400 black sharecroppers observed for the natural course of untreated syphilis.

1932: Japanese troops invade Manchuria. Dr. Shiro Ishii, a prominent physician and army officer begins preliminary germ warfare experiments.

1936: Japan's Wartime Human Bio warfare Experimentation Program.

1938: Japan establishes Unit 731 in Pingfan, 25 km. from Harbin. Unit 731, a biological-warfare unit disguised as a water-purification unit, is formed outside the city of Harbin.

1939: Third Reich orders births of all twins be registered with Public Health Offices for purpose of genetic research.

1939: Twenty-two children living at the Iowa Soldiers' Orphans' Home in Davenport were the subjects of the "monster" experiment that used psychological pressure to induce children who spoke normally to stutter. It was designed by one of the nation's most prominent speech pathologists, Dr. Wendell Johnson, to test his theory on the cause of stuttering.

1940: Poisonous gas experiments at Unit 731. One experiment conducted September 7-10, 1940, on 16 Chinese prisoners who were exposed to mustard gas in a simulated battle situation.
1940-1941: Unit 731 used aircraft to spread cotton and rice husks contaminated with the black plague at Changde and Ningbo, in central China. About 100 people died from the black plague in Ningbo as a result.
1940s: In a crash program to develop new drugs to fight Malaria during World War II, doctors in the Chicago area infected nearly 400 prisoners with the disease. Although the Chicago inmates were given general information that they were helping with the war effort, they were not informed about the nature of the experiment. Nazi doctors on trial at Nuremberg cited the Chicago studies as precedents to defend their own research aimed at aiding the German war effort.
1941: Sterilization experiments at Auschwitz.
1941-1945: Typhus experiments at Buchenwald and Natzweiler concentration camps.
1941: Dr. William c. Black inoculated a twelve month old baby with herpes. He was criticized by Francis Payton Rous, editor of the Journal of Experimental Medicine, who called it "an abuse of power, an infringement of the rights of an individual, and not excusable because the illness which followed had implications for science." Dr. Rous rejected outright the fact that the child had been "offered as a volunteer."
1942 –1945: Unit 731. Ishii begins "field tests" of germ warfare and vivisection experiments on thousands of Chinese soldiers and civilians. Chinese people who rebelled against the Japanese occupation were arrested and sent to Pingfan where they became human guinea pigs; there is evidence that some Russian prisoners were also victims of medical atrocities.
"I cut him open from the chest to the stomach and he screamed terribly and his face was all twisted in agony. He made this unimaginable sound, he was screaming so horribly. But then finally he stopped. This was all in a day's work for the surgeons, but it really left an impression on me because it was my first time." NYT
These prisoners were called 'maruta' (literally 'logs') by the Japanese. After succumbing to induced diseases - including bubonic plague, cholera, anthrax - the prisoners were usually dissected while still alive, their bodies then cremated within the compound. Tens of thousands died. The atrocities were committed by some of Japan's most distinguished doctors recruited by Dr. Ishii.
1942: High altitude or low pressure experiments at Dachau concentration camp.
1942: Harvard biochemist Edward Cohn injects sixty-four Massachusetts prisoners with beef blood in U.S. Navy-sponsored experiment.
1942: Japanese sprayed cholera, typhoid, plague, and dysentery pathogens in the Jinhua area of Zhejian province (China). A large number of Japanese soldiers also fell victim to the sprayed diseases.
1942-1943: Bone regeneration and transplantation experiments on female prisoners at Ravensbrueck concentration camp.
1942-1943: Freezing experiments at Dachau concentration camp.
1943 Refrigeration experiment conducted on sixteen mentally disabled patients who were placed in refrigerated cabinets at 30 degree Farenheit, for 120 hours, at University of Cincinnati Hospital., "to study the effect of frigid temperature on mental disorders."
1942-1943: Coagulation experiments on Catholic priests at Dachau concentration camp.

1942-1944: U.S. Chemical Warfare Service conducts mustard gas experiments on thousands of servicemen.
1942-1945: Malaria experiments at Dachau concentration camp on more than twelve hundred prisoners.
1943: Epidemic jaundice experiments at Natzweiler concentration camp.
1943-1944: Phosphorus burn experiments at Buchenwald concentration camp.
1944: Manhattan Project injection of 4.7 micrograms of plutonium into soldiers at Oak Ridge.
1944: Seawater experiment on sixty Gypsies who were given only saltwater to drink at Dachau concentration camp.
1944-1946: University of Chicago Medical School professor Dr. Alf Alving conducts malaria experiments on more than 400 Illinois prisoners.
1945: Manhattan Project injection of plutonium into three patients at Billings Hospital at University of Chicago.
1945: Malaria experiment on 800 prisoners in Atlanta.
1946: Opening of Nuremberg Doctors Trial by U.S. Military Tribunal.
1945: Japanese troops blow up the headquarters of Unit 731 in final days of Pacific war. Ishii orders 150 remaining "logs" (i.e., human beings) killed to cover up their experimentation. Gen. Douglas MacArthur is named commander of the Allied powers in Japan.
1946: U.S. secret deal with Ishii and Unit 731 leaders cover up of germ warfare data based on human experimentation in exchange for immunity from war-crimes prosecution.
1946-1953: Atomic Energy Commission sponsored study conducted at the Fernald school in Massachusetts. Residents were fed Quaker Oats breakfast cereal containing radioactive tracers.
1946: Patients in VA hospitals are used as guinea pigs for medical experiments. In order to allay suspicions, the order is given to change the word "experiments" to "investigations" or "observations" whenever reporting a medical study performed in one of the nation's veteran's hospitals.
1947: Colonel E.E. Kirkpatrick of the U.S. Atomic Energy Comission issues a secret document (Document 07075001, January 8, 1947) stating that the agency will begin administering intravenous doses of radioactive substances to human subjects.
1947: The CIA begins its study of LSD as a potential weapon for use by American intelligence. Human subjects (both civilian and military) are used with and without their knowledge.
1947: Judgment at Nuremberg Doctors Trial sets forth "Permissible Medical Experiments" – i.e., the Nuremberg Code, which begins: "The voluntary consent of the human subject is absolutely essential."
1949: Intentional release of radiodine 131 and xenon 133 over Hanford Washington in Atomic Energy Commission field study called "Green Run."
1949: Soviet Union's war crimes trial of Dr. Ishii's associates.
1949-1953: Atomic Energy Commission studies of mentally disabled school children fed radioactive isotopes at Fernald and Wrentham schools.
1940s-1950s: "psychic driving" and "mental departterning" experiments conducted by Dr. Ewen Cameron, depriving patients of sleep, using massive ECT combined with psychoactive drugs such as, LSD. After his "treatments" patients were unable to function. In the 1950's Dr.Cameron's experiments were sponsored by the CIA.

1950: Dr. Joseph Stokes of the University of Pennsylvania infects 200 women prisoners with viral hepatitis.
1950: U.S. Army secretly used a Navy ship outside the Golden Gate to spray supposedly harmless bacteria over San Francisco and its outskirts. Eleven people were sickened by the germs, and one of them died.
1951-1960: University of Pennsylvania under contract with U.S. Army conducts psychopharmacological experiments on hundreds of Pennsylvania prisoners.
1952-1974: University of Pennsylvania dermatologist Dr. Albert Kligman conducts skin product experiments by the hundreds at Holmesburg Prison; "All I saw before me," he has said about his first visit to the prison, "were acres of skin."
1952: Henry Blauer injected with a fatal dose of mescaline at New York State Psychiatric Institute of Columbia University. U.S. Department of Defense, the sponsor, conspired to conceal evidence for 23 years.
I
1953 Newborn Daniel Burton rendered blind at Brooklyn Doctor's Hospital due to high oxygen study on RLF.
1953-1957: Oak Ridge-sponsored injection of uranium into eleven patients at Massachusetts General Hospital in Boston.
1953-1960: CIA brainwashing experiments with LSD at eighty institutions on hundreds of subjects in a project code named "MK-ULTRA."
1953-1970: U.S. Army experiments with LSD on soldiers at Fort Detrick, Md.
1954-1974: U.S. Army study of 2,300 Seventh-Day Adventist soldiers in 157 experiments code named "Operation Whitecoat."
1950s –1972: Mentally disabled children at Willowbrook School (NY) were deliberately infected with hepatitis in an attempt to find a vaccine. Participation in the study was a condition for admission to institution.
1956: Dr. Albert Sabin tests experimental polio vaccine on 133 prisoners in Ohio.
1958-1962: Spread of radioactive materials over Inupiat land in Point Hope, Alaska in Atomic Energy Commission field study code named "Project Chariot."
1962: Thalidomide withdrawn from the market after thousands of birth deformities blamed in part on misleading results of animal studies; the FDA thereafter requires three phases of human clinical trials before a drug can be approved for the market.
1962 to 1966, a total of 33 pharmaceutical companies tested 153 experimental drugs at Holmesburg prison (PA) alone.
1962-1980 Pharmaceutical companies conduct phase I safety testing of drugs almost exclusively on prisoners for small cash payments.
1962: Injection of live cancer cells into 22 elderly patients at Jewish Chronic Disease Hospital in Brooklyn. Administration covered up, NYS licensing board placed the principal investigator on probation for one year. Two years later, American Cancer Society elected him Vice President.
1962: Stanley Milgram conducts obedience research at Yale University.
1963: NIH supported researcher transplants chimpanzee kidney into human in failed experiment.
1963-1973: Dr. Carl Heller, a leading endocrinologist, conducts testicular irradiation experiments on prisoners in Oregon and Washington giving them $5 a month and $100 when they receive a vasectomy at the end of the trial.

1964: World Medical Association adopts Helsinki Declaration, asserting "The interests of science and society should never take precedence over the well being of the subject."

1965-1966: University of Pennsylvania under contract with Dow Chemical conducts dioxin experiments on prisoners at Holmesburg.

1966: Henry Beecher's article "Ethics and Clinical Research" in New England Journal of Medicine.

1966: U.S. Army introduces bacillus globigii into New York subway tunnels in field study.

1966: NIH Office for Protection of Research Subjects ("OPRR") created and issues Policies for the Protection of Human Subjects calling for establishment of independent review bodies later known as Institutional Review Boards.

1967: British physician M.H. Pappworth publishes "Human Guinea Pigs," advising "No doctor has the right to choose martyrs for science or for the general good."

1969: Judge Sam Steinfield's eloquent dissent in Strunk v. Strunk, 445 S.W.2d 145, the first judicial suggestion that the Nuremberg Code should influence American jurisprudence.

1969. Milledgeville Georgia, investigational drugs tested on mentally disabled children. No institutional approval.

1969: San Antonio Contraceptive Study conducted on 70 poor Mexican-American women. Half received oral contraceptives the other placebo. No informed consent.

1973 Ad Hoc Advisory Panel issues Final Report of Tuskegee Syphilis Study, concluding "Society can no longer afford to leave the balancing of individual rights against scientific progress to the scientific community."

1974: National Research Act establishes National Commission for the Protection of Human subjects and requires Public Health Service to promulgate regulations for the protection of human subjects.

1975: The Department of Health, Education and Welfare (DHEW) raised NIH's 1966 Policies for the Protection of Human subjects to regulatory status. Title 45 of the Code of Federal Regulations, known as "The Common Rule," requires the appointment and utilization of institutional review boards (IRBs).

1976: National Urban League holds National Conference on Human Experimentation, announcing "We don't want to kill science but we don't want science to kill, mangle and abuse us."

1978: Experimental Hepatitis B vaccine trials, conducted by the CDC, begin in New York, Los Angeles and San Francisco. Ads for research subjects specifically ask for promiscuous homosexual men.

1979: National Commission issues Belmont Report setting forth three basic ethical principles: respect for persons, beneficence, and justice.

1980: The FDA promulgates 21 CFR 50.44 prohibiting use of prisoners as subjects in clinical trials shifting phase I testing by pharmaceutical companies to non-prison population.

1981: Leonard Whitlock suffers permanent brain damage after deep diving experiment at Duke University.

1986: Congressional subcommittee holds one-day hearing in Washington, called by Rep. Pat Williams of Montana, aimed at determining whether U.S. prisoners of war in Manchuria were victims of germ-warfare experimentation. Hearing is inconclusive.

1981-1996: Protocol 126 at Fred Hutchinson Cancer Center in Seattle.

1987: Supreme Court decision in United States v. Stanley, 483 U.S. 669, holding soldier given LSD without his consent could not sue U.S. Army for damages.

1987:" L-dopa challenge and relapse" experiment conducted on 28 U.S. veterans who were subjected to psychotic relapse for study purposes at the Bronx VA.

1990: The FDA grants Department of Defense waiver of Nuremberg Code for use of unapproved drugs and vaccines in Desert Shield.

1991: World Health Organization announces CIOMS Guidelines which set forth four ethical principles: respect for persons, beneficence, nonmaleficence and justice.

1991: Tony LaMadrid commits suicide after participating in study on relapse of schizophrenics withdrawn from medication at UCLA.

1993: Kathryn Hamilton dies 44 days after participating in breast cancer experiment at Fred Hutchinson Cancer Center in Seattle.

1994. The Albuquerque Tribune publicizes 1940s experiments involving plutonium injection of human research subjects and secret radiation experiments. Indigent patients and mentally retarded children were deceived about the nature of their treatment.

1994. President Clinton appoints the Advisory Commission on Human Radiation Experiments (ACHRE) The ACHRE Report http://tis.eh.doe.gov/ohre/roadmap/achre/index.html

1995. U.S. Department of Energy (DOE) published Human Radiation Experiments, listing 150 plus an additional 275 radiation experiments conducted by DOE and the Atomic Energy Commission, during the 1940s-1970s. http://tis.eh.doe.gov/ohre/roadmap/experiments/0491doca.html#0491_List

1995: 19-year-old University of Rochester student Nicole Wan dies after being paid $150 to participate in MIT-sponsored experiment to test airborne pollutant chemicals.

1995. President Clinton appoints the National Bioethics Advisory Commission.

1995: NYS Supreme Court rules (TD v NYS Office of Mental Health) against the state's policy of conducting nontherapeutic experiments on mentally incapacitated persons - including children - without informed consent. Justice Edward Greenfield ruled that parents have no authority to volunteer their children: "Parents may be free to make martyrs of themselves, but it does not follow that they may make martyrs of their children."

1995: Thirty-four healthy, previously non-aggressive New York City minority children, boys aged 6 to 11 years old, were exposed to fenfluramine in a nontherapeutic experiment at the New York State Psychiatric Institute. The children were exposed to this neurotoxic drug to record their neurochemical response in an effort to prove a speculative theory linking aggression to a biological marker.

1996. Cleveland Plain Dealer investigative report series, 'Drug Trials: Do People Know the Truth About Experiments,' December 15 to 18, 1996. The Plain-Dealer found: of the "4,154 FDA inspections of researchers testing new drugs on people [since 1977] . . . more than half the researchers were cited by FDA inspectors for failing to clearly disclose the experimental nature of their work."

1996: Yale University researchers publish findings of experiment that subjected 18 stable schizophrenia patients to psychotic relapse in an amphetamine provocation experiment at West Haven VA.

1997. President Clinton issues a formal apology to the subjects of the Tuskegee syphilis experiments. NBAC continues investigation into genetics, consent, privacy, and research on persons with mental disorders.

1997. Researchers at the University of Cincinnati publish findings of experiment attempting to create a "psychosis model" on human beings at the Cincinnati VA. Sixteen patients, experiencing a first episode

schizophrenia, were subjected to repeated provocation with amphetamine. The stated purpose was to produce "behavioral sensitization. This process serves as a model for the development of psychosis, but has been little studied in humans. Symptoms, such as severity of psychosis and eye-blink rates, were measured hourly for 5 hours."

1997. U.S. government sponsored placebo-controlled experiment withholds treatment from HIV infected, pregnant African women. NY Times, Sept. 18.

1997. Victims of unethical research at major U.S. medical centers - including the NIMH - testify before the National Bioethics Advisory Commission, Sept. 18.

1997. FDA Modernization Act gives pharmaceutical companies a huge financial incentive - a 6 month patent exclusivity extension - if they conduct drug tests on children. The incentive can yield $900 million.

1998. National Bioethics Advisory Commission (NBAC) Report. Research Involving Subjects with Mental Disorders That May Affect Decisionmaking Capacity. November 12, 1998
http://bioethics.georgetown.edu/nbac/capacity/TOC.htm

1998: The Japanese government has never formally apologized for Unit 731's activities, and did not even admit to its existence until August 1998, when the Supreme Court ruled that the existence of the unit was accepted in academic circles.

1998. Complaint filed with OPRR about experiments that exposed non-violent children in New York City to fenfluramine to find a predisposition to violence.

1998: Boston Globe (four part) series, "Doing Harm: Research on the Mentally Ill" shed light on the mistreatment and exploitation of schizophrenia patients who have been subjected to relapse producing procedures in unethical experiments.

1999: Nine month-old Gage Stevens dies at Children's Hospital in Pittsburgh during participation in Propulsid clinical trial for infant acid reflux.

1999: 18-year-old Jesse Gelsinger dies after being injected with 37 trillion particles of adenovirus in gene therapy experiment at University of Pennsylvania.

1999: Administrator of National Institute of Mental Health suspends 29 clinical trials that failed to meet either ethical or scientific standards.

2000: University of Oklahoma melanoma trial halted for failure to follow government regulations and protocol.

2000: OPRR becomes Office of Human Research Protection ("OHRP") and made part of the Department of Health and Human Services.

2000: President Clinton implement the Energy Employees Occupational Illness Compensation Act of 2000, which authorized compensation for thousands of Department of Energy workers who sacrificed their health in building the nation's nuclear defenses.

2000: The Washington Post (6 part) series, "Body Hunters" exposes unethical exploitation in experiments conducted by U.S. investigators in underdeveloped countries. Part 4 dealt with U.S. government funded, genetic experiments conducted by Harvard University in rural China.
http://www.washingtonpost.com/wp-dyn/articles/A26797-2000Dec19.html

2001: A biotech company in Pennsylvania asks the FDA for permission to conduct placebo trials on infants in Latin America born with serious lung disease though such tests would be illegal in U.S.

2001: Ellen Roche, a healthy 27-year old volunteer, dies in challenge study at Johns Hopkins University in Baltimore, Maryland.

2001: April 4, Elaine Holden-Able, a healthy retired nurse, consumed a glass of orange juice that had been mixed with a dietary supplement for the sake of medical research. This Case Western University Alzheimer's experiment, financed by the tobacco industry, wound up killing her in what was called a "tragic human error." Federal Office of Human Research Protections did not interview hospital staff, mostly accepted hospital's internal report, imposed no penalty, and closed the case and did not mention the death in its letter of determination. http://ohrp.osophs.dhhs.gov/detrm_letrs/nov01f.pdf

2001: Maryland Court of Appeals renders a landmark decision affirming "best interest of the individual child" as a standard for medical research involving children. The Court unequivocally prohibited nontherapeutic experimentation on children. (Higgins and Grimes v. Kennedy Krieger Institute).The case involved exposure of babies and small children to lead poisoning in EPA funded experiment. (http://www.courts.state.md.us/opinions/coa/2001/128a00.pdf)

Appendix B

Berlin Code Of 1900

The Royal Prussian Minister of Religious, Educational and Medical Affairs

Directive to all medical directors of university hospitals, polyclinics, and other hospitals

I. I advise the medical directors of university hospitals, polyclinics, and all other hospitals that all medical interventions for other than diagnostic, healing, and immunization purposes, regardless of other legal or moral authorization, are excluded under all circumstances, if

(1) the human subject is a minor or not competent due to other reasons;

(2) the human subject has not given his unambiguous consent;

(3) the consent is not preceded by a proper explanation of the possible negative consequences of the intervention.

II. At the same time I determine that

(1) interventions of this kind are to be only performed by the medical director himself or with his special authorization;

(2) in all cases of these interventions the fulfillment of the requirements of I (1-3) and II (1), as well as all further circumstances of the case, are documented in the medical record.

III. The existing instructions about medical interventions for diagnostic, healing, and immunization purposes are not affected by these instructions.

Berlin, 29 December 1900
The Minister for Religious ec. Affairs
Studt

Appendix C

High-Altitude Experiments

To investigate the limits of human endurance and existence at extremely high altitudes the victims were placed in the low-pressure chamber and thereafter the simulated altitude therein was raised. Many victims died as a result of these experiments and others suffered grave injury, torture, and ill-treatment.

Source: United States Holocaust Memorial Museum, Washington, D.C.:

http//www.ushmm.org

Appendix D

Incendiary Bomb Experiments:

To test the effect of various pharmaceutical preparations on phosphorous burns were inflicted on the victims with phosphorous matter taken from incendiary bombs, and caused severe pain, suffering, and serious bodily injury.

Source: United States Holocaust Memorial Museum, Washington, D.C.:

http//www.ushmm.org

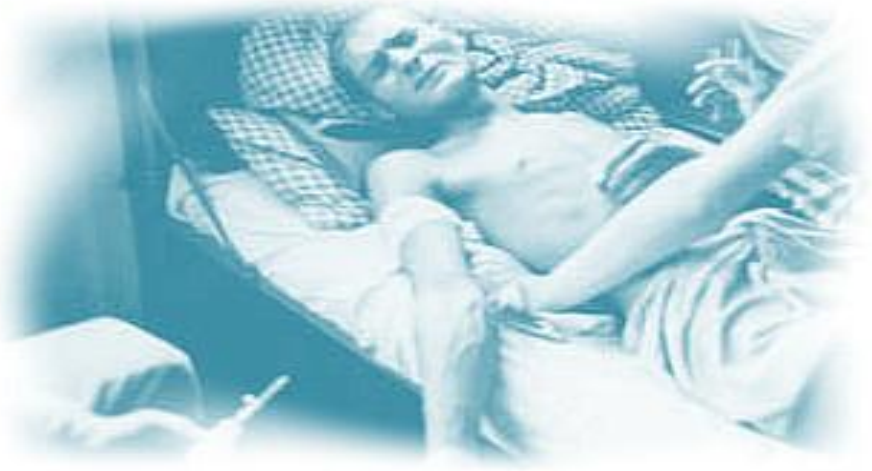
Appendix E

Freezing Experiments

To investigate the most effective means of treating persons who had been severely chilled or frozen the victims were forced to remain in a tank of ice water for up to 3 hours. Extreme rigor developed in a short time. Numerous victims died in the course of these experiments. After the survivors were severely chilled, re-warming was attempted by various means. In another series of experiments, the victims were kept naked outdoors for many hours at temperatures below freezing. The victims screamed with pain as their bodies froze.

Source: United States Holocaust Memorial Museum, Washington, D.C.: http//www.ushmm.org

Appendix F



Sea-water Experiments

To study various methods of making sea water drinkable the victims were deprived of all food and given only chemically processed sea water. Such experiments caused great pain and suffering and resulted in serious bodily injury to the victims.

Source: United States Holocaust Memorial Museum, Washington, D.C.: http//www.ushmm.org

Appendix G

Malaria Experiments:

To investigate immunization for and treatment of malaria the victims were infected by mosquitoes or by injections of extracts of the mucous glands of mosquitoes. After having contracted malaria the victims were treated with various drugs to test their relative efficacy. Over 1,000 victims were used in these experiments. Many died and others suffered severe pain and permanent disability.

Source: United States Holocaust Memorial Museum, Washington, D.C.: http//www.ushmm.org

Appendix H

THE NUREMBERG CODE (1947)

BRITISH MEDICAL JOURNAL NO 7070 VOLUME 313: P 1448,

7 December 1996.

Introduction

The judgment by the war crimes tribunal at Nuremberg laid down 10 standards to which physicians must conform when carrying out experiments on human subjects in a new code that is now accepted worldwide.
This judgment established a new standard of ethical medical behavior for the post World War II human rights era. Amongst other requirements, this document enunciates the requirement of voluntary informed consent of the human subject. The principle of voluntary informed consent protects the right of the individual to control his own body.

This code also recognizes that the risk must be weighed against the expected benefit, and that unnecessary pain and suffering must be avoided.
This code recognizes that doctors should avoid actions that injure human patients.

The principles established by this code for medical practice now have been extended into general codes of medical ethics.

Permissible Medical Experiments

The great weight of the evidence before us to effect that certain types of medical experiments on human beings, when kept within reasonably well-defined bounds, conform to the ethics of the medical profession generally. The protagonists of the practice of human experimentation justify their views on the basis that such experiments yield results for the good of society that are unprocurable by other methods or means of study. All agree, however, that certain basic principles must be observed in order to satisfy moral, ethical and legal concepts:

1. The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent, should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion, and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him

the nature, duration, and purpose of the experiment, the method and means by which it is to be conducted, all inconveniences and hazards reasonably to be expected, and the effects upon his health or person which may possibly come from his participation in the experiment.

The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs, or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.
3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results justify the performance of the experiment.
4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur, except, perhaps, in those experiments where the experimental physicians also serve as subjects.
6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability or death.
8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.
10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

Appendix I

DECLARATION OF HELSINKI (1964)

[CIRP Note: Ethical research on human subjects into or about the effects of circumcision must be conducted under the provisions of this declaration and those of the *Nuremberg Code*.]
Recommendations guiding physicians in biomedical research involving human subjects.
Adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964, amended by the 29th World Medical Assembly, Tokyo, Japan, October 1975, and the 35th World Medical Assembly, Venice, Italy, October 1983.

Introduction
It is the mission of the physician to safeguard the health of the people. His or her knowledge and conscience are dedicated to the fulfillment of this mission.
The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration "and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient. "

The purpose of biomedical research involving human subjects must be to improve diagnostic, therapeutic and prophylactic procedures and the understanding of the audiology and pathogenesis of disease.
In current medical practice most diagnostic, therapeutic or prophylactic procedures involve hazards. This applies especially to biomedical research.
Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects. In the field of biomedical research a fundamental distinction must be recognized between medical research in which the aim is essentially diagnostic or therapeutic for a patient, and medical research the essential object of which is purely scientific and without implying direct diagnostic or therapeutic value to the person subjected to the research.
Special caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, the World Medical Association has prepared the following recommendations as a guide to every physician in biomedical research involving human subjects. They should be kept under review in the future. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Physicians are not relieved from criminal, civil and ethical responsibilities under the law of their own countries.

I. Basic Principles

1. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.
2. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted to a specially appointed independent committee for consideration, comment and guidance.
3. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.
4. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

5. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interests of science and society.
6. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
7. Physicians should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Physicians should cease any investigation if the hazards are found to outweigh the potential benefits.
8. In publication of the results of his or her research, the physician is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.
9. In any research on human beings, each potential subject mustbe adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw visor her consent to participation at any time. The physician should then obtain the subject's freely given informed consent, preferably inheriting.
10. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a physician who isn't engaged in the investigation and who is completely independent of this official relationship.
11. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation. Whenever the minor child is in fact able to give a consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.
12. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present declaration are complied with.

II. Medical Research Combined with Professional Care (Clinical Research)

1. In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure, if in his or her judgment it offers hope of saving life, re-establishing health or alleviating suffering.
2. The potential benefits, hazards and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.
3. In any medical study, every patient- including those of a control group, if any- should be assured of the best proven diagnostic and therapeutic method.
4. The refusal of the patient to participate in a study must never interfere with the physician-patient relationship.
5. If the physician considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee (1, 2).
6. The physician can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

III. Non-Therapeutic Biomedical Research Involving Human Subjects (Non-Clinical Biomedical Research)

1. In the purely scientific application of medical research carried out on a human being, it is the duty of the physician to remain the protector of the life and health of that person on whom biomedical research is being carried out.
2. The subjects should be volunteers- either healthy persons or patients for whom the experimental design is not related to the patient's illness.
3. The investigator or the investigating team should discontinue the research if in his/her or their judgment it may, if continued, be harmful to the individual.
4. In research on man, the interest of science and society should never take precedence over considerations related to the well-being of the subject.

Appendix J

NATIONAL RESEARCH ACT

PUBLIC LAW 93-348-JULY 12, 1974 - Public Law 93-348 July 12.1974

JULY 12, 1974 - [H. R. 7724]

AN ACT

To amend the Public Health Service Act to establish a program of National Research Service Awards to assure the continued excellence of biomedical and behavioral research and to provide for the protection of human subjects involved in biomedical and behavioral research and for other purposes.

Be it enacted by the Senate and House of Representatives of the Re- United States of America in Congress assembled, search Act. 42 usc 2891-1 SECTION 1. This Act may be cited as the "National Research Act". note. National Re- TITLE I-BIOMEDICAL AND BEHAVIORAL RESEARCH search Service Award Act of 1974. TRAINING SHORT TITLE SEC. 101. This title may be cited as the '<National Research Service 42 U.S.C 28g1-1 Award Act of 1974". note. FINDINGS .AND DECLARATION OF PURPOSE 42 U.S.C 2891-1 note. SEC. 102. (a) Congress finds and declares that- (1) the success and continued viability of the Federal biomedical and behavioral research effort depends on the availability of excellent scientists and a network of institutions of excellence capable of producing superior research personnel ; (2) direct support of the training of scientists for careers in biomedical and behavioral research is an appropriate and necessary role for the Federal Government ; and (3) graduate research assistance programs should be the key elements in the training programs of the institutes of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration. (b) It is the purpose of this title to increase the capability of the institutes of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration to carry out their responsibility of maintaining a superior national program of research into the physical and mental diseases and impairments of man. BIOMEDICAL AND BEHAVIORAL RESEARCH TRAINING Ante, p. 135. SEC. 103. The part H of the Public Health Service Act relating to the appointment of the Administrators of the National Institutes of Health and the National Cancer Institute is redesignated as part I, section 461 of such part is redesignated as section 471, and such part is amended by adding at the end the following new sections: 42 U.S.C 289C1. "SEC. 472. (a) (1) The Secretary shall- "(A) provide National Research Service Awards for- "(1) biomedical and

behavioral research at and with the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration in matters relating to the cause, diagnosis, prevention, and treatment of the disease (or diseases) or other health problems to which the activities of the Institutes and Administration are directed, "(ii) training at the Institutes and Administration of individual~ to undertake such research, PUBLIC LAW 93-348-JULY 12, 1974 - \ Public Law 93-348 July 12.1974 AN ACT [H' R. 77241 TO amend the Public Health Service Act to establish a program of National Research Service Awards to assure the continued excellence of biomedical and behavioral research and to provide for the protection of human subjects involved in biomedical and behavioral research and for other purposes. Be it enacted by the Senate and House of Representatives of the Re- United States of America in Congress assembled, search Act. 42 usc 2891-1 SECTION 1. This Act may be cited as the "National Research Act". note. National Re- TITLE I-BIOMEDICAL AND BEHAVIORAL RESEARCH search Service Award Act of 1974. TRAINING SHORT TITLE SEC. 101. This title may be cited as the '<National Research Service 42 U.S.C 28g1-1 Award Act of 1974". note. FINDINGS .AND DECLARATION OF PURPOSE 42 U.S.C 2891-1 note. SEC. 102. (a) Congress finds and declares that- (1) the success and continued viability of the Federal biomedi- cal and behavioral research effort depends on the availability of excellent scientists and a network of institutions of excellence capable of producing superior research personnel ; (2) direct support of the training of scientists for careers in biomedical and behavioral research is an appropriate and necessary role for the Federal Government ; and (3) graduate research assistance programs should be the key elements in the training programs of the institutes of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration. (b) It is the purpose of this title to increase the capability of the institutes of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration to carry out their responsibility of maintaining a superior national program of research into the physical and mental diseases and impairments of man.

Appendix K

THE BELMONT REPORT

Ethical Principles and Guidelines for the protection of human subjects of research

The Belmont Report

Office of the Secretary

Ethical Principles and Guidelines for the Protection of Human Subjects of Research

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

April 18, 1979

AGENCY: Department of Health, Education, and Welfare.

ACTION: Notice of Report for Public Comment.

SUMMARY: On July 12, 1974, the National Research Act (Pub. L. 93-348) was signed into law, there-by creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles. In carrying out the above, the Commission was directed to consider: (i) the boundaries between biomedical and behavioral research and the accepted and routine practice of medicine, (ii) the role of assessment of risk-benefit criteria in the determination of the appropriateness of research involving human subjects, (iii) appropriate guidelines for the selection of human subjects for participation in such research and (iv) the nature and definition of informed consent in various research settings.

The Belmont Report attempts to summarize the basic ethical principles identified by the Commission in the course of its deliberations. It is the outgrowth of an intensive four-day period of discussions that were held in February 1976 at the Smithsonian Institution's Belmont Conference Center supplemented by the monthly deliberations of the Commission that were held over a period of nearly four years. It is a statement of basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects. By publishing the Report in the Federal Register, and providing reprints upon request, the Secretary intends that it may be made readily available to scientists, members of Institutional Review Boards, and Federal employees. The two-volume Appendix, containing the lengthy reports of experts and specialists who assisted the Commission in fulfilling this part of its charge, is available as DHEW Publication No. (OS) 78-0013 and No. (OS) 78-0014, for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

Unlike most other reports of the Commission, the Belmont Report does not make specific recommendations for administrative action by the Secretary of Health, Education, and Welfare.

Rather, the Commission recommended that the Belmont Report be adopted in its entirety, as a statement of the Department's policy. The Department requests public comment on this recommendation.

National Commission for the Protection of Human Subjects
of Biomedical and Behavioral Research
Members of the Commission

Kenneth John Ryan, M.D., Chairman, Chief of Staff, Boston Hospital for Women.
Joseph V. Brady, Ph.D., Professor of Behavioral Biology, Johns Hopkins University.
Robert E. Cooke, M.D., President, Medical College of Pennsylvania.
**** Dorothy I. Height, President, National Council of Negro Women, Inc.*
Albert R. Jonsen, Ph.D., Associate Professor of Bioethics, University of California at San Francisco.
Patricia King, J.D., Associate Professor of Law, Georgetown University Law Center.
Karen Lebacqz, Ph.D., Associate Professor of Christian Ethics, Pacific School of Religion.
**** David W. Louisell, J.D., Professor of Law, University of California at Berkeley.*
Donald W. Seldin, M.D., Professor and Chairman, Department of Internal Medicine, University of Texas at Dallas.
****Eliot Stellar, Ph.D., Provost of the University and Professor of Physiological Psychology, University of Pennsylvania.*
**** Robert H. Turtle, LL.B., Attorney, VomBaur, Coburn, Simmons & Turtle, Washington, D.C.*
**** Deceased.*

Ethical Principles & Guidelines for Research Involving Human Subjects

Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions. Public attention was drawn to these questions by reported abuses of human subjects in biomedical experiments, especially during the Second World War. During the Nuremberg War Crime Trials, the Nuremberg code was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on concentration camp prisoners. This code became the prototype of many later codes(1) intended to assure that research involving human subjects would be carried out in an ethical manner.

The codes consist of rules, some general, others specific, that guide the investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply. Broader ethical principles will provide a basis on which specific rules may be formulated, criticized and interpreted.

Three principles, or general prescriptive judgments, that are relevant to research involving human subjects are identified in this statement. Other principles may also be relevant. These three are comprehensive, however, and are stated at a level of generalization that should assist scientists, subjects, reviewers and interested citizens to understand the ethical issues inherent in research involving human subjects. These principles cannot always be applied so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects.

This statement consists of a distinction between research and practice, a discussion of the three basic ethical principles, and remarks about the application of these principles.

Part A: Boundaries Between Practice & Research

A. Boundaries Between Practice and Research

It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, in order to know what activities ought to undergo review for the protection of human subjects of research. The distinction between research and practice is blurred partly because both often occur together (as in research designed to evaluate a therapy) and partly because notable departures from standard practice are often called "experimental" when the terms "experimental" and "research" are not carefully defined.

For the most part, the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals.(2) By contrast, the term "research' designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is "experimental," in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.(3)

Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

Part B: Basic Ethical Principles

B. Basic Ethical Principles

The expression "basic ethical principles" refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions. Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect of persons, beneficence and justice.

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. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

An autonomous person is an individual capable of deliberation about personal goals and of acting under the direction of such deliberation. To respect autonomy is to give weight

to autonomous persons' considered opinions and choices while refraining from obstructing their actions unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person's considered judgments, to deny an individual the freedom to act on those considered judgments, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

However, not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Respect for the immature and the incapacitated may require protecting them as they mature or while they are incapacitated.

Some persons are in need of extensive protection, even to the point of excluding them from activities which may harm them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequence. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.
In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

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. Such treatment falls under the principle of beneficence. 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.
The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not injure one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic

Oath requires physicians to benefit their patients "according to their best judgment." Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.
The obligations of beneficence affect both individual investigators and society at large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk

that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel medical, psychotherapeutic, and social procedures.

The principle of beneficence often occupies a well-defined justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research involving children -- even when individual research subjects are not direct beneficiaries. Research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices that on closer investigation turn out to be dangerous. But the role of the principle of beneficence is not always so unambiguous. A difficult ethical problem remains, for example, about research that presents more than minimal risk without immediate prospect of direct benefit to the children involved. Some have argued that such research is inadmissible, while others have pointed out that this limit would rule out much research promising great benefit to children in the future. Here again, as with all hard cases, the different claims covered by the principle of beneficence may come into conflict and force difficult choices.

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." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally.
There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are (1) to each person an equal share, (2) to each person according to individual need, (3) to each person according to individual effort, (4) to each person according to societal contribution, and (5) to each person according to merit.

Questions of justice have long been associated with social practices such as punishment, taxation and political representation. Until recently these questions have not generally been associated with scientific research. However, they are foreshadowed even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries the burdens of serving as research subjects fell largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a particularly flagrant injustice. In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease that is by no means confined to that population. These subjects were deprived of demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available.

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

position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

Part C: Applications

C. Applications

Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk/benefit assessment, and the selection of subjects of research.

1. Informed Consent. -- Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied.

While the importance of informed consent is unquestioned, controversy prevails over the nature and possibility of an informed consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

Information. Most codes of research establish specific items for disclosure intended to assure that subjects are given sufficient information. These items generally include: the research procedure, their purposes, risks and anticipated benefits, alternative procedures (where therapy is involved), and a statement offering the subject the opportunity to ask questions and to withdraw at any time from the research. Additional items have been proposed, including how subjects are selected, the person responsible for the research, etc.

However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locale, is inadequate since research takes place precisely when a common understanding does not exist. Another standard, currently popular in malpractice law, requires the practitioner to reveal the information that reasonable persons would wish to know in order to make a decision regarding their care. This, too, seems insufficient since the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for needed care. It may be that a standard of "the reasonable volunteer" should be proposed: the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation.

A special problem of consent arises where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research of which some features will not be revealed until the research is concluded. In all cases of research involving incomplete disclosure, such research is justified only if it is clear that (1) incomplete disclosure is truly necessary to accomplish the goals of the research, (2) there are no undisclosed risks to subjects that are more than minimal, and (3) there is an

adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them. Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases in which disclosure would destroy or invalidate the research from cases in which disclosure would simply inconvenience the investigator.

Comprehension. The manner and context in which information is conveyed is as important as the information itself. For example, presenting information in a disorganized and rapid fashion, allowing too little time for consideration or curtailing opportunities for questioning, all may adversely affect a subject's ability to make an informed choice.

Because the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information. While there is always an obligation to ascertain that the information about risk to subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases. On occasion, it may be suitable to give some oral or written tests of comprehension.

Special provision may need to be made when comprehension is severely limited -- for example, by conditions of immaturity or mental disability. Each class of subjects that one might consider as incompetent (e.g., infants and young children, mentally disable patients, the terminally ill and the comatose) should be considered on its own terms. Even for these persons, however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in research. The objections of these subjects to involvement should be honored, unless the research entails providing them a therapy unavailable elsewhere. Respect for persons also requires seeking the permission of other parties in order to protect the subjects from harm. Such persons are thus respected both by acknowledging their own wishes and by the use of third parties to protect them from harm.

The third parties chosen should be those who are most likely to understand the incompetent subject's situation and to act in that person's best interest. The person authorized to act on behalf of the subject should be given an opportunity to observe the research as it proceeds in order to be able to withdraw the subject from the research, if such action appears in the subject's best interest.

Voluntariness. An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence. Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable.

Unjustifiable pressures usually occur when persons in positions of authority or commanding influence -- especially where possible sanctions are involved -- urge a course of action for a subject. A continuum of such influencing factors exists, however, and it is impossible to state precisely where justifiable persuasion ends and undue influence begins. But undue influence would include actions such as manipulating a person's choice through the controlling influence of a close relative and threatening to withdraw health services to which an individual would otherwise be entitle.

2. Assessment of Risks and Benefits. -- The assessment of risks and benefits requires a careful arrayal of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the investigator, it is a means to examine whether the proposed research is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to subjects are justified. For prospective subjects, the assessment will assist the determination whether or not to participate.

The Nature and Scope of Risks and Benefits. The requirement that research be justified on the basis of a favorable risk/benefit assessment bears a close relation to the principle of beneficence, just as the moral requirement that informed consent be obtained is derived primarily from the principle of respect for persons. The term "risk" refers to a possibility that harm may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm and the severity (magnitude) of the envisioned harm.

The term "benefit" is used in the research context to refer to something of positive value related to health or welfare. Unlike, "risk," "benefit" is not a term that expresses probabilities. Risk is properly contrasted to probability of benefits, and benefits are properly contrasted with harms rather than risks of harm.

Accordingly, so-called risk/benefit assessments are concerned with the probabilities and magnitudes of possible harm and anticipated benefits. Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked.

Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society). Previous codes and Federal regulations have required that risks to subjects be outweighed by the sum of both the anticipated benefit to the subject, if any, and the anticipated benefit to society in the form of knowledge to be gained from the research. In balancing these different elements, the risks and benefits affecting the immediate research subject will normally carry special weight. On the other hand, interests other than those of the subject may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subjects' rights have been protected. Beneficence thus requires that we protect against risk of harm to subjects and also that we be concerned about the loss of the substantial benefits that might be gained from research.

The Systematic Assessment of Risks and Benefits. It is commonly said that benefits and risks must be "balanced" and shown to be "in a favorable ratio." The metaphorical character of these terms draws attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, nonarbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically. This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and investigators less subject to misinterpretation, misinformation and conflicting judgments. Thus, there

should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

Finally, assessment of the justifiability of research should reflect at least the following considerations: (i) Brutal or inhumane treatment of human subjects is never morally justified. (ii) Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures. (iii) When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject -- or, in some rare cases, to the manifest voluntariness of the participation). (iv) When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. A number of variables go into such judgments, including the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits. (v) Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the informed consent process.

3. Selection of Subjects. -- Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects.

Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that researchers exhibit fairness: thus, they should not offer potentially beneficial research only to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons. Thus, it can be considered a matter of social justice that there is an order of preference in the selection of classes of subjects (e.g., adults before children) and that some classes of potential subjects (e.g., the institutionalized mentally infirm or prisoners) may be involved as research subjects, if at all, only on certain conditions.

Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by investigators and treated fairly in the course of research. Thus injustice arises from social, racial, sexual and cultural biases institutionalized in society. Thus, even if individual researchers are treating their research subjects fairly, and even if IRBs are taking care to assure that subjects are selected fairly within a particular institution, unjust social patterns may nevertheless appear in the overall distribution of the burdens and benefits of research. Although individual institutions or investigators may not be able to resolve a problem that is pervasive in their social setting, they can consider distributive justice in selecting research subjects.

Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments. When research is proposed that involves risks and does not include a therapeutic component, other less burdened classes of persons should be called upon first to accept these risks of research, except where the research

is directly related to the specific conditions of the class involved. Also, even though public funds for research may often flow in the same directions as public funds for health care, it seems unfair that populations dependent on public health care constitute a pool of preferred research subjects if more advantaged populations are likely to be the recipients of the benefits.

One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted.

Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.

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(1) Since 1945, various codes for the proper and responsible conduct of human experimentation in medical research have been adopted by different organizations. The best known of these codes are the Nuremberg Code of 1947, the Helsinki Declaration of 1964 (revised in 1975), and the 1971 Guidelines (codified into Federal Regulations in 1974) issued by the U.S. Department of Health, Education, and Welfare Codes for the conduct of social and behavioral research have also been adopted, the best known being that of the American Psychological Association, published in 1973.

(2) Although practice usually involves interventions designed solely to enhance the well-being of a particular individual, interventions are sometimes applied to one individual for the enhancement of the well-being of another (e.g., blood donation, skin grafts, organ transplants) or an intervention may have the dual purpose of enhancing the well-being of a particular individual, and, at the same time, providing some benefit to others (e.g., vaccination, which protects both the person who is vaccinated and society generally). The fact that some forms of practice have elements other than immediate benefit to the individual receiving an intervention, however, should not confuse the general distinction between research and practice. Even when a procedure applied in practice may benefit some other person, it remains an intervention designed to enhance the well-being of a particular individual or groups of individuals; thus, it is practice and need not be reviewed as research.

(3) Because the problems related to social experimentation may differ substantially from those of biomedical and behavioral research, the Commission specifically declines to make any policy determination regarding such research at this time. Rather, the Commission believes that the problem ought to be addressed by one of its successor bodies.

Appendix L

CODE OF FEDERAL REGULATIONS

TITLE 45
PUBLIC WELFARE
DEPARTMENT OF HEALTH AND HUMAN SERVICES
PART 46
PROTECTION OF HUMAN SUBJECTS
Subparts A, B C D E
Revised January 15, 2009
Effective July 14, 2009

Basic HHS Policy for Protection of Human Research Subjects

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Authority: 5 U.S.C. 301, 42 U.S.C. 289(a).

Editorial Note: The Department of Health and Human Services issued a notice of waiver regarding the requirements set forth in part 46, relating to protection of human subjects, as they pertain to demonstration projects, approved under section 1115 of the Social Security Act, which test the use of cost--sharing, such as deductibles, copayment and coinsurance, in the Medicaid program. For further information see 47 FR 9208, Mar. 4, 1982.

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Subpart A	Basic HHS Policy for Protection of Human Research Subjects
	Authority: 5 U.S.C. 301, 42 U.S.C. 289(a), 42 U.S.C. 300v-1(b).
	Source: 56 FR 28012, 28022, June 18, 1991, unless otherwise noted.

§46.101 To what does this policy apply?
(a) Except as provided in paragraph (b) of this section, this policy applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any Federal department or agency which takes appropriate administrative action to make the policy applicable to such research. This includes research conducted by Federal civilian employees or military personnel, except that each department or agency head may adopt such procedural modifications as may be appropriate from an administrative standpoint. It also includes research conducted, supported, or otherwise subject to regulation by the Federal government outside the United States.

(1) Research that is conducted or supported by a Federal department or agency, whether or not it is regulated as defined in §46.102(e), must comply with all sections of this policy.

(2) Research that is neither conducted nor supported by a Federal department or agency but is subject to regulation as defined in §46.102(e) must be reviewed and approved, in compliance with §46.101, §46.102, and §46.107 through §46.117 of this policy, by an institutional review board (IRB) that operates in accordance with the pertinent requirements of this policy.

(b) Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:

(1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
(i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects, and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

(3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:
(i) the human subjects are elected or appointed public officials or candidates for public office, or
(ii) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

(4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

(5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:

(i) Public benefit or service programs, (ii) procedures for obtaining benefits or services under those programs, (iii) possible changes in or alternatives to those programs or procedures, or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

(6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

(c) Department or agency heads retain final judgment as to whether a particular activity is covered by this policy.

(d) Department or agency heads may require that specific research activities or classes of research activities conducted, supported, or otherwise subject to regulation by the department or agency but not otherwise covered by this policy, comply with some or all of the requirements of this policy.

(e) Compliance with this policy requires compliance with pertinent Federal laws or regulations which provide additional protections for human subjects.

(f) This policy does not affect any state or local laws or regulations which may otherwise be applicable and which provide additional protections for human subjects.

(g) This policy does not affect any foreign laws or regulations which may otherwise be applicable and which provide additional protections to human subjects of research.

(h) When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. [An example is a foreign institution which complies with guidelines consistent with the World Medical Assembly Declaration (Declaration of Helsinki amended 1989) issued either by sovereign states or by an organization whose function for the protection of human research subjects is internationally recognized.] In these circumstances, if a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy. Except when otherwise required by statute, Executive Order, or the department or agency head, notices of these actions as they occur will be published in the FEDERAL REGISTER or will be otherwise published as provided in department or agency procedures.

(i) Unless otherwise required by law, department or agency heads may waive the applicability of some or all of the provisions of this policy to specific research activities or classes or research activities otherwise covered by this policy. Except when otherwise required by statute or Executive Order, the department or agency head shall forward advance notices of these actions to the Office for Human Research Protections, Department of Health and Human Services (HHS), or any successor office, and shall also publish them in the FEDERAL REGISTER or in such other manner as provided in department or agency procedures.[1]

[1] Institutions with HHS-approved assurances on file will abide by provisions of Title 45 CFR part 46 subparts A-D. Some of the other departments and agencies have incorporated all provisions of Title 45 CFR part 46 into their policies and procedures as well. However, the exemptions at 45 CFR 46.101(b) do not apply to research involving prisoners, subpart C. The exemption at 45 CFR 46.101(b)(2), for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, subpart D, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

[56 FR 28012, 28022, June 18, 1991; 56 FR 29756, June 28, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.102 Definitions.

(a) *Department or agency head* means the head of any Federal department or agency and any other officer or employee of any department or agency to whom authority has been delegated.
(b) *Institution* means any public or private entity or agency (including Federal, state, and other agencies).
(c) *Legally authorized representative* means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.
(d) *Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.
(e) *Research subject to regulation*, and similar terms are intended to encompass those research activities for which a Federal department or agency has specific responsibility for regulating as a research activity, (for example, Investigational New Drug requirements administered by the Food and Drug Administration). It does not include research activities which are incidentally regulated by a Federal department or agency solely as part of the department's or agency's broader responsibility to regulate certain types of activities whether research or non-research in nature (for example, Wage and Hour requirements administered by the Department of Labor).
(f) *Human subject* means a living individual about whom an investigator (whether professional or student) conducting research obtains
(1) Data through intervention or interaction with the individual, or
(2) Identifiable private information.
Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. *Private information* includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.
(g) *IRB* means an institutional review board established in accord with and for the purposes expressed in this policy.
(h) *IRB approval* means the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.
(i) *Minimal risk* means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
(j) *Certification* means the official notification by the institution to the supporting department or agency, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

§46.103 Assuring compliance with this policy -- research conducted or supported by any Federal Department or Agency.
(a) Each institution engaged in research which is covered by this policy and which is conducted or supported by a Federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in this policy. In lieu of requiring submission of an assurance, individual department or agency heads shall accept the existence of a current assurance, appropriate for the research in question, on file with the Office for Human Research Protections, HHS, or any successor office, and approved for Federalwide

use by that office. When the existence of an HHS-approved assurance is accepted in lieu of requiring submission of an assurance, reports (except certification) required by this policy to be made to department and agency heads shall also be made to the Office for Human Research Protections, HHS, or any successor office.
(b) Departments and agencies will conduct or support research covered by this policy only if the institution has an assurance approved as provided in this section, and only if the institution has certified to the department or agency head that the research has been reviewed and approved by an IRB provided for in the assurance, and will be subject to continuing review by the IRB. Assurances applicable to Federally supported or conducted research shall at a minimum include:

(1) A statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution, regardless of whether the research is subject to Federal regulation. This may include an appropriate existing code, declaration, or statement of ethical principles, or a statement formulated by the institution itself. This requirement does not preempt provisions of this policy applicable to department- or agency-supported or regulated research and need not be applicable to any research exempted or waived under §46.101(b) or (i).

(2) Designation of one or more IRBs established in accordance with the requirements of this policy, and for which provisions are made for meeting space and sufficient staff to support the IRB's review and recordkeeping duties.

(3) A list of IRB members identified by name, earned degrees, representative capacity, indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations, and any employment or other relationship between each member and the institution, for example: full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant. Changes in IRB membership shall be reported to the department or agency head, unless in accord with §46.103(a) of this policy, the existence of an HHS-approved assurance is accepted. In this case, change in IRB membership shall be reported to the Office for Human Research Protections, HHS, or any successor office.

(4) Written procedures which the IRB will follow (i) for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution, (ii) for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review, and (iii) for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

(5) Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB, and (ii) any suspension or termination of IRB approval.
(c) The assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this policy and shall be filed in such form and manner as the department or agency head prescribes.
(d) The department or agency head will evaluate all assurances submitted in accordance with this policy through such officers and employees of the department or agency and such experts or consultants engaged for this purpose as the department or agency head determines to be appropriate. The department or agency head's evaluation will take into consideration the adequacy of the proposed IRB in light of the anticipated scope of the institution's research activities and the types of subject populations likely to be involved, the appropriateness of the

proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution.
(e) On the basis of this evaluation, the department or agency head may approve or disapprove the assurance, or enter into negotiations to develop an approvable one. The department or agency head may limit the period during which any particular approved assurance or class of approved assurances shall remain effective or otherwise condition or restrict approval.
(f) Certification is required when the research is supported by a Federal department or agency and not otherwise exempted or waived under §46.101(b) or (i). An institution with an approved assurance shall certify that each application or proposal for research covered by the assurance and by §46.103 of this Policy has been reviewed and approved by the IRB. Such certification must be submitted with the application or proposal or by such later date as may be prescribed by the department or agency to which the application or proposal is submitted. Under no condition shall research covered by §46.103 of the Policy be supported prior to receipt of the certification that the research has been reviewed and approved by the IRB. Institutions without an approved assurance covering the research shall certify within 30 days after receipt of a request for such a certification from the department or agency, that the application or proposal has been approved by the IRB. If the certification is not submitted within these time limits, the application or proposal may be returned to the institution.
(Approved by the Office of Management and Budget under Control Number 0990-0260.)
[56 FR 28012, 28022, June 18, 1991; 56 FR 29756, June 28, 1991, as amended at 70 FR 36328, June 23, 2005]

§§46.104--46.106 [Reserved]

§46.107 IRB membership.
(a) Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.
(b) Every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of members of one profession.
(c) Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.
(d) Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.
(e) No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.
(f) An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB

§46.108 IRB functions and operations.

In order to fulfill the requirements of this policy each IRB shall:
(a) Follow written procedures in the same detail as described in §46.103(b)(4) and, to the extent required by, §46.103(b)(5).
(b) Except when an expedited review procedure is used (see §46.110), review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting

§46.109 IRB review of research.
(a) An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy.
(b) An IRB shall require that information given to subjects as part of informed consent is in accordance with §46.116. The IRB may require that information, in addition to that specifically mentioned in §46.116, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects.
(c) An IRB shall require documentation of informed consent or may waive documentation in accordance with §46.117.
(d) An IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.
(e) An IRB shall conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research. High heat
[56 FR 28012, 28022, June 18, 1991; 56 FR 29756, June 28, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.
(a) The Secretary, HHS, has established, and published as a Notice in the FEDERAL REGISTER, a list of categories of research that may be reviewed by the IRB through an expedited review procedure. The list will be amended, as appropriate, after consultation with other departments and agencies, through periodic republication by the Secretary, HHS, in the FEDERAL REGISTER. A copy of the list is available from the Office for Human Research Protections, HHS, or any successor office.
(b) An IRB may use the expedited review procedure to review either or both of the following:
(1) some or all of the research appearing on the list and found by the reviewer(s) to involve no more than minimal risk,
(2) minor changes in previously approved research during the period (of one year or less) for which approval is authorized.
Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth in §46.108(b).
(c) Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure.
(d) The department or agency head may restrict, suspend, terminate, or choose not to authorize an institution's or IRB's use of the expedited review procedure.
[56 FR 28012, 28022, June 18, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.111 Criteria for IRB approval of research.
(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:
(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 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 (for example, the possible effects of the research on public policy) 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, in accordance with, and to the extent required by §46.116.
(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117.
(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.

§46.112 Review by institution.
Research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB.

§46.113 Suspension or termination of IRB approval of research.
An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.
(Approved by the Office of Management and Budget under Control Number 0990-0260.)
[56 FR 28012, 28022, June 18, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.114 Cooperative research.
Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the department or agency head, an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

§46.115 IRB records.
(a) An institution, or when appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities, including the following:
(1) Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.
(2) Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings, actions taken by the IRB, the vote on these actions including the number of members voting for, against, and abstaining, the basis for requiring changes in or disapproving research, and a written summary of the discussion of controverted issues and their resolution.
(3) Records of continuing review activities.
(4) Copies of all correspondence between the IRB and the investigators.
(5) A list of IRB members in the same detail as described in §46.103(b)(3).
(6) Written procedures for the IRB in the same detail as described in §46.103(b)(4) and §46.103(b)(5).
(7) Statements of significant new findings provided to subjects, as required by §46.116(b)(5).
(b) The records required by this policy shall be retained for at least 3 years, and records relating to research which is conducted shall be retained for at least 3 years after completion of the research. All records shall be accessible for inspection and copying by authorized representatives of the department or agency at reasonable times and in a reasonable manner.
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[56 FR 28012, 28022, June 18, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.116 General requirements for informed consent.
Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.
(a) Basic elements of informed consent. Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:
(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental,
(2) A description of any reasonably foreseeable risks or discomforts to the subject,
(3) A description of any benefits to the subject or to others which may reasonably be expected from the research,
(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject,
(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained,
(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained,
(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject, and

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
(b) Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:
(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable,
(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent,
(3) Any additional costs to the subject that may result from participation in the research,
(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject,
(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject, and
(6) The approximate number of subjects involved in the study.
(c) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:
(1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs, (ii) procedures for obtaining benefits or services under those programs, (iii) possible changes in or alternatives to those programs or procedures, or (iv) possible changes in methods or levels of payment for benefits or services under those programs, and
(2) The research could not practicably be carried out without the waiver or alteration.
(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:
(1) The research involves no more than minimal risk to the subjects,
(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects,
(3) The research could not practicably be carried out without the waiver or alteration, and
(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
(e) The informed consent requirements in this policy are not intended to preempt any applicable Federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.
(f) Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable Federal, state, or local law.
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[56 FR 28012, 28022, June 18, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.117 Documentation of informed consent.
(a) Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.
(b) Except as provided in paragraph (c) of this section, the consent form may be either of the following:
(1) A written consent document that embodies the elements of informed consent required by §46.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed, or

(2) A short form written consent document stating that the elements of informed consent required by §46.116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.
(c) An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:
(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern, or
(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.
In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

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[56 FR 28012, 28022, June 18, 1991, as amended at 70 FR 36328, June 23, 2005]

§46.118 Applications and proposals lacking definite plans for involvement of human subjects.
Certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. These include activities such as institutional type grants when selection of specific projects is the institution's responsibility, research training grants in which the activities involving subjects remain to be selected, and projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. These applications need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived under §46.101(b) or (i), no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in this policy, and certification submitted, by the institution, to the department or agency.

§46.119 Research undertaken without the intention of involving human subjects.
In the event research is undertaken without the intention of involving human subjects, but it is later proposed to involve human subjects in the research, the research shall first be reviewed and approved by an IRB, as provided in this policy, a certification submitted, by the institution, to the department or agency, and final approval given to the proposed change by the department or agency.

§46.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency.
(a) The department or agency head will evaluate all applications and proposals involving human subjects submitted to the department or agency through such officers and employees of the department or agency and such experts and consultants as the department or agency head determines to be appropriate. This evaluation will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained.
(b) On the basis of this evaluation, the department or agency head may approve or disapprove the application or proposal, or enter into negotiations to develop an approvable one.

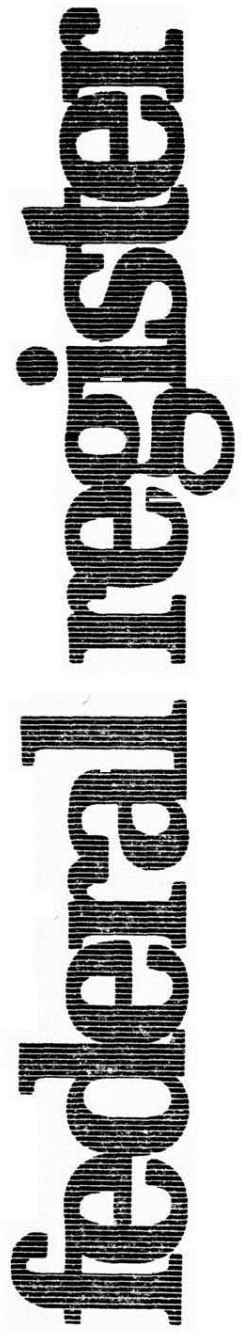
§46.121 [Reserved]

§46.122 Use of Federal funds.
Federal funds administered by a department or agency may not be expended for research involving human subjects unless the requirements of this policy have been satisfied.

§46.123 Early termination of research support: Evaluation of applications and proposals.
(a) The department or agency head may require that department or agency support for any project be terminated or suspended in the manner prescribed in applicable program requirements, when the department or agency head finds an institution has materially failed to comply with the terms of this policy.
(b) In making decisions about supporting or approving applications or proposals covered by this policy the department or agency head may take into account, in addition to all other eligibility requirements and program criteria, factors such as whether the applicant has been subject to a termination or suspension under paragraph (a) of this section and whether the applicant or the person or persons who would direct or has/have directed the scientific and technical aspects of an activity has/have, in the judgment of the department or agency head, materially failed to discharge responsibility for the protection of the rights and welfare of human subjects (whether or not the research was subject to Federal regulation).

§46.124 Conditions.
With respect to any research project or any class of research projects the department or agency head may impose additional conditions prior to or at the time of approval when in the judgment of the department or agency head additional conditions are necessary for the protection of human subjects.

APPENDIX M



Tuesday
August 14, 1979

Part II

Department of Health, Education, and Welfare

Food and Drug Administration, Office of the Secretary

Protection of Human Research Subjects

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Office of the Secretary

[45 CFR Part 46]

Proposed Regulations Amending Basic HEW Policy for Protection of Human Research Subjects

AGENCY: Department of Health, Education, and Welfare.

ACTION: Proposed rule.

SUMMARY: The Department of Health, Education, and Welfare (HEW or Department) is proposing regulations amending HEW policy for the protection of human research subjects and responding to the recommendations of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (Commission) concerning institutional review boards (IRBs or Boards). These proposed rules adopt, for the most part, the recommendations of the Commission and, if adopted in their present form, would have the following primary effects: (1) continue to provide protections for human subjects of research conducted or supported by the Department of Health, Education, and Welfare; (2) require IRB review and approval of research involving human subjects, even if it is not supported by Department funds, if it is conducted at or supported by an institution receiving HEW funds for research not exempt from these regulations—research not supported by Department funds are subject to the same exemption clauses as Department funded research; (3) require review of human subject research irrespective of risk—unless the research is specifically exempted from coverage; (4) exempt from coverage certain kinds of social, economic and educational research; (5) either exempt or require only expedited review of certain kinds of research involving solely the use of survey instruments, solely the observation of public behavior, solely the study of documents, records and specimens, or solely a combination of any of these activities [public comment is especially invited concerning whether to exempt or to require only expedited review for these categories of research]; (6) require only expedited review for certain categories of proposed research involving no more than minimal risk and for minor changes in research already approved by the IRB; (7) provide specific procedures for full IRB review and for expedited IRB review; (8) designate basic elements of informed consent which are a necessary prerequisite to research subject participation and additional elements which, when appropriate, are a necessary prerequisite to subject participation; (9) indicate circumstances under which the IRB may approve withholding or altering certain information otherwise required to be presented to research subjects; (10) require that IRB membership include at least one nonscientist; and (11) establish regulations which to the extent possible, are compatible and consistent with the soon to be published, FDA proposed standards for IRB's.

Note.— These are "proposed" regulations and public comment on them is encouraged.

DATES: Written comments on the proposed rules should be received on or before November 12, 1979, if they are to be given full consideration.

ADDRESS: Please send comments or requests for additional information to:

F. William Dommel, Jr., J.D., Assistant Director for Regulations, Office for Protection from Research Risks; National Institutes of Health, 5333 Westbard Avenue, Room 3A18, Bethesda, Maryland 20205, Telephone: (301) 496–7163,

where all comments received will be available for inspection weekdays (Federal holidays excepted) between the hours of 9 a.m. and 4:30 p.m.

FOR FURTHER INFORMATION CONTACT: F. William Dommell, Jr. (301) 496–7163.

SUPPLEMENTARY INFORMATION: Basic regulations governing the protection of human subjects involved in research, supported by HEW through grants and contracts were published in the **Federal Register** on May 30, 1974 (30 FR 18914). Subsequently, regulations were published to accord additional protections for "special groups" which may have diminished capacity to consent or which may be at high risk (i.e., fetuses, pregnant women, and prisoners). These "special group" regulations which, have previously been published in final form, will be amended to conform (where necessary) with the basic regulations proposed below, when these basic regulations are published in final form. In addition, regulations have been proposed to provide additional safeguards for others who may have diminished capacity. These were published in the **Federal Register** as follows: Research Involving Children (43 FR 31786, July 21, 1978) and Research Involving Those Institutionalized as Mentally Disabled (43 FR 53950, November 17, 1978). Final regulations on those two categories are being withheld pending further comment on them as well as the proposed regulations below.

Therefore, the public comment period for each of these proposed regulations (including their relationship to the basic regulations published in proposed form below) has been extended to November 12, 1979. The decision to postpone final regulations on these special categories of participants was reached on the basis of procedural considerations. By finalizing first the regulations applicable to the review and monitoring of all research involving human subjects and covered by these regulations, the Department may then issue only those additional regulations necessary for the protection of specific categories of subjects who may have diminished capacity to consent. By following this order of regulation development, the Department hopes to avoid the possibility of duplicative and inconsistent requirements among the several sections of these regulations.

On August 8, 1978, the Food and Drug Administration published proposed standards for Institutional Review Boards for Clinical Investigations (43 FR 35186). Shortly thereafter, the Commission submitted its report and recommendations on IRBs and informed consent, and that document was published in the **Federal Register** on November 30, 1978 (43 FR 56174). In its report, the Commission recommended revisions of the current HEW regulations for IRBs. Because the FDA stated in the August 8, 1978 proposal that its regulations should be compatible with, if not identical to, those of the Department, FDA is withdrawing its IRB proposal of August 8, 1978 and is publishing a revised proposal which has been developed in conjunction with HEW. The Department and FDA both agree in principle with the recommendation of the Commission that IRBs should operate under one set of federal regulations. Within the constraints of their independent statutory obligations and missions, the Department and FDA have developed IRB proposals which have virtually the same structure and functions, so that IRBs will have essentially uniform requirements in areas such as scope of responsibility, quorum requirements, and records retention.

It should be emphasized that, although the regulations proposed below will be essentially compatible and consistent with the regulations to be proposed by FDA, the two sets of regulations cannot be identical. The statutory authorities under which FDA regulates clinical research are different from the authorities relied upon by the

Department to regulate research which it either funds or conducts. In addition, because the Department's regulations encompass behavioral research, the scope of coverage and types of review required are somewhat different.

The regulations proposed below attempt to achieve a common, flexible framework within which IRBs can operate whether they are reviewing HEW supported research or FDA regulated research. Because FDA is a regulatory agency, the compliance aspects of its regulations must be explicitly stated. In its proposal, FDA will provide for inspection and disqualification of IRBs. However, the Department, which employs the institutional assurance mechanism for dealing with institutions, and which may cut off funding of projects for noncompliance, has made no such provision.

The Department will continue to consult with FDA during the development of final regulations so that consistency of IRB structure and function can be maintained, as much as possible.

Background: The National Research Act (Pub. L. 93–348) was signed into law on July 12, 1974, creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the topics of study identified in the mandate to the Commission was "Institutional Review Boards." The Commission was required to recommend to the Secretary of Health, Education, and Welfare ". . . mechanisms for evaluating and monitoring the performance of Institutional Review Boards in accordance with section 474 of the Public Health Service Act and appropriate enforcement mechanisms for carrying out their decisions." And was further required to make recommendations regarding the protection of subjects involved in research not subject to regulation by HEW.

In discharging its duties under this mandate, the Commission studied the performance of IRBs which are required to review all research involving human subjects that is conducted at institutions receiving funds for such reserach from HEW under the Public Health Service Act. The Commission found that the review of proposed research by IRBs is the primary mechanism for assuring that the rights of human subjects are protected. Thus, the Commission's previous recommendations regarding particular categories of research subjects are intended ulimately to be carried out by the IRBs through the estalishment of conditions and requirements that IRBs should determine to have been satisified before approving research.

The commission, therefore, undertook a substantial effort to develop information about the performance of IRBs, the research they review, and the strengths and weaknesses of this mechanism. This effort included the support of an extensive survey of IRB members, investigators and research subjects at a sample of 61 institutions including medical schools, hospitals, universities, prisons, institutions for the mentally ill and retarded, and researh organizations. Also, the background, development, and administration of the present HEW regulations governing IRBs were examined. Three public hearings were held at which Federal officials, representatives of IRBs, investigators, and other concerned persons presented their views on IRBs. The National Minority Conference on Human Experimentation, convoked by the Commission to assure that viewpoints of minorities would be heard, made recommendations to the Commission that pertained to IRBs. The Commission also reviewed several papers prepared under contract on such topics as informed consent, evaluation of risks and benefits, issues that arise in particular kinds of research (such as social experimentation or deception research), and the legal aspects of IRB operation. A substantial amount of correspondence on IRBs was received and reviewed by the Commission.

In addition, a survey was made of the standards and procedures for the protection of human subjects in research conducted or sponsored by Federal departments and agencies. Finally, the Commission conducted public deliberations to develop its recommendations on IRBs.

Action on recommendations of the Commission: Pursuant to section 205 of the National Research Act (Pub. L. 93–348), the recommendations of the Commission regarding Institutional Review Boards were published in the **Federal Register** (43 FR 56174) on November 30, 1978. Comments were received from 104 individuals, institutions, organizations and groups. After reviewing the recommendations and the comments, the Secretary has prepared the notice of proposed rulemaking set forth below, which in essence accepts the recommendations. The proposed rules depart from the recommendations of the Commission to the Department in a few respects.

Recommendations of the Commission and HEW Responses

Recommendation (1)

(A) Federal law should be enacted or amended to authorize the Secretary of Health, Education, and Welfare to promulgate regulations governing ethical review of all research involving human subjects that is subject to Federal regulation.

(B) Federal law should be enacted or amended to provide that each institution which sponsors or conducts involving human subjects that is supported by any Federal department or agency or otherwise subject to Federal regulation, and each Federal department or agency which itself conducts research involving human subjects, shall give assurances satisfactory to the Secretary of Health, Education, and Welfare that all research involving human subjects sponsored or conducted by such institution, or conducted by such department or agency, will be reviewed by and conducted in accordance with the determinations of a review board established and operated in accordance with the regulations promulgated by the Secretary under the authority recommended in paragraph (A) of this recommendation.

(C) Federal law should be enacted or amended to provide that all research involving human subjects sponsored or conducted by an institution that receives funds from any Federal department or agency to provide health care or conduct health-related research shall be subject to Federal regulation regarding the review and conduct of such research, as provided under paragraphs (A) and (B) of this recommendation.

(D) Federal law should be enacted or amended to authorize and appropriate funds to support the operation of Institutional Review Boards by direct cost funding.

HEW Response

The legislative mandate to the Commission included a charge to make recommendations to the Congress regarding the protection of subjects involved in research not subject to HEW regulation. Recommendation (1) responds to that charge. The Department contemplates no HEW action on this recommendation which is directed to the Congress. However, most of the twenty-two Federal agencies conducting or supporting research with human subjects have adopted the HEW regulations in whole or in part. The Department encourages this voluntary

approach and will continue to serve these agencies in an advisory capacity.

Recommendation (2)

(A) Federal law should be enacted or amended to authorize the Secretary of Health, Education, and Welfare to establish a single office to carry out the following duties:

(i) Accreditation of Institutional Review Boards based upon the submission of assurances containing descriptions of their membership, authority, staff, meeting facilities, review and monitoring procedures and provisions for recordkeeping; (ii) Compliance activities, including site visits and audits of Institutional Review Board records, to examine the performance of the Boards and their fulfillment of institutional assurances and regulatory requirements; and (iii) Educational activities to assist members of Institutional Review Boards in recognizing and considering the ethical issues that are presented by research involving human subjects.

(B) Federal law should be enacted or amended to authorize and appropriate funds to support the duties described in paragraph (A) of this recommendation.

HEW Response

Recommendation (2), just as Recommendation (1), is directed to the Congress. However, current HEW policy and regulations, as well as the regulations proposed below, implement for the main part this recommendation.

Recommendations (2)(A)(i) and (2)(A)(ii) are implemented by §§ 46.105 and 46.106 which establish the minimum requirements for institutional assurances regarding IRBs. Currently, FDA compliance activities and the aforementioned assurances, required under current HEW regulations and negotiated by the Office for Protection from Research Risks (OPRR), National Institutes of Health (NIH) and the FDA compliance activities meet and will continue to meet the requirements of these recommendations.

Educational activities such as those proposed in Recommendation (2)(A)(iii), although not described in the regulations, are currently being conducted by FDA and are being planned by OPRR, NIH.

Recommendation (3)

The Secretary of Health, Education, and Welfare should require by regulation that an Institutional Review Board:

(A) Consist of at least five men and women of diverse backgrounds and sufficient maturity, experience and competence to assure that the Board will be able to discharge its responsibilities and that its determinations will be accorded respect by investigators and the community served by the institution or in which it is located;

(B) Include at least one member who is not otherwise affiliated with the institution;

(C) Have the authority to review and approve, require modifications in, or disapprove all research involving human subjects conducted at the institution;

(D) Have the authority to conduct continuing review of research involving human subjects and to suspend approval of research that is not being conducted in accordance with the determinations of the Board or in which there is unexpected serious harm to subjects;

(E) Maintain appropriate records, including copies of proposals reviewed, approved consent forms, minutes of Board meetings, progress reports submitted by investigators, reports of injuries to subjects, and records of continuing review activities;

(F) Be provided with meeting space and sufficient staff to support its review and recordkeeping duties;

(G) Be authorized and directed to report to institutional authorities and the Secretary any serious or continuing noncompliance by investigators with the requirements and determinations of the Board;

(H) Be provided with protection for members in connection with any liability arising out of their performance of duties on the Board.

HEW Response

Recommendation (3)(A) would be implemented by § 46.107(a), (b), and (c) of the proposed regulations set forth below. Several of the Commission's comments on the recommendation were included on the proposed regulations for purposes of clarification. One comment, however, suggested that ". . . at least one-third but no more than two-thirds of the IRB members should be scientists." The Department recognizes the need for diversity of professions among IRB members, and provision is made for this diversity at § 46.107(a) and (b) of the proposed regulations. It was decided, however, that to require in the regulation that "No board may consist entirely of members of one profession, and at least one member must be a nonscientist" provides a flexible means for institutions to establish diverse membership.

Recommendation (3)(B) would be implemented in its entirety by § 46.107(d) of the proposed regulations.

Recommendation (3)(C) would be implemented in part by §§ 46.101 and 46.108(a) of the proposed regulations. This recommendation would assign to IRBs the review, approval, disapproval, and modification authority (to secure approval) over all research ". . . conducted at the institution." The proposed regulations would afford this authority to the IRBs for research sponsored by, as well as conducted at the institution. The issue of what categories of research and which institutions must comply with the proposed regulations is described below in ADDITIONAL HEW COMMENTS or provided for at § 46.101 of the proposed regulations.

Recommendation (3)(D) would be implemented in its entirety by § 46.108(b) of the proposed regulations.

Recommendation (3)(E) would be implemented in its entirety by §§ 46.105(f) and 46.106(g) of the proposed regulations.

Recommendation (3)(F) would be implemented in its entirety by §§ 46.105(g) and 46.106(i) of the proposed regulations.

Recommendation (3)(G) would be implemented in its entirety by § 46.108(c) of the proposed regulations.

Recommendation (3)(H) would not be implemented by the regulations proposed below. The Commission recommended that protection be provided for IRB members in connection with any liability arising out of their performance of duties on the Board. The Department is hesitant to make this an absolute requirement because there is not certainty, at this time, that reasonable mechanisms are available to provide this protection. Furthermore the Department is not aware of any negligence action which has named an IRB member as a defendant and therefore believes that liability protections might prove to be an unnecessary, yet costly, requirement.

Recommendation (4)

The Secretary of Health, Education, and Welfare should require by regulation that all research involving human subjects that is subject to Federal regulation shall be reviewed by an Institutional Review Board and that the approval of such research shall be based upon affirmative determinations by the Board that:

(A) The research methods are appropriate to the objectives of the research and the field of study;

(B) Selection of subjects is equitable;

(C) Risks to subjects are minimized by using the safest procedures consistent with sound research design and, whenever appropriate, by using procedures being performed for diagnostic or treatment purposes;

(D) Risks to subjects are reasonable in relation to anticipated benefits to subjects and importance of the knowledge to be gained;

(E) Informed consent will be sought under circumstances that provide sufficient opportunity for subjects to consider whether or not to participate and that minimize the possibility of coercion or undue influence;

(F) Informed consent will be based upon communicating to subjects, in language they can understand, information that the subjects may reasonably be expected to desire in considering whether or not to participate, generally including:

(i) That an Institutional Review Board has approved the solicitation of subjects to participate in the research, that such participation is voluntary, that refusal to participate will involve no penalties or loss of benefits to which subjects are otherwise entitled, that participation can be terminated at any time, and that the conditions of such termination are stated;

(ii) The aims and specific purposes of the research, whether it includes procedures designed to provide direct benefit to subjects, and available alternative ways to pursue any such benefit;

(iii) What will happen to subjects in the research, and what they will be expected to do;

(iv) Any reasonably foreseeable risks to subjects, and whether treatment or compensation is available if harm occurs;

(v) Who is conducting the study, who is funding it, and who should be contacted if harm occurs or there are complaints; and

(vi) Any additional costs to subjects or third parties that may result from participation;

(G) Informed consent will be appropriately documented, unless the Board determines that written consent is not necessary or appropriate because (I) the existence of signed consent forms would place subjects at risk, or (II) the research presents no more than minimal risk and involves no procedures for which written consent is normally required;

(H) Notwithstanding the requirements of paragraphs (E), (F) and (G) above, informed consent is unnecessary (I) where the subjects' interests are determined to be adequately protected in studies of documents, records or pathological specimens and the importance of the research justifies such invasion of the subjects' privacy, or (II) in studies of public behavior where the research presents no more than minimal risk, is unlikely to cause embarrassment, and has scientific merit;

(I) There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data; and

(J) Applicable regulatory provisions for the protection of fetuses, pregnant women, prisoners, children and those institutionalized as mentally infirm will be fulfilled.

HEW Response

Recommendations (4)(A–D) would be implemented in their entirety by § 46.110(1–4) of the proposed regulations.

Recommendations (4)(E) and (4)(F)(I–III) would be implemented in their entirety by § 46.112(a)(1).

Recommendation (4)(F)(IV) would be implemented in part by 46.112(a)(1)(c) concerning description of foreseeable risks. The second part of this recommendation suggests notification of whether treatment or compensation is available if harm occurs. At § 46.112(a)(1)(I), the proposed regulation would require this notification if the research involves more than minimal risk and would further require an explanation of the extent of available coverage (if any). The Department feels that where the risk is no greater than minimal, an explanation of injury benefits would be inappropriate.

Recommendations (4)(F)(V–VI) would be implemented in part by 46.112(a)(1)(J) concerning who should be contacted if harm occurs or there are complaints (referred to in the regulations as questions or problems instead of complaints). The other parts of the recommendations suggest that the subject be informed of who is conducting the study and of any additional costs to subjects or third parties that may result from participation. These later notifications, while at times appropriate, are not seen by the Department as being essential to every informed consent procedure. Therefore, these two notifications as well as notice of the possible involvement of currently unforeseeable risks, notice of foreseeable circumstances under which the subjects participation may be terminated by the investigator, and notice of the approximate number of subjects involved are included under an optional set of informed consent elements (§ 46.112(a)(2)). The IRB, when appropriate, shall require that some or all of these elements of information be provided to the subject.

Recommendation (4)(G) regarding the waiver of the required documentation of consent would be implemented by § 46.113(b) where the Department has added additional requirements for the waiver.

Recommendation (4)(H) would waive the informed consent requirement for certain kinds of research presenting no more than minimal risk. The proposed regulations do not provide for this total waiver of consent requirements because the categories of research to which it would apply are under consideration for exemption from these regulations (§ 46.101(c) [option A]). However, the Department would support waiving consent for these categories if they are not exempted (§ 46.101(c) [option B]).

Recommendation (4)(I) would be implemented in its entirety by § 46.119 of the proposed regulations.

Recommendation (4)(J) is implemented for fetuses and pregnant women by 45 CFR 46 Subpart B and for prisoners by 45 CFR 46 Subpart C. The recommendation would be implemented for children by 45 CFR 46 Subpart D (proposed) and for those institutionalized as mentally disabled by 45 CFR 46 Subpart E (proposed).

Recommendation (5)

The Secretary of Health, Education, and Welfare should require by regulation that an Institutional Review Board shall review proposed research at convened meetings at which a majority of the members of the Board are present and that approval of such research shall be reached by a majority of those members who are present at the meeting, provided, however, that the Secretary may specifically approve expedited review procedures adopted by an Institutional Review Board for carefully defined categories of research that present no more than minimal risk. The Secretary should require, further, that an Institutional Review Board inform investigators of the basis of decisions to disapprove or require the modification of proposed research and give investigators an opportunity to respond in person or in writing.

HEW Response

Recommendation (5) would be implemented in its entirety by §§ 46.105e, 46.106(b), and 46.111 of the proposed regulations.

Additional HEW Comments

Alternative Exemptions

The Department is considering and requesting comments on two alternative lists of exemptions or some combination thereof. The two lists reflect differing opinions concerning: (1) whether to exempt research involving solely observation, (2) what types of survey or related research should be exempted, (3) under what conditions research involving solely the study of documents, records or specimens should be exempted (assuming the investigator is not collecting identifiers).

The list of exemptions in alternative A (especially items 4, 5 and 6) reflect the belief held by some that almost all of this research is innocuous. Those who advocated this alternative felt that there is no need to include such research under the regulations because there is no evidence of adverse consequences and little evidence of risk apart from possible breaches of confidentiality. Furthermore they contended that institutions which currently have no IRB would have to create one to review minimal-risk research. It was argued that to require an institution to review a large volume of minimal-risk research in order to find the rare proposal that might be potentially harmful, could create an unwarranted burden on the institution.

Alternative B reflects the view of those who feel that not all survey research and records research should be exempted. Furthermore thay believe that observational research should be entirely subject to the regulations because at least some of this research can present serious risks for subjects. Examples of these research are: research involving collection of information about mental disorders or child abuse, observation of illegal conduct, or collection of data on alcohol abuse from medical records or specimens. Inadvertent or compulsory disclosure of information collected in such research can have serious consequences for subjects' future employability, family relationships or financial credit; also, some surveys can cause psychological distress for subjects.

The argument for IRB review of such research is based not only on the need to protect from harm, but on the need for an independent, social mechanism to ensure that research is ethically acceptable and that the rights and welfare of subjects will be protected.

Alternative B, along with inclusion of certain procedures in the expedited review list will permit sugnificant reduction in the workload by IRBs, though not as much of a reduction as alternative A.

Filing Justification for Exemption

The Department is also considering whether to require a principal investigator who proposes to carry out research involving human subjects which he judges to be exempt from the regulations should be required to document the reasons underlying the judgement that his research project is exempt. The investigator who claims exemption would be required to file a justification with an appropriate IRB or with the Secretary. It is felt that such a requirement would reduce the possibility of investigators claiming exemptions for non-exempt research. Comments on this procedure are requested.

Notice is given that it is proposed to make any amendments that are adopted effective upon publication in the **Federal Register.**

Dated July 26, 1979.

Julius B. Richmond,

Assistant Secretary for Health.

Approved July 27, 1979.

Joseph A. Califano, Jr.,

Secretary.

It is therefore proposed to amend Part 46 of 45 CFR, by repealing current Subparts A and D, and replacing them with the following new Subpart A.

Subpart A—Basic HEW Policy for Protection of Human Research Subjects

Sec.

46.101 To what do these regulations apply?
46.102 Definitions.
46.103 Submission of assurances.
46.104 Types of assurances.
46.105 Minimum requirements for general assurances.
46.106 Minimum requirements for special assurances.
46.107 Institutional Review Board membership.
46.108 Institutional Review Board functions
46.109 Evaluation and disposition of assurances.
46.110 Review of proposed research by the Institutional Review Board.
46.111 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.
46.112 Informed consent.
46.113 Documentation of informed consent.
46.114 Applications and proposals lacking definite plans for involvement of human subjects.
46.115 Research undertaken without the intention of involving human subjects.
46.116 Evaluation and disposition of applications and proposals.
46.117 Cooperative research projects.
46.118 Investigational new drug 30-day delay requirement.
46.119 Confidentiality of records.
46.120 Use of Federal funds.
46.121 Early termination of research support; evaluation of subsequent applications and proposals.
46.122 Research not conducted or supported by the Department.
46.123 Conditions.

Authority: 5 U.S.C. 301.

Subpart A—Basic HEW Policy for Protection of Human Research Subjects

§46.101 To what do these regulations apply?

(a) Except as provided in paragraph (c), this subpart applies to all research involving human subjects conducted or supported by the Department of Health, Education, and Welfare.

(b) Except as provided in paragraph (c) below, only §§ 46.104(c) and 46.122 of these regulations apply to research involving human subjects which is not funded by the Department, but is conducted at or supported by any institution receiving funds from the Department for the conduct of research involving human subjects.

(c) These regulations do not apply to:

[The Department will include a list of exempted categories of research in the final regulations. Two alternative lists are provided below for public comment. (The first three items and the last item in each list are identical.) If the list in Alternative B is adopted, additions will also be made to the list of procedures which can receive expedited review (see § 46.111).]

Alternative A

(1) Research designed to study on a large scale: (A) the effects of proposed social or economic change, or (B) methods or systems for the delivery of or payment for social or health services.

(2) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (A) research on regular and special education instructional strategies, or (B) research on the effectiveness of or the comparison among instructional techniques, curriculum, or classroom management.

(3) Research involving solely the use of standard educational diagnostic, aptitude, or achievement tests, if information taken from these sources is recorded in such a manner that subjects cannot be reasonably identified, directly or through identifiers linked to the subjects.

(4) Research involving solely the use of survey instruments if: (A) results are recorded in such a manner that subjects cannot be reasonably identified, directly or through identifiers linked to the subjects, or (B) the research (although not exempted under clause (A)) does not deal with sensitive topics, such as sexual behavior, drug or alcohol use, illegal conduct, or family planning.

(5) Research involving solely the observation (including observation by participants) of public behavior, if observations are recorded in such a manner that subjects cannot be reasonably identified, directly or through identifiers linked to the subjects.

(6) Research involving solely the study of documents, records. or pathological or diagnostic specimens, if information taken from these sources is recorded in such a manner that subjects cannot be reasonably identified, directly or through identifiers linked to the subjects.

(7) Research involving solely a combination of any of the activities described above.

Alternative B

(1) Research designed to study on a large scale: (A) the effects of proposed social or economic change, or (B) methods or systems for the delivery of or payment for social or health services.

(2) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (A) research on regular and special education instructional strategies, or (B) research on the effectiveness of or the comparison among instructional techniques, curriculum, or classroom management.

(3) Research involving solely the use of standard educational diagnostic, aptitude, or achievement tests, if information taken from these sources is recorded in such a manner that subjects cannot be reasonably identified, directly or through identifiers linked to the subjects.

(4) Survey activities involving solely product or marketing research, journalistic research, historical research, studies of organizations, public opinion polls, or management evaluations, in which the potential for invasion of privacy is absent or minimal.

(5) Research involving the study of documents, records, data sets or human materials, when the sources or materials do not contain identifiers or cannot reasonably be linked to individuals.

(6) Research involving solely a combination of any of the activities described above.

(d) The Secretary has final authority to determine whether an activity is exempt from these regulations under paragraph (b), and may override an institution's decision, for example, that the activity is exempt.

(e) The Secretary may require that specific research or nonresearch activities or classes of research or nonresearch activities conducted or supported by the Department, but not otherwise covered by these regulations, comply with these regulations.

(f) The Secretary may also exempt specific activities or classes of activities, otherwise covered by these regulations, from some or all of these regulations. Notices of these actions will be published in the **Federal Register** as they occur.

(g) Compliance with these regulations will in no way render inapplicable pertinent State or local laws or regulations or other Federal laws or regulations, including those of the Food and Drug Administration bearing upon activities covered by these regulations.

(h) Each subpart of these regulations contains a separate section describing to what the subpart applies. Research which is covered by more than one subpart must comply with all applicable subparts.

§ 46.102 Definitions.

(a) "Secretary" means the Secretary of Health, Education, and Welfare and any other officer or employee of the Department of Health, Education, and Welfare to whom authority has been delegated.

(b) "Department" means the Department of Health, Education, and Welfare.

(c) "Institution" means any public or private entity or agency (including Federal, State, and other agencies).

(d) "Legally authorized representative" means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the particular research or procedure.

(e) "Research" means a formal investigation designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute "research" for purposes of this part, whether or not they are supported or conducted under a program which is considered research for other purposes. For example, some "demonstration" and "service" programs may include research activities.

(f) "Human subject" means an individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the person, or (2) identifiable information.

(g) "Minimal risk" is the probability and magnitude of harm that is normally encountered in the daily lives of healthy individuals, or in the routine medical, dental or psychological examination of healthy individuals.

§ 46.103 Submission of assurances.

(a) Each institution engaged in research covered by these regulations shall provide written assurance satisfactory to the Secretary that it will comply with the requirements set forth in the regulations, including the requirements that: (1) the research will be reviewed by an Institutional Review Board established and operated in accordance with these regulations, and (2) the research will be conducted in accordance with the Board's determinations.

(b) The assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by these regualtions, and shall be filed in such form and manner as the Secretary may prescribe.

§ 46.104 Types of assurances.

(a) *General assurances.* A general assurance is a comprehensive plan for the review and implementation procedures applicable to all research covered by these regulations at a particular institution, regardless of the number, location, or types of its components or field activities. Institutions having a significant number of concurrent research projects involving human subjects will be required to file general assurances.

(b) *Special assurances.* A special assurance describes the review and implementation procedures applicable to, and reports the findings of the Institutional Review Board on, a single research project. Institutions not having on file with the Department an approved general assurance will be required to file special assurances.

(c) *Assurances applicable to research not funded by the Department.* Each institution which applies to the Department for a grant or contract for any research project or program involving human subjects, unless such project or program is an exempted category listed at § 46.101(c), must

provide assurance in a document submitted with its application or proposal that it will comply with § 46.122 of these regulations.

(d) *Department-conducted research.* Research by Department employees must be conducted in conformity with these regulations, except each Principal Operating Component head may adopt such nonsubstantive, procedural modifications as may be appropriate, from an administrative standpoint.

(e) *Awards to individuals.* No individual may receive Department support for research covered by these regulations unless he or she is affiliated with or sponsored by an institution which assumes responsibility for the research under an assurance satisfying the requirements of this part.

§ 46.105 Minimum requirements for general assurances.

In order to satisfy the requirements of these regulations, a general assurance shall provide specifically for the following:

(a) A statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of subjects. This may include appropriate existing codes, declarations, or statements of basic ethical principles, or statements formulated by the institution itself. However, these principles do not supersede Department policy or applicable law.

(b) One or more Institutional Review Boards, each satisfying the requirements of § 46.107 regarding membership and § 46.108 regarding functions.

(c) A list of the Board members identified by name; earned degrees (if any); position or occupation; specialty field (if any); representative capacity; and by other pertinent idications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to Board deliberations. Any employment or other relationship between each member and the institution shall be identified (e.g., full-time employee, part-time employee, member of governing panel or board, stockholder, paid consultant, unpaid consultant). Changes in Board membership must be reported to the Department in such form and at such times as the Secretary may require.

(d) Written procedures which the Board will follow (1) for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution, (2) for determining which projects require review more often than annually and which projects need verification from sources other than the researchers that no material changes have occurred since initial Board review, (3) to insure prompt reporting to the Board of proposed changes in an activity and of unanticipated problems involving risks to subjects or others, and (4) to insure that nay such problems, including adverse reactions to biologicals, drugs, radioisotope labelled drugs, or medical devices, are promptly reported to the Department. These procedures may be promulgated by the institution or by the Board, if this authority is delegated to it by the institution.

(e) Board review of proposed research at convened meetings at which a majority of the members of the Board are present, including at least one member whose primary concerns are in nonscientific areas, except when an approved expedited review procedure is utilized (see § 46.111). In order for the research to be approved, it must receive the approval of a majority of those members present at the meeting. The Board shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure Board approval of the activity. If the Board decided to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

(f) Maintenance of appropriate records, including information on Board members required by paragraph (c), copies of proposals reviewed and approved sample consent forms, minutes of Board meetings, progress reports submitted by investigators, reports of injuries to subjects, and records of continuing review activities. These records must be accessible for inspection by Department representatives and retained for at least five years after completion of the research, or such longer period as may be specified by program requirements. Minutes must be in sufficient detail to show attandance at Board meetings, actions taken by the Board, the number of members voting for and against these actions, and the basis for the actions (including a written summary of the discussion of substantive issues and their resolution).

(g) Provision for meeting space and sufficient staff to support the Board's review and recordkeeping duties.

§ 46.106 Minimum requirements for special assurances.

In order to satisfy the requirements of these regulations, a special assurance shall:

(a) Identify the specific research project covered by the assurance.

(b) Include a statement, executed by an appropriate institutional official, indicating that the institution has established a Board satisfying the requirements of §§ 46.107 and 46.108 and that the Board will follow the procedures set forth in §§ 46.105(d) and 46.105(e).

(c) Describe the makeup of the Board, including the information required by § 46.105(c).

(d) Describe the risks to subjects that the Board recognizes as inherent in the activity, and justify its finding that these risks are reasonable in relation to the anticipated benefits to subjects and the importance of the knowledge to be gained.

(e) Describe the informed consent procedures to be used and attach samples of the documentation to be required under § 46.113.

(f) Describe procedures which the Board will follow to insure prompt reporting to the Board of proposed changes in the activity and of any unanticipated problems, involving risks to subjects or others, and to insure that any such problems, including adverse reactions to biologicals, drugs, radioisotope labelled drugs, or medical devices are promptly reported to the Department.

(g) Maintain appropriate records, including information on Board members required by paragraph (c), copies of proposals reviewed and approved sample consent forms, minutes of Board meetings, progress reports submitted by investigators, reports of injuries to subjects, and records of continuing review activities. These records must be accessible for inspection by Department representatives and retained for at least five years after completion of the research, or such longer period as may be specified by program requirements. Minutes must be insufficient detail to show attendance at Board meetings, actions taken by the Board, the number of members voting for and against these actions, and the basis for the actions (including a written summary of the discussion of substantive issues and their resolution).

(h) Provide for meeting space and necessary staff (if any) to support the Board's review and reporting duties.

§ 46.107 Institutional Review Board membership.

(a) Each Institutional Review Board must have at least five members, with varying backgrounds to promote complete and adequate review of activities commonly conducted by the institution. The Board must be sufficiently qualified through the maturity, experience, and expertise of its members, and the sufficient diversity of the members' racial and cultural backgrounds, to promote respect for its advice and counsel for safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific activities, the Board must be able to ascertain the acceptability of applications and proposals in terms of institutional commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes. The Board must therefore include persons knowledgeable in these areas. If a Board regularly reviews research that has an impact on a vulnerable category of subjects, the Board should have one or more individuals who are primarily concerned with the welfare of these subjects.

(b) No Board may consist entirely of members of one profession, and at least one member must be an individual whose primary concerns are in nonscientific areas (e.g., lawyers, ethicists, members of the clergy).

(c) The membership of the Board may not consist entirely of men or entirely of women.

(a) Each Board shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution. The records of the Board must identify the employment or other relationship between each member and the insitution (e.g., full-time employee, part-time employee, a member of governing panel or board, stockholder, paid consultant, or unpaid consultant).

(e) No member of a Board may participate in the Boards initial or continuing review of any project in which the member has a conflicting interest, or any project involving an investigator who participated in the member's selection for the Board, except to provide information requested by the Board. The Board has responsibility for determining whether a member has a conflicting interest. The Secretary may waive the requirements of this paragraph upon request. Any request should contain information describing the reasons why it is essential for the member to participate in the particular review in question.

(f) A Board may, in its discretion, invite individuals with competence in special areas to assist in the review of complex issues which require expertise beyond or in addition to that available on the Board. These individuals may not vote with the Board.

§ 46.108 Institutional Review Board functions.

In order to fulfill the requirements of these regulations each Institutional Review Board shall:

(a) Review and have authority to approve, require modifications in (to secure approval), or disapprove all research described in § 46.101(a) which is conducted at or sponsored by the institution. [1]

(b) Conduct continuing review (as provided in § 46.105(d)) of research covered by these regulations and have authority to suspend, and if appropriate, terminate approval of research that is not being conducted in accordance with the determination of the Board or in which there is unexpected serious harm to subjects. Any such suspension or termination of approval must be reported promptly to the investigator, appropriate institutional officials, and the Secretary, including a statement of the reasons for the Board's action. As part of its continuing review responsibility, the Board must have authority to observe the consent process or the research itself on a sample or routine basis, or have a third party (not otherwise associated with the research or the investigator) do so. Continuing review shall be undertaken at intervals appropriate to the degree of risk, but not less than once per year.

(c) Be responsible for reporting to the appropriate institutional officials and the Secretary any serious or continuing noncompliance by investigators with the requirements and determinations of the Boards.

(d) Carry out such other duties as may be assigned by the institution or the Secretary.

§ 46.109 Evaluation and disposition of assurances.

(a) The Secretary will evaluate all assurances submitted in accordance with § 46.105 and § 46.106 through such officers and employees of the Department and such experts or consultants engaged for this purpose as the Secretary determines to be appropriate. The Secretary's evaluation will take into consideration the adequacy of the proposed Institutional Review Board in the light of the anticipated scope of the institution's activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution.

(b) On the basis of this evaluation, the Secretary may approve or disapprove the assurance, or enter into negotiations to develop an approvable one. The Secretary may limit the period during which any particular approved assurance or class of approved assurances shall remain effective or otherwise condition or restrict approval. The Secretary may, pending completion of negotiations for a general assurance, require an institution otherwise eligible for such assurance, to submit special assurances.

§ 46.110 Review of proposed research by the Institutional Review Board.

(a) Except as provided in this section or § 46.111, the Department will conduct or support research covered by these regulations only if the institution has an assurance approved under § 46.109, and only if the institution has certified to the Secretary that the research has been reviewed and approved by the Institutional Review Board provided for in the assurance. In order to give its approval, the Board must determine that all of the following requirements are satisfied:

(1) The research methods are appropriate to the objectives the research and the field of study.

(2) Selection of subjects is equitable, taking into account the purposes of the research.

(3) Risks to subjects are minimized by using the safest procedures consistent with sound research design and, whenever appropriate, by using procedures already being performed for diagnostic or treatment purposes.

(4) Risks to subjects are reasonable in relation to anticipated benefits to subjects and importance of the knowledge to be gained. In making this determination, the Board should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits the subjects would be exposed to or receive even if not participating in the research), Also, the Board should not consider possible effects of applying knowledge gained in the research as among those research risks which fall within the purview of its responsibility.

(5) Informed consent will be sought from each prospective subject or his or

[1] Where applicable, the Board shall also review other research, described at § 46.101(b), which is conducted at or sponsored by the institution.

her legally authorized representative, in accordance with, and to the extent required by, § 46.112.

(6) Informed consent will be appropriately documented, in accordance with, and to the extent required by, § 46.113.

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

(8) There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(9) Applicable regulations for the protection of fetuses, pregnant women, children, prisoners, and those institutionalized as mentally disabled are satisfied.

(b) Within 60 days after the date of submission of an application or proposal, an institution with a general assurance must certify that the application or proposal has been reviewed and approved by the Board. Other institutions must certify that the application or proposal has been approved by the Board within 30 days after receipt of a request for such a certification from the Department. If the certification is not submitted within these time limits, the application or proposal may be returned to the institution.

(c) Department funds may not be used to support research covered by these regulations until certification of the Board's review and approval (under this section or § 46.111) is received by the Department from the institution; except that only Board review (but not approval) will be required for research projects which the Secretary is specifically directed by statute to carry out.

§46.111 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

(a) The Secretary will publish in the **Federal Register** a list [1] of categories of research, involving no more than minimal risk, that may be reviewed by the Institutional Review Board through an expedited review procedure. The Secretary will amend this list, as appropriate, through republication in the **Federal Register.**

(b) A Board at an institution with an approved general assurance may review some or all of the research appearing on the list through an expedited review procedure. The Board may also use the expedited review procedure to review minor changes in previously approved research. However, the institution must describe the Board's expedited review procedure in its general assurance.

(c) Under an expedited review procedure, the review may be carried out by the Board chairperson or by one or more experienced reviewers designated by the chairperson from among members of the Board. The reviewer has authority to approve the research if it meets the requirements set forth in § 46.110, to request the investigator to modify the research, or to refer the proposal to the Board for full review. If the reviewer has any significant doubt about whether the research should be approved, it should be referred to the Board for full review.

(d) The Secretary may restrict, suspend, or terminate an institution's or Board's right to use an expedited review procedure when necessary to protect the rights of subjects.

§ 46.112 Informed consent.

(a) Except as provided elsewhere in this section, no subject may be involved in research covered by these regulations without the legally effective informed consent of the subject or the subject's legally authorized representative. This consent shall be sought under circumstances that provide the subject (or the subject's legally authorized representative) sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the subject's legally authorized representative must be in a language understandable to the subject or the legally authorized representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the subject's legally authorized representative is made to waive, or to appear to waive, the subject's legal rights, including any release of the institution or its agents from liability for negligence.

(1) *Basic elements of informed consent.* In seeking informed consent, the following information shall be provided:

(A) A statement that the activity involves research, and that the Institutional Review Board has approved the solicitation of subjects to participate in the research;

(B) An explanation of the scope, aims, and purposes of the research, and the procedures to be followed (including identification of any treatments or procedures which are experimental), and the expected duration of the subject's participation;

(C) A description of any reasonably foreseeable risks or discomforts to the subject (including likely results if an experimental treatment should prove ineffective);

(D) A description of any benefits to the subject or to others which may reasonably be expected from the research;

(E) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(F) A statement that new information developed during the course of the research which may relate to the subject's willingness to continue

[1] The Department proposes to include the following procedures in the list to be promulgated under this section:

"Research in which the only involvement of human subjects will be in one or more of the following activities (carried out through standard methods):

(1) Collection (in a nondisfiguring manner) of hair, nail clippings, and deciduous teeth.

(2) Collection of excreta and external secretions including sweat, saliva, placenta expelled at delivery, umbilical cord blood after the cord is clamped at delivery, and amniotic fluid at the time of artificial rupture of the membrane prior to or during labor.

(3) Recording of data from adults through the use of physical sensors that are applied either to the surface of the body or at a distance and do not involve input of matter or significant amounts of energy into the subject or an invasion of the subject's privacy. Such procedures include weighing, electrocardiogram, electroencephalogram, thermography, detection of naturally occurring radioactivity, diagnostic echography, and electroretinography.

(4) Collection of blood samples by venipuncture, in amounts not exceeding 450 milliliters in a six-week period and no more often than two times per week, from subjects 18 years of age or older who are not anemic, pregnant, or in a significantly weakened condition.

(5) Collection of both supra- and subgingival plaque, provided the procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques.

(6) Voice recordings made for research purposes such as investigations of speech defects.

(7) Moderate exercise by healthy volunteers.

(8) Program evaluation activities that entail no deviation for subjects from the normal requirements of their involvement in the program being evaluated or benefits related to their participation in such program."

Note.— [The Department would add the following procedures to the above list if Alternative B under § 46.101(b) is adopted:

(9) Survey activities in which responses are recorded in such a manner that individuals cannot reasonably be identified or in which the records will not contain sensitive information about the individuals.

(10) Research activities involving the observation of human subjects carrying out their normal day-to-day activities, where observations are recorded in such a manner that individuals cannot reasonably be identified.

(11) Research involving the study of documents, records, data sets, or human materials where the sources contain identifiers, but the researcher will take information from them in such a way as to prevent future identification of any individual.]

participation will be provided to the subject;

(G) A statement describing the extent to which confidentiality of records identifying the subject will be maintained.

(H) An offer to answer any questions the subject (or the subject's representative) may have about the research the subject's rights, or related matters;

(I) For research involving more than minimal risk, an explanation as to whether conpensation and medical treatment are available if injury occurs and, if so, what they consist of or where further information may be obtained;

(J) Who should be contacted if harm occurs or there are questions or problems; and

(K) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(2) *Additional elements.* When appropriate, the Institutional Review Board shall require that some or all of the following elements of information also be provided:

(A) A statement that the particular treatment or procedure being tested may involve risks to the subject (or fetus, if the subject is pregnant or becomes pregnant) which are currently unforeseeable. This statement will often be appropriate in connection with tests of experimental drugs, or where the subjects are children, pregnant women, or women of childbearing age.

(B) Foreseeable circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

(C) Any additional costs to the subject or others that may result from their participation in the research.

(D) Who is conducting the study, the approximate number of subjects involved, the institution responsible for the study, and who is funding it.

(E) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

(b) The Board may approved a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in paragraph (a), provided the Board finds (and documents) the following:

(1) The withholding or altering will not materially affect the ability of the subject to assess the harm or discomfort of the research to the subject or others;

(2) Sufficient information will be disclosed to give the subject a fair opportunity to decide whether or not to participate;

(3) The research could not reasonably be carried out without the withholding or alteration;

(4) Information is not withheld or altered for the purpose of eliciting participation; and

(5) Whenever feasible the subject will be debriefed after his or her participation.

(c) Nothing in these regulations is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable (e.g., State or local) law.

§ 46.113 Documentation of informed consent.

(a) Except as provided in paragraph (b), informed consent shall be documented in writing (and a copy provided to the subject or the subject's legally authorized representative) through either of the following methods:

(1) A written consent document embodying the elements of informed consent. This may be read to the subject or to his or her legally authorized representative, but in any event the subject or his or her legally authorized representative must be given adequate opportunity to read it. This document is to be signed by the subject or his or her legally authorized representative, and a copy supplied to the subject or representative. The Board shall retain approved sample copies of the consent form.

(2) A "short form" written consent document indicating that the elements of informed consent have been presented orally to the subject or his or her legally authorized representative. Written summaries of what is to be said to the subject (or representative) are to be approved by the Board. The short form is to be signed by the subject or his or her legally authorized representative and by a witness to the oral presentation and to the subject's signature, or that of the representative. A copy of the approved summary is to be signed by the persons officially obtaining the consent and by the witness. Copies of the form and the summary shall be provided to the subject or representative. The Board shall retain approved sample copies of the consent form and the summaries.

(b) The Board may waive the requirement for the researcher to obtain documentation of consent for some or all subjects if it finds (and documents) either:

(1) That the only record linking the subject and the research would be the consent document, the only significant risk would be potential harm resulting from a breach of confidentiality, each subject will be asked whether he or she wants there to be documentation linking the subject with the research, and the subject's wishes will govern; or

(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In many cases covered by this paragraph it may be appropriate for the Board to require the investigator to provide subjects with a written statement regarding the research, but not to request their signature, or to require that oral consent be witnessed.

(c) In those cases when new information is provided to the subject during the course of the research, the information shall be reviewed and approved by the Board and a copy retained in its records.

§ 46.114 Applications and proposals lacking definite plans for involvement of human subjects.

Certain types of applications for grants or contracts are submitted to the Department with the knowledge that subjects may be involved within the support period, but definite plans would not normally be set forth in the application or proposal. These include such activities as institutional type grants (including bloc grants) where selection of specific projects is the institution's responsibility; training grants where the activities involving subjects remain to be selected and projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. These applications need not be reviewed by an Institutional Review Board before an award may be made. However, except for research described in § 46.101(c), no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the Institutional Review Board, as provided in these regulations, and certification submitted to the Department.

§ 46.115 Research undertaken without the intention of involving human subjects.

In the event research (conducted or supported by the Department) is undertaken without the intention of involving human subjects, but it is later

proposed to use human subjects in the research, the research must first be reviewed and approved by the Institutional Review Board, as provided in these regulations, a certification submitted to the Department, and final approval given to the proposed change by the Department.

§ 46.116 Evaluation and disposition of applications and proposals.

(a) The Secretary will evaluate all applications and proposals involving human subjects submitted to the Department through such officers and employees of the Department and such experts and consultants as the Secretary determines to be appropriate. This evaluation will take into consideration the apparent risks to the subjects, the adequacy of protection against these risks, the potential benefits of the proposed research to the subjects and to others, and the importance of the knowledge to be gained.

(b) On the basis of this evaluation, the Secretary may approve or disapprove the application or proposal, or enter into negotiations to develop an approvable one.

§ 46.117 Cooperative research projects.

(a) Cooperative research projects are those projects, normally supported through grants, contracts, or similar arrangements, which involve institutions in addition to the grantee or prime contractor (such as a contractor with the grantee or a subcontractor with the prime contractor). In such instances, the grantee or prime contractor remains responsible to the Department for safeguarding the rights and welfare of subjects. However, except as provided in paragraph (b), when cooperating institutions in fact conduct some or all of the research involving some or all of these subjects, each cooperating institution must comply with these regulations as though it received support for its participation in the project directly from the Department.

(b) With prior approval by the Secretary, institutions involved in cooperative research projects may comply with these regulations through joint review or other arrangements aimed at avoidance of duplication of effort.

§ 46.118 Investigational new drug 30-day delay requirement.

Where an institution is required to prepare or to submit a certification under these regulations and the application or proposal involves an investigational new drug within the meaning of the Food, Drug, and Cosmetic Act, the drug must be identified in the certification together with a statement that the 30-day delay required by 21 CFR 312.1(a)(2) has elapsed and the Food and Drug Administration has not, prior to expiration of such 30-day interval, requested that the sponsor continue to withhold or to restrict use of the drug in human subjects; or that the Food and Drug Administration has waived the 30-day delay requirement: Provided, however, that in those cases in which the 30-day delay interval has neither expired nor been waived, a statement shall be forwarded to the Department upon such expiration or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received.

§ 46.119 Confidentiality of records.

Except as otherwise provided by Federal, State, or local law, information in the records or possession of an institution acquired in connection with an activity covered by these regulations (including all subparts of these regulations), which information refers to or can be identified with a particular subject, may not be disclosed except:

(a) With the consent of the subject or his legally authorized representative; or

(b) As may be necessary for the Secretary to carry out his responsibilities.

§ 46.120 Use of Federal funds.

Federal funds administered by the Department may not be expended for research involving human subjects unless the requirements of these regulations (including all subparts of these regulations) have been satisfied.

§ 46.121 Early termination of research support; evaluation of subsequent applications and proposals

(a) If, in the judgment of the Secretary, an institution has failed materially to comply with the terms of these regulations (including any subpart of these regulations), with respect to any particular research project, the Secretary may require that Department support for the project be terminated or suspended in the manner prescribed in applicable program requirements.

(b) In making decisions about funding applications or proposals covered by these regulations (including any subpart of these regulations), the Secretary may take into account, in addition to all other eligibility requirements and program criteria, such factors as: (1) Whether the applicant has been subject to a termination or suspension under paragraph (a) of this section; (2) whether the applicant or the person who would direct the scientific and technical aspects of an activity has in the judgment of the Secretary failed materially to discharge his, her, or its responsibility for the protection of the rights and welfare of subjects in his, her, or its care (whether or not Department funds were involved): and (3) whether, where past deficiencies have existed in discharging this responsibility, adequate steps have in the judgment of the Secretary been taken to eliminate these deficiencies.

§ 46.122 Research not conducted or supported by the Department.

Except for the categories of research exempted under § 46.101(c), prior and continuing review and approval by an Institutional Review Board is required for the conduct of all research involving human subjects not funded by the Department, if the research is conducted at or supported by any institution receiving funds from the Department for the conduct of research involving human subjects.

§ 46.123 Conditions.

The Secretary may with respect to any research project or any class of research projects impose additional conditions prior to or at the time of funding when in the Secretary's judgment conditions are necessary for the protection of human subjects.

[FR Doc. 79-24788 Filed 8-13-79; 8:45 am]

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Food and Drug Administration

[21 CFR Parts 16, 56, 71, 171, 180, 310, 312, 314, 320, 330, 361, 430, 431, 601, 630, 1003, and 1010]

[Docket No. 77N-0350]

Standards for Institutional Review Boards for Clinical Investigations; Withdrawal of Proposal

AGENCY: Food and Drug Administration.

ACTION: Withdrawal of Proposal.

SUMMARY: The Food and Drug Administration (FDA) is withdrawing a proposal to establish standards for institutional review boards (IRB's) which review clinical investigations regulated by FDA. The National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research (National Commission) published its IRB report after FDA published its IRB proposal. FDA is withdrawing its IRB proposal and issuing a new proposal that reflects a

Appendix N

Domestic FWA Filing Sample

OMB No. 0990-0278
Approved for use through May 31, 2011

Federalwide Assurance (FWA) for the Protection of Human Subjects for Institutions Within the United States

[ ] New Filing **[ ] Update or Renewal for FWA Number: _____**

1. Institution Filing Assurance

Legal Name:

City: State:

HHS Institution Profile File (IPF) code, if known:

Federal Entity Identification Number (EIN), if known:

If this Assurance replaces an MPA or CPA, please provide the "M" or "T" number:

2. Institutional Components

List below all components over which the Institution has legal authority that operate under a different name. Also list with an asterisk (*) any alternate names under which the Institution operates. The Institution should have available for review by the Office for Human Research Protections (OHRP) upon request a brief description and line diagram explaining the interrelationships among the Assurance Signatory Official, the Institutional Review Board(s) (IRB), IRB support staff, and investigators in these various components.

NOTE: The Signatory Official signing this Assurance must be legally authorized to represent the Institution providing this Assurance and all components listed below. Entities that the Signatory Official is not legally authorized to represent may not be listed here without the prior approval of OHRP.

[ ] Please check here if there are no such components or alternate names.

Name of Component or Alternate Names Used	City	State (or Country if Outside U.S.)

3. Statement of Principles

This Institution assures that all of its activities related to human subjects research, regardless of the source of support, will be guided by the ethical principles in the following document(s): (*indicate below*)

[ ] *The Belmont Report*
[ ] *Other: (Please submit copy to OHRP with this Assurance)*

http://www.hhs.gov/ohrp/humansubjects/assurance/filasur.htm[12/15/2010 9:06:51 PM]

4. Applicability

(a) This Institution assures that whenever it engages in human subjects research conducted or supported by any federal department or agency that has adopted the Federal Policy for the Protection of Human Subjects, known as the Common Rule, the Institution will comply with the **Terms of the Federalwide Assurance for Institutions Within the United States (contained in a separate document on the OHRP website)**, unless the research is otherwise exempt from the requirements of the Common Rule or a department or agency conducting or supporting the research has determined that the research shall be covered by a separate assurance.

(b) *Optional:* This Institution elects to apply the following to all of its human subjects research regardless of the source of support, except for research that is covered by a separate assurance:

[ ] *The Common Rule (see section 3 of the Terms of the FWA for Institutions Within the United States for a list of departments and agencies that have adopted the Common Rule and the applicable citations to the Code of Federal Regulations)*

[ ] *The Common Rule and subparts B, C, and D of the HHS regulations at 45 CFR part 46*

5. Designation of Institutional Review Boards (IRBs)

This Institution designates the following IRB(s) for review of research under this Assurance *(if the IRB has not previously registered with HHS or has not provided a membership roster to HHS, please submit to OHRP the appropriate IRB registration materials which are available on the OHRP website)*.

NOTE: Reliance on the IRB of another institution or organization or an independent IRB must be documented by a written agreement that is available for review by OHRP upon request. OHRP's sample IRB Authorization Agreement may be used for this purpose, or the parties involved may develop their own agreement. Future designation of other IRBs requires an update of the FWA.

HHS IRB Registration Number	Name of IRB as Registered with HHS

6. Human Protections Administrator (e.g., Human Subjects Administrator or Human Subjects Contact Person)

First Name: Middle Initial: Last Name:

Degrees or Suffix: Institutional Title:

Institution:

Telephone: FAX: E-Mail:

Address:

City: State: Zip Code:

7. Signatory Official (i.e., Official Legally Authorized to Represent the Institution)

I understand that the Assurance Training Modules on the OHRP website describe the responsibilities of the Signatory Official, the IRB Chair(s), and the Human Protections Administrator under this Assurance. Additionally, I recognize that providing research investigators, IRB members and staff, and other relevant personnel with appropriate initial and continuing education about human subject protections will help ensure that the requirements of this Assurance are satisfied.

Acting officially in an authorized capacity on behalf of this Institution and with an understanding of the Institution's responsibilities under this Assurance, I assure protections for human subjects as specified above. The IRB(s) designated above are to provide review for all research to which this Assurance applies. The designated IRB(s) will comply with the **Terms of the Federalwide Assurance for Institutions Within the United States** and possess appropriate knowledge of the local context in which this Institution's research will be conducted.

All information provided with this Assurance is up-to-date and accurate. *I am aware that false statements could be cause for invalidating this Assurance and may lead to other administrative or legal action.*

Signature _____ Date: _____

First Name: Middle Initial: Last Name:

Degrees or Suffix: Institutional Title:

Institution:

Telephone: FAX: E-Mail:

Address:

City: State: Zip Code:

NOTE: Institutions operated by the U.S. Government may need to obtain department or agency clearance prior to submission of the FWA to OHRP. Please contact the relevant department or agency Human Subject Protections Officer before forwarding this Assurance to OHRP.

8. FWA Approval

The Federalwide Assurance for the Protection of Human Subjects for Institutions Within the United States submitted to HHS by the above Institution is hereby approved.

Assurance Number: Expiration Date:

Signature of HHS Approving Official: _____ Date:_____

Public burden for this collection of information is estimated to average two hours for a new FWA filing and less than an hour for an FWA renewal or update. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: OS Reports Clearance Officer, Room 537H, 200 Independence Avenue, SW., Washington, DC 20201. *Do not return the completed form to this address.*

Appendix O

Written Testimony

Felice J. Levine, PhD
American Sociological Association
on behalf of the
Consortium of Social Science Associations
in Cooperation with the American Sociological Association

Submitted to

The Committee on Assessing the System for Protecting Human Research Subjects
The Institute of Medicine
The National Academies
January 31, 2001

Written Testimony Felice J. Levine, PhD American Sociological Association on behalf of the Consortium of Social Science Associations in Cooperation with the American Sociological Association Submitted to The Committee on Assessing the System for Protecting Human Research Subjects The Institute of Medicine The National Academies January 31, 2001

Dr. Federman and Members of the Committee:
Thank you very much for the opportunity to submit comments on the draft accreditation standards regarding the protection of human participants in research. As Executive Officer of the American Sociological Association and as a member of the Executive Committee of the Consortium of Social Science Associations (COSSA), I am pleased to be able to do so on behalf of COSSA. COSSA is an advocacy organization for the social and behavioral sciences, supported by over 105 professional associations, scientific societies, universities, and research institutes.

COSSA appreciates the opportunity to talk about some of the issues and challenges for the social and behavioral sciences under the proposed standards of accreditation for the protection of human subjects in research. COSSA believes in promoting sound science with sound ethical practices. Most of our professional associations have developed ethical guidelines for researchers to follow in conducting their studies, particularly where human subjects are part of the research design. All embrace the Belmont Report's admonitions of respect for persons, beneficence, and justice. We are, however, concerned with the growing fault lines in the system that protects human subjects and by the gap that has developed between law and policy on-the-books and in-action. For example, researchers utilizing secondary data are being asked to seek approval by IRBs to use these data where the information is in anonymous form and where subjects are already protected under earlier protocols. We hope the Committee will examine such issues closely, not only in assessing these draft standards, but also in your larger study of the whole system of protecting human research participants.

For the social and behavioral sciences, the overall problem with the system is the attempt to fit our research into a framework that was over specified and designed for biomedical-

clinical research. The presence of IRBs in academic and other research organizations dates back to 1974 when Federal guidelines were established for the protection of human subjects. While social and behavioral science research was included from the outset, much of the impetus for such guidelines grew out of concerns about informed consent and risks involved in biomedical research. Despite the passage of time, this model of science continues to color the operations of the system, the understanding of best ethical practices, and the functioning of Institutional Review Boards (IRBs). The proposed standards that we are here to discuss today provide further evidence of this inherent problem. If these standards are intended to be universal and fit all research involving human participants, then they need to be framed in a way that meaningfully includes all research fields. Standing alone, for example, the very long mention at the beginning of Section 3 of Henry Beecher and his 1966 article on "Ethics and Clinical Research" focuses too exclusively on physicians and on "performing experiments" on humans. This type of preamble sends the wrong signal. We need to take this opportunity to send inclusive signals about a broader band of research involving humans.

Before offering our specific observations of the draft accreditation standards, we address some general concerns about the standards and about the system for protecting human research subjects. We have framed our observations as a series of ten recommendations. Most are broadly applicable to accreditation and the overall system; some deal with issues that are particularly important for improving the ethical consideration of research in the social and behavioral sciences. We believe that these recommendations could and should usefully guide the IOM Committee in both the assessment of the system and the development of accreditation standards.

GENERAL RECOMMENDATIONS

1) Seize the Moment for Effective Leadership on Behalf of All Science. IOM has the opportunity to provide guidance on an accreditation system and a human research participant protection system that effectively reaches to all areas of scientific research and effectively serves all Federal funding agencies engaged in the support of such research-not just the biomedical sciences. The social and behavioral sciences have been committed to this system and its objectives, but often, in practice, the ethical requirements of our sciences have not been consistently and effectively understood.

2) There is Virtue to Moving Ahead, but There is Also Virtue to Slowing the "Train" Sufficiently to Ensure We Can Turn a New Corner. If the standards for accreditation are to be more effective than the current process for obtaining assurances of compliance under the Common Rule, then the two important IOM studies yet to be undertaken should logically proceed before the final crafting and finalizing of accreditation standards. Simply put, perhaps the final accreditation standards should follow after studies two and three and not before.

3) Where's the Fit? The proposed accreditation standards integrate many pieces of the Common Rule but use these regulations in a different context and often coupled with other ideas. Accreditation standards should accredit to the regulations in place; the goal of accreditation is to ensure that the regulations are followed, not to produce additional regulations. The disjuncture between the Common Rule and the accreditation standards needs careful analysis. It may be wisest to have accreditation standards that ensure the effective implementation of the Common Rule guidelines. Then, perhaps as part of introducing accreditation standards, an evaluation could be undertaken to assess whether the system is working effectively and what gaps exist. The problem in the past has been less the actual rules governing the human research protection system than implementation of them.

4) The Devil is in the Details. The proposed accreditation standards are not per se couched in the language of any one science or arena of research, but, when coupled with the Commentary, these standards are quite biomedical and heavily clinical and pay only lip service to other substantive arenas of work. This is especially problematic for the social and behavioral sciences. Will the Commentary be presented? If so, the role of the Commentary needs to be clear, and the examples across areas of research need to be specified.

5) While Good Ethics Makes for Good Research, Judgments of Best Ethical Practices are Distinct from Judgments about the Quality of the Research. The proposed accreditation standards overreach to what constitutes quality science and do not sufficiently distinguish between those judgments and what constitutes ethical practices in science. Standards shift from the criteria for the accreditation of IRBs to the assessment of the research and the researcher. The standards need to emphasize accrediting the structure put in place and the procedures to be followed for the
protection of human participants in research.

6) Clarity, Simplicity, and Transparency are Fundamental to Accreditation Standards of Excellence. Many of the standards require judgments that are impossible to make. The standards should not tell an institution how it should achieve its goals, but should set forth what the standards or goals are. The standards should focus on the actual facts of what is required and not engage in standard setting or determinations that are highly subjective or elusive. The Commentary is often so detailed that, by omission, it is limiting in its scope; at other points, the standards are so vague as to be subject to widely different interpretations. Ironically, the movement to accreditation in large part aims to transcend such problems-with the promulgation of reproducible standards intended to be the backbone.
http://www.cossa.org/humanparticipants.html

7) The Educative Role of Accreditation Standards Can be More Powerful than its Regulatory or Enforcement Functions. We know from research on compliance and non-compliance, that the primary power of a rule system is in its moral persuasion and educative effects. Yet, the proposed accreditation standards, especially the Commentary, provide little education for IRBs regarding how the human research protection system should operate-especially for the social and behavioral sciences.

8) Less Can be More: Accreditation Standards Should Ensure that the Human Research Protection System Does Not Overreach Its Role and that it Stays on Task. The human research protection system needs to ensure that research proceeds and knowledge is advanced in accordance with the highest standards of ethical practice with respect to human subjects protection. The system needs also to ensure that work that comports to ethical standards is facilitated and not impeded by the process. For example, research involves risk at various levels-standards should hold IRBs to the task of effectively implementing what was intended to be exempt or expedited and what requires full review. Consent is another area where IRBs need to have knowledge about how to undertake research ethically. Studies of runaway youth, for example, raise different issues about parental consent than do observational studies of
preschoolers in a classroom.

9) Human Research Participants Refer to Actual Participation in a Study Underway or Being Proposed. The accreditation standards need to make clear to IRBs what the scope of the human research protection system is and is not. The analysis, for example, of public use data or public use files where information is maintained in anonymous form and without personal identifiers is research about people but not on people. The definition

of human subjects under the Common Rule defines the scope of its purview as research on living individuals when an investigator obtains data through an intervention or interaction or obtains identifiable private information. For a human research protection system to focus on this domain and to do it well-with appropriate attention to level of risk-is to achieve an important goal.
10) Focus on the Ethical Considerations regarding Human Research Participants in Various Types of Research. The answer to concerns in the social and behavioral sciences is not to create a dual human research protection system but to ensure a system that is more sophisticated about ethical practices across fields of science. Social and behavioral science research is increasingly interdisciplinary within fields and across especially biomedical, environmental, public health, and engineering fields. Separation of the review by field could create redundancy and limit researchers mutually benefiting from the ethical expertise of each other. But, this puts a burden on ensuring that an altered human research protection system includes the necessary and appropriate expertise on ethical practices in the social and behavioral sciences. The composition of IRBs is very important; other parts of the system also need to be savvy about ethical practices in the social and behavioral sciences.

SPECIFIC ILLU.S.TRATIVE CONCERNS
Our general recommendations raise questions that speak to the overall thrust, tone, scope, and reach-if not overreaching-of the accreditation standards as currently crafted. They also speak to how and when the IOM might be best situated to develop and recommend accreditation standards for Institutional Review Boards. Because our general concerns speak to each of the standards, we offer below some illustration of the type of revisions and development work that would be required in any revision process.

Section on Principles Underlying . . . . should be expanded to set the tone of what is meant to be included within the scope of the Belmont Report and the Common Rule (45 CFR Part 26). Note, for example, the reference in paragraph two to only "experimental subjects." This should be changed to "who agree to be research participants (subjects)" or similar language.

Definitions should explicitly include "colleges and universities" not just "universities."
Proposed Standard 1.7 calls for the review of the policies and procedures of the Human Research Protection Plan. We suggest that it include a clause that periodic review must include input from the scientific community and researchers as to whether the policies and procedures are effectively protecting research participants and enabling the progress of
research.

Proposed Standard 1.9 would benefit from explicit recognition of the social and behavioral sciences. The language and Commentary of 1.9 should be appropriately amended. Such a modification would make clear that the social and behavioral sciences are different from the biomedical/clinical sciences and that, in a meaningful protection of research participants, ethical principles need to be applied and implemented appropriate to the substance and methodologies of the work. We urge that the Human Research Protection Plan recognize that research in the social and behavioral sciences often involves different situations (from clinical experiments) regarding the protection of human subjects. The Plan could allows for specialty IRBs or certainly IRBs with appropriate expertise in the social and behavioral sciences and ethical practices therein.

Proposed Standard 1.11 should make clear that expertise for the chair needs to include expertise regarding ethical issues as they pertain to human participants in social and behavioral science research. Language could be added to the effect of "across all fields

of science germane to the work of the IRB." As in the Commentary, perhaps the proposed standard should refer to both the chair and the members. The Commentary can make clear that every chair cannot be expert in the specifics of all arenas of inquiry, but that chairs need to display a breadth of interest and exposure that signals knowledge and openness across fields. Also, the reference to "organization culture" seems superfluous to an accreditation standard. It is not clear how one would measure "their [IRB chairs] contribution to the organization's culture." It is also unclear why this determination is included in the Commentary and the fit between this language and requirements for assurances under the Common Rule.

Proposed Standard 1.14 focuses on the performance of an organization's HRPP-emphasizing the importance of assessment and evaluation. The Commentary, however, should refer only to the HRPP overall and the IRBs, not to the investigator. The evaluation, of course, focuses on whether the HRPP is effectively performing its functions of protecting human participants in research and thus necessarily examines how the system identifies and deals with problems. The Commentary, however, should not imply that there is a further assessment of the performance of investigators beyond examining how the system operates with respect to the ethical monitoring of investigations. Also, the Commentary should not explicitly cite any group like PRIM&R and what roles it might perform because such roles are not mandated by the accreditation process. Also, the Commentary should allow for successful assessments
and how they will be duly recorded and reported.

Proposed Standard 1.15 does not recognize the breadth and nature of communities of research when it charges this function to the "organization." As currently written, the proposed standard seems also to confuse an implied "local" community with populations at risk and groups requiring special sensitivity because of their vulnerabilities. If it is to be retained as a standard, it needs to be clear how community is defined. Does it include international communities in multi-national research? Unlike in clinical trials where the subject population might be drawn from the proximal community, in the social and behavioral sciences, the sites for research and the locations of relevant research participants and research communities can be geographically wide ranging. Typically samples are drawn not based on geographic convenience to the investigator, but on the substantive ideas motivating the research. Researchers need to demonstrate sensitivity to relevant research communities, but it is unclear how or why the "organization" would be charged with doing so. Therefore, as an accreditation standard for HRPP, this should be deleted.

Proposed Standard 2.3 has examples in the Commentary that could usefully be broadened. The Commentary should also use explicit language that signals the social and behavioral sciences. Here and throughout "i.e." is used when it seems that "e.g." is meant.

Proposed Standard 2.4 seems to focus on traits beyond substantive expertise in relevant ethical areas embraced by the IRB. Why is this section necessary as an accreditation standard, how does it link to the assurances specified in the Common Rule, and what does it add beyond Proposed Standard 1.11? Especially in the Commentary, it reads far too much like a job description. The accreditation standards need to focus on required structures and processes; it seems unnecessary and unwise to frame the standards in terms of personality attributes of those who serve. The Standard itself talks about "sufficient respect" and other elusive traits which we believe are far too subjective and not very
useful. Therefore, we recommend that this whole section should be eliminated.

Proposed Standard 2.5 and the Commentary could usefully signal the breadth of research involving human subjects. The text should read: The IRB administrator, staff, chair(s), and Board members must possess and maintain knowledge, skills and abilities appropriate to the actual conduct of research across all areas of study with human subjects. IRB chairs and members should be encouraged to attend scientific society meetings and their ethics workshops so that they understand the ethical requirements put on the researcher by his/her professional community. Language in Commentary should not explicitly privilege-even by example-any one certification process like CCIP. Standards should be neutral on their face and should not promote any specific programs.

Proposed Standards 2.8 and 2.9 should be in reverse order. The appropriateness of the consent process should take precedence over the legibility of the consent documents.

Proposed Standard 2.10 needs clarification. The Commentary is misguided. The IRB should not be determining who should serve as principal investigator and whether that person is qualified to lead a research project. That should be left to peer review of the substance of the research itself. The IRBs' attention should be directed to the processes and procedures to be followed for the protection of human research participants. The language could usefully be modified from "to be responsible for the research" to "to be responsible for the protection of human subjects involved in the conduct of the research." This standard is a further location where the breadth of the fields could be signaled and the
social and behavioral sciences more explicitly included.

Proposed Standard 2.11 and specifically its opening Commentary should include a wide array of examples that go beyond health and visibly include examples from the social and behavioral sciences on health and other issues. For example, written specific guidelines for IRBs would be useful in the area of survey research (including with respect to different populations), and IRBs would benefit from being better informed (and having greater expertise) regarding how risk or adverse circumstances may be different in survey research. As elsewhere, the current examples (after the "i.e.," are essentially all clinical or biomedical.)

Proposed Standard 2.11 (E) (F) essentially has no Commentary. This is an area where the accreditation standards can ensure that the HRPP system and the operations of IRBs reach-not overreach-to what is meant to be included. The specification of Commentary here could usefully educate IRBs about human subjects protection with respect to a considerable amount of work in the social and behavioral sciences. Research qualified for exemption or expedited review needs to be explicitly stipulated and reference made to the Common Rule.

Proposed Standard 2.12 and 2.13 could usefully be aligned with the Common Rule; in their present form, they are too prescriptive. They should be simplified so that the goals and purposes of the IRB record keeping are clear and so that someone not party to the process or the meeting could be expected to understand what has happened and why. Proposed Standard 3, as noted above, needs to have the General Commentary recast to explicit capture all fields of research, not just the biomedical and clinical fields. In Commentary about investigators, all researchers and all IRBs need to see that these accreditation standards includes social and behavioral science research and other germane fields.

Proposed Standard 3.4 needs to explicitly account for exempt research and the alignment between the responsibility of the IRBs and the investigators. Also, the

Commentary gives final authority to the IRBs. We recommend that the IRB should not have the sole authority in the organization to determine what constitutes protection of human participants in research. There should be some avenue of appeal of IRB decisions. Thus, if an IRB determined that a given project, such as secondary analysis of data, should not be exempt, there needs to be another body where the researcher can make his/her case and which is charged with determining if the IRB operated consistent with regulations.

Proposed Standard 3.5 substantially overlaps Standard 2.10, which, as noted earlier, needs clarification. The one difference is the emphasis on "delegation." Were this Standard to be retained, it should read: "Principal Investigators (PIs) may delegate responsibility for aspects of human subjects protection only to individuals who are qualified through training and experience for this role."

Proposed Standard 3.7 is vague and unclear as to its purpose and intent. It sounds almost like a "litmus test" that goes well beyond the high level of ethical practices that an investigator may set for his or her own research. Furthermore, it is unclear how it would be measured. We recommend that it be eliminated.

CONCLU.S.ION

In addressing both our general recommendations and specific concerns, we in the social and behavioral sciences and in the scientific societies can be very useful. We stand ready to do so under the auspices of COSSA. Other key agencies outside of the health sciences that fund and support research with human participants can also help to bring appropriate knowledge to bear. The National Science Foundation is key in that regard. We believe that such guidance can help structure the next round of revisions for a final set of "testable" accreditation standards. We at COSSA as well as many, many top quality researchers behind us are eager to help in any way we can. Thank you for the opportunity to present our views.

http://www.cossa.org/humanparticipants.html

Appendix P

Office for Human Research Protections (OHRP)
Determination Letters 2000 – 2010

1.	12/04/2000	University of South Florida
2.	12/11/2000	Louisiana State University Medical Center of New Orleans
3.	12/11/2000	The University of Alabama at Birmingham
4.	12/11/2000	University of Wisconsin - Madison
5.	12/12/2000	Yale University
6.	12/12/2000	National Institutes of Health
7.	12/12/2000	State University of New York
8.	12/15/2000	Massachusetts Eye and Ear Infirmary
9.	12/15/2000	Virginia Commonwealth University
10.	12/18/2000	Vanderbilt University
11.	12/20/2000	Yale University
12.	12/20/2000	Washington University School of Medicine
13.	12/22/2000	Wake Forest University
14.	12/22/2000	The University of North Carolina at Chapel Hill
15.	11/03/2000	National Institutes of Health
16.	11/06/2000	University of Arkansas for Medical Sciences
17.	11/08/2000	Yale University
18.	11/13/2000	University of Florida
19.	11/22/2000	University of Missouri - Columbia
20.	11/17/2000	University of South Florida
21.	11/27/2000	University of Rochester
22.	11/27/2000	RAND
23.	11/27/2000	Evanston Northwestern Healthcare Corporation
24.	11/27/2000	Case Western Reserve University
25.	11/27/2000	Raritan Bay Medical Center
26.	11/27/2000	Brown University
27.	11/29/2000	Temple University
28.	11/30/2000	Charles R. Drew University of Medicine and Science
29.	10/03/2000	The Johns Hopkins University
30.	10/03/2000	State University of New York at Binghamton
31.	10/03/2000	Brooke Army Medical Center
32.	10/04/2000	Georgetown University
33.	10/11/2000	Northeast Georgia Health Services
34.	10/11/2000	Evanston Northwestern Healthcare Corporation
35.	10/11/2000	St. Francis Health System
36.	10/19/2000	University of Maryland
37.	10/19/2000	Research Foundation for Mental Hygiene, Inc.
38.	10/19/2000	East Tennessee State University
39.	10/19/2000	The University of Oklahoma Health Sciences Center
40.	10/23/2000	Kaiser Foundation Hospitals

41. 10/24/2000 University of South Florida
42. 10/26/2000 University of Colorado Health Sciences Center
43. 10/26/2000 Toxicology Associates
44. 10/27/2000 Louisiana State University Medical Center
45. 10/27/2000 The Pennsylvania State University
46. 10/27/2000 George Mason University
47. 09/07/2000 University of Florida
48. 09/14/2000 University of Texas Medical Branch at Galveston
49. 09/21/2000 University of Tennessee, Memphis
50. 09/22/2000 Virginia Commonwealth University
51. 09/26/2000 University of Texas Medical Branch at Galveston
52. 09/28/2000 University of South Florida
53. 08/02/2000 The University of Alabama at Birmingham
54. 08/04/2000 Northeast Georgia Health Services
55. 08/07/2000 Good Samaritan Regional Medical Center
56. 08/07/2000 INOVA Institute of Research and Education, Fairfax Hospital
57. 08/07/2000 Morehouse School of Medicine
58. 08/07/2000 University of Cincinnati
59. 08/11/2000 University of Wisconsin - Madison
60. 08/23/2000 University of Pennsylvania
61. 08/25/2000 The Cleveland Clinic Foundation
62. 08/28/2000 The University of Alabama at Birmingham
63. 08/28/2000 Memorial Health University Medical Center
64. 08/28/2000 St. Francis Health System
65. 08/28/2000 The Miriam Hospital
66. 07/07/2000 University of Oklahoma Health Sciences Center
67. 07/10/2000 University of Nebraska Medical Center
68. 07/10/2000 University of Texas Medical Branch at Galveston
69. 07/12/2000 University at Buffalo, State University of New York
70. 07/13/2000 University of Oklahoma Health Sciences Center
71. 07/13/2000 University of Illinois at Chicago
72. 07/17/2000 State University of New York
73. 07/18/2000 University of Illinois at Chicago
74. 07/21/2000 Encino-Tarzana Regional Medical Center
75. 07/27/2000 Yale University
76. 07/28/2000 University of Miami
77. 07/31/2000 University of Miami
78. 07/31/2000 University at Buffalo, State University of New York
79. 12/05/2001 Brooke Army Medical Center
80. 12/11/2001 Thomas Jefferson University/Wills Eye Hospital
81. 12/14/2001 John Hopkins University School of Medicine
82. 12/14/2001 Memorial Medical Center, New Orleans
83. 12/14/2001 University of Texas Health Science Center, Houston
84. 12/20/2001 University of Cincinnati
85. 12/21/2001 Columbia University
86. 12/21/2001 Columbia University Health Sciences Division
87. 11/16/2001 Brookhaven Science Associates, LLC
88. 11/21/2001 Children's National Medical Center
89. 11/26/2001 The Johns Hopkins University School of Medicine
90. 11/29/2001 Virginia Mason Research Center
91. 11/30/2001 Eastern Virginia Medical School
92. 11/30/2001 Case Western Reserve University
93. 10/03/2001 The Johns Hopkins University School of Medicine
94. 10/03/2001 Suburban Hospital

95. 10/10/2001 Beth Israel Deaconess Medical Center
96. 10/15/2001 The Johns Hopkins University School of Medicine and National Institute on Aging
97. 10/15/2001 Thomas Jefferson University/Wills Eye Hospital
98. 10/17/2001 Georgetown University
99. 10/23/2001 St. Elizabeth's Medical Center of Boston
100. 10/23/2001 The University of Texas Health Center - San Antonio
101. 10/24/2001 Sturdy Memorial Hospital
102. 10/24/2001 University of California - Los Angeles
103. 10/24/2001 University of California - San Francisco
104. 10/25/2001 National Institute on Drug Abuse (NIDA)
105. 10/29/2001 Georgetown University
106. 10/30/2001 Brown University
107. 10/30/2001 State University of New York at Stony Brook
108. 09/04/2001 Memorial Medical Center, New Orleans
109. 09/21/2001 University of South Florida/Tampa General Healthcare
110. 09/21/2001 Aaron Diamond AIDS Research Center
111. 09/26/2001 University of Pennsylvania
112. 08/01/2001 Thomas Jefferson University/Wills Eye Hospital
113. 08/06/2001 Georgetown University
114. 08/15/2001 Georgetown University
115. 08/15/2001 National Institutes of Health
116. 08/16/2001 University of Miami
117. 08/17/2001 Michael Reese Hospital
118. 08/17/2001 Rosewell Park Cancer Institute
119. 08/17/2001 University of California, Irvine
120. 08/17/2001 University of Michigan
121. 08/17/2001 University of Washington
122. 08/20/2001 University of Pennsylvania
123. 08/21/2001 University of Iowa
124. 08/21/2001 Okanagan Similkameen Health Region-Corporate
125. 08/21/2001 South Georgia Medical Center
126. 08/22/2001 St. Jude Children's Research Hospital
127. 08/22/2001 National Institutes of Health
128. 08/27/2001 University of California, San Francisco
129. 08/28/2001 The University of Texas Health Science Center at San Antonio
130. 08/29/2001 National Institutes of Health
131. 08/29/2001 University of California, Davis
132. 08/29/2001 Minnesota Department of Health
133. 08/29/2001 State University of New York at Stony Brook
134. 08/31/2001 Childrens Hospital Los Angeles
135. 07/11/2001 University of Missouri - Columbia
136. 07/12/2001 St. Elizabeth's Medical Center of Boston
137. 07/12/2001 The University of Texas M.D. Anderson Cancer Center
138. 07/13/2001 St. Judes Children's Research Hospital
139. 07/19/2001 Johns Hopkins University School of Medicine/The Johns Hopkins Bayview Medical Center
140. 07/20/2001 University of South Florida
141. 07/22/2001 Johns Hopkins University School of Medicine/The Johns Hopkins Bayview Medical Center
142. 06/01/2001 Florida Department of Children and Families
143. 06/01/2001 Michael Reese Hospital
144. 06/05/2001 Roswell Park Cancer Institute

145. 06/05/2001 Sturdy Memorial Hospital
146. 06/06/2001 University of Pennsylvania
147. 06/11/2001 Cleveland Clinic Foundation
148. 06/11/2001 Scientific Analysis Corporation
149. 06/11/2001 University of California, Irvine
150. 06/11/2001 University of Michigan
151. 06/14/2001 University of Arkansas for Medical Sciences & Arkansas Children's Hospital
152. 05/03/2001 University of Colorado Health Sciences Center
153. 05/07/2001 University of Pennsylvania
154. 05/10/2001 University of Missouri-Columbia
155. 05/29/2001 University of Colorado Health Sciences Center
156. 05/31/2001 University of Texas M.D. Anderson Cancer Center
157. 05/31/2001 Georgetoown University
158. 04/13/2001 Mary Bridge Children's Hospital & Health Center
159. 04/17/2001 University of Texas - Houston Health Science Center
160. 04/19/2001 University of South Florida
161. 04/20/2001 University of Washington
162. 04/23/2001 Wills Eye Hospital - Thomas Jefferson University
163. 04/30/2001 University of Cincinnati, Department of Veterans Affairs Medical Center and Shriners Burns Institute
164. 04/30/2001 University of Cincinnati, Department of Veterans Affairs Medical Center and Shriners Burns Institute
165. 04/30/2001 University of Cincinnati, Department of Veterans Affairs Medical Center and Shriners Burns Institute
166. 04/30/2001 NIH Cancer Therapy Evaluation Program - Eastern Cooperative Oncology Group
167. 03/26/2001 University of Southern California Health Sciences
168. 03/27/2001 Indiana University
169. 03/28/2001 Department of Veterans Affairs Medical Center, Philadelphia
170. 03/28/2001 The University of Texas Southwestern Medical Center
171. 03/29/2001 RAND
172. 03/29/2001 Garden State Cancer Center
173. 03/29/2001 St. Jude Children's Research Hospital
174. 03/30/2001 St. Jude Children's Research Hospital
175. 03/30/2001 University of Utah
176. 03/30/2001 University of Illinois at Chicago
177. 02/08/2001 Children's Hospital, Boston
178. 02/12/2001 Louisiana State University Medical Center
179. 02/15/2001 Baylor College of Medicine
180. 02/15/2001 University of Cincinnati
181. 02/15/2001 Department of Veterans Affairs Medical Center, Philadelphia
182. 02/16/2001 Florida Dept. of Health/FDCF
183. 02/22/2001 Yale University
184. 02/28/2001 Raritan Bay Medical Center
185. 02/28/2001 Brown University Graduate School
186. 01/12/2001 Mary Bridge Children's Hospital & Health Center
187. 01/17/2001 National Institutes of Health
188. 01/17/2001 University of Texas Medical Branch at Galveston
189. 01/19/2001 University of Miami
190. 01/22/2001 The John Hopkins University School of Medicine
191. 01/22/2001 McMaster University
192. 01/22/2001 University of Pennsylvania
193. 01/22/2001 National Institutes of Health

194. 01/23/2001 The University of Texas Southwestern Medical Center
195. 01/23/2001 National Institutes of Health
196. 01/24/2001 Garden State Cancer Center
197. 01/24/2001 National Institutes of Health
198. 01/25/2001 University of South Florida
199. 01/25/2001 Cook Children's Medical Center
200. 01/25/2001 St. Francis Health System
201. 01/26/2001 University of South Florida
202. 01/31/2001 Morehouse School of Medicine
203. 01/31/2001 St. Luke's Medical Center
204. 01/31/2001 The University of Memphis
205. 12/03/2002 Columbia University Health Sciences
206. 12/03/2002 Lawrence Berkeley National Laboratory/University of California, Berkeley
207. 12/03/2002 National Institutes of Health
208. 12/04/2002 Ohio State University
209. 12/04/2002 University of Miami
210. 12/10/2002 Oregon Health & Science University
211. 12/20/2002 Lankenau Medical Research Center
212. 12/27/2002 Wake Forest University School of Medicine
213. 11/13/2002 Johns Hopkins University
214. 11/14/2002 Lankenau Medical Research Center
215. 11/14/2002 Loma Linda University
216. 11/21/2002 New York City Department of Health and Mental Hygiene
217. 11/21/2002 New York Hospital Medical Center of Queens
218. 11/21/2002 University of Cincinnati
219. 11/27/2002 University of Michigan, Ann Arbor
220. 10/04/2002 Oregon Health & Science University
221. 10/07/2002 Vanderbilt University
222. 10/10/2002 New York City Department of Health and Mental Hygiene
223. 10/24/2002 Oregon Health & Science University
224. 10/28/2002 Uganda National Council of Science and Technology
225. 10/28/2002 University of Louisville
226. 10/30/2002 National Institutes of Health
227. 09/04/2002 Beth Israel Deaconess Medical Center
228. 09/04/2002 University of Florida
229. 09/05/2002 Loyola University Chicago
230. 09/16/2002 University of Michigan
231. 09/24/2002 University of Louisville
232. 08/05/2002 University of Hawaii
233. 08/05/2002 University of Miami
234. 08/19/2002 Johns Hopkins University School of Medicine/Kennedy Krieger Institute
235. 08/19/2002 University of Chicago
236. 08/19/2002 University of Utah
237. 08/20/2002 Hawaii State Department of Health
238. 08/23/2002 Johns Hopkins University School of Medicine
239. 08/26/2002 University of Michigan
240. 07/01/2002 Boston University Medical Center
241. 07/01/2002 New York City Department of Health
242. 07/11/2002 Walter Reed Army Medical Center
243. 07/16/2002 National Institutes of Health
244. 07/16/2002 Uganda National Council of Science and Technology
245. 07/17/2002 Johns Hopkins University School of Medicine

246. 07/24/2002 Beijing Medical University
247. 07/24/2002 Brigham & Women's Hospital
248. 07/24/2002 Harvard School of Public Health
249. 07/24/2002 Massachusetts Mental Health Center/Massachusetts Mental Health Research Corporation
250. 07/24/2002 Shanghai No. 1 Textile Hospital
251. 07/24/2002 Sun Yat-sen University of Medical Sciences
252. 07/24/2002 Yunnan Institute for Drug Abuse
253. 07/29/2002 Lankenau Hospital
254. 07/29/2002 St. Louis University
255. 07/31/2002 Duke University Health System, Inc.
256. 07/31/2002 University of Washington
257. 06/10/2002 Thomas Jefferson University
258. 06/10/2002 University of Pennsylvania
259. 06/18/2002 Johns Hopkins University
260. 06/18/2002 New York University School of Medicine
261. 06/26/2002 Vanderbilt University/Nashville Veterans Affairs Medical Center
262. 06/27/2002 Columbia University, Health Sciences
263. 05/07/2002 Mount Sinai School of Medicine
264. 05/08/2002 New York University School of Medicine
265. 05/09/2002 Columbia University College of Physicians and Surgeons/New York-Presbyterian Hospital
266. 05/09/2002 Beth Israel Deaconess Medical Center
267. 05/13/2002 Children's Hospital of Pittsburgh
268. 05/13/2002 Ochsner Clinical Foundation
269. 05/16/2002 Parker Hughes Institute
270. 05/23/2002 University of California, San Francisco
271. 05/31/2002 Johns Hopkins University School of Medicine
272. 05/31/2002 State University of New York Downstate Medical Center
273. 05/31/2002 Winifred Masterson Burke Medical Research Institute
274. 04/02/2002 Indiana University
275. 04/02/2002 Mayo Foundation
276. 04/02/2002 Memorial Hospital of Rhode Island
277. 04/02/2002 University of Kansas Medical Center
278. 04/03/2002 LDS Hospital
279. 04/03/2002 Massachusetts General Hospital
280. 04/03/2002 Rush-Presbyterian-St. Luke's Medical Center
281. 04/03/2002 Washington University School of Medicine
282. 04/03/2002 University of Colorado Health Sciences Center
283. 04/03/2002 University of Minnesota
284. 04/04/2002 Baylor College of Medicine
285. 04/04/2002 Cornell University Medical Center
286. 04/04/2002 University of Texas Southwestern Medical Center
287. 04/10/2002 Boston University Medical Center
288. 04/11/2002 Cleveland Clinic Foundation
289. 04/11/2002 University of California, San Francisco
290. 04/12/2002 State University of New York at Stony Brook
291. 04/17/2002 State University of New York Health Sciences Center at Brooklyn/Downstate Medical Center
292. 04/17/2002 Walter Reed Army Medical Center
293. 04/23/2002 Case Western Reserve University
294. 04/23/2002 University of Chicago
295. 04/25/2002 University of California, Davis

296. 04/29/2002 Johns Hopkins University, School of Medicine
297. 04/29/2002 University of California, Irvine
298. 04/29/2002 University of California, San Diego
299. 04/29/2002 University of Michigan Ann Arbor
300. 04/30/2002 Beth Israel Deaconess Medical Center
301. 04/30/2002 Cleveland Clinic Foundation
302. 04/30/2002 McLean Hospital
303. 04/30/2002 University of Pennsylvania
304. 03/12/2002 National Institutes of Health
305. 03/18/2002 Suburban Hospital
306. 03/19/2002 University of California, Los Angeles
307. 03/21/2002 Duke University Health System, Inc.
308. 03/25/2002 Emory University
309. 03/25/2002 Southern Illinois University
310. 03/25/2002 University of Kentucky
311. 03/25/2002 University of Maryland, Baltimore
312. 03/25/2002 University of Pittsburgh
313. 03/25/2002 University of South Florida
314. 03/25/2002 Walter Reed Army Medical Center
315. 03/25/2002 Yale University
316. 03/26/2002 Case Western Reserve University
317. 03/27/2002 University of California, San Diego
318. 03/28/2002 Brigham and Women's Hospital
319. 03/28/2002 Harvard School of Public Health
320. 03/28/2002 Massachusetts Mental Health Center
321. 02/01/2002 Duke University Health System, Inc.
322. 02/02/2002 Brookhaven Science Associates, LLC
323. 02/04/2002 John Hopkins University School of Medicine
324. 02/04/2002 LDS Hospital
325. 02/04/2002 University of Maryland, Baltimore
326. 02/04/2002 University of Washington
327. 02/04/2002 Vanderbilt University/Nashville Veterans Affairs Medical Center
328. 02/05/2002 University of Cincinnati
329. 02/05/2002 Yale University
330. 02/07/2002 Cleveland Clinic Foundation
331. 02/08/2002 University of California, San Francisco
332. 02/11/2002 University of California, San Diego
333. 02/11/2002 University of Michigan, Ann Arbor
334. 02/26/2002 University of Arkansas for Medical Sciences
335. 02/27/2002 National Institutes of Health
336. 01/07/2002 Beth Israel Deaconess Medical Center
337. 01/07/2002 University of Colorado Health Sciences Center
338. 01/08/2002 University of California, San Diego
339. 01/10/2002 Baylor College of Medicine
340. 01/11/2002 Thomas Jefferson University
341. 01/14/2002 North Shore University Hospital
342. 01/18/2002 Duke University Health System, Inc.
343. 01/18/2002 John Hopkins University School of Medicine/Kennedy Krieger Institute
344. 01/22/2002 Beth Israel Deaconess Medical Center
345. 01/24/2002 John Hopkins University School of Medicine
346. 01/29/2002 Children's National Medical Center
347. 01/29/2002 Massachusetts General Hospital

348. 01/30/2002 Thomas Jefferson University
349. 01/30/2002 University of Pennsylvania
350. 01/31/2002 University of Colorado Health Sciences Center
351. 12/01/2003 Columbia University Health Sciences
352. 11/03/2003 Baystate Medical Center
353. 11/03/2003 University of Maryland at Baltimore/Baltimore Veterans Affairs Medical Center
354. 11/05/2003 Center for Molecular Medicine and Immunology
355. 11/05/2003 Moses Cone Health System
356. 11/10/2003 Duke University Health System
357. 11/10/2003 Wake Forest University School of Medicine
358. 11/17/2003 Louisiana State University Health Sciences Center
359. 11/17/2003 Thomas Jefferson University
360. 11/17/2003 University of Virginia
361. 11/17/2003 Vanderbilt University
362. 11/19/2003 University of California, San Francisco
363. 10/01/2003 Ochsner Clinic Foundation
364. 10/06/2003 Boston University Medical Center
365. 10/06/2003 National Institutes of Health
366. 10/06/2003 University of South Florida
367. 10/20/2003 Cleveland Clinic Foundation
368. 10/20/2003 University of Maryland
369. 10/21/2003 The Cleveland Clinic Foundation
370. 10/23/2003 Johns Hopkins University School of Medicine
371. 10/30/2003 Parma Community General Hospital
372. 09/03/2003 University of Rochester
373. 09/05/2003 Parma Community General Hospital
374. 09/15/2003 University of Michigan
375. 09/29/2003 Ohio State University
376. 8/07/2003 University of South Florida
377. 8/21/2003 National Institutes of Health
378. 8/28/2003 Garden State Cancer Center
379. 07/01/2003 University of Florida
380. 07/01/2003 University of Maryland
381. 07/02/2003 University of Texas - Austin
382. 07/03/2003 ARDS Network
383. 07/15/2003 The University of Alabama at Birmingham
384. 07/25/2003 Baystate Medical Center
385. 07/25/2003 Case Western Reserve University
386. 07/25/2003 The Cleveland Clinic Foundation
387. 07/25/2003 Department of Veterans Affairs - New Orleans
388. 07/25/2003 Duke University Health System, Inc
389. 07/25/2003 Harris County Hospital District
390. 07/25/2003 Intermountain Health Care - McKay-Dee Hospital Center
391. 07/25/2003 Intermountain Health Care - Utah Valley Regional Medical Center
392. 07/25/2003 Johns Hopkins University School of Medicine
393. 07/25/2003 LDS Hospital
394. 07/25/2003 Louisiana State University Health Sciences Center
395. 07/25/2003 Moses Cone Health System
396. 07/25/2003 Northwestern University
397. 07/25/2003 Ochsner Clinic Foundation
398. 07/25/2003 St. Anthony Central Hospital
399. 07/25/2003 Thomas Jefferson University

400. 07/25/2003 Tulane University Hospital
401. 07/25/2003 The University of British Columbia
402. 07/25/2003 University of California, San Francisco
403. 07/25/2003 The University of Chicago
404. 07/25/2003 University of Colorado Health Sciences Center
405. 07/25/2003 University of Maryland at Baltimore
406. 07/25/2003 University of Michigan
407. 07/25/2003 University of Pennsylvania
408. 07/25/2003 University of Pittsburgh
409. 07/25/2003 University of Texas Health Science Center at San Antonio
410. 07/25/2003 University of Virginia
411. 07/25/2003 University of Washington
412. 07/25/2003 Vanderbilt University
413. 07/25/2003 Veterans Affairs Medical Center - Denver
414. 07/25/2003 Wake Forest University School of Medicine
415. 06/02/2003 University of Arizona
416. 06/04/2003 University of Texas - Austin
417. 05/02/2003 Harvard School of Public Health
418. 05/13/2003 Columbia University Health Sciences
419. 05/15/2003 National Institutes of Health
420. 05/30/2003 City of Hope National Medical Center
421. 04/02/2003 Beth Israel Deaconess Medical Center
422. 04/08/2003 Virginia Commonwealth University
423. 04/17/2003 Oregon Health & Science University
424. 04/21/2003 University of Cincinnati Medical Center
425. 04/29/2003 Saint Joseph's University
426. 03/17/2003 National Institutes of Health
427. 03/21/2003 University of Washington
428. 03/24/2003 Duke University Health Systems, Inc.
429. 03/24/2003 Mary Imogene Bassett Hospital
430. 03/24/2003 Uganda National Council of Science & Technology
431. 03/26/2003 New York University School of Medicine
432. 02/06/2003 University of California San Francisco
433. 02/12/2003 Mount Sinai School of Medicine
434. 02/12/2003 University of Colorado Health Sciences Center
435. 02/12/2003 University of Michigan
436. 02/13/2003 The Children's Hospital of Philadelphia
437. 02/22/2003 University of California - Los Angeles
438. 02/25/2003 Saint Joseph's University
439. 01/07/2003 Washington University School of Medicine
440. 01/13/2003 University of California, San Francisco
441. 01/23/2003 Loma Linda University
442. 01/29/2003 Saint Louis University Health Sciences Center
443. 12/02/2004 Colorado Cancer Research Program, Inc.
444. 12/06/2004 Evanston Northwestern Healthcare
445. 12/06/2004 St. John's Health System
446. 12/07/2004 M. D. Anderson Cancer Center
447. 12/15/2004 University of Colorado Health Sciences Center
448. 12/22/2004 Baptist Hospital of Miami, Inc.
449. 11/03/2004 City of Hope National Medical Center and Beckman Research Institute
450. 11/03/2004 University of Maryland Baltimore Professional Schools
451. 11/04/2004 Baptist Hospital of Miami

452. 11/05/2004 University of Southern California - Health Science/Charles R. Drew University
453. 11/22/2004 University of Arizona
454. 10/13/2004 Florida Department of Health
455. 10/15/2004 National Institutes of Health
456. 10/15/2004 Virginia Commonwealth University
457. 09/09/2004 Columbia University Health Sciences
458. 09/16/2004 Scott & White Memorial Hospital
459. 08/02/2004 Columbia University Health Sciences
460. 08/03/2004 Association of American Medical Colleges
461. 08/03/2004 Finch University Health Sciences/Chicago Medical School
462. 08/03/2004 George Washington University
463. 08/03/2004 University of California, Los Angeles
464. 08/03/2004 University of Massachusetts Medical School
465. 08/03/2004 University of Medicine & Dentistry of New Jersey - Newark Campus/New Brunswick Campus
466. 08/03/2004 University of Miami
467. 08/12/2004 Community Hospital of the Monterey Peninsula
468. 08/19/2004 Tufts-New England Medical Center
469. 08/20/2004 Virginia Commonwealth University
470. 08/23/2004 City of Hope National Medical Center
471. 08/26/2004 AIDS Research Alliance-Chicago/Saint Joseph Hospital
472. 08/31/2004 Florida Department of Health
473. 07/01/2004 Fred Hutchinson Cancer Research Center
474. 07/06/2004 Evanston Northwestern Healthcare Research Institute
475. 07/06/2004 Medical University of South Carolina
476. 07/06/2004 Ohio State University
477. 07/08/2004 Tufts-New England Medical Center
478. 07/21/2004 Joan and Sanford I. Weill College of Medicine of Cornell University
479. 07/22/2004 Texas Tech University Health Sciences Center
480. 06/29/2004 Johns Hopkins University School of Medicine
481. 06/29/2004 M. D. Anderson Cancer Center
482. 06/29/2004 University of Michigan
483. 05/03/2004 University of Pittsburgh/Carnegie Mellon University
484. 05/10/2004 University of Colorado Health Sciences Center
485. 05/24/2004 Joan and Sanford I. Weill College of Medicine of Cornell University
486. 05/26/2004 Harvard Medical School
487. 05/28/2004 Oregon Health & Science University
488. 04/05/2004 AIDS Research Alliance-Chicago
489. 04/05/2004 University of Cincinnati
490. 04/15/2004 Intermountain Health Care/McKay-Dee Hospital Center
491. 04/15/2004 Thomas Jefferson University
492. 04/15/2004 University of Alabama - Birmingham
493. 04/16/2004 Northwestern University
494. 04/20/2004 Evanston Northwestern Healthcare Research Institute
495. 04/21/2004 Medical University of South Carolina
496. 04/23/2004 Baptist Hospital of Miami
497. 03/10/2004 University of Alabama, Birmingham
498. 03/26/2004 Harvard Medical School
499. 02/13/2004 Denver Veterans Affairs Medical Center
500. 02/13/2004 University of Texas Health Science Center at San Antonio
501. 02/26/2004 University of California, San Francisco

502. 01/06/2004 Harris County Hospital District
503. 01/06/2004 University of California, San Francisco
504. 01/06/2004 University of Colorado Health Sciences Center
505. 01/06/2004 University of Michigan
506. 01/06/2004 University of Pennsylvania
507. 01/07/2004 Children's Hospital and Regional Medical Center
508. 01/12/2004 Ohio State University
509. 01/15/2004 Oregon Health & Sciences University
510. 01/20/2004 Johns Hopkins University School of Medicine
511. 01/20/2004 University of Chicago
512. 01/20/2004 University of Pittsburgh
513. 01/21/2004 University of Pittsburgh
514. 01/28/2004 Tulane University Hospital
515. 01/30/2004 University of Washington
516. December 13, 2005 Mid-Delta Family Practice Clinic
517. November 22, 2005 Gothenburg University
518. October 3, 2005 Gothenburg University
519. October 19, 2005 National Institutes of Health
520. October 20, 2005 University of South Florida/ All Children's Health System
521. October 24, 2005 University of Washington
522. October 27, 2005 Drexel University College of Medicine
523. October 31, 2005 Gothenburg University
524. October 31, 2005 Louisiana State University Health Science Center Shreveport
525. September 9, 2005 University of Washington
526. August 5, 2005 University of Miami
527. August 18, 2005 University of Illinois at Urbana-Champaign
528. August 18, 2005 University of Minnesota
529. August 25, 2005 National Institutes of Health
530. August 26, 2005 University of South Florida
531. August 30, 2005 Northwestern University
532. July 19, 2005 St. Joseph's Hospital Atlanta
533. July 28, 2005 Oregon Health and Science University
534. June 29, 2005 Northwestern University
535. May 2, 2005 University of Maryland Baltimore Professional Schools
536. May 19, 2005 St. Joseph's Hospital Atlanta, Inc.
537. May 23, 2005 Columbia University Medical Center / New York Presbyterian Hospital
538. April 1, 2005 University of Washington
539. April 15, 2005 Joan and Sanford I. Weill College of Medicine of Cornell University
540. April 27, 2005 University of Colorado Health Sciences Center
541. April 28, 2005 National Jewish Medical and Research Center
542. April 29, 2005 National Institutes of Health
543. March 1, 2005 University of Colorado Health Sciences Center
544. March 7, 2005 National Institutes of Health
545. March 8, 2005 University Hospitals of Cleveland
546. March 14, 2005 University of Illinois at Urbana-Champaign
547. March 30, 2005 National Institutes of Health
548. February 24, 2005 University of Maryland Baltimore Professional Schools
549. February 25, 2005 St. John's Health System
550. February 28, 2005 National Jewish Medical and Research Center

551. January 5, 2005 Saint Joseph Hospital
552. January 6, 2005 Joan and Sanford I. Weill College of Medicine of Cornell University
553. January 7, 2005 University Hospitals of Cleveland
554. January 10, 2005 National Institutes of Health
555. December 7, 2006 Medical College of Wisconsin
556. December 13, 2006 New England Research Institute
557. December 13, 2006 University of Washington
558. December 20, 2006 University of Illinois at Urbana-Champaign
559. December 21, 2006 Children's Hospital Oakland
560. December 22, 2006 Anne Arundel Medical Center
561. November 8, 2006 Lenox Hill Hospital
562. November 17, 2006 San Antonio Metropolitan Health District
563. November 22, 2006 Women & Infants Hospital of Rhode Island
564. October 11, 2006 University of Utah
565. October 12, 2006 University of Illinois at Urbana-Champaign
566. October 19, 2006 Main Line Health Systems
567. October 24, 2006 Scripps Health
568. October 25, 2006 Illinois Institute of Technology
569. September 6, 2006 Illinois Institute of Technology
570. September 25, 2006 Women & Infants Hospital of Rhode Island
571. August 15, 2006 Children's Hospital of Philadelphia
572. August 16, 2006 University of Miami
573. August 21, 2006 Main Line Health Systems
574. August 24, 2006 Scripps Health
575. August 28, 2006 Cook County Bureau of Health Services
576. August 28, 2006 Drexel University College of Medicine
577. August 29, 2006 New England Research Institutes, Inc.
578. August 29, 2006 University of Washington
579. July 6, 2006 University of Colorado at Boulder
580. July 21, 2006 Custom Kynetics/Cardinal Hill Rehab
581. July 21, 2006 San Juan City Hospital
582. June 15, 2006 Eastern Virginia Medical School
583. June 19, 2006 Bronx-Lebanon Hospital Center
584. June 19, 2006 Universidad Central del Caribe
585. June 19, 2006 Children's Hospital of the King's Daughters
586. June 19, 2006 Children's Hospital and Research Center at Oakland
587. June 19, 2006 University of Medicine and Dentistry of New Jersey
588. June 19, 2006 Bellevue Hospital Center
589. June 19, 2006 Children's Hospital and Regional Medical Center
590. June 19, 2006 SUNY Upstate Medical University
591. June 19, 2006 Drexel University College of Medicine
592. June 19, 2006 Cook County Bureau of Health Services
593. June 19, 2006 Children's Hospital of Philadelphia
594. June 19, 2006 Duke University School of Medicine
595. June 19, 2006 University of Miami
596. June 19, 2006 University of Chicago
597. June 19, 2006 Children's Hospital of Orange County
598. June 19, 2006 Children's Memorial Hospital
599. June 19, 2006 San Juan City Hospital
600. June 19, 2006 University of California, San Francisco
601. June 21, 2006 University of Miami
602. June 26, 2006 University of Maryland Baltimore School of Medicine
603. June 27, 2006 Scripps Health

604. June 28, 2006 University of Tennessee Health Science Center
605. May 5, 2006 Research Foundation for Mental Hygiene, Inc
606. May 17, 2006 The University of Tennessee Health Science Center
607. May 23, 2006 University of California, Los Angeles
608. April 10, 2006 Scripps Health
609. April 11, 2006 Research Foundation for Mental Hygiene, Inc.
610. April 11, 2006 University of Colorado at Boulder
611. April 12, 2006 Delta Health Center
612. April 26, 2006 Philadelphia Health and Education Corporation (Drexel University College of Medicine)
613. March 3, 2006 State University of New York at Stony Brook
614. March 27, 2006 University of Houston
615. February 14, 2006 Delta Health Center
616. February 14, 2006 Mid-Delta Family Practice Clinic
617. February 14, 2006 University of California, Los Angeles
618. February 17, 2006 Bellevue Hospital Center
619. February 17, 2006 Bronx-Lebanon Hospital Center
620. February 17, 2006 Children's Hospital - Denver
621. February 17, 2006 Children's Hospital - Oakland
622. February 17, 2006 Children's Hospital - Philadelphia
623. February 17, 2006 Children's Hospital & Regional Medical Center
624. February 17, 2006 Columbia University Medical Center/New York Presbyterian Hospital
625. February 17, 2006 Cook County Bureau of Health Services
626. February 17, 2006 H. Lee Moffitt Cancer Center and Research Institute
627. February 17, 2006 Harbor-UCLA Medical Center
628. February 17, 2006 Johns Hopkins Health System
629. February 17, 2006 North Shore-Long Island Jewish Health System
630. February 17, 2006 SUNY Stony Brook
631. February 17, 2006 SUNY Upstate Medical University
632. February 17, 2006 University of Chicago
633. February 17, 2006 University of Maryland Baltimore Professional Schools
634. February 17, 2006 University of Medicine and Dentistry New Jersey/New Brunswick
635. February 17, 2006 University of Miami
636. February 24, 2006 Philadelphia Health and Education Corporation (Drexel University College of Medicine)
637. February 27, 2006 Gothenburg University
638. January 25, 2006 Louisiana State University Health Science Center Shreveport
639. January 25, 2006December 17, 2007 The J. David Gladstone Institutes/ University of California, San Francisco/San Francisco General Hospital Medical Center
640. January 26, 2006 University of Tennessee Health Science Center
641. December 17, 2007 University of Connecticut Health Center
642. December 18, 2007 Interior Health Authority
643. December 19, 2007 University of Arizona
644. December 19, 2007 Carondelet Health Network
645. December 20, 2007 New York University School of Medicine
646. November 1, 2007 New Mexico State University
647. November 6, 2007 Michigan Health & Hospital Association
648. November 6, 2007 John Hopkins University School of Medicine/ Johns Hopkins Bloomberg School of Public Health/ Johns Hopkins University

649. November 28, 2007 Saint John's Health System
650. October 15, 2007 Bridge Back Recovery Homes, Inc.
651. September 14, 2007 Saint John's Health System
652. September 14, 2007 University of Miami
653. September 17, 2007 Bluefield State College
654. September 24, 2007 Hawaii State Department of Health/ University of Hawaii
655. August 9, 2007 University of Connecticut Health Center
656. August 27, 2007 New Mexico State University
657. July 9, 2007 Bluefield State College
658. July 18, 2007 University of Miami
659. July 19, 2007 Johns Hopkins
660. July 24, 2007 Arizona State University
661. June 22, 2007 University of Arizona
662. June 25, 2007 Hawaii State Department of Health/ University of Hawaii
663. June 29, 2007 University of California at Berkeley
664. May 2, 2007 University of Florida/ Malcom Randall VA Medical Center
665. May 15, 2007 Arizona State University
666. May 16, 2007 University of Texas Health Science Center at Houston
667. May 30, 2007 University of Florida
668. April 10, 2007 University of Miami
669. April 23, 2007 University of Washington
670. March 7, 2007 New Mexico State University
671. March 20, 2007 Bluefield State College
672. February 5, 2007 Anne Arundel Medical Center
673. February 6, 2007 Washington University School of Medicine
674. February 13, 2007 HCA-HEALTHONE LLC
675. January 3, 2007 University of Utah
676. January 4, 2007 Cleveland Clinic Foundation/Case Western Reserve University
677. University of Houston
678. December 1, 2008 YRG CARE India
679. December 4, 2008 Mayo Clinic
680. December 16, 2008 University of KwaZulu-Natal
681. December 30, 2008 University of Puerto Rico
682. November 24, 2008 Haverford College
683. October 3, 2008 George Washington University
684. September 15, 2008 YR Gaitonde Center for AIDS Research and Education
685. September 15, 2008 Haverford College
686. September 26, 2008 Interior Health Authority
687. August 1, 2008 University of Washington
688. August 13, 2008 University of KwaZulu-Natal
689. August 21, 2008 Cook County Bureau of Health Services/ Rush University Medical Center
690. July 3, 2008 The J. David Gladstone Institutes/ University of California, San Francisco
691. July 17, 2008 Lehigh Valley Hospital & Health Network
692. July 23, 2008 Mayo Clinic
693. June 2, 2008 Columbia University Health Sciences
694. May 1, 2008 Lehigh Valley Hospital & Health Network
695. May 2, 2008 University of Arizona
696. May 6, 2008 George Washington University
697. May 13, 2008 Carondelet Health Network

698. May 19, 2008 The J. David Gladstone Institutes/ University of California, San Francisco
699. April 21, 2008 University of California at Berkley
700. April 28, 2008 University of Connecticut Health Center
701. April 28, 2008 Saint John's Health System
702. March 3, 2008 University of Connecticut Health Center
703. March 5, 2008 New York University
704. February 11, 2008 Charles R. Drew University of Medicine & Science
705. February 14, 2008 John Hopkins University School of Medicine /Johns Hopkins Bloomberg School of Public Health /Johns Hopkins University
706. February 14, 2008 Michigan Health & Hospital Association
707. February 21, 2008 Bluefield State College
708. February 25, 2008 Columbia University Medical Center
709. February 25, 2008 Gothenburg University
710. February 27, 2008 University of Washington
711. January 2, 2008 Mount Sinai School of Medicine
712. December 8, 2009 - Northern Arizona University
713. December 16, 2009 - Carle Clinic Association/ Carle Foundation Hospital
714. November 9, 2009 - University of California, San Francisco
715. November 9, 2009 - Children's Hospital of Philadelphia
716. November 9, 2009 - Cincinnati Children's Hospital Medical Center
717. October 30, 2009 - Mt. Sinai Medical Center
718. September 2, 2009 - The University of Iowa
719. September 16, 2009 - Northern Arizona University
720. September 21, 2009 - Carle Clinic Association/ Carle Foundation Hospital
721. July 31, 2009 Howard University
722. June 4, 2009 Weizmann Institute of Science
723. June 5, 2009 Board of Regents of the University of Oklahoma Health Sciences Center
724. June 9, 2009 Carle Clinic Association / Carle Foundation Hospital
725. May 26, 2009 Scottsdale Healthcare
726. May 27, 2009 Mount Sinai Medical Center/ Duke University Health System, Inc./ University of Miami
727. April 15, 2009 University of Washington
728. April 15, 2009 Northern Virginia Pelvic Surgery
729. April 29, 2009 Duke University Health System, Inc.
730. April 30, 2009 Weizmann Institute of Science
731. March 2, 2009 Board of Regents of the University of Oklahoma Health Sciences Center
732. March 17, 2009 Children's Hospital of Philadelphia
733. March 17, 2009 University of California, San Francisco
734. March 17, 2009 Cincinnati Children's Hospital Medical Center
735. March 19, 2009 Cook County Bureau of Health
736. March 25, 2009 Native American Cancer Research/ University of Colorado Denver
737. March 30, 2009 Children's Hospital Oakland Research Institute
738. March 30, 2009 Scottsdale Healthcare
739. February 3, 2009 University of KwaZulu-Natal
740. February 11, 2009 Indiana University
741. February 17, 2009 Duke University Health System, Inc.
742. February 19, 2009 Children's Hospital Oakland Research Institute
743. February 19, 2009 Northern Virginia Pelvic Surgery Associate
744. February 25, 2009 Rush University Medical Center

745. January 29, 2009 Mayo Clinic
746. November 24, 2010 Drexel University/Philadelphia Health & Education Corp.
747. October 4, 2010 University of California, Berkeley
748. October 26, 2010 Drexel University/Philadelphia Health & Education Corp.
749. September 2, 2010 Weill Cornell Medical Center and Mount Sinai School of Medicine
750. September 6, 2010 Massachusetts General Hospital
751. June 3, 2010 Board of Regents of the University of Oklahoma Health Sciences Center
752. May 10, 2010 North Shore-Long Island Jewish Health System
753. April 8, 2010 University at Buffalo - State University of New York
754. April 8, 2010 University of California, San Francisco
755. April 16, 2010 University of British Columbia
756. April 30, 2010 Howard University
757. March 29, 2010 University of California, San Francisco
758. March 29, 2010 Intermountain Health Care
759. February 25, 2010 Research Triangle Institute International/ University of Rochester
760. February 25, 2010 University at Buffalo - State University of New York
761. January 11, 2010 East Carolina University
762. January 28, 2010 Intermountain Health Care
763. January 29, 2010 Howard University

Appendix Q

Determination Letter

DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852
Telephone: 240 453-8297
FAX: 240 453-6909

March 27, 2006

Arthur C. Vailas, Ph.D.
Vice President for Research
University of Houston
4800 Calhoun 316 East Cullen
Houston, TX 77204-2015

RE: Human Research Subject Protections Under Federalwide Assurance FWA-5994

(1) Research Project: Investigation of Variables Involved in the Behavioral Treatment of Children with Autism
Project Number: 03-097
Principal Investigator: Gerald Harris, Ph.D.
(2) TYAP Project: Acquisition of ABA Treatment Skills: In-Vivo vs. Video Modeling
(3) Research Project: Generalization of Parent Training: A Comparison Study
Principal Investigator: Gerald Harris, Ph.D.
(4) Research Project: Training and Generalizing Interaction Skills with Siblings of Children with Autism
Principal Investigator: Gerald Harris, Ph.D.
(5) Research Project: The Relationship of Parental Stress to Autism Treatment Type and Duration Principal Investigator: Gerald Harris, Ph.D.

Dear Dr. Vailas:

The Office of Human Research Protections has reviewed the University of Houston's (UH) March 2, 2006 and January 27, 2005 reports regarding the above referenced research and OHRP's inquiry regarding allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects involving the above-referenced research.

(1) In its January 25, 2006 letter, OHRP made the following determination:
HHS regulations at 45 CFR 46.103(a), 46.103(b)(4)(ii) and 46.103(b)(5) require that institutions have written institutional review board (IRB) procedures that adequately describe IRB operations with respect to:

(a) determining which projects require review more often than annually and which need verification from sources other than the investigators that no material changes have occurred since previous IRB review, and

(b) ensuring prompt reporting to the IRB, appropriate institutional officials, any Department or Agency head, and OHRP of (a) any unanticipated problems involving risks to subjects or others; (b) any serious or continuing noncompliance with 45 CFR Part 46 or the requirements or determinations of the IRB; and (c) any suspension or termination of IRB approval.

OHRP found that the UH IRB Policies and Procedures supplied to OHRP do not contain specific procedures for how the IRB conducts these activities.

Corrective Action: OHRP acknowledges that UH's IRB Policies and Procedures have now been revised to describe IRB operations adequately with respect to the above requirements under HHS regulations at 45 CFR 46.103(a), 46.103(b)(4)(ii), and 46.103(b)(5).

OHRP makes the following additional findings about the above-referenced research and projects:

(2) HHS regulations at 45 CFR 46.109(a) require institutional review boards (IRBs) to review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by the HHS regulations. With respect to allegations that research was conducted without IRB review and approval and without legally effective informed consent, OHRP finds that this allegation cannot be substantiated. OHRP acknowledges UH's statements that (a) the IRB-approved study # 03-097 titled "*Investigation of Variables Involved in the Behavioral Treatment of Children with Autism*" involves the collection of data from the clinical files of the investigator's private clients at the Texas Young Autism Project; (b) the second referenced project (hereinafter referred to as "TYAP Project") is a presentation of activities conducted by TYAP and was not subject to UH IRB review or approval, and (c) the last three projects (two presentations and one poster) were not based on independent research, but utilized a subset of the research database created under the first, IRB-approved research project.

(3) HHS regulations at 45 CFR 46.116 require investigators to obtain legally effective informed consent prior to the initiation of research. For research involving children, HHS regulations at 45 CFR 46.408 require IRBs to determine that adequate provisions are made for soliciting the assent of children and the permission of each child's parents or

guardian. OHRP finds that when the UH IRB approved study #03-097, it reviewed and approved a parental permission form which contained all of the required elements of informed consent set forth under 45 CFR 46.116. OHRP notes that there is no evidence in the IRB file to determine whether the UH IRB considered, as required by 45 CFR 46.408(a), whether the child subjects involved in study #03-097 were capable of providing assent; however, OHRP acknowledges that UH IRB Policies and Procedures require assent from children capable of providing it, and describe appropriate criteria to include in assent forms.

(4) HHS regulations at 45 CFR 46.111(a)(1)(i) state that, in order to approve research covered by the regulations, the IRB shall determine that risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk. OHRP questioned whether the UH IRB, in reviewing project #03-097, obtained sufficient information from the investigator regarding data recording technique and statistical method to determine that these regulatory requirements were satisfied.

Corrective Action: OHRP acknowledges that IRB project #03-097 involved only the collection of pre-existing data from TYAP files, and that the UH IRB identified the only significant risk of this research to be the possible loss of confidentiality. OHRP further acknowledges that UH modified its "IRB Application To Conduct Research Using Human Subjects" form to request that investigators include a description of date recording techniques and/or statistical methods to be employed in the research.

(5) HHS regulations at 45 CFR 46.110(c) require IRBs that use expedited review procedures to keep all IRB members advised of research proposals which have been approved via expedited review.

OHRP finds that the UH IRB did not keep all IRB members advised of the approval of project # 03-097, as required by 45 CFR 46.110.

Corrective Action: The UH IRB has modified its reporting procedures to ensure that the minutes for the expedited review subcommittee reflect subcommittee decisions regarding the research proposals it reviews under an expedited review procedure, and that these minutes are presented to the full IRB by one of the reviewing subcommittee members.

(6) HHS regulations at 45 CFR 46.404-407 (subpart D) require specific findings on the part of the IRB for approval of research involving children. OHRP expressed concern that the UH IRB file for project #03-097 provides no evidence that the IRB made the required Subpart D findings.

Corrective Action: OHRP acknowledges UH's statement that, as a matter of policy and practice, the IRB reviews the requirements of subpart D for all research activities involving children. OHRP notes that UH initiated the following changes to

address OHRP's concern in this and future research activities: (a) the IRB application form now
requires investigators seeking approval for research involving children to designate what they believe to be the category of the research under HHS regulations (45 CFR 46.404, 46.405, or 46.406) and to explain how the regulatory criteria are met by the study; (b) a new reviewer's worksheet has been developed to require reviewers to identify the appropriate regulatory category for involvement of children in research and to ensure that child assent is obtained if appropriate, and (c) the regulatory category for involvement of children in research will now be noted in IRB meeting minutes.

OHRP finds that the above corrective actions are adequate and appropriate under UH's FWA. As a result, there should be no need for further OHRP involvement in this matter, although you should notify OHRP if new information becomes available which might alter this determination.

OHRP appreciates the continued commitment of your institution to the protection of human research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Carol J. Weil, J.D. Compliance Oversight
Coordinator Division of Compliance Oversight

cc: Ms. Debra Comeaux, Research Compliance Specialist,
U Houston Dr. Merrill Hiscock, IRB Chair,
U Houston IRB #2A and 2B
Dr. Gerald Harris, U Houston
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
Dr. Kristina Borror, OHRP
Ms. Shirley Hicks, OHRP
Dr. Irene Stith-Coleman, OHRP
Ms. Pat El-Hinnawy, OHRP
Ms. Janet Fant, OHRP

Appendix R

List of Acronyms

CARMA	Complementary Analysis Research Method Application
CRS	Congress of Research Service
DHHS	Department of Health and Human Services
DL	Determination Letters
FDA	Food and Drug Administration
FWA	Federalwide Assurance
HHS	Health and Human Services
HRPP	Human Research Protection Program
IRB	Institutional Review Board
NBAC	National Bioethics Advisory Commission
NCJJ	National Center for Juvenile Justice
NIH	National Institutes of Health
OHRP	Office of Human Research Protections
OPRR	Office for the Protection of Research Risks
SACHRP	Secretary's Advisory Committee on Human Research Protections
SSR	Social Science Research

APPENDIX S

UNLV
UNIVERSITY OF NEVADA LAS VEGAS

Social/Behavioral IRB – Expedited Review

Approval Notice

NOTICE TO ALL RESEARCHERS:

Please be aware that a protocol violation (e.g., failure to submit a modification for any change) of an IRB approved protocol may result in mandatory remedial education, additional audits, re-consenting subjects, researcher probation, suspension of any research protocol at issue, suspension of additional existing research protocols, invalidation of all research conducted under the research protocol at issue, and further appropriate consequences as determined by the IRB and the Institutional Officer.

DATE: March 24, 2011

TO: **Dr. LeAnn Putney**, Educational Psychology

FROM: Office of Research Integrity - Human Subjects

RE: Notification of IRB Action by Charles Rasmussen Chair
Protocol Title: **The Impact of Regulating Social Science Research with Biomedical Regulations**
Protocol #: 1103-3762M
Expiration Date: March 23, 2012

This memorandum is notification that the project referenced above has been reviewed and approved by the UNLV Social/Behavioral Institutional Review Board (IRB) as indicated in Federal regulatory statutes 45 CFR 46 and UNLV Human Research Policies and Procedures.

The protocol is approved for a period of one year and expires March 23, 2012. If the above-referenced project has not been completed by this date you must request renewal by submitting a Continuing Review Request form 30 days before the expiration date.

PLEASE NOTE:
Upon approval, the research team is responsible for conducting the research as stated in the protocol most recently reviewed and approved by the IRB, which shall include using the most recently submitted Informed Consent/Assent forms and recruitment materials. The official versions of these forms are indicated by footer which contains approval and expiration dates.

Should there be *any* change to the protocol, it will be necessary to submit a **Modification Form** through ORI - Human Subjects. No changes may be made to the existing protocol until modifications have been approved by the IRB. Modified versions of protocol materials must be used upon review and approval. Unanticipated problems, deficiencies to protocols, and adverse events must be reported to the ORI – HS within 10 days of occurrence.
If you have questions or require any assistance, please contact the Office of Research Integrity - Human Subjects at IRB@unlv.edu or call 895-2794.

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