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The Protection of Individual Inviolability: Nazi Doctors and their Mark on Biomedical Research

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**The Protection of Individual Inviolability:
Nazi Doctors and their Mark on Biomedical Research**

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Readers: Dr. Janet Gray, Dr. Jill Schneiderman

Thesis submitted in partial fulfillment of the requirements for a major in the
program in Science, Technology, and Society (STS).

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“When may a society actively or acquiescence, expose some of its members to harm in order to seek benefits for them, for others, or for society as a whole?”

-Jay Katz

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Introduction

“It is comforting to think that it is not possible to defend involuntary euthanasia, forced sterilization, and genocide in moral terms. It is comforting to think that anyone who espouses racist, eugenic ideas cannot be a competent, introspective physician or scientist. Such beliefs are especially comforting to ethicists. Nazi medical crimes show that each of these beliefs is false”

-Arthur Caplan, How Did Medicine Go So Wrong?

The purpose of this thesis is not to preach but to examine. The following pages attempt to provide a picture not only of some of the darkest moments in medical ethics but also of the events occurring after-the attempts to address the actions of the Nazi doctors and prevent any future crimes against ethics and humanity. The world of biomedical research is seventy years and millions of innovations past the events of World War II. As a result, the experiments in concentration camps may seem but a blemish of the past. This work aims to examine the interplay of circumstances that allowed for these experiments to happen, taking at face value evidence asserting that not all of the doctors were sadists or mad men and that many felt their actions and experiments were ethically justified.

A study of the history of medical ethics reveals that certain conditions and pressures place both doctors and patients in situations that can, and often do, result in breaches of medical ethics. The experiments conducted during World War II provide some of the most extreme examples in breaches of human rights and ethics the world has so far seen. There is no benefit in considering the Nazi experiments as “other” or irrelevant. The greatest good that can come out of

these atrocities is the lessons they have to teach about what plays into and creates a hostile research environment. Before the rise of Hitler and the Nazi party, Germany was at the forefront of both medical research and medical ethics. It is important to remember this while examining what factors, both culturally and politically, transformed one of the most forward moving and medically advanced countries into a genocidal machine.

The great irony of the actions perpetrated by Nazi doctors in concentration camps during the second world war is the fact that, only ten years previously, Germany had been actively developing and defining principles to guide ethical biomedical research. Early in the twentieth century, the issue of patient rights in experimentation was brought to the forefront of the Prussian Government as a result of the experiments of Albert Neisser. In his search for a vaccine for syphilis, Neisser injected cell free serum into his patients without their consent, causing many to contract the disease. Revelations of Neisser's experiments were met with general uproar and debate both within and outside of the medical community. (Baumslag, 2005, p. 131) In 1928, the Berlin Medical Association issued a statement stating that although they did not agree with a legal limit being placed on scientific research,

“Any trial on human must be limited to what is absolutely necessary, must be well grounded theoretically and scientifically, and must be well defined biologically...for the well-being of the patient is more important than science. Moreover, medical ethics commands that the patient or a legal representative be informed of the spirit and purpose of the particular therapeutic test” (Winau, 2007, p. 53).

The debates over medical ethics continued into the 1930s. During this time, Emil Abderhalden published *Ethiks*, the first international physician-run journal to focus on ethics. In a 1930 poll taken by Abderhalden, the German medical community was shown to be split on the legitimacy and need for biomedical experimentation. (Frewer, 2007, p. 31) In 1931, the Reich government published the “Guidelines for New Therapy and Human Experimentation”. The document stated,

“Undertaking any test without informed consent is impermissible under any circumstances. Any test on humans that could have been replaced by a test on animals is to be rejected...Experiments performed on children or adolescents under the age of 18 are not allowed if they will endanger the welfare of the child or adolescent in the slightest. Experiments on the dying are incompatible with the principles of medical ethics and thus not permitted” (Winau, 2007, p. 54).

It is clear that even in its earliest inception on, the concepts of informed consent of the patient were already under discussion in the realm of the bioethics. The “Guidelines” were repeated and cited in future ethical documents. They are more stringent than those set forth by most bioethical documents since this time. However, while they clearly enumerated many expectations for human experimentation, they were later claimed by defendants at the Nuremberg Trials (the tribunal held by the U.S. Trials System at the close of World War II) to be “relative” and “not the standard” for German medical practices. (Grodin, 1992b, p.128)

The general conception of medical professions at the time was that physicians were to be given complete authority over their own decisions and did

not need supervision. Though the bioethical movement did take root in Germany, it has been argued by historians that the development was too philosophical, and the confidence in the collective morality of both physicians and the national community was, “Ultimately the cause and internal logic of an ‘ethics without humanity...[which] paved the way by justifying and shaping the events that unfolded” (Frewer, 2007, p. 30). The rise of the National Socialist movement led to “An ethical decline in physicians’ perception of their professional identity” (Frewer, 2007, p. 36). This was reinforced by concepts like “lives not worth living”, a term that was repeated often in Nazi propaganda and which played a central role in justifying many atrocities committed under the Nazi regime. During this time, Viktor von Weizsacker, a physician/philosopher who wrote extensively on eugenics, stated, “If the physician presupposes there to be worth in a given worldly and temporal life, but one void of eternal value, then that merely temporal worth can be so low that the life in question deserves annihilation” (Bohme, 2007, p. 24).

In his book, When Medicine Went Mad, prominent bioethicist Arthur Caplan argues that the Nazi operation was made possible because of the work of German scientists; educated men and women who were, in one way or another, able to sufficiently morally justify their actions despite their “degree of civilization”. (1992b, p. 157) In her analysis of the events, Ruth Macklin writes, “The Nazi era in general, and the behavior of Nazi doctors in particular, serve to show that despite a general historical progression toward greater humaneness and

humanity, egregious regressions and moral backsliding have occurred” (1992, p. 243).

It is with this background in mind that I begin the investigation into the history of bioethics in the United States. The second chapter of this thesis provides a summary of some of the experiments done both on behalf of the German government and at the whim of the Nazi researchers in concentration camps during the Second World War. Most of the accounts come from records of the doctors’ diaries or from first hand testimonies provided by survivors and later summarized into works about these events. Chapter three outlines three documents of significance to the progression of medical ethics: The Nuremberg Code, The Declaration of Helsinki, and the Belmont Report. In addition, the chapter examines the concept of informed consent, how it is presented in each document and what significance it holds to the justification and creation of ethical biomedical research. This section phrases the argument with the same ethical terminology that is frequently used to philosophically justify the existence of biomedical research as a whole. Chapter four addresses the state of current affairs. It outlines the IRB process used by the United States, focusing on the ways that the process deviates from previous guidelines as well as the methods it employs to address the problems currently encountered in biomedical research. Though dense, this process forms the cornerstone for all analysis about the efficacy of current policy. Chapter five looks at recent research about the state of ethics in modern biomedical research. It uses data from empirical and behavioral studies on the current research environment in order to assess

areas of concern and examine how well the modern IRB process addresses present concerns surrounding the state of ethics in biomedical research. Chapter six summarizes and discusses the significance of the information presented in the previous chapters, drawing connections between past events and modern concerns in order to emphasize the role a historical understanding of research ethics can have in the development of future policies and systems of ethics. The epilogue briefly discusses problems presented by the political system, specifically those conditions that arise during times of upheaval and violence.

Biomedical research contains within it an inherent tension. A researcher is required to negotiate a careful balance between protecting the rights of the individual subject and conducting experiments for the benefit of “the greater good”. The negotiation of these two elements is both challenging and crucial to ethical research. As stated in the Massachusetts General Hospital’s Guiding Principles for Human Studies of 1981, “A study is ethical or not at its inception. It does not become ethical because it succeeds in producing valuable data” (Angell, 1992, p.278). If the ultimate goal of biomedical research is the pursuit and development of procedures and technologies to benefit mankind, doing so unethically undermines the entire process. In this case the ends cannot not justify the means; individual inviolability must have equal weight with the greater good.

It is for this reason that the history of bioethics is essential to modern medical research. The events that unfolded both during and following World War

It reveals the frequent failings of biomedical research to successfully navigate this tension. As a result, many have been harmed in a way that goes against the purpose of medicine. In order to avoid similar occurrences, knowledge of these events and the factors that lead to them must be imparted to all involved in research. History shows that bioethical policy acquires its strength through the degree that researchers adhere to it. It is therefore essential that new scientists learn and appreciate the extensively scarred history of their profession, and the implications this has on their own research. The preservation of the integrity of the subject is dependent on the integrity of the researchers.

Summary of Concentration Camp Experiments and Doctors

*“He wasn’t a monster...none of the Nazi Doctors were,
you know -but merely a fallible and corruptible human
being”*

-Dr. Magda V. on Dr. Josef Mengele

In his reports, Dr. Sigmund Rascher, a captain of the medical service of the German airforce, described one of the high altitude experiments that was conducted at the Dachau concentration camp during the war,

“It was a continuous experiment without oxygen at a height of 12 kilometers conducted on a 37-year-old Jew in good general condition. Breathing continued up to 30 minutes. After 4 minutes the experimental subject began to perspire and wiggle his head, after 5 minutes cramps occurred, between 6 and 10 minutes breathing increased in speed and the experimental subject became unconscious; from 11 to 30 minutes breathing slowed down to three breaths per minute, finally stopping altogether.

Severest cyanosis developed in between and foam appeared at the mouth.

At 5 minute intervals electrocardiograms from three leads were written. After breathing had stopped Ekg was continuously written until the action of the heart had come to a complete standstill. About ½ hour after breathing had stopped, dissection was started” (Katz, 1992b, p. 233).

The high altitude experiments were just one type of experiment sponsored by the *Ahnenerbe* (ancestral heritage) office of the SS, an agency created by Heidrich Himmler in 1939 to “develop historical and scientific studies of the Nordic Indo-Germanic race...and combine the Gestapo mission of controlling Germany’s

intellectual life with Himmler's visionary ideas" (Lifton, 1986, p.286). The idea for these particular experiments was proposed by Dr. Rauscher in 1941. He wrote to Himmler requesting that subjects be put at his disposal on which to conduct these experiments. Rauscher was given the go ahead and a movable pressure chamber was placed at Dachau that allowed experimenters to simulate the rapid changes in pressure that occur when humans fall great distances without parachute and oxygen. (Taylor, 1946, p.71) The subjects chosen for the study were at first Poles and Russians, however, later on "Jewish professional criminals", those guilty of racial shame (marriage or intercourse between Aryans and non-Aryans) were found to be in greater supply. (Taylor, 1946, p. 73)

After the conclusion of the high altitude experiments, inmates at the Dachau concentration camp became subjects in freezing experiments that were also conducted at the bequest of the German Air Force. (Taylor, 1946, p. 74) These experiments aimed to discover possible ways to rewarm German pilots who had been forced to land in the cold North Sea. Subjects were immersed in water ranging from 2 to 12 degrees Celsius for 3 hours at a time, as well as made to stand naked in below freezing temperatures for up to 14 hours. Different methods were then tested in order to determine the best method of rewarming. Experiments were conducted with and without narcotics; attempts at rewarming included placing the body between two naked women and throwing the subject into boiling water. (Taylor, 1946, p. 74) Documentation for the study reveals that very little scientific process was observed. Factors such as subject age, weight and height were not recorded; EKGs provided the only assessments

of cardiac activity and no measurements were taken during immersion in cold water. Nonetheless, a report referred to as the Dachau Comprehensive Report was prepared by Dr. Rascher for presentation of the research. (Berger, 1990) A comprehensive analysis of the experiments was compiled by Dr. Leo Alexander after the war that revealed many variables were not assessed or considered during the experiments. A more contemporary analysis conducted by historian Dr. Robert Berger also concluded that the experiments do not provide reliable evidence stating, "In summary, the basic information essential for documenting an orderly experimental protocol and evaluating the results is not provided. We know enough, however, to conclude that the methods of study were clearly defective" (1990). Though this is still a topic of debate, it has been strongly argued that the results acquired in the experiments are scientifically unreliable. There is considerable evidence that despite their knowledge of the scientific process, the majority of the doctors performing these tests failed to create experiments that would appropriately and accurately produce data. (Berger, 1990) During the Doctor's Trial, the prosecution argued, "The moral shortcomings of the defendants and the precipitous ease with which they decided to commit murder in quest of "scientific results" dulled also that scientific hesitancy, that thorough thinking-through, that responsible weighing of every single step which alone can ensure scientifically valid results" (Taylor, 1946, p. 91).

Other Nazi experiments included attempts to make seawater drinkable, to find vaccines for malaria and typhus, experiments with sulfanilamide (a chemical

compound that was thought to clot blood), mustard gas and other poisons, sterilization experiments and the creation of a “Jewish skeleton collection”. (Taylor, 1946, p. 84) Each experiment was conducted with a similar lack of regard for patient safety. If the subjects survived the experiments, they were often euthanized so that their bodies could be dissected for further research. Many subjects were purposely infected with diseases such as typhus and malaria in order to perform experiments on them. In studies of the coagulation of the blood, inmates were fired upon to simulate battlefield wounds and then treated with polygal and sulfanilamide (compounds whose properties as blood clotting agents were being tested). Any side effects, diseases, or infections that developed as a result of these experiments were left untreated. (Taylor, 1946, p. 77)

The motivation behind these experiments varied. Some reflected the personal interests of the doctors presiding over them. Dr. Eduard Wirths, the chief SS doctor at Auschwitz, conducted trials that studied pre-cancerous conditions of the cervix. Many were commissioned by Himmler in order to serve the needs of the German government. (Lifton, 1986, p. 269) For the most part, the experiments were performed with nationalistic intentions. Sterilization and castration experiments conducted by Drs. Clauberg and Schumann in Auschwitz were encouraged as a direct expression of racial theory and policy. (Lifton, 1986, p. 269) In a letter to Himmler in 1941, Dr. Adolf Pokorny, a retired German medic wrote, “The thought alone that 3 million Bolsheviks, at present German prisoners, could be sterilized so that they could be used as laborers but

be prevented from reproduction opens the most far-reaching perspectives” (Lifton, 1986, p. 275).

Despite the violence involved in the majority of the experiments, records show that Nazi doctors still viewed their work as scientific. Heidrich Himmler, the man in charge of commissioning most trials, saw himself as “a patron of science”. He was, “The pseudo-medical scientist par excellence, the personal and ideological epitome of the healing-killing reversal” (Lifton, 1986, p. 279). The doctors that conducted these experiments were established medical professionals. They identified the opportunities for unrestrained research made possible by the availability of bodies and lack of oversight. Dr. Robert Lifton wrote of one physician, Dr. Helmuth Vetter, who was employed by the Bayer Group and ran medical trials for them in several concentration camps, “He found in Auschwitz a testing area where he need not be restrained either by compunctions about harming or killing research subjects, or by rigorous judgments about therapeutic effects” (1986, p. 292). SS doctors and medical students used concentration camp prisoners to gain surgical experience by using those afflicted with various diseases as “practice” to hone their skills. Lifton states,

“In the absence of ethical restraint, one could arrange exactly the kind of surgical experience one sought, on exactly the appropriate kinds of “cases” at exactly the time one wanted. If one felt Hippocratic twinges of conscience, one could usually reassure oneself that, since all of these people were condemned to death in any case, one was not really harming them. Ethics aside, and apart from a few other inconveniences, it would have been hard to find so ideal a surgical laboratory” (1986, p. 295).

Records of researcher's diaries show that many of them could identify the fault in the events but accepted it as reality and felt themselves detached from the proceedings. Dr. Johann Kremer, a doctor at Auschwitz, kept a diary that alternately spoke of the "routine" horrors he experienced in the concentration camp life and what he had eaten for dinner. Accounts of Dr. Josef Mengele, infamous both for his experiments and for his success in evading capture following the war, provide a clear example of the dichotomy between civilized scientist and murderer that manifested itself in many of the Nazi physicians.

Mengele was trained at the University of Munich; though he did not join the Nazi party until 1937, his research and attitude towards his research reflect his ardent faith in the Nazi doctrine. He achieved infamy very soon after the war as stories from former subjects, as well as documentation from Auschwitz began to expose his role in the experiments conducted at the camp. In addition to being largely in charge of the selection process (a process in which he was asked to choose which of the inmates would be sent to the gas chambers on a certain day), Mengele conducted "twin experiments" in which he attempted to understand the role heredity played in different traits in order to reinforce Nazi ideals of the superiority of the Aryan Race. (Lifton, 1986, p. 352) The stories told by some of his former subjects depict a man capable of heartless murder as well as countless other crimes. However, other accounts given by former colleagues and prisoners paint him as less of a monster. A fellow doctor at the camp stated that Mengele showed himself to be, "Cultivated, pleasant, and knowledgeable in discussions not only on medical subjects but about literary questions, even

Flaubert” (Lifton, 1986, p. 371). Mengele’s intense interest in twins resulted in their receiving special treatment in the camps. He was seen showing kindness and favoritism to certain pairs of twins, giving them rides in his cars and bringing them presents. However, he also was observed emotionlessly killing those who he deemed no longer useful, or whom he decided would be of better use dissected. (Lifton, 1986, p. 353) He was described as a man who liked to be in control, who was passionate about his research; a “duality of affection and violence”. (Lifton, 1986, p. 355) One prisoner doctor questioned, “Was he a kind man, good with children...who was only driven to do the things he did by his passion for research? Or was he a monster who only plays a role with the children to hide his game better, to get his ends more easily?” (Lifton, 1986, p. 374) This wavering doubt about the nature of Mengele’s character applied to his peers’ opinions of his research practices and scientific integrity as well.

There were many doctors and peers at Auschwitz who respected Mengele and his passion for his research. He was described by an assistant working at the camp as, “Having a sense of legitimacy of his method and of his having been a man with a genuine ‘scientific background’ who was ‘absolutely capable of doing serious and appropriate scientific work” (Lifton, 1986, p. 365). Mengele was passionate about his work, however, his conception of the scientific process involved demanding absolute control over his research environment. He is said to have been stubborn-a man whose purpose in his experiments was the search for proof for his preconceived values and beliefs. He often refused to

acknowledge any evidence of contradiction to his expected results. (Lifton, 1986, p. 370)

Despite his infamy, by all accounts, Mengele does not represent the worst of the Nazi doctors. Instead, he is an example in large part of a man who fell naturally into the mold of a concentration camp doctor-someone who was perfectly fitted to the environment and conditions of the Auschwitz camp and the Nazi government. In concluding his analysis of Mengele, Robert Lifton states,

“In the camp he could be a visionary ideologue, an efficiently murderous functionary, a “scientist” and even a “professor,” an innovator in several areas, a diligent careerist, and, above all, a physician who became a murderer. He reveals himself as a man and not a demon, a man whose multifaceted harmony with Auschwitz can give us insight into-and make us pause before-the human capacity to convert healing into killing” (1986, p. 383).

Perhaps one of the most significant aspects of Mengele’s story is his ability to completely detach from his patients while maintaining parts of his humanity. His ability to show affection, to hold intelligent conversation, to interact on an everyday basis was not impeded by his frequent murders of children, nor his “god-like” role in determining those sent to the gas chambers. Mengele’s training as a doctor occurred during a time when the topics of ethics in human experimentation were being actively discussed in the German medical field. It is unlikely these principles would have been unknown to him. However, the opportunities, resources, and lack of oversight he received while working as a doctor in Auschwitz caused him to set all of this aside.

It is important to keep in mind when studying these events that the men responsible for the experiments at Nazi concentration camps during World War II represented many of the established members of the German medical community. The defendants at the Doctor's Trial included the head of the University of Berlin Department of Surgery, acclaimed military medical administrators, specialists in the fields of public health and tropical diseases. (Taylor, 1992, p. 87) Many of the men had already reached the peak of their profession. Though some of them, such as Clausberg and Kremer, seem to have been universally disliked for their attitudes both towards their subjects and their peers, others got very different and far more mixed reviews. They were not monsters, bred from a different cloth and living in a separate world. The horrifying nature of these events has sometimes caused them to be viewed as "irrelevant" to modern medical research; this is a mistake. As Arthur Caplan explains in his book,

"It is comforting to believe that health care professionals who have pledged an oath to 'do no harm' and who are minimally concerned with the morality of their own conduct could not kill babies or conduct brutal, often lethal, experiments on starving inmates in concentration camps...It is comforting to think that anyone who espouses racist, eugenic ideas cannot be a competent, introspective physician or scientist. Such beliefs are especially comforting to ethicists. Nazi medical crimes show that each of these beliefs is false" (1992b, p. 55)

During the Doctor's Trial at Nuremberg, the German researchers showed little remorse for their actions. Instead, they offered ethical arguments for the research, explaining that the rules during war are different and they believed their

experiments justified as they were acting in the interest of the “greater good”. The events that transpired in Dachau and Auschwitz are not foreign, they are not the work of creatures unfit for the “modern world”. The men involved were not monsters but educated German physicians. Their actions have permanently stained the history of biomedical research.

The Nuremberg Code and Beyond

“One has to strive toward obtaining an international basis to represent the present international opinion on human experiments, one which for decades, if not for centuries, will form the criterion for the permissibility of human experiments. We, as jurists, can only render a service to the development of medical science and therewith to humanity if we endeavor to establish an incontrovertibly clear view of today’s international opinion on human experiments”

-Closing Brief, Nuremberg Trial

Throughout the second half of the 20th century, following the publication of the many violations of human rights committed during World War II, there were several documents published whose goals were not only to condemn the actions of the Nazi Doctors but to also set new standards for the rights of the individual in human experimentation and reaffirm the commitment to repercussions from the international community for any future violations of human rights. In the realm of bioethics and human experimentation, three documents stand out in the strength of the statements they made as well as the impacts that they had on the formation of future medical ethics policies. (A. Caplan, personal communication, December 10, 2014) These three documents, the Nuremberg Code, the Declaration of Helsinki, and the Belmont Report will form the basis of my examination of the processes that have led to the IRB process.

These three documents represent the foundations of modern biomedical ethics. When examining these documents, their contents, and the effects they have had, both directly and indirectly, on the formation of the IRB process, it is important to consider them within a historical context.

The impetus behind the creation of the Nuremberg Code is perhaps the most obvious. Following the conclusion of the war, a series of military Tribunals were held by the Allied forces in order to assess and prosecute the crimes committed by leaders of the Nazi party during the war. Though ostensibly a collective effort, these trials were held in the U.S. occupation zone of Nuremberg and were conducted by the U.S. Trials Court. (Annas & Grodin, 1992, p.7) One of these trials, *United States of America v. Karl Brandt et al.* is known as the Doctors' Trial and focused on the crimes committed by concentration camp doctors during the war. There were 23 defendants, all German and the majority doctors. The tribunal convened 139 times after the indictment and arraignment of the defendants. At the conclusion of the trial, seven were issued the death sentence. (Annas, Grodin, 1992, p. 5) In addition, the verdict included a set of ten principles of medical ethics in the area of human experimentation. These principles are now known as the Nuremberg Code.

The Code was issued as part of the judicial process at the conclusion of the Doctors' Trial at Nuremberg. (Annas, Grodin, 1992, p. 6) During the trial, the defendants argued that there was a large degree of "relativism" in codes of ethics concerning human research. (Grodin, 1992, p. 128) Although, as it has already been discussed, a code of ethics did exist in Germany at the time, because it was not "universal" the Nazi doctors believed it did not confer the same legitimacy as other legal documents. It was with this argument in mind that the Nuremberg Code was created. Though it was overseen by the U.S. Trials Court, it was declared to be the first "Universal Code of Ethics".

Today, the Nuremberg Code is largely recognized as “A hallmark for all subsequent discourse on the ethics of human experimentation” (Grodin, 1992, p. 122). However, while it is seen to have great ideological significance in the world of medical ethics, the code has been criticized for the lack of impact the document has actually had on medical experimentation. As Sharon Perley, Sev Fluss, Zbigniew Bankowski and Francoise Simon pointed out in their essay on the Code, “A set of “universal principles”, with no legal or professional authority, is successful only if researchers choose to abide by them” (1992, p. 157). In his book, Justice at Nuremberg, Ulf Schmidt claims,

“By 1953 US governments officials were fully aware of the fact that the Code constituted part of international law and that a violation of its principles, irrespective of national security requirements, could undermine the self-proclaimed moral superiority of the Western governments” (2004, p. 278).

However, despite this, the medical profession did not view it as significant.

The Nuremberg Code has been described as inadequate. Many doctors resented the implications it made and were indignant to find themselves compared to the Nazi doctors and to be asked to follow ethical laws that they saw as “obvious”. The Code was described as, “A good code for barbarians but an unnecessary code for ordinary physician-scientists” (Katz 1992b, p. 228). Even by the 1950s, the lack of appreciation and respect for the principles of the Nuremberg code can be seen in research. (Annas, 1992, p. 218) It was believed that, “Researchers generally regarded the Nuremberg Code as a set of principles appropriate for moral monsters, not for democratically minded American physicians” (Stark, 2012, p.104). There was an idea that Nazi doctors and their

actions were unique in the history of medicine, and it was therefore insulting to even compare them to current research. In addition, doctors objected to the judicial nature of the Code, arguing that it was created by men who had no knowledge of the realities of the medical profession. (Glantz, 1992, p. 197)

Needless to say, there was considerable resistance to the Nuremberg Code and its adoption in the field of medical research. Those involved in policy formation in the international community acknowledged these problems with the code, however, also agreed that the actions of Nazi doctors during World War II were too significant to the world of medicine to be ignored. If doctors would not respect the Nuremberg Code, something else must be created. There was a need for *professional guidelines* designed by physicians for physicians (Perley et al, 1992, p. 157).

The Declaration of Helsinki represents the World Medical Association's response to the Nuremberg code. The document, originally published in 1964, lists the principles its creators believe must be observed within the sphere of human experimental research. Noting the judicial nature of the Nuremberg code and the stringent limits it placed on human experimentation, the Association claimed that the Declaration of Helsinki provided a more doctor-centered and "realistic" set of principles for human experimentation. The document was meant to address the problems with the restrictive nature of the code and the lack of adherence to the Code's principles by the medical field. (Schmidt, 2004, p. 282)

Henry K. Beecher, a prominent anesthesiologist known for exposing unethical research conducted at the time, stated about the Declaration,

“The Nuremberg Code presents a rigid act of legalistic demands...The Declaration of Helsinki, on the other hand, presents a set of guides. It is an ethical as opposed to a legalistic document and is thus a more broadly useful instrument than the one formulated at Nuremberg...Until recently the Western world was threatened with the imposition of the Nuremberg Code as a Western credo. With the declaration of Helsinki, this danger is apparently now past” (Annas, 1992, p.205).

This statement reflects the apparent “sigh of relief” issued by the medical community upon discovering that they would not be encouraged to conduct research under the stringent requirements of the Nuremberg Code. Instead, the Declaration of Helsinki offered a more “lenient” set of principles for them to abide by.

While the current director of the WMA does confirm that the Nuremberg Code was referenced in the creation of the Declaration of Helsinki, there are significant differences between the two documents. (Perley et al, 1992, p. 158) When introducing the Declaration, the World Medical Association stated that it had created the document, “Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity” (Mariner, 1992, p. 289). Though the wording is subtle, a comparison of the two documents reveals that the differences in their content are explained primarily by the differences in their purpose. The Nuremberg Code was created in the aftermath of the exposure of heinous crimes in which medicine played a key role. It aimed to address the experiments by creating regulations that would prevent the repetition of these events in the future. The Declaration of Helsinki, however, was written “by physicians for physicians”. (Mariner, 1992, p.

289). The document, “Embodies a general faith in the methods and achievements of medical science and an acceptance of the premise that scientific success depends upon testing new substances in human subjects” (Mariner, p. 289).

Like the Nuremberg Code, the Declaration requires that proposed research be based on laboratory and animal experiments or other scientifically established facts. The documents both require that research be conducted by qualified persons and that the benefits of the research be measured against the risks to the subject. Both give the subject freedom to withdraw from the experiment at any time and mandate that the experimenter immediately discontinue any experiment in which it becomes apparent the subject may be harmed. (Perley et al. 1992, p. 158)

However, the Declaration of Helsinki omits many of the requirements made of doctors in the Nuremberg Code. There are no prohibitions on the use of force, deceit or other forms of coercion to attract subjects. (Katz, 1992a, p. 232) In addition, the Declaration lifts the ban on the use of prisoners and mental health inmates in experiments. (Schmidt, 2004, p. 283) The principle of informed consent included in the original Declaration of Helsinki is far less stringently worded than in the Nuremberg Code, and is not listed as one of the document’s basic principles (Perley et al., 1992, p. 158.)

The Declaration of Helsinki has been revised a number of times since its original inception. The most significant of these revisions occurred in 1975 and 2000. The 1975 regulations created a document known as Helsinki II which is

recognized as “Providing the fundamental guiding principles for the conduct of biomedical research involving human subjects” (Perley et. al, 1992, p.159). The revisions repositioned the principle of informed consent in the first paragraphs of the document and greater emphasis was placed on responsibility to the individual. (“Declaration of Helsinki”) In addition, it also included an ethical review committee, a passage that played a significant role in the creation of the IRB method in the United States. (Perley et. al, 1992, p. 159)

Together, the Nuremberg Code and Declaration of Helsinki constitute “the basis of universality in the field of ethical-moral standards in human experimentation” (Perley et. al, 1992, p. 160). Both documents make strong statements about the precautions that must be taken in order to ensure the protection of subject rights. However, the ways that they approach this are very different. The Declaration of Helsinki reflects, “A more benign modern attitude toward biomedical research” and seems to accept that medical progress must ultimately depend on research on human subjects (Mariner, 1992, p. 289). However, this difference in attitude is important when considering the history of medical ethics as a whole. In his book on the development of the Nuremberg Code, Ulf Schmidt writes,

“In 1964 a crucial shift was initiated in the Helsinki Declaration about the quality of international medical ethics codes, from the rights of the patients and the protection of human subjects in experimental research to the protection of patient welfare through physicians’ responsibility. It was a move away from the essential requirement of informed consent as stated in the Nuremberg Code, beginning a watering-down process of the Code that continues to this day” (2004, p. 283).

The shift in focus of ethical documents so soon after the release of the Nuremberg Code and the conclusion of the Nuremberg Trials outlines how quickly the world began to shift away from post-World War II philosophies. Jay Katz wrote on this shift saying,

“The Declaration of Helsinki was enacted in the shadow of the Holocaust experiments; yet, less than 20 years after the Nuremberg Code was promulgated, concerns over the advancement of science began to overshadow concerns over the integrity of the person” (Katz 1992a, p. 234).

The aim of the Nuremberg Code was to create a set of principles that, if observed, would prevent the repetition of events like the Nazi experiments. Therefore, this shift in focus is significant. The shift in ideology has been accompanied by a shift in policy; it was the Declaration of Helsinki, and not the Nuremberg Code, that was adopted by the Food and Drug Administration when it issued its regulations governing experimental drug research. (Mariner, 1992, p. 290)

The purpose of emphasizing the significance of the shift from the Nuremberg Code to the Declaration of Helsinki is simply to provide a greater understanding and perspective of the ways that ethics has been created and developed in the United States during the second half of the twentieth century. It is not to say that this shift in trajectory of medical ethics has either harmed or helped the field of medicine. Instead, understanding the Nuremberg Code, the Declaration of Helsinki and the historical events surrounding both documents provides the tools needed for an informed analysis of one of the first United States Government issued documents on medical ethics, the Belmont Report.

This document that is now credited as the foundation of modern day IRB research and is the final document this chapter will examine. (Office for Human Research Protections [OHRP], 1993)

The Belmont Report was released in 1978 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

(“Belmont Report”) This Commission had been established in 1974 as a part of the National Research Act and was meant to formulate a new set of bioethical standards in the aftermath of the exposure of the Tuskegee experiments.

(“National Research Act”) These experiments, also known as the USPHS Syphilis Study, took place in Macon County, Alabama, and involved the participation of 600 men, around half of whom entered the study already having contracted syphilis. (Katz, 1992b, p. 246) The long term study aimed to compare those with the disease to the control group in order to determine the effects of the disease. Though the cure for syphilis was discovered in the 1940s, the study was continued until 1972. During this time, those in the study with the disease were deliberately left untreated. Furthermore, the subjects were not told about their condition, nor what the experiment was attempting to learn from their participation. (“About the USPHS Syphilis Study”, 2015) This lack of informed consent, as well as the blatant negligence of subject well-being by the researchers conducting the study are in violation of the Nuremberg Code and the Declaration of Helsinki. The National Research Act, as well as the Commissions established as a result of it were seen by many as recognition by the American government that the ethical standards set forth by the Nuremberg Code, as well

as the Declaration of Helsinki, were not being observed by scientists in America and that further action must be taken in order to prevent future unethical research. (“About the USPHS Syphilis Study”, 2015)

The Belmont Report is fairly succinct. Following the introduction, it lists three basic ethical principles (respect for persons, beneficence and justice) that should guide modern research . It then identifies three areas of application for these principles: informed consent, assessments of risks and benefits, and selection of subjects as the main concerns of ethics in human research. (Belmont Report). The Belmont Report serves as the document of reference for the modern day IRB Guidelines. (OHRP, 1993) Notably, the Belmont Report is significantly shorter than both the Nuremberg Code and the Declaration of Helsinki. This was done deliberately by the Commission following an agreement that the other codes were “lists of regulations that may not allow the resolution of complex ethical questions” (Fischer, 2006, p.72). The Belmont Report gives far less specific and stringent guidelines in an attempt to allow for greater recognition of the “fundamental principles” of medical ethics. It was believed that, “Researchers could then appeal to these principles to resolve dilemmas for which other codes have no answer” (Fischer, 2006, p. 72).

The Belmont Report represents a further shift in the world of medical ethics towards providing researchers with tools to address medical issues instead of simply placing requirements and limitations on their experiments in the way that the Nuremberg Code did. Historically, this makes sense-the second half of the twentieth century saw a rapid rise in medical discovery and these new

technologies and processes were in large part a result of biomedical research. Therefore, at the same time that the actions of the Nazi doctors were becoming a distant pre-Cold War memory, the field of medical technology and research was rapidly expanding. As a result of this many researchers were finding themselves in ethical situations not covered by either the Nuremberg Code or the Declaration of Helsinki. The Belmont Report aims to address this by removing specific guidelines and instead providing researchers with a more general summary of what the commission believed to be the most essential elements of ethics in research. The Report becomes more of a tool to be utilized by researchers when making ethical decisions rather than a document attempting to govern their research. This continues the trend in ethical literature (begun by the shift from Nuremberg to Helsinki) of returning the responsibility for patient safety and research ethics to the researcher. It is for this reason that the returned emphasis of the importance of informed consent in the Belmont Report is so important.

Informed Consent:

The following section of this chapter pays particular attention to the concept of informed consent and the role it plays in the ethical justification of biomedical research as a whole. As it has already been discussed, conducting research on humans, especially the types of research in which the subject can gain nothing from their participation, provides several obstacles to the world of ethics. However, despite these problems the importance of bioethical research

to the world of medicine and medical technology is acknowledged by most ethicists. In addition, past events such as the atrocities of Nazi German experiments and the Tuskegee experiments are evidence that research is an area in great need of constant and persistent ethical influence and scrutiny. It is for this reason that I now present the ways in which ethicists are able to justify some types of biomedical research in their terminology.

The first principle of the Nuremberg Code begins, “The voluntary consent of the human subject is absolutely essential” (HHS site, Nuremberg). The document goes on to define informed consent saying,

“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, over-reaching, 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.” (Nuremberg Code).

The significance of this first principle comes from the priority it places in the autonomous rights of the individual over the interests of science and society.

(Grodin, 1992, p. 277) The actions of Nazi doctors during World War II forced the world to reexamine where medicine places the values of the individual and society in the area of biomedical research. In his book on this time period, NYU bioethicist Arthur Caplan writes,

“The torture and killing that were at the core of Nazi medical experiments involves not only murder but also the exploitation of human beings to serve the goals of science. The evil inherent in Nazi medical experimentation was not simply that people suffered and died but that they were exploited for science and medicine as they died” (1992b, p. 65).

The Nazi experiments revealed a moral and ethical fallibility in the world of medicine that had previously been thought to be addressed by the professional interests of doctors to the science of healing. Early in the 20th century it began to be apparent that the advent of biomedical research required doctors to be simultaneously physicians and scientists. This created ethical problems for researchers not previously encountered in the world of medicine. This occurred simultaneously with the increased recognition that science was not an independent body, but instead a field heavily influenced by the social and political situations it existed within. The actions of German doctors during World War II provide a ready example of the potential for the politicization of science. Robert Proctor writes, “It used to be argued (by both logical positivists and many liberal sociologists) that science is either inherently democratic or, at worst, apolitical, and that the politicizations of science implies its destruction” (Proctor, 1992a, p. 17). The ways the doctors both assisted and utilized the Nazi regime for their individual and scientific interests made this view unsustainable.

Subsequent events have shown that even in situations less extreme than those in Nazi Germany, biomedical research inherently raises tensions between the values of the freedom of scientific inquiry and the protection of individual inviolability. (Katz, 1992b, p. 234) Following World War II, it was decided that if biomedical research were to continue, action must be taken to protect the rights of the individual. Though the entirety of the Nuremberg Code aims to address this, it is the principle of informed consent that has received the most recognition as a key component of ethical research. The consent principle of the Code has the status of an absolute, *a priori* principle. (Schmidt, 2004, p. 5) Consent, according to the code, is non-negotiable. (Caplan, 1992a, p. 269)

The principle of informed consent is essential to the existence of biomedical research. The principle directly addresses the concept of “humanity”, a word which, in the world of ethics, is defined as “a measurement of the moral progress of society based on the ways that the society recognizes and respects the integrity, autonomy and intrinsic worth of human beings as expressed by the laws and customs of that society”. (Macklin, 1992, p. 242) Therefore, by preserving integrity and autonomy, we can continue biomedical research without sacrificing the “humanity” of current society. Autonomous action has been defined as action by “normal choosers” (those mentally capacitated to make decisions for themselves) who act “intentionally, with understanding, and without controlling influences that determine their action” (Pedroni & Pimple, 2001, p. 2). The principle of informed consent provides an ethically viable possibility for continued human experimentation by letting the research subject make informed

decisions about their role and therefore preserving the subject's autonomy and integrity. Jon Vegar Hugaas outlines the necessity of informed consent saying, "The two principles of respect for autonomy and integrity and the principle of informed consent form a triangle in biomedical ethics, in such a way that if we accept one of them, we accept them all, and therefore we cannot turn down one without turning down the others as well" (2002,p. 68). Arthur Caplan describes informed consent as "a counter to utilitarianism", explaining that the principle responds to ethical questions surrounding the role of human subjects in research should be by allowing them to choose. (personal communication, December 10, 2014)

Since the creation of the Nuremberg code, the notion of informed consent has for some become the "*sine qua non*" for human experimentation. (Perley et al., 1992, p.155). The Code provides the "most complete and authoritative statement of the law of informed consent" and is "part of international common law" (Annas, 1992, p. 201). Since that time, informed consent has been preserved in documents of ethical standards. However, while it has remained a consistent ethical guideline, lack of adherence to this principle by the medical community has led to several instances of unethical research. Examples of this are apparent in events such as the Tuskegee experiments. In addition, the fight for recognition of the importance of informed consent has met resistance from a government standpoint as well. In 1966 the FDA, recognizing the failure of the biomedical industry in obtaining these forms of patient consent promulgated patient consent regulations to the biomedical industry. (Glantz, 1992 ,p.186)

However, in 1990, the FDA also granted the Department of Defense a waiver for the informed consent requirements so that they could experiment with unapproved drugs and vaccines on soldiers as part of project Desert Storm. (Neuhaus, 1992, p. 216). Throughout the second half of the 20th century, other occurrences, such as LSD experiments conducted on soldiers without their knowledge in Manhattan, as well as countless other examples also serve as examples of the lack of priority given to informed consent. (Katz, 1992a, p. 231)

Informed consent is difficult. On the one hand, it provides an ethically viable way to protect the rights of the individual by preserving that person's autonomy and integrity. It places the concerns for a subject's welfare over the interests of science and society. (Grodin, 1992, p. 277) However, it is also time consuming, it can limit the subject pool, and it means extra paperwork. The concept is also very relative. The levels to which a subject must understand an experiment in order to make an informed decision about it are difficult to define. When looked at from an ethical standpoint, the principle of informed consent seems essential. However, in the highly competitive, fast-paced environment that many researchers find themselves in today, the responsibility of the scientist to the patient may pale against pressures they experience from outside forces to produce results from their experiments. Therefore, with the the recognition that there has been a shift towards returning the power of discretion to the physician (as a result of the Belmont Report) as well as a history of neglect of the principles of informed consent, modern day IRB processes have been developed to attempt to absolve the researcher from at least a part of the responsibility and therefore

mediate some of the unfortunate tension between rights of the individual and interests of society that is so inherent in biomedical research.

Current IRB Policies

“When the fences and the safety rails have been removed, when the signposts have been changed or taken down, what reason is there to believe that people in our time will not do what was done then?”

-Richard Neuhaus, “The Way They Were, The Way We Are”

In 1989, it was agreed that all federally connected research in the United States should come under the purview of a single set of regulations. In 1991, the Department of Health and Human Services (DHHS) published Title 45: Public Welfare, Part 46: Protection of Human Subjects. Subpart A of this represents the basic policy for protection of human research subjects. This law became known as the “Common Rule”, with 16 federal agencies agreeing to operate under its regulations. (Fischer, 2006, p. 73) The Common Rule applies to any research done that is supported by or subject to oversight by any of the 16 government agencies involved. (Ex. private pharmaceutical research overseen by the FDA) The Common Rule, is based in large part on the Belmont Report. It created and set guidelines for an Institutional Review Board (IRB). IRBs are given the responsibility of evaluating “the risk/benefit ratio of proposals, selection of subjects, and protection of subjects’ confidentiality” as well as insuring that “potential subjects will be informed about the research prior to their consent being sought and that the consent is documented”. (Fischer, 2006, p.74) The breaches of medical ethics in the 20th century were seen by some as proof that researchers could not be trusted to make ethical decisions because of their investment in their own research. IRBs were developed with the hope that,

“Groups of scientists deliberating together could make better judgments than individuals in lone reflection” (Stark, 2012, p. 109).

The Code of Federal Regulations (CFR) defines an IRB as, “Any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects” (IRB:General Provisions § 56.101, 2014). The CFR outlines the structure of an IRB. It states that an IRB should be composed of at least five members who possess different backgrounds so as to “promote complete and adequate review of research activities.” (Protection of Human Subjects § 46.107, 2009) The document requires that an Institutional Review Board 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” (Protection of Human Subjects § 46.107, 2009) Given these components, the document asserts that an IRB will therefore be able to provide advice and counsel in “safeguarding the rights and welfare of human subjects” as well as 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” (Protection of Human Subjects § 46.107, 2009). The document requires each IRB to contain at least one person whose primary concerns are scientific, and one whose primary concerns are nonscientific. (PHS § 46.107, 2009)

The CFR describes the role of the IRB as something of a “watchdog” for the research conducted at the institution. It is the role of the IRB to perform initial and continuing review of research, as well as review and approve any changes to research that may occur during experimentation. IRBs are required to conduct regular inquiries into the research process based on the risk level of the research and ensure that ethical protocols are being observed. In addition, the IRBs are responsible for documentation of research and for reporting “unanticipated problems involving risks to human subjects and any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB and subsequent suspension and termination of IRB approval to institutional officials and the FDA” (IRB:IRB Functions § 56.108, 2014). In essence, the intended role of the IRB is to oversee research and provide physicians with both a guiding force and a watchful eye.

IRBs are technically run by the institution that sponsors the experiments they review, however, they are subject to government oversight. The Code of Federal Regulations lists the FDA as the primary source of this oversight. Just as IRBs are required to oversee research, the institution is required to oversee the IRB and the FDA is required to ensure the correct operation of the institution. However, the FDA does this by conducting reviews of the conduct of the IRBs themselves. Any identification of a lack of adherence to the CFR by an IRB results in negative action against the institution as well as the IRB itself. Disciplinary actions by the FDA include withholding approval for any new studies, termination of ongoing studies, retracting the ability to recruit new subjects to a

particular study and the notification of relevant state and federal regulatory agencies to the indiscretions of the institution and the institution's IRB. (IRB: Administrative Actions §56.120, 2014) In addition, institutions can have funding revoked and possibly face clinical penalties. (Glantz, 1992, p. 189) This oversight as well as the potential consequences of failing to adhere to protocols is meant to motivate institutions to create and maintain responsible and effective IRBs. In turn, the presence of the IRB and the requirements for funding are intended to encourage researchers develop ethical protocols from the beginning.

Institutional Review Boards are given a comparatively large degree of freedom in the decisions that they make regarding the approval of biomedical experiments. However, the Code of Federal Regulations does list a series of requirements that experiments must meet to qualify for approval. A study must use procedures "consistent with sound research design and which do not unnecessarily expose subjects to risk"(IRB:IRB Functions §56.110, 2014). Risks to subjects must be "reasonable in relation to anticipated benefits"(IRB:IRB Functions § 56.110, 2014). In determining this, IRBs should not consider the long-range effects of the knowledge gained in the research, only assessing risks or benefits that may directly result from the research. IRBs are in charge of ensuring that the selection of subjects is equitable and that a particular vigilance is maintained for any research associated with "vulnerable populations" (children, prisoners, pregnant women, handicapped, mentally disabled or economically and/or educationally disadvantaged persons). One of the ways they are charged with doing this is through informed consent.

The Code of Federal Regulations states that an IRB must request and review proof of informed consent from subjects from every relevant experiment and must continue to monitor these experiments in order to ensure that the guidelines set are being followed. The CFR's definition of informed consent retains the definition originally expressed by the Nuremberg Code. The document maintains the rights of the subject to withdraw from a study at any time. (Glantz, 1992, p.189) However, unlike the Nuremberg Code, or any other previous documents of medical ethics, the CFR gives an IRB the power to waive the requirement for informed consent given that the board determines the experiment will have sufficient oversight similar to that provided by an IRB, or that the research could not be performed without a waiver. (Protection of Human Subjects § 46.116, 2009) This responsibility to assess the necessity of informed consent, as well as monitoring the procedures for obtaining it deviates from previous guidelines by removing the responsibility from the researcher and instead placing it on the Institutional Review Board. In theory, this transfer of responsibility to a larger group would decrease the likelihood of unethical research. Once again, we see the idea that groups of scientists make better decisions than the individual alone.

In addition to the doctrine and definition of informed consent in the main document of the CFR, there are also two separate sections that aim to directly address policies regarding the rights of children and prisoners in biomedical research. These two populations are mentioned specifically because past events have shown these populations to be especially at risk of being taken advantage

of in research. This additional protection aims to address problems identified in these populations with informed consent and the ability of the these subjects to make truly autonomous decisions.

In section 46.401 of the document, research on children is divided into 4 classes: research not involving greater than minimal risk, research involving greater than minimal risk but presenting the prospect of direct benefit to the subject, research involving greater than minimal risk and no prospect of direct benefit to the subject but likely to yield generalizable knowledge about the subject's disorder or condition, and research not otherwise approvable which presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children (2009). An IRB is responsible for assessing the risk a particular experiment poses to its subjects and then classifying it into one of these categories. Each category receives slightly different treatment by the IRB, including variations in amount of documentation and frequency of oversight. Any experiments falling in the fourth category (research not otherwise approvable) requires the approval of the Secretary of the Department of Human Health Services (DHHS) before it can proceed. (PHS: Additional Protections for Children §46.401, 2009)

Similarly, the Code of Federal Regulations places additional requirements on research done on prisoners in order to ensure the protection of the rights of those individuals. Prison research, like research on children, is classified as one of four categories: studies of possible causes, effects, or processes of incarceration and of criminal behavior, studies of prisons as institutions or of

prisoners as incarcerated persons, research on conditions particularly affecting prisoners as a class and research on innovative and accepted practices that have the “intent and reasonable probability” of improving the health or well-being of the subject. (PHS:Addition Protections...Involving Prisoners §46.301, 2009)

The third of these categories, research on conditions particularly affecting prisoners must be approved by the Secretary of the DHHS. The prisoner regulations found in the CFR are even more stringent than those in the Nuremberg Code. They require that there be a compelling reason for using prisoners, as opposed to a more general population. The document states the reasoning behind the strictness of these regulations saying,

“Inasmuch as prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subject in research, it is the purpose of this subpart to provide additional safeguards for the protections of prisoners involved in activities to which this subpart is applicable” (PHS:Addition Protections...Involving Prisoners §46.302, 2009)

IRBs reviewing prisoner research are structured differently than a normal IRB. In IRBs concerned with prisoner research, the regulations state that one member of the IRB, “Shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one Board only one Board need satisfy this requirement” (§46.302, 2009). This requirement along with the others made in the document aim to create additional regulations to protect the rights of vulnerable groups.

When analyzing the implications of each change in the regulations and procedures made by the Code of Federal Regulations, the main considerations is how effective the IRB system is in identifying and addressing ethical problems posed to modern medical research. There are both positive and negative aspects to the IRB system. On the one hand, IRBs are able to serve as watchdogs, ensuring that researchers are observing ethical research practices by assessing the risks of experiments and monitoring research to ensure adherence to protocols. IRBs place responsibility for the protection of human subjects on the institution, rather than the investigator conducting the research. (Glantz, 1992, p.189) IRBs are also a far more decentralized system of ethical review than had been previously used in the medical research. Certainly, they ensure that researchers are observing the CFR. However, they are also given a great amount of leeway in the decisions they make regarding the specifics of research protocol and oversight. Theoretically this gives IRBs a greater ability to tackle some of the nuanced and difficult problems that may arise in creating and maintaining ethical research. However, the lack of rigidity in the design of the system also raises questions as to the proper role of each component of an Institutional Review Board and creates a lack of uniformity in the decisions made by each IRB. IRBs are frequently tasked to make many decisions by interpreting and inferring ethical practices using the CFR. This can be tricky as well as subjective. Factors such as past experiences of the individuals comprising an IRB or personal knowledge of a researcher by members of an IRB have been observed to influence the board's decisions.

One such example of this can be seen in the ways that community members act within an IRB. The inclusion of community members in IRBs is meant to provide an outside perspective on the research, one whose primary concern is not science or scientific progress. In addition, community members can assist in helping the IRB be sensitive to community attitudes when considering and approving research proposals. In her observations of the processes involved in IRB decision making, Laura Stark, a sociologist who researched the origin of the IRB, observed that community members, “Keep the scientists and the medical folks honest because their perspective is not to drive or improve the science” (2012, p. 24). However, the ways that IRBs include and interact with their community members varies. Often, community members were formally involved in the medical or scientific fields and therefore may have trouble representing a layperson on the IRB. (Klitzman, 2012) Community members often struggle with the ability to accurately represent community attitudes in full. Because community members aren’t associated with the scientific community, IRBs struggle with the level that they are required to engage and include them and how thoroughly to explain complicated medical terminology and procedures. (Klitzman, 2012)

When considering how effective the IRB format is in ensuring ethical research, Arthur Caplan, pointed out both positive and negative aspects of the system. He named the IRB as the “Protector of the doctrine of informed consent”, saying, “[IRBs] help because they explain to the researcher that you have a motive to do this--the more that subjects understand, the less likely that

they are to be noncompliant with the research protocol... So there's the idea if [the researchers] don't buy into the model, then you don't get great science out" (personal communication, December 10, 2014). Caplan argues that IRBs are beneficial because of their ability to inquire into the "soundness of the methodology or the reliability of the hypothesis and experimental design of a certain project". (personal communication, December 10, 2014) They are in a position which allows them to question researchers and experiments with a legitimacy that researchers respect. In addition, it is to the advantage of a researcher to observe the decisions made by an IRB. Caplan states, "If you get an adverse event, its much better to have the IRB processes documented...It will help you, as a researcher, to survive any outcome thats not predictable or not due to any maleficence" (personal communication, December 10, 2014). This is important as many of the problems that were seen with the Nuremberg code and the Declaration of Helsinki stemmed from the lack of respect granted to them by researchers and the inability to enforce any of the guidelines they outlines.

While they may exert a greater degree of influence than previous ethical policies, IRBs present additional problems in the lack of uniformity in their decisions. Laura Stark writes, "The point of the rules is to enable civil servants to make rote, seemingly impersonal decisions in our stead. In theory, the rules are so precise that they would allow all qualified people to reach the same conclusion. Administrative laws are designed to make human decisions appear to be objective and beyond the judgment of a given individual" (2012, p. 3). However, Stark also observed, "The issue of who gets authorized to sit around

the table has a remarkable effect on the decision making process” (2012, p. 37) IRBs, and the decisions they make, are so detailed and nuanced that they rarely result in a uniformity. As Gernot Bohme, a German philosopher of science, points out in his essay on unethical medical research, “Universalistic principles, precisely because they are meant to be valid irrespective of culture, religion, and class-identity, can lead only to the most minimalist form of ethics” (2007, p. 27). Therefore, in order to make the detailed decisions, Institutional Review Boards often draw upon many different influences in the decision making process. Stark writes, “The people whom board members called to mind when they imagined a research subject—a relative or a student, for example—reinforced the race, class, and gender biases of the board membership” (2012, p. 14).

Though this variance in the decisions made has always been a topic of issue for ethicists, the issue has recently been brought to the forefront by the expansion of multisite and multinational experiments. Arthur Caplan stated, “Part of the local IRB notion was to have me watch you or you watch be...it could be a kind of local police force. You know, single investigator, working down the hall. Well, now its a thousand investigators working around the world..I’m not watching anyone I know and I can’t monitor anything that closely” (Personal Communication, December 10, 2014). Today many experiments are worldwide, taking place at multiple sites, with each site having its own IRB and review process. Though trials are usually run using the same protocol at each site, the decisions made by that site’s IRB may vary. This is often the case in the ways they approve consent forms and research practices. (Check et al., 2013, p. 561)

Researchers must then take additional time to address the issues raised by each IRB in order to create a unified experiment. This can result in extensive changes to consent forms as a result of opposing requests by multiple IRBs, making the documents longer, more complex, and often introducing errors. (Check et al., 2013, p. 563) This can delay participant enrollment and delay start up. (Check et al., 2013, p.560) In a study done on a multi-center therapeutic West Nile virus trial, waiting for multiple local IRB approvals contributed to major delays in sites' ability to begin enrollment (Check et al., 2013, p.563). This process results in frequent frustrations from researchers who are under pressure to produce timely results. The issue of multisite IRBs is important because it provides one example of the inability of the IRB system to handle recent changes in the biomedical experimental process. Other problems, such as lack of resources need to properly review research protocols and lack of scientific understanding by IRB members of technologies and methods used in the experiments have also been observed. (Caplan, personal communication, December 10, 2014)

The Code of Federal Regulations and the IRBs that result from it do address some of the problems observed with previous ethical documents like the Nuremberg Code and the Declaration of Helsinki. As Laura Stark points out, IRBs are, in theory, guided by a respect for persons, beneficence and justice in their interpretations of the Code of Federal Regulations. (2012, p.11) Their inclusion of community members ideally provides non-scientific voices and the power given to it by the Federal Government helps avoid any problems of

disobedience or apathy by researchers. However, the format is certainly not perfect.

IRBs are given the flexibility necessary to respond to a myriad of ethical issues, however, as a result of this decision making ability, the results are unpredictable. This unpredictability causes its own set of issues, some which are becoming more and more prominent as the face of research continues to shift globally. As biomedical research progresses there has been an increase in the observed limitations of the IRB process.

IRBs and the Modern Research Environment

“Solutions, pedagogical and structural, for the challenges of research integrity need to be customized to the variability of climate at the subunit level”

-Organization Research Climates Survey

The development of the IRB process is deeply rooted in the global history of bioethics, stemming in large part from the Nuremberg Code and the actions of the Nazi doctors. The regulations contained in the CFR attempt to address past violations of the principle of bioethics. This is especially apparent in the emphasis the regulations place on informed consent and the extra protections it provides to vulnerable groups such as children and prisoners. However, while it does address past actions and problems in bioethics, whether the IRB process effectively addresses current research conditions and dilemmas is still a matter of concern. The justification for the IRB process centers on the idea that a group of physicians is better able to make ethical decisions than the individuals. However, the question is, does this shift actually promote more ethical research? In this chapter I present several problems that have begun to emerge as a result of the modern research environment and the IRB system’s inability to address these issues both as a result of its status as a reactionary document and of its inability to address the root causes of unethical behavior.

One of the most important things to consider when examining the changes is that biomedical research in the United States has rapidly expanded in the twenty first century. (“Biomedical Research”) Funding for research both from the

National Institute of Health (Government Funding) and from pharmaceutical companies, has been increasing in the past thirty years. Today, industry sponsored research accounts for sixty percent of funding. This increase in funding has been met by an explosion of research centers and influx of researchers to the profession. This has led to greater pressure on researchers to get things done in the quickest, most efficient manner. In 2012, the NIH began publishing “Success Rates”, a statistic measuring the results published per dollar spent by the Institute. Industry funded research also pushes heavily for results.

According to Arthur Caplan, industry grants are, “More outcomes oriented and speed oriented than a foundation or government grant-they have a timeline, they paid you the money and they want an answer...They don’t even necessarily want favorable results, they just want results” (Personal Communication, December 10, 2014). Caplan also explained that there is additional pressure from medical schools to produce “headlines” and compete with other institutions. (Personal Communication, December 10, 2014) Coupled with a decreased availability of jobs, the culture of biomedical research has been described as “publish or perish”. (Schmidt, 2004, p. 285) Other individuals in the world of bioethics have raised similar concerns about the current research environment. Historian Ulf Schmidt claims that the increase in pressure on researchers to produce has led to a “culture of shortcuts” that can manifest itself in neglect of policies such as informed consent and equal recruitment of subjects. (Schmidt, 2004, p. 285) In her essay on the sources of unethical research, author and physician Marcia Angell stated, “It stems from the desire to obtain unambiguous

answers to scientific questions as rapidly as possible in a highly competitive research environment” (1992, p.279).

Unfortunately, recent studies have corroborated these theories. A study done in Belgium in 2012 found that “Excessive pressure to publish scientific articles contributes to scientific misconduct, at least among European medical scientists” (Tijdink, Verbeke, Smulders, 2014, p. 68). In a study done by scientists Koocher and Keith-Spiegel it was found that 84% of researchers reported questionable behavior among colleagues. (2010, p. 438) Another 2011 study reported that 33% of the researchers surveyed self reported “questionable research practices”(DuBois, Anderson, Chibnall, 2013, p. 209). One study showed that 4.9% of biomedical early career scientists reported modifying research results and 81% said they would be willing to fabricate data to win grants or be published. (Kalichman & Friedman, 1992)

As discussed in the previous chapter, the IRB structure was created with the idea that groups of researchers are better able to make ethical decisions than the individual alone. The idea was to remove some of the great weight of responsibility from the researcher and instead place it on a collective body, one that is theoretically better able to monitor the research. However, one unfortunate side effect of this process is that it places the researcher outside the realm of ethical decision making. While the CFR still does include sections on informed consent and other principles that have historically been shown to be essential in medical ethics, because of the structure of the system these issues become the responsibility of the Institutional Review Board to protect and not the

researcher. In an article published in the *Journal of Academic Ethics* in 2008, researcher Gary Allen argues, “A schism has emerged between the actual ethical conduct in research and the mechanism of following the rules” (p. 107). The results of this schism have been observed in the work place. A 2007 study of 3,000 NIH-funded scientists found high levels of “normative dissonance” and suggested that the environments that scientists work in often do not reflect their own beliefs and values (Anderson, Martinson, & De Vries, 2005).

This level of normative dissonance and the separation of scientists from the ethics process is especially important given that the intense research environment often places scientists in a position in which their ability to efficiently and expediently get their experiments through the IRB process is advantageous both to the institution they work for and to their own careers. In addition, as a result of recent trends of institution wide shutdown of research following government identification of unethical conduct, institutions have begun to increase the pressure they place on IRBs to ensure complete compliance with federal regulations. The system places the researchers and the IRBs in opposition to each other, with the IRB responsible for ensuring research compliance so as not to threaten the entire institution and the researchers focused on “getting past” the IRB to produce results for their funders. Gary Allen writes, “Within these constraints, any reflection on the role or operation of ethics committees tends to be almost exclusively focused upon the goal of ensuring compliance, and compliance tends to be understood in terms of a researcher completing an application form for review by an ethics committee” (2008, p.

107). A 2004 paper by scientists Loff and Black observed that the functioning of ethics committees may actually encourage an abrogation of the responsibility of researchers to reflect upon the ethical issues associated with their own research (Loff & Black, 2004).

As a result of this situation, researchers may be more prone to misrepresent their experiments in a way that will allow them to more expediently pass the IRB process. As discussed previously, the IRB process can often delay research, especially in the case of multi-site trials. This can be a large source of frustration for researchers already under pressure to produce quickly and at low cost. Allen states, "There are indications that research designs are being compromised or 'disfigured' by existing ethical review processes, or that researchers may actually be presenting a distorted description of their research to get it past an ethics committee" (2008, p. 109). One study found that "A researcher who feels that a study protocol was unfairly reviewed by an IRB is more likely to find ways to bypass the IRB when conducting future research. (Dubois et. al, 2012, pg 10)

This analysis of the current research environment and the rate of unethical research is concerning. However, it is because of the identification of these problems that a historical understanding of the development of the IRB process as well as the significance of its principles becomes even more important. Past ethical transgressions reveal the consequences of failing to place appropriate emphasis on medical ethics. However, they also show that enforcing ethical principles through institutional or government oversight is limited and ultimately

useless if not done in a way that is conducive to the research environment. The Nazi experiments occurred despite ethics research, the Tuskegee experiments despite codes of ethics created by doctors, themselves. Now, even despite increased oversight and the creation of IRBs, research has shown that unethical research still exists and growing pressure on researchers increases the likelihood of it continuing in the future.

One possible reason for the failings of the IRB system is that the regulations put in place fail to accurately address where ethics stems from. Recent research looking at ethical decision making in the laboratory states that researchers gain most of their ethical guidance from looking at past experience, examples given to them by peers, and the training they received when beginning their careers. One study found that exposure of first year doctoral students regularly exposed to unethical events were, “More likely to report having behaved unethically, to have lost ethical principles, and to feel guilty” (Mumford et al., 2009, p.352). It was found the such exposure provided “negative case models” from which the students would draw on later in their careers when dealing with similar situations. The study suggests that the issue is not that graduate students are taught unethical principles through exposure to these events but rather, that these instances teach unethical work practices. The authors state, “These findings suggest that exposure to unethical events led people to incorporate these events into their body of knowledge about how work is conducted. This knowledge is, in turn, used as people make decisions about how to conduct their work, with exposure to unethical events giving rise to unethical decisions” (Mumford et al., 2009, p. 357).

Research also suggests this is especially true for younger, less experienced, graduate students and those in charge of them (e.g. preceptors, mentors). Reviews of U.S. Office of Research Integrity cases of misconduct showed a positive correlation between research misconduct and poor mentoring by mentors and senior colleagues (Wright, Titus & Cornelison, 2008).

Studies have also shown that the perceptions researchers have of their research environment play a significant role in guiding their decisions. In a study done on the effects of climate and environmental conditions on research integrity, it was found that competition, production pressure and poor study design were the most commonly seen causes for breaches in ethics. (Mumford et al., 2007, p. 341). The study findings suggested that young graduate students were especially prone to take actions (even unethical ones) when rewards and reinforcements were not readily available in the work environment. Furthermore, it was hypothesized that doctoral students entering an environment they perceived as being committed to the work were more likely to make ethical decisions, while placing undue competitive pressure lead to more frequent unethical decision making across a number of domains. The researchers concluded that their findings suggest, “Ethical decision making might be improved if people are not placed under excessive or undue pressure in the early phases of their career...Excessive competitive pressure may lead to the acquisition of beliefs likely to engender the potential for unethical decisions throughout an individual’s career” (Mumford et. al, 2007, p. 362).

This research is concerning for several reasons. The previous evidence that that competitive pressures increase the likelihood of unethical decision making make the recent increase in research pressures more significant. Secondly, evidence that researchers gather most of their guidance in ethical decision making from their peers and mentors means that the IRB oversight process, a system that is already struggling with its relationship to investigators and researchers, can have little benefit in encouraging ethical decision. Instead, the system places additional pressure and oversight on research, further alienating the two from each other. All of these factors are manifested in the apparent willingness of younger researchers to make unethical decisions in order to achieve career boosts.

Given this evidence, the current system seems less than ideal. However, if used correctly, the results of these studies as well as the records of frequent unethical research can be used to help guide further revision in the system. Currently, it would seem that the system creates something of a self-perpetuating unethical research climate: pressure increases the likelihood of unethical decisions, unethical decisions tend to beget more unethical decisions, and observation of these decisions and climates by younger students drives them to make similar decisions in the future. However, if appropriate action is taken the research gives the potential for a change in the way we do things through the reduction of pressure on researchers and the fostering of a more ethical research environment. Doing this requires examining our system in order to figure out specifically who and where it is currently failing.

The Belmont Report and the IRB process represents America's current response to addressing the tensions between biomedical research and bioethics. The system reflects the many bouts of trial and error that have occurred in the last one hundred years between these two sectors. The rules and processes involved are still changing, as ethics struggles to keep up with and reflect the modern research environment. This is understandable; both of these fields are relatively modern and rapidly progressing. It is apparent from recent studies and research that this system too, will need to be altered if not completely changed in the upcoming years. However, unlike in other situations, it is important to understand that unlike other disciplines this system of "push and pull" and "trial and error" involves human life. Therefore it would behoove all parties involved to exercise caution in their decisions. In order to do this, it is essential that we understand the history of bioethics, what has and hasn't worked, so that we may give appropriate weight to each actor, learn from the past what has and hasn't worked, and use these lessons in the revision of the system.

Where are We Now?

“The scientists of the world must remember that the research is being done for the sake of mankind and not for the sake of science; scientists must never detach themselves from the humans they serve.”

-Eva Kor, Mengele twin

Understanding the history of the IRB process as well as the documents and events leading to its creation is essential to any discussion of issues in medical ethics. Current policies aim to address past failures; current issues underline the problems that remain in the current system. By studying the history of medical ethics, one can get a grasp on the different interactions and ideas that have led to the modern system. We can see what did and didn't work, and from that gain guidance for future action.

There are several important lessons we can learn from the history of biomedical research. The history shows that while policies and systems can be changed, it is often necessary for the revelation of some great breach of medical ethics to occur before action is taken. Such was the case for both the Nuremberg Code and the Belmont Report. History shows that the backlash against these events is often large, vocal, and easily forgotten. This can be seen with the unethical experiments done within five years of the Nuremberg Trials. History shows the to the importance of having bioethical policies and emphasizes how essential collaboration with the medical profession is in order to ensure compliance to these policies.

Past events provide copious evidence that ethics, especially in the case of biomedical research, is a matter of constant vigilance. This is shown in the way

that, despite several different forms of rules and regulations, unethical events still emerge. In a world in which science represents progress and power, where scientists are constantly pushed to produce and achieve, there are far more impetuses towards breaking and stretching the rules than adhering to them. It is for this reason that the IRB process is not enough. Doctors, medical ethicists, researchers and subjects must work to regulate and monitor the system. In order to do this, an understanding of the policies, their histories and the reasons they were created is essential. The continued study of what factors in our researchers, research environments, and ethical regulation systems make unethical decisions more likely should be guided by history. The research presented in the previous chapter is encouraging. By identifying these issues and their causes we may begin to address them. Beginning this process now could prevent biomedical research from more severe breaches of medical ethics like those that have occurred in the past.

As a discipline, medicine has been struggling for as long as it has existed to foster within its members a commitment to ethical conduct. As a country, the United States has been working since World War II both nationally and internationally to establish a set of guidelines and a system that researchers and physicians will adhere to. However, frequently, the worlds of biomedicine and bioethics have found themselves in opposition to each other. The Nuremberg Code failed because doctors refused to adhere to it. The Declaration of Helsinki was replaced by the Belmont Code because of revelations that researchers in the United States were unethical despite it. Though the creation of the IRB

system introduced a certain amount of power to the ethical regulations laid out by the Code of Federal Regulations and the Belmont Code, increased opposition and disconnect to the structure, as well as unethical decision making has been observed. Currently, increasing research pressure coupled with the inability of the process to directly address the roots of unethical decisions limit the impact and extent of our system. The IRB process watches doctors closely, using an outside body to examine each experiment; even so, unethical research still occurs. Though it is apparent from the structure and content of the CFR that bioethics did make an attempt to learn from history by placing additional oversight on researchers, it also ignored historical evidence that any system made in opposition to physician/researcher ideas will ultimately fail. The policies created to address and create ethical research are dependent on the level of significance those they govern place on them.

Historical knowledge of bioethics also serves as a constant reminder of the importance of the field. Today, with the fast paced research environment, there is reluctance to give principles such as informed consent the respect their ethical foundations demand. Experiments such as the Nazi concentration camp experiments and the Tuskegee trials serve as a reminder that there are consequences to belittling these principles. Examination of the individuals involved revealed that they did not represent extremists or medical outsiders. The defendants at the Nuremberg Trials represented some of the top physicians and scientists in Germany at the time; few were described as sadistic or insane, only as passionate and committed to their research. Furthermore, there were

already discussions around and guidelines for biomedical experimentation and the rights of the individual in Germany before World War II. The specter of the actions of Nazi doctors serves as a reminder that these ethical principles and policies must be taken seriously.

The question then seems, taking these influences into account, along with a knowledge of the strengths and shortcomings of the current IRB process, where does bioethics stand? In his essay on the impact of the Nuremberg Code, Leonard Glantz (1992) writes,

“The Nuremberg Code is an exclusively substantive document, whereas the federal regulations contain procedural safeguards. These safeguards are embodied primarily in IRB review and public scrutiny by requiring at least one member of the IRB to be from the community. The mere fact of such scrutiny and the risk of exposure deter unethical research. However, such review acts as a safeguard only when the values of the reviewers are directed at protecting human well-being. It is unlikely that IRB review in Nazi Germany would have led to more humane treatment of subjects” (p.199).

Glantz argues that our current process only works to safeguard the rights of patients and ensure ethical research if researchers share these goals. Research has shown that the main source of ethical guidance for researchers is gained through their peers and mentors. Their decisions are guided by what they perceive from the climate and environment of their laboratory and institution. Ethical policies, documents and review boards can only supplement and guide scientists. Currently, the increases we see in pressure on researchers as well as the inability of the IRB to effectively relieve this pressure is correlated with an increased observation in unethical decision making. Glantz argues that the IRB

process would have had no effect in Germany because the research culture in the concentration camps encouraged unethical research. Physicians and researchers were pressured to produce results that could aid Germany in the war effort, and they were told to do so by any means necessary. The Nazi doctors believed strongly in their cause. They were ready to present ethical reasons to justify their actions. The extremes seen in their research, especially their neglect of the rights of their patients, come from a failure to give appropriate weight to individual rights versus the “greater good”. Their interest centered almost entirely on the progress of science; no consideration was given to the rights or care of their subjects.

In cases of individual rights in biomedical research, the preservation of the ethics and the integrity of the patient ultimately falls on the researcher. Committees can be created to oversee experiments, laws and regulations can be enacted to guide committees, however, the end product depends on the commitment the researcher has to adhere to these guidelines and the protection of patient rights. The Nazi experiments are a reminder of how essential the preservation of these rights are. Elie Wiesel (1992), a survivor of the camps who wrote extensively about his experiences, says of the doctors, “They knew how to differentiate between good and evil. Their sense of reality was impaired. Human beings were not human beings in their eyes. They were abstractions. This is the legacy of the Nuremberg Tribunal and the Nuremberg Code. The respect for human rights in human experimentation demands that we see persons as unique, as ends in themselves” (p. ix).

Examining the history of bioethics shows that while each subsequent document does address past problems and attempt to use those changes to

promote more ethical research, ultimately there is very little to be done if researchers are unwilling to comply. Referencing the extensive *Guidelines* that were already in place in German biomedicine before the start of World War II, Sharon Perley et al. (1992) points out, “The fact that such a governmental regulation actually existed, at a time when the Nazis were carrying out human experiments in an irresponsible manner in concentration camps underlines the irrelevance of legal regulations if they are not enforced by the authorities” (p. 151). Ulf Schmidt reiterates this in his own work saying,

“What becomes apparent is that the political climate of the time is central not only to the efficiency with which medical ethics regulations are being introduced and disseminated, but, more importantly, to the extent to which the rules are actually being followed by medical professions, funding and state agencies” (2004, p.281).

The extent to which these rules are being followed, even with the modern IRB system, is dependent on researchers. However, in our current system, pressure is placed on researchers from all sides. In many cases, the pressure to produce and follow the rules may overshadow the pressure to maintain an ethical environment; a researcher may be tempted to discount the impacts of performing research without high ethical standards and instead place the responsibility for ensuring ethical research solely on Institutional Review Boards. The history of biomedical research shows how essential it is to have the researchers themselves committed to ethical decision making and to creating an ethical research environment. The history of biomedical research also shows the consequences when this is not done.

The goal of this thesis is not to draw direct parallels between the current state of biomedical research and experiments done by Nazi doctors during World War II. Instead, it aims to use the events as an opportunity to gain insight into possible areas of weakness in the modern day system by drawing on the extreme. One of the great advantages of the Nazi experiments is that seeing such a degree of disregard for human autonomy and life in a “civilized and advanced” country is difficult to ignore. The events provide strength to arguments for constant vigilance in the worlds of bioethics and biomedical research.

The current system of bioethics is not enough. Already, studies are showing cracks in the modern research system. Many suggest that the current procedures of oversight limit researchers and fail to address where these ethical decisions are made from. IRB processes result in increased pressure on researchers to meet the standards set by the CFR for “ethical research”; however, the system simply sets guidelines and provides paperwork for meeting these standards. Many times this limits or slows the research process as well as distances researchers from the ethical decisions made in their experiments. It fails to support or guide researchers in their decisions. As a result researchers are required to turn to their peers and mentors for guidance. Increasing pressure from funding sources only serve to exacerbate these issues. We know from an examination of the history that neglecting to place appropriate emphasis on the principles of medical ethics in the laboratory, at the heart of research, results in violations of individual rights. It is for these reasons that it is essential we begin to identify, to discuss, and eventually to address these problems, instead of

letting the situation escalate further. The commitment to the protection of individual rights and principles of ethics in biomedical research is essential to the preservation of our “humanity”. Without it, the discipline becomes a sad irony; a science striving for the advancement of society through methods that harm its subjects.

Epilogue

There is one factor in the Nazi experiments as well as other subsequent breaches in medical ethics that I feel it is important to identify but difficult to discuss within the scope of this thesis. That is the role that war and “wartime conditions” plays in the way we weigh the tension between individual rights and actions for the “greater good” in medical experimentation. The Nazi experiments serve as a particularly well fitted example of one way acting in the interests of one’s country has been used by both governments and scientists in the past as ethical justification for ignoring and knowingly violating medical ethics.

Throughout the Nuremberg Doctors’ Trial, the defendants presented a number of arguments attempting to ethically justify their actions during the war. The argument that wartime conditions and protection of country took greater precedence than ethical policies, has borne repetition in recent years. In the second half of the 20th century, the United States Army performed experiments in which various doses of LSD were given to soldiers without their knowledge or consent. For some, the effects of these experiments were permanently damaging and had lifelong effects on the mental health of the soldiers. The justification given by the CIA and the US Army for these experiments pointed to reasons of national security. (Annas, 1992, p. 216) In December of 1990, the Federal Drug Administration granted the Department of Defense a waiver from the informed consent requirements necessitated by the Nuremberg Code and all other existing law and regulations in order to allow the department to test unapproved drugs and vaccines on the soldiers involved in experiment Desert

Shield. (Annas, 1992, p. 216). The “wartime mentality” argument given by the American government is almost identical to one of the major defenses given by Nazi physicians at Nuremberg (Annas, 1992, p. 218).

When examining the events of Nazi Germany as well as other breaches of medical ethics, it is important to focus on the role that medicine played in perpetrating these atrocities. In times of war, countries must unite against a greater force. Individuals must act in coordination with each other to combat the greater threat. However, it is in these cases especially that the lines in ethics may be blurred. Individuals are asked to act on behalf of their country, and as a result, may not consider the ramifications of their actions in the same way—they are blinded to the rights and concerns of the individual and may instead begin to perceive the persons they are dealing with only as representatives of their countries, nothing more.

There is unfortunately very little that can be done to prevent further transgressions through legislation. During times of political turmoil, laws and rules tend to be broken. This can be seen in the horrifying facts of the Nazi experiments or in the suspension of informed consent by the FDA. However, efforts can be made by the medical community to prevent physician and researcher involvement in future conflicts. The Nazi experiments are significant to medical ethics not because of the unbelievability of the atrocities committed, but because of the essential role that doctors played in these acts. Without science, without medicine, these things could not have occurred in the same magnitude.

In order to prevent repetition, the medical community must recognize their obligations to ethics and the rights of the individual in all instances. By studying the history we may be able to identify warning signs, and possibly prevent future incidents. Creation of a more ethical research environment may be able to help with this, as could explaining to researchers the historical precedents and significance of the role they play in safeguarding ethics in times of political uncertainty. Ultimately, as indicated in the rest of this piece, the most important part is preserving a constant vigilance over the position of ethics in the world of biomedical research.

References

1. "About the USPHS Syphilis Study" (2015). Retrieved on January 3, 2015
http://www.tuskegee.edu/about_us/centers_of_excellence/bioethics_center/about_the_usphs_syphilis_study.aspx
2. Allen, G. (2008). Getting Beyond Form Filling: The Role of Institutional Governance in Human Research Ethics. *Journal of Academic Ethics*, 105-116.
3. Angell, M. (1992) Editorial Responsibility: Protecting Human Rights by Restricting Publication of Unethical Research. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (276-285)*. New York, NY: Oxford University Press
4. Annas, G. (1992). The Nuremberg Code in U.S. Courts: Ethics versus Expediency. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (201-222)*. New York, NY: Oxford University Press
5. Annas, G. & Grodin, M. (1992) Introduction. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (3-12)*. New York, NY: Oxford University Press
6. Barber, B., Lally, J., Makarushka, J., Sullivan, D. (1973). *Research on Human Subjects: Problems of Social Control in Medical Experimentation*. New York, NY: Russell Sage Foundation
7. Baumslag, N. (2005) *Murderous Medicine: Nazi Doctors, Human Experimentation, and Typhus*. Westport, CT: Praeger
8. Belmont Report (n.d.) Retrieved January 8, 2015 from Wikipedia.
http://en.wikipedia.org/wiki/Belmont_Report
9. Berger, R. (1990) Nazi Science-The Dachau Hypothermia Experiments. *New England Journal of Medicine*, 322, 1435-1440. Retrieved from:
<http://www.nejm.org/doi/full/10.1056/NEJM199005173222006>
10. Biomedical Research (n.d.) Retrieved January 13, 2015 from Wikipedia
11. http://en.wikipedia.org/wiki/Medical_research
12. Bohme, G. (2007) Rationalizing Unethical Medical Research: Taking Seriously the Case of Viktor von Weizacker. In W. Lafleur, G. Bohme, & S. Shimazono (Eds.), *Dark Medicine: Rationalizing Unethical Medical Research (15-29)*. Indianapolis, IN: Indiana University Press
13. Caplan, A. (1992a) The Doctors' Trial and Analogies to the Holocaust in Contemporary Bioethical Debates. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (258-275)*. New York, NY: Oxford University Press
14. Caplan, A. (1992b) How did Medicine Go So Wrong? In A. Caplan (Ed.), *When Medicine Went Mad: Bioethics and the Holocaust (53-92)*. Totowa, NJ: Humana Press
15. Check, D., Weinfurt, K., Dombeck, C., Kramer, J., Flynn, K. (2013) Use of central institutional review boards for multicenter clinical trials in the United States: A review of the literature. *Journal of Clinical Trials*, 10, 560-567. doi: 10.1177/1740774513484393
16. Declaration of Helsinki. (n.d.) Retrieved January 7, 2015 from Wikipedia.
http://en.wikipedia.org/wiki/Declaration_of_Helsinki
17. Dubois, J., Anderson, E., Carroll, K., Gibb, T., Kraus, E., Rubbelke, T., & Vasher, M. (2012). Environmental Factors Contributing to Wrongdoing in Medicine: A Criterion-Based Review of Studies and Cases. *Ethics & Behavior*, 22(3), 163-188.

18. Dubois, J., Anderson, E., & Chibnall, J. (2013). Assessing the Need for a Research Ethics Remediation Program. *Clinical and Translational Science*, 6, 209-213.
19. Fischer, B. (2006) A Summary of Important Documents in the Field of Research Ethics. *Schizophrenia Bulletin*, 32(1), 69-80. doi: 10.1093/schbul/sj005
20. Frewer, A. (2007) Medical Research, Morality, and History: The German Journal *Ethik* and the Limits of Human Experimentation. In W. Lafleur, G. Bohme, & S. Shimazono (Eds.), *Dark Medicine: Rationalizing Unethical Medical Research (30-46)*. Indianapolis, IN: Indiana University Press
21. Glantz, L. (1992) The Influence of the Nuremberg Code on U.S. Statues and Regulations. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (183-200)*. New York, NY: Oxford University Press
22. Grodin, M. (1992) Historical Origins of the Nuremberg Code. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (121-144)*. New York, NY: Oxford University Press
23. Hugaas, J. (2002) An Essay on the Principle of Informed Consent versus the Significance of Trust for the Subjects of Biomedical Research. *Eubios Journal of Asian and International Bioethics*, 65-70. Retrieved from: www.eubios.info/EJ122/ej122i
24. Institutional Review Boards: Administrative Actions for Noncompliance. 21 C.F.R. §§ 120-124. (2014)
25. Institutional Review Boards: IRB Functions and Operations. 21 C.F.R. §§ 108-114. (2014).
26. Kalichman MW, Friedman PJ. A pilot study of biomedical trainees' perceptions concerning research ethics. *Acad Med*. 1992; 67(11): 769–775.
27. Katz, J. (1992a) The Consent Principle of the Nuremberg Code: Its Significance Then and Now. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (227-239)*. New York, NY: Oxford University Press
28. Katz, J. (1992b) Abuse of Human Beings for the Sake of Science. In A. Caplan (Ed.), *When Medicine Went Mad: Bioethics and the Holocaust (233-270)*. Totowa, NJ: Humana Press
29. Klitzman, R. (2012) Institutional Review Board Community Members: Who are They, What do They Do, and Whom Do They Represent? *Academic Medicine*, 87(7), 975-981. doi:10.1097/ACM.0b013e3182578b54
30. Koocher GP, Keith-Spiegel P. Peers nip misconduct in the bud. *Nature*. 2010; 466(7305): 438–440
31. Lifton, J. (1986). *The Nazi Doctors: Medical Killing and the Psychology of Genocide*. New York, NY: Basic Books, Inc.
32. Loff, B., & Black, J. (2004). Research ethics committees: what is their contribution. *Medical Journal of Australia*, 181(8), 440-441.
33. Macklin, R. (1992) Universality of the Nuremberg Code. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (240-257)*. New York, NY: Oxford University Press
34. Mariner, W. (1992) AIDS Research and the Nuremberg Code. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (286-304)*. New York, NY: Oxford University Press
35. Martinson BC, Anderson MS, de Vries R. Scientists behaving badly. *Nature* 2005;435:737–738.

36. Mumford, M., Murphy, S., Connelly, S., Hill, J., Antes, A., Brown, R., & Devenport, L. (2007). Environmental Influences on Ethical Decision Making: Climate and Environmental Predictors of Research Integrity. *Ethics & Behavior*, 337-366.
37. Mumford, M., Waples, E., Antes, A., Murphy, S., Connelly, S., Brown, R., & Devenport, L. (2009). Exposure to Unethical Career Events: Effects on Decision Making, Climate, and Socialization. *Ethics & Behavior*, 351-378.
38. National Research Act. (n.d.) Retrieved January 8, 2015 from Wikipedia. http://en.wikipedia.org/wiki/National_Research_Act
39. Neuhaus, R. (1992) The Way They Were, The Way We Are. In A. Caplan (Ed.), *When Medicine Went Mad: Bioethics and the Holocaust (211-231)*. Totowa, NJ: Humana Press
40. Nuremberg Code (PDF). U.S. National Institutes of Health. Retrieved December 25, 2014. <http://history.nih.gov/research/downloads/nuremberg.pdf>
41. Office for Human Research Protections. (1993). *IRB Guidebook*. Washington, D.C.:Author
42. Pedroni, J. and Pimple, K. (2001) *A Brief Introduction to Informed Consent in Research with Human Subjects*. Indiana: The Trustees of Indiana University
43. Perley, S., Fluss, S., Bankowski, Z., Simon, F. (1992) The Nuremberg Code: An International Overview. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (149-173)*. New York, NY: Oxford University Press
44. Pozos, R. (1992) Scientific Inquiry and Ethics: *The Dachau Data*. In A. Caplan (Ed.), *When Medicine Went Mad: Bioethics and the Holocaust (95-108)*. Totowa, NJ: Humana Press
45. Proctor, R. (1992a). Nazi Doctors, Racial Medicine, and Human Experimentation. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (17-31)*. New York, NY: Oxford University Press
46. Proctor, R. (1992b). Nazi Biomedical Policies. In A. Caplan (Ed.), *When Medicine Went Mad: Bioethics and the Holocaust (23-42)*. Totowa, NJ: Humana Press
47. Pross, C. (1992). Nazi Doctors, German Medicine, and Historical Truth. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (32-53)*. New York, NY: Oxford University Press
48. Protection of Human Subjects: Additional Protections for Children Involved as Subjects in Research, 46 C.F.R.§§ 401-409. (2009).
49. Protection of Human Subjects: Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects, 46 C.F.R. §§ 301-306. (2009).
50. Protection of Human Subjects: Basic HHS Policy for Protection of Human Research Subjects, C.F.R 46 §§ 101-124 (2009).
51. Schmidt, U. (2004) *Justice at Nuremberg: Leo Alexander and the Nazi Doctors' Trial*. New York, NY: Palgrave Macmillan
52. Stark, L. (2012). *Behind Closed Doors: IRBS and the Making of Ethical Research*. Chicago, IL: The University of Chicago Press
53. Taylor, T. (1946) Opening Statement of the Prosecution, December 9, 1946. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (67-93)*. New York, NY: Oxford University Press
54. Tjink, J., Verbeke, R., & Smulders, Y. (n.d.). Publication Pressure and Scientific Misconduct in Medical Scientists. *Journal of Empirical Research on Human Research Ethics*, 9(5), 64-71.
55. Wells, J., Thrush, C., Martinson, B., Mays, T., Stickler, M., Callahan, E., & Klomparens, K. (2014). Survey of Organizational Research Climates in Three Research Intensive, Doctoral Granting Universities. *Journal of Empirical Research on Human Research Ethics*, 9(5), 72-88.

56. Wiesel, E. (1992) Foreword. In George J. Annas & Michael A. Grodin (Eds.), *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation (vii-ix)*. New York, NY: Oxford University Press
57. Winau, R. (2007) Experimentation on Humans and Informed Consent: How We Arrived Where We Are. In W. Lafleur, G. Bohme, & S. Shimazono (Eds.), *Dark Medicine: Rationalizing Unethical Medical Research (46-56)*. Indianapolis, IN: Indiana University Press