Waiver of Informed Consent for Military Service Members

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Abstract

The evolution of the informed consent process began with the development of the Nuremburg Code in 1949 and further evolved following the publication of the Belmont Report in 1979. The purpose of informed consent is to ensure that voluntary consent of the human subject is absolutely essential. The Department of Defense (DoD) has initiated a process whereby the informed consent for investigational products may be modified or waived for military service members entering combat.

The objective of this research has been to compare the DoD process for requesting a waiver of informed consent with the informed consent process for prisoners and children and attempt to determine whether this waiver is actually necessary and in the best interest of the military service member.

Although similarities were found during the comparative research of the informed consent process with prisoners and children, the government (DoD) is far behind in protecting the safety of the military service members.

Similarities between prisoners and military service members revealed coercion due to the environment. The DHHS has continued to update regulations for prisoner protection in human research, originally published by Health, Education, and Welfare (HEW) in 1981. However, military regulations stipulate that the military service member is "required to obey all lawful orders and perform all assigned duties." This element of coercion cannot be removed due to the organization of military hierarchy and yet it has not been addressed. The ethical principle "Respect for Person" of the Belmont Report is continually violated when investigational drugs are administered to the military service members without informed consent.

Similarities between children and military service members revealed lack of

voluntariness. The FDA has responded by organizing a department, Office of Pediatric Therapeutics, within the Center for Drug Evaluation and Research in continued attempts to stimulate involvement and protection of children in research. However, several military doctrines govern the conduct of military service members with regards to their duty and obligations and yet nothing has been instituted to protect the military service members and allow them to provide voluntary consent or withdrawal from the administration of investigational products.

These military practices and the waiver of informed consent are unethical and do not follow the intent of established codes and regulations. Military service members can make an informed decision that is in their best interest and still meet the demands of DoD, which is ultimately to accomplish the mission.

Background

Purpose

Federal regulations stipulate that if any federal agency, including the military, desires to use an unapproved drug, that agency must first fully brief the individual receiving the investigational drug of the risks and obtain a written consent (Cummings, 2002). The Department of Defense (DoD) requests a waiver of informed consent from the Food and Drug Administration (FDA) for the administration of investigational products to military service members entering combat. The objective of this research has been to compare the DoD process for requesting a waiver of informed consent with the informed consent process for prisoners and children and attempt to determine whether this waiver is actually necessary and in the best interest of the military service member.

Literature Review

Military History

In 1777 during the Revolutionary War, soldiers were variolated against smallpox. General George Washington had ordered all his soldiers ("soldiers" and "military service members" will be used interchangeably) to be variolated due to the threat of smallpox. General Washington proclaimed smallpox to be his "most dangerous enemy" when a smallpox epidemic had reduced his troops strength to half (Anderson, n.d.).

Variolation was the practice of collecting ooze and scabs from smallpox lesions of an infected person and scratching this material into the skins of health persons who then contracted the disease and developed immunity. Although it had already been used by the British troops

who became immune to smallpox, many recipients of variolation eventually died through the course of the variolation process (Anderson, n.d.).

In January 1942 during World War II, a yellow fever vaccine that was in early development had been given to all U.S. troops deployed to combat. By March 1942, tens of thousands of soldiers had hepatitis and thousands died. It was later discovered that the yellow fever vaccine had been contaminated with the hepatitis B virus (Anderson, n.d.).

During the same war, thousands of the soldiers had also been vaccinated against influenza with an experimental vaccine (Anderson, n.d.). The experimental vaccine was developed to avoid a repeat occurrence of the Influenza Pandemic of 1918 that killed between 20 and 40 million people worldwide, 43,000 of which were soldiers (Billings, 1997). This vaccine was later approved for marketing by the FDA based on evidence of efficacy collected during an epidemiological survey of the military's use (Anderson, n.d.).

Between 1954 and 1973, over 2,300 Seventh Day Adventists (SDA) served as volunteer subjects in research studies directed at developing and testing vaccines and therapeutic drug candidates against Q-fever, tularemia, various viral encephalitides, Rift Valley Fever Virus, sand fly fever, and Plague. Although they were conscientious objectors to the war, many SDA entered active duty in the Army. They were known as the Operation Whitecoat Volunteers. The "Operation Whitecoat" program was designed to determine the extent to which humans are susceptible to infection with biological warfare agents to develop vaccines and treatments (Linden, 2005). The SDAs participated as volunteers in studies testing human vulnerability to biological warfare agents in realistic scenarios. Multiple new products for defense (DoD) against biological warfare and hazardous infectious diseases were developed with their participation. The information that was exchanged between the investigators and research volunteers

confirmed that the "process" of informed consent, and respect for the principles of the Nuremburg Code, were effectively implemented (Anderson, n.d.).

In the early 1990's during the Gulf War, the DoD administered two investigational drugs, pyridostigimide bromide (PB) and botulinum toxoid (BT) to military service members against the threat of chemical warfare and biological warfare (CW/BW) agents thought to be in Iraq. They were intended for treatment and/or pretreatment purposes (Seftel, 1991).

After the war, PB was implicated as a possible risk factor in Gulf War veterans' illnesses (a.k.a. Gulf War Syndrome), especially when used in combination with diethyl-m-toluamide (DEET), a pesticide used in the Gulf War by deployed troops. BT and Anthrax (AX) were also cited as possible causes for some veterans' illnesses (Rettig, 1999). Approximately 100,000 of the 697,000 soldiers that served in the Gulf War have reported multiple symptoms. In 2001, research had not validated any specific cause of these symptoms (Wood, 2001).

According to *The Hastings Report*, the controversy of the Gulf War and the Gulf War Syndrome raised two ethical questions about whether military service members should be given these investigational products: and if yes, whether they should be given the opportunity to grant or withhold their consent (Howe, et al., 1991).

History of Informed Consent

The evolution of informed consent began with the development of the Nuremburg Code in 1949 and further evolved with the publication of the Belmont report in 1979. The purpose of informed consent is to ensure that voluntary consent of the human subject is absolutely essential. This means that each person must be allowed to exercise freedom of choice in giving voluntary consent to participation of a clinical trial knowing the risks and benefits of the investigational

product. The decision by the subject cannot be under duress, deceit, fraud, force, or any other form of coercion. In addition, the subject should be able to withdraw at anytime without fear of repercussions (www.ohsr.od.nih.gov).

The Nuremburg Code was established following an American military tribunal by U.S. judges acting under the authority of the U.S. Army at the trial of Nazi doctors at Nuremberg. At the end of this trial, the judges presented the Nuremburg Code, a ten-pint guidance document on the "principles of the law of nations as they result from the usages established among civilized peoples, from the laws of humanity, and from the dictates of public conscience" (Annas, 1998). The first Nuremburg principle provides "the voluntary consent of the human subject is absolutely essential." The remaining nine Nuremburg principles state:

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods of means of study, and not random and unnecessary in nature.
3. The experiment should be so designed and based on the results of animal experimentation and knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.
4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.
6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.
10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any state, if he has probably cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

Thirty years later, the nature and definition of informed consent was again addressed in the Belmont Report. Developed in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (the commission) in response to carrying out the tasks as directed by the National Research Act, it was an attempt to summarize basic ethical principles and provide guidelines to assist in resolving the ethical problems that surround the conduct of research with human subjects (www.ohsr.od.nih.gov).

This directive resulted from growing public concern regarding abuses during clinical research, specifically involving vulnerable patient populations (Paar, et al., 2005). Vulnerable patient populations are identified as groups or individuals who cannot give consent that is truly informed or truly involuntary (Phipps, 2002).

This concern was influenced by well-publicized revelations of the serious side effects associated with medications, such as birth defects caused by the tranquilizer thalidomide and the Tuskegee Syphilis experiments (Paar, et al., 2005).

The Belmont Report summarizes the basic ethical principles identified by the Commission while considering "… the nature and definition of informed consent in various research settings". Appendix A

In Part B of the Belmont Report (see Appendix A), the basic ethical principles are expressed and include: the principles of respect of persons, beneficence and justice.

1. Respect for Persons. -- Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection.
2. Beneficence. -- Persons are treated in an ethical manner not only be respecting their decisions and protecting them from harm, but also b making efforts to secure their well-being.
3. Justice. -- Who out to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved."

Informed Consent for Vulnerable Patient Populations

Informed Consent for Prisoners

During World War II, in the United States prison system, experimentation with the use of consenting prisoners became extensive. As citizens of the United States, prisoners wanted to show their patriotism and did so by volunteering as subjects for testing drugs that were needed in war. Prisoners viewed this as a special moral privilege bestowed upon those incarcerated

(McCarthy, 1989).

At the Nuremburg trials, the Nazi physicians' legal defense team tried to analogize the concentration camp experiments with, for example, "the wartime experiments in the Unites States such as those carried out at the Joliet, Illinois prison, in which treatments for malaria were sought by physicians who had first to infect the volunteer prisoners with the disease." However, these arguments were not successful because in the Nazi camp situations you had non-volunteer prisoners, whereas in the Joliet case, there were volunteer subjects (prisoners) (McCarthy, 1989).

After World War II, the use of American prisoners in research studies continued. Prisons offered ideal controlled environments for investigational purposes. Experimentation also continued as a result of the absence of protections afforded the subjects by state and federal laws (McCarthy, 1989). In fact, after the FDA restructured regulations in 1962 with the Kefauver-Harris Amendment, prisoners became almost the exclusive subjects in non-federally funded Phase I pharmaceutical trials designed to test the toxicity of new drugs. By 1972, FDA officials estimated that more than 90 percent of all investigational drugs were first tested on prisoners (ACHRE Report, n.d.).

During this time, the Commission was established and it initiated an investigation of the experimentation on prisoners as research subjects. The commission gathered a wealth of data on prison medical research, made site visits to prisons, held extensive public hearings, and engaged in long debates amongst themselves. The commission concluded that it was "inclined toward protection as the most appropriate expression of respect for prisoners as persons" (ACHRE Report, n.d.). The Commission's report made five recommendations:

1. Unconditionally permitted low to no risk studies of prison life itself;
2. Allowed research that would be truly therapeutic, provided that the fourth

recommendation was also fulfilled;

3. Set minimum conditions to ensure fairness and voluntariness (for prisoners) in experimental drug research;
4. Urged the creation of institutional review boards (IRB's) to monitor research;
5. Stated that research projects not satisfying the third condition should not be permitted to continue longer than one year (Schroeder, 1983).

In May of 1980, although the Commission did not explicitly recommend a total ban on experimental research in prison, the FDA supported the Commission's conclusion and proposed a ban on nontherapeutic, experimental drug research on prisoners. Two months later, four inmates at the State Prison of Southern Michigan at Jackson filed a lawsuit challenging the FDA rule, purportedly designed to protect prison research subjects (Schroeder, 1983).

Both the prisoners and the pharmaceutical company (Upjohn Company) alleged that:

> [t]he effect of the [FDA] proposal would be to eliminate clinical testing at Jackson and similar facilities, because most of the pharmaceutical studies at prisons involve 'no therapeutic' research (i.e., studies not designed solely to improve the health of study participants);… [and] closing down such programs would deprive prisoners of their right freely to decide whether to participate in such programs, would deprive state correctional institutions of the rehabilitative and economic benefits for prisoners of such programs, and would injure the public by depriving pharmaceutical companies of the most suitable populations for certain kinds of studies …

The prisoners and Upjohn Company questioned the FDA's proposed regulations, claiming that the proposed ban on no therapeutic drug research in prison violates the equal protection and the process clauses of the fifth amendment (Schroeder, 1983).

A year after the lawsuit was filed, the FDA stayed its rule and announced plans to repropose the regulation, which was issued on December 18, 1981. The FDA recognized the

notion that prisoners might freely decide whether to participate in experimental research. This notion attempted to avoid "paternalism" and recognize that prisoners can give voluntary and informed consent to participate in no therapeutic research (Schroeder, 1983).

Also in 1981, the Department of Health, Education, and Welfare (HEW) published regulations for prisoner protection in human research, similar to the FDA regulations and modified to an extent by the Department of Health and Human Services (DHHS), the successor to HEW (McCarthy, 1989).

On the state level, some governments have become involved in controlling research and experimentation on human research subjects. For example, Oregon bans research on prisoners completely, while Iowa allows research to continue with limited restrictions addressed in its statute. It is not uncommon to find statues on protection of prisoners as research subjects vary from state to state. (McCarthy, 1989).

As of May 23, 2003, the DHHS has updated the OHRP Guidance on the Involvement of Prisoners in Research. This guidance describes DHHS regulations as covered by 45 CFR Part 46, Subpart C. The regulations provide that "biomedical or behavioral research conducted or supported by DHHS shall not involve prisoners as subjects" unless the research is specifically authorized within the subpart (www.hhs.gov).

Informed Consent for Children

Instances of experimentation with children date back centuries. One widely cited example from the 1790s is Edward Jenner's experimental injection of his gardener's son and his own son with cowpox material to vaccinate them against smallpox (IOM, 2004).

As medical research accelerated in the 1950s and 1960s, the Nuremburg principles were

both increasingly recognized and increasingly questioned. Some questions concerned the lack of provision for research involving children and other not competent to consent to research in their own right (IOM, 2004).

During the 1960s, criticisms of unethical research practices in studies involving children gained new attention. One of several studies exposed, included the Willowbrook State School where researchers had infected some of the child participants with a mild form of hepatitis during the initial stages of a study of the natural history, prevention, and treatment of viral hepatitis. The results of this research eventually contributed to the development of a successful hepatitis vaccine. At the same time, the research also contributed to the public debate over research ethics and obtaining parental consent for the involvement of healthy institutionalized children as research subjects (IOM, 2004).

Then in 1973, DHEW issued a working document on experimentation with children that proposed several protections for children. The draft provided that children would be excluded from participating in research under several conditions, one of which was if they were age 6 or over and had not consented to participation - unless the agency waived the requirement. The draft also proposed that an "ethical review board" should review research protocols involving children and that a "protection committee" should monitor aspects of research once it was initiated (IOM, 2004).

Later in 1975, the National Institute of Health (NIH) required that investigators obtain a child's agreement to participate in research (IOM, 2004). In its simplest form, informed consent is the treatment authorization given by a patient to a physician and it can only be given by those with legal entitlement and decisional capacity, otherwise a parent or guardian must provide permission (Kuther, 2003). However, government regulations have stipulated that a child must

actively show his or her willingness to participate in the research by providing assent. According to 45 CFR 46.402(b) “assent” means a child‘s affirmative agreement to participate in research (www.hhs.gov).

The DHHS adopted further regulations specifically on research involving children (Subpart D) in 1983. And in 2000, the children’s Health Act required FDA to update its regulations providing additional protections for children participating in research.

The FDA now has an Office of Pediatric Therapeutics within the Center for Drug Evaluation and Research (CDER). It has a web page dedicated to pediatric research with links to a variety of resources. However, many investigators and sponsors of research have been reluctant to undertake research with children and policy makers continue their attempts to stimulate research that involves infants, children, and adolescents (IOM, 2004).

Informed Consent for Military Service Members

Military Service Members in Peacetime

In 1962 the Army issued Army Regulation (AR) 70-25 as a formal regulation for the first time, which applied to all types of research and not simply that related to atomic, biological, and chemical warfare, as it had been previously. However, the regulation specifically excluded clinical research. A year later, an ad hoc committee of Army and civilian personnel concluded that the rule applied where research was done by contractors. That same year, the Army issued another regulation for radioisotope use that required local institutions to convene review committees and obtain approval from the secretary of the Army pursuant to AR 70-25 when radioisotopes were to be used with "volunteer" experimental subjects (ACHRE Report, n.d.).

The Army established the regulation, AR 40-38 "Medical Services--Clinical Investigation

Program" in 1973, which applied to "any person who may be at risk because of participation . . . [in] clinical investigation," including "patients" and "normal individuals." It required that subjects of research be given an explanation of the proposal in understandable language and sign a "volunteer agreement." Moreover, clinical research with patients, as well as healthy people, was to be reviewed by a "Human Use Committee" (ACHRE Report, n.d.).

Military service members may participate as research subjects (AR 70-25, 1990). At the Walter Reed Army Institute of Research (WRAIR), protocols for studies conducted through the Department of Clinical Trials (DCT) have been reviewed and approved by multiple review committees, each of which is tasked to assure scientific relevance, as well as to ensure that the rights and welfare of study volunteers are protected. In most cases, the FDA also reviews these protocols and grants permission for the studies to be conducted (www.army.mil).

Once research protocols have been approved, the DCT advertises for volunteers in multiple ways, to include newspaper ads, posters, and flyers. Calls from interested people are answered by full-time recruitment staff. The informed consent process is completed and the participant is reminded their participation is completely voluntary and they may withdraw at any time (www.army.mil).

Informed consent is documented by the use of a written consent form, preferably DA Form 5303-R Appendix B, approved by the Human Use Committee (HUC) and signed by the subject. A copy is then given to the subject who signed the form (www.dtic.mil).

Military Service Members in Wartime

It is the policy of the United States government (DoD) to provide our military personnel with safe and effective vaccines, antidotes, and treatments that will negate or minimize the

effects of CW/BW health threats as written in Executive Order (E.O.) 13139 (See Appendix C). Vaccinating military service members before an attack is the best way to ensure that our troops are protected and they can continue their missions (DoD, n.d.). According to a report by the Information Assurance Technology Analysis Center (IATAC). "History has shown that an infusion of technology can provide a significant military advantage to the side that first realizes it's potential and exploits it." Historical examples fail to recognize the ethical complexities presented by biotechnological research, development, and used in the military (Melson, 2003).

The DoD uses a strategy of Force Health Protection (FHP) to protect military service members being deployed to combat. The strategy of FHP is a continuum of programs designed to maintain health and to provide protection to military service members and basically covers three broad areas: Fitness and Health; Protection and Prevention; and Force Health Protection Strategy and Doctrine (Winkenwerder, 2003). The strategy of Force Health Protection has initiatives that are either currently in operation or are under development, which include (www.ha.osd.mil):

- Collection, evaluation and surveillance of environmental contaminants;
- Immunizations;
- Pre- and post deployment health assessments; and
- Anticipation of the enemy's operational threats, including measures required to counter biological, chemical or nuclear weapons effects.

The DoD's philosophy follows the principle of preventing unnecessary harm to military service members, which overrides all other values. It fulfills the (Belmont Report) principle of "Respect for Persons" by maintaining the military's explicitly and implicit promise to military service members to protect them from unnecessary harm (Howe, et al., 1991).

The DoD requests that the FDA waive the requirements for informed consent for the use of investigational drugs in certain military exigencies. This is called the Interim Rule (62 FR 40996, July 31, 1997), which was written in response to the threat of the use of CW/BW agents in Iraq during the Gulf War. At that time, DoD had concluded that it needed to be prepared to use several investigational products for defense against the potential CW/BE threats and that it should seek FDA approval for using these investigational products. DoD had determined that obtaining informed consent of military service members was not feasible (Rettig, 1999). The FDA responded to the DoD request by issuing the Interim Rule, which was written into the Code of Federal Regulations (CFR) under 12 CFR § 50.23(d) (Seftel, 1991).

The Interim Rule was implemented by the FDA and established a process, pursuant to a written request by the Assistant Secretary of Defense (DoD) given to the President, by which a determination could be made that obtaining informed consent for the use of investigational drugs is "not feasible for a specific military operation involving combat or the immediate threat of combat." The request must indicate that an IRB has reviewed and approved the use of the investigational drugs without informed consent (Rettig, 1999).

The FDA, in reaching the decision, determined that obtaining informed consent is not feasible "only when withholding treatment would be contrary to the best interests of the military personnel" and when "no available satisfactory alternative therapy" is available (Rettig, 1999).

Military Controversy with Principles & Guidelines

The DoD argues that the Nuremburg Code does not apply to the wartime military (Howe, et al., 1991). Therefore when a waiver of informed consent is issued during wartime, it has not violated established codes and regulation because they apply only to human experimentation or

research on human beings and DoD is not conducting research in these circumstances (Annas, 1998). It‘s philosophy follows the principle of preventing unnecessary harm to military service members, which overrides all other values. And for that reason, it fulfills the (Belmont Report) principle of “respect for persons“ by maintaining the military‘s explicit and implicit promise to military service members to protect them from unnecessary harm (Howe, et al., 1991).

The FDA generally approves an investigational new drug application (IND) to permit drug developers to perform human studies of the drug. Yet INDs have been employed by the DoD to permit routine use of untested drugs, without any intention of putting the drug through the experimental process required for licensure (Nass, n.d.).

21 CFR 50.23(d) Exception from General Requirements allows the President to waive prior (informed) consent for the administrations of an IND to a member of the armed forces in connection with the service member’s participation in a particular military operation (www.fda.gov).

One question that needs a legal resolution is the difference between “research” and “unlicensed use in the absence of research” of investigational products (Nass, n.d.). According to Meryl Nass, MD, the FDA generally approves an investigational new drug application (IND) to permit drug developers to perform human studies of the drug. The intention is to gain evidence of safety and efficacy for eventual licensure. This is referred to as “research”. Yet INDs have been employed by the DoD to permit routine use of untested drugs, without any intention of putting the drug through the experimental process required for licensure, which is referred to as “unlicensed use in the absence of research” (Nass, n.d.).

In an example, Dr. Nass presented a story where a Pentagon spokesman for DoD objected to a newspaper’s use of the term “experimental”. the spokesman said, “It is what is known as an

IND," claiming that the drug in contention is safe. Questions present themselves as to differentiate between an "experimental" drug and an "IND". Scientists routinely use the term investigational when referring to experimental research (thewinds.org, 1998).

The Pentagon (DoD) told the office that military service members were informed of the experimental nature of the drugs used in the Gulf War. However, a vaccination record of a gulf War veteran displayed "received immunization "B" classified secret while in participation in Operation Desert Storm." (sic) (thewinds.org, 1998).

In 2004, a FDA final positive determination on the anthrax vaccination was set to be legally challenged over the legitimacy of the Pentagon's (DoD) policy to force U.S. Troops to get an anthrax vaccination. At issue had been whether or not the anthrax vaccine was considered and investigational drug, which would have required DoD to obtain informed consent (or waiver of informed consent) before the vaccine was administered. The DoD argued that the vaccine was not investigational, and that it was licensed for inhalation anthrax (Basu, 2004).

The courts had initially issued an injunction until the FDA displayed the results of a panel per 21 CFR 601.25, that had reviewed information on biological products were licensed under the Public Health Service Act before 1972, when the National Institutes of Health (NIH) had the responsibility of licensing biological products (Basu, 2004). The Panel convened on July 12, 1973 and included the following individuals: Panel Chairman, Gene H. Stollerman, MD; Geoffery Edsal, MD (deceased); Theodore C. Eickhoff, MD; John C. Feeley, Ph.D.; Hjordis M. Foy, MD, Ph.D.; Edward A Mortimer, Jr., MD; Jay P. and Sandford, MD (www.fda.gov). This panel recommended that the vaccine be classified as a Category I product, which meant that it was safe and effective as labeled. The courts lifted the junction and DoD vaccinated military service members to protect them against the threat of anthrax (Basu, 2004).

Conclusion

It is surprising the DoD can obtain a waiver for informed consent, regardless of the circumstances. Clinical research has evolved immensely and the most critical aspect has been the safety of the subject, especially for the vulnerable patient populations and their voluntariness.

As discussed in the literature review, the evolution of the informed consent began when the military initiated the Nuremburg Trial which resulted in the Nuremburg Code. This set of principles established a foundation for all research subjects and was followed by the publication of the Belmont Report in 1979. It is the Belmont Report that issued guidelines for the protection of vulnerable patient populations, such as prisoners and children.

During the comparative research of the informed consent process with prisoners and children, I found that there were similarities but the government was far behind in protecting the safety of their own employees: the military service members.

In comparing the treatment of military service members with the informed consent process for prisoners, I was reminded of the voluntariness of the prisoners during their participation in clinical research and the government's interception of this process on behalf of the prisoners in order to protect them from coercion. The government discovered through several investigations that there were underlying effects of coercion due to the environment the prisoners lived within, which included compensation, fear, altruism or the desire to do something worthwhile (McCarthy, 1989).

The government has also stepped in to protect another vulnerable patient population: children. Again, the issue is voluntariness and the government has addressed it by allowing children to assent to their participation in clinical research studies.

However, military service members, who also exist under effects of coercion through

their own established hierarchy, have had no government entity attempt to intercede on their behalf. The shady area is whether the DoD uses the military service members as research subjects and whether these service members are a vulnerable patient population to be protected.

During this research, most of the information related to the Gulf War because it was the first time the military (DoD) had actually sought a waiver of informed consent from the FDA for the administration of investigational products to military service members. It appears that the DoD expected military service members to request to be allowed the ability to make an informed decision and the DoD wanted to preempt this industry-standard requirement by not offering informed consent on the basis that they were offering a treatment.

The U.S. Code of Military Justice (UCMJ) and other military doctrines have provided military service members with regulations regarding their duty and obligations. The Enlistment Document DD Form 4/1 (See Appendix D) signed by the service member upon entering the military states, "Many laws, regulations, and military customs will govern my conduct and require me to do things a civilian does not have to do."

One such requirement is Force Health Protection (FHP), which includes annual exams and immunization. This strategy of FHP now also covers measures by the DoD to protect military service members in combat against the threat of CW/BW agents. As in the Gulf War, there are several investigational products that the DoD has decided are the only products available that offer any type of protection against CW/BW against. Therefore, the military service members must accept these treatments as ordered by DoD per their military contract.

Most individuals that enter the service are consenting adults. They have the capacity to make an informed choice. To remove this option is an obvious violation of both the Nuremburg Code and the Belmont Report.

Within DD Form 4/1 Appendix D Section 9.a (1), the military service member is "required to obey all lawful orders and perform all assigned duties." This presents an environment with the possibility of coercion by the upper echelon towards the lower-ranking enlisted military service member. Therefore, there is the absence of adherence to the Belmont Report and the ethical principle "Respect for Persons".

This element of coercion cannot be removed due to the organization of our military. It is common knowledge to each military service member that he or she must obey their superiors. Not to adhere to this regulation can result in several repercussions, which include: forfeiture of pay, dishonorable discharge, or sentencing the military service member to a military prison.

With the information I learned from this research, I suggest the DHHS, FDA, and DoD combine efforts to propose recommendations that will protect military service members as a vulnerable patient population for all scenarios, including military exigencies. These recommendations may include:

1. Continue or conduct research on investigational products that may be considered useful for treatment during combat in order to obtain FDA approval for safety and efficacy, similar to marketed products.
2. Allow military service members to voluntarily accept or decline the administration of investigational products for deployment to combat without fear of repercussion.
3. Initiate a regulation for all military service members to provide guidelines for deployment of soldiers that receive the drugs and soldiers that decline the drugs in order to uphold the military environment of unity and cohesiveness.
4. Provide for better recordkeeping during combat and continuing after the military service member exits the military for all soldiers who were administered the

investigational product.

In addition, the President of the United States should institute legislation for the protection of military service members that will hold the DoD accountable for any retroactive condition or illness resulting from the consumption of an investigational product administered to the military service member.

In my opinion, there is no acceptable reason for a consenting adult to be disallowed the standard requirement for all subjects to voluntarily make an informed decision for the receipt of an administered investigational drug. Therefore, no waiver of informed consent is necessary. Military service members can make an informed decision that is in their best interest and still meet the demands of DoD, which is ultimately to accomplish the mission.

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Appendix A

THE BELMONT REPORT
ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
April 18, 1979

AGENCY: Department of Health, Education, and Welfare.

ACTION: Notice of Report for Public Comment.

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

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

Unlike most other reports of the Commission, the Belmont Report does not make specific recommendations for administrative action by the Secretary of Health, Education, and Welfare. Rather, the Commission recommended that the Belmont Report be adopted in its entirety, as a statement of the Department's policy. The Department requests public comment on this

recommendation.

NATIONAL COMMISSION FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH

MEMBERS OF THE COMMISSION

Kenneth John Ryan, M.D., Chairman, Chief of Staff, Boston Hospital for Women.
Joseph V. Brady, Ph.D., Professor of Behavioral Biology, Johns Hopkins University.
Robert E. Cooke, M.D., President, Medical College of Pennsylvania.
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ETHICAL PRINCIPLES & GUIDELINES FOR RESEARCH INVOLVING HUMAN SUBJECTS

Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions. Public attention was drawn to these questions by reported abuses of human subjects in biomedical experiments, especially during the Second World War. During the Nuremberg War Crime Trials, the Nuremberg code was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on concentration camp prisoners. This code became the

prototype of many later codes**(1)** intended to assure that research involving human subjects would be carried out in an ethical manner.

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

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

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

PART A: BOUNDARIES BETWEEN PRACTICE & RESEARCH

A. BOUNDARIES BETWEEN PRACTICE AND RESEARCH

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

For the most part, the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals. **(2)** By contrast, the term "research' designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective. When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is "experimental," in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project. **(3)**

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

PART B: BASIC ETHICAL PRINCIPLES

B. BASIC ETHICAL PRINCIPLES

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

1. Respect for Persons. -- Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

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

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

Some persons are in need of extensive protection, even to the point of excluding them from activities which may harm them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequence. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

2. Beneficence. -- Persons are treated in an ethical manner not only by

respecting their decisions and protecting them from harm, but also by making efforts to secure their wellbeing. Such treatment falls under the principle of beneficence. The term "beneficence" is

often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: **(1)** do not harm and **(2)** maximize possible benefits and minimize possible harms.

The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not injure one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment." Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

The obligations of beneficence affect both individual investigators and society at large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel medical, psychotherapeutic, and social procedures.

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

3. Justice. -- Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted

formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are **(1)** to each person an equal share, **(2)** to each person according to individual need, **(3)** to each person according to individual effort, **(4)** to each person according to societal contribution, and **(5)** to each person according to merit.

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

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

PART C: APPLICATIONS

C. APPLICATIONS

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

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

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

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

> However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locale, is inadequate since research takes place precisely when a common understanding does not exist. Another standard, currently popular in malpractice law, requires the practitioner to reveal the information that reasonable persons would wish to know in order to make a decision regarding their care. This, too, seems insufficient since the research subject, being in essence a volunteer, may

wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for needed care. It may be that a standard of "the reasonable volunteer" should be proposed: the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation.

A special problem of consent arises where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research of which some features will not be revealed until the research is concluded. In all cases of research involving incomplete disclosure, such research is justified only if it is clear that **(1)** incomplete disclosure is truly necessary to accomplish the goals of the research, **(2)** there are no undisclosed risks to subjects that are more than minimal, and **(3)** there is an adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them. Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases in which disclosure would destroy or invalidate the research from cases in which disclosure would simply inconvenience the investigator.

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

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

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

from harm.

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

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

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

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

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

The term "benefit" is used in the research context to refer to something of positive value related to health or welfare. Unlike, "risk," "benefit" is not a term that expresses probabilities. Risk is properly contrasted to probability of benefits, and benefits are properly contrasted with harms rather than risks of harm. Accordingly, so-called risk/benefit assessments are concerned with the probabilities and magnitudes of possible harm and anticipated benefits. Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked.

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

substantial benefits that might be gained from research.

The Systematic Assessment of Risks and Benefits. It is commonly said that benefits and risks must be "balanced" and shown to be "in a favorable ratio." The metaphorical character of these terms draws attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, nonarbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically. This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and investigators less subject to misinterpretation, misinformation and conflicting judgments. Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

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

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

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

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

Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments. When research is proposed that involves risks and does not include a therapeutic component, other less burdened classes of persons should be called upon first to accept these risks of research, except where the research is directly related to the specific conditions of the class involved. Also, even though public funds for research may often flow in the same directions as public funds for health care, it seems unfair that populations dependent on public health care constitute a pool of preferred research subjects if more advantaged populations are likely to be the recipients of the benefits.

One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.

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

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

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

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Appendix B

VOLUNTEER AGREEMENT AFFIDAVIT

For use of this form, see AR 70-25 or AR 40-38; the proponent agency is DTSG.

PRIVACY ACT OF 1974

Authority:	10 USC 3013, 44 USC 3101, and 10 USC 1071-1087.
Principle Purpose:	To document voluntary participation in the Clinical Investigation and Research Program. SSN and home address will be used for identification and locating purposes.
Routine Uses:	The SSN and home address will be used for identification and locating purposes. Information derived from the study will be used to document the study; implementation of medical programs; adjudication of claims; and for the mandatory reporting of medical conditions as required by law. Information may be furnished to Federal, State and local agencies.
Disclosure:	The furnishing of your SSN and home address is mandatory and necessary to provide identification and to contact you if future information indicates that your health may be adversely affected. Failure to provide the information may preclude your voluntary participation in this investigational study.

PART A(1) - VOLUNTEER AFFIDAVIT

Volunteer Subjects in Approved Department of the Army Research Studies

Volunteers under the provisions of AR 40-38 and AR 70-25 are authorized all necessary medical care for injury or disease which is the proximate result of their participation in such studies.

I,_____, SSN_____,

having full capacity to consent and having attained _____ birthday, do hereby volunteer/give consent as legal

representative _____ to participate _____

_____

(Research study)

_____

under the direction _____

conducted at _____.

(Name of Institution)

The implications of my voluntary participation/consent as legal representative; duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconveniences and hazards that may reasonably be expected have been explained to me by

_____

I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights/the rights of the person I represent on study related injury, I may contact

_____

at _____

(Name, Address and Phone Number of Hospital (Include Area Code))

I understand that I may at any time during the course of this study revoke my consent and withdraw/have the person I represent withdrawn from the study without further penalty or loss of benefits; however, I/the person I represent may be required (military volunteer) or requested *(civilian volunteer)* to undergo certain examination if, in the opinion of the attending physician, such examinations are necessary for my/the person I represent's health and well-being. My/the person I represent's refusal to participate will involve no penalty or loss of benefits to which I am/the person I represent is otherwise entitled.

_____

PART A(2) - ASSENT VOLUNTEER AFFIDAVIT *(MINOR CHILD)*

I,_____, SSN_____, having full

capacity to assent and having attained _____ birthday, do hereby volunteer _____

_____ to participate _____

_____

(Research Study)

_____

under the direction of _____

conducted at _____.

(Name of Institution)

(Continue on Page 2)

PART A(2) - ASSENT VOLUNTEER AFFIDAVIT *(MINOR CHILD) (Cont'd.)*

The implications of my voluntary participation; the nature, duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconveniences and hazards that may reasonably be expected have been explained to me by

I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights I may contact

at

(Name, Address and Phone Number of Hospital (Include Area Code))

I understand that I may at any time during the course of this study revoke my consent and withdraw from the study without further penalty or loss of benefits; however, I may be requested to undergo certain examination if, in the opinion of the attending physician, such examinations are necessary for my health and well-being. My refusal to participate will involve no penalty or loss of benefits to which I am otherwise entitled.

PART B - TO BE COMPLETED BY INVESTIGATOR

INSTRUCTIONS FOR ELEMENTS OF INFORMED CONSENT: *(Provide a detailed explanation in accordance with Appendix C, AR 40-38 or AR 70-25.)*

I **do** ☐ **do not** ☐ *(check one & initial)* consent to the inclusion of this form in my outpatient medical treatment record.

SIGNATURE OF VOLUNTEER	DATE	SIGNATURE OF LEGAL GUARDIAN *(If volunteer is a minor)*
PERMANENT ADDRESS OF VOLUNTEER	TYPED NAME OF WITNESS	
	SIGNATURE OF WITNESS	DATE

Appendix C

THE WHITE HOUSE
Office of the Press Secretary
For Immediate Release
September 30, 1999

EXECUTIVE ORDER

IMPROVING HEALTH PROTECTION OF MILITARY PERSONNEL PARTICIPATING IN PARTICULAR MILITARY OPERATIONS

By the authority vested in me as President by the Constitution and the laws of the United States of America, including section 1107 of title 10, United States Code, and in order to provide the best health protection to military personnel participating in particular military operations, it is hereby ordered as follows:

Section 1. Policy. Military personnel deployed in particular military operations could potentially be exposed to a range of chemical, biological, and radiological weapons as well as diseases endemic to an area of operations. It is the policy of the United States Government to provide our military personnel with safe and effective vaccines, antidotes, and treatments that will negate or minimize the effects of these health threats.

Sec. 2. Administration of Investigational New Drugs to Members of the Armed Forces.

(a) The Secretary of Defense (Secretary) shall collect intelligence on potential health threats that might be encountered in an area of operations. The Secretary shall work together with the Secretary of Health and Human Services to ensure appropriate countermeasures are developed. When the Secretary considers an investigational new drug or a drug unapproved for its intended use (investigational drug) to represent the most appropriate countermeasure, it shall be studied through scientifically based research and development protocols to determine whether it is safe and effective for its intended use.

(b) It is the expectation that the United States Government will administer products approved for their intended use by the Food and Drug Administration (FDA). However, in the event that the Secretary considers a product to represent the most appropriate countermeasure for diseases endemic to the area of operations or to protect against possible chemical, biological, or radiological weapons, but the product has not yet been approved by the FDA for its intended use, the product may, under certain circumstances and strict controls, be administered to provide potential protection for the health and well-being of deployed military personnel in order to ensure the success of the military operation. The provisions of 21 CFR Part 312 contain the FDA requirements for investigational new drugs.

Sec. 3. Informed Consent Requirements and Waiver Provisions.

(a) Before administering an investigational drug to members of the Armed Forces, the Department of Defense (DoD) must obtain informed consent from each individual unless the Secretary can justify to the President a need for a waiver of informed consent in accordance with 10 U.S.C. 1107(f). Waivers of informed consent will be granted only when absolutely necessary.

(b) In accordance with 10 U.S.C. 1107(f), the President may waive the informed consent requirement for the administration of an investigational drug to a member of the Armed

Forces in connection with the member's participation in a particular military operation, upon a written determination by the President that obtaining consent:

(1) is not feasible;

(2) is contrary to the best interests of the member; or

(3) is not in the interests of national security.

(c) In making a determination to waive the informed consent requirement on a ground described in subsection (b)(1) or (b)(2) of this section, the President is required by law to apply the standards and criteria set forth in the relevant FDA regulations, 21 CFR 50.23(d). In determining a waiver based on subsection (b)(3) of this section, the President will also consider the standards and criteria of the relevant FDA regulations.

(d) The Secretary may request that the President waive the informed consent requirement with respect to the administration of an investigational drug. The Secretary may not delegate the authority to make this waiver request. At a minimum, the waiver request shall contain:

(1) A full description of the threat, including the potential for exposure. If the threat is a chemical, biological, or radiological weapon, the waiver request shall contain an analysis of the probability the weapon will be used, the method or methods of delivery, and the likely magnitude of its affect on an exposed individual.

(2) Documentation that the Secretary has complied with 21 CFR 50.23(d). This documentation shall include:

(A) A statement that certifies and a written justification that documents that each of the criteria and standards set forth in 21 CFR 50.23(d) has been met; or

(B) If the Secretary finds it highly impracticable to certify that the criteria and standards set forth in 21 CFR 50.23(d) have been fully met because doing so would significantly impair the Secretary's ability to carry out the particular military mission, a written justification that documents which criteria and standards have or have not been met, explains the reasons for failing to meet any of the criteria and standards, and provides additional justification why a waiver should be granted solely in the interests of national security.

(3) Any additional information pertinent to the Secretary's determination, including the minutes of the Institutional Review Board's (IRB) deliberations and the IRB members' voting record.

(e) The Secretary shall develop the waiver request in consultation with the FDA.

(f) The Secretary shall submit the waiver request to the President and provide a copy to the Commissioner of the FDA (Commissioner).

(g) The Commissioner shall expeditiously review the waiver request and certify to the Assistant to the President for National Security Affairs (APNSA) and the Assistant to the President for Science and Technology (APST) whether the standards and criteria of the relevant FDA regulations have been adequately addressed and whether the investigational new drug protocol may proceed subject to a decision by the President on the informed consent waiver request. FDA shall base its decision on, and the certification shall include an analysis describing, the extent and strength of the evidence on the safety and effectiveness of the investigational new drug in relation to the medical risk that could be encountered during the military operation.

(h) The APNSA and APST will prepare a joint advisory opinion as to whether the waiver of informed consent should be granted and will forward it, along with the waiver request and the FDA certification to the President.

(i) The President will approve or deny the waiver request and will provide written notification of the decision to the Secretary and the Commissioner.

Sec. 4. Required Action After Waiver is Issued.

(a) Following a Presidential waiver under 10 U.S.C. 1107(f), the DoD offices responsible for implementing the waiver, DoD's Office of the Inspector General, and the FDA, consistent with its regulatory role, will conduct an ongoing review and monitoring to assess adherence to the standards and criteria under 21 CFR 50.23(d) and this order. The responsible DoD offices shall also adhere to any periodic reporting requirements specified by the President at the time of the waiver approval.

The Secretary shall submit the findings to the President and provide a copy to the Commissioner.

(b) The Secretary shall, as soon as practicable, make the congressional notifications required by 10 U.S.C. 1107(f)(2)(B).

(c) The Secretary shall, as soon as practicable and consistent with classification requirements, issue a public notice in the Federal Register describing each waiver of informed consent determination and a summary of the most updated scientific information on the products used, as well as other information the President determines is appropriate.

(d) The waiver will expire at the end of 1 year (or an alternative time period not to exceed 1 year, specified by the President at the time of approval), or when the Secretary informs the President that the particular military operation creating the need for the use of the investigational drug has ended, whichever is earlier. The President may revoke the waiver based on changed circumstances or for any other reason. If the Secretary seeks to renew a waiver prior to its expiration, the Secretary must submit to the President an updated request, specifically identifying any new information available relevant to the standards and criteria under 21 CFR 50.23(d). To request to renew a waiver, the Secretary must satisfy the criteria for a waiver as described in section 3 of this order.

(e) The Secretary shall notify the President and the Commissioner if the threat countered by the investigational drug changes significantly or if significant new information on the investigational drug is received.

Sec. 5. Training for Military Personnel. (a) The DoD shall provide ongoing training and health risk communication on the requirements of using an investigational drug in support of a military operation to all military personnel, including those in leadership positions, during chemical and biological warfare defense training and other training, as appropriate. This ongoing training and health risk communication shall include general information about 10 U.S.C. 1107 and 21 CFR 50.23(d).

(b) If the President grants a waiver under 10 U.S.C. 1107(f), the DoD shall provide training to all military personnel conducting the waiver protocol and health risk communication to all military personnel receiving the specific investigational drug to be administered prior to its use.

(c) The Secretary shall submit the training and health risk communication plans as part of the investigational new drug protocol submission to the FDA and the reviewing IRB. Training and health risk communication shall include at a minimum:

(1) The basis for any determination by the President that informed consent is not or may not be feasible;

(2) The means for tracking use and adverse effects of the investigational drug;

(3) The benefits and risks of using the investigational drug; and

(4) A statement that the investigational drug is not approved (or not approved for the intended use).

(d) The DoD shall keep operational commanders informed of the overall requirements of successful protocol execution and their role, with the support of medical personnel, in ensuring successful execution of the protocol.

Sec. 6. Scope. (a) This order applies to the consideration and Presidential approval of a waiver of informed consent under 10 U.S.C. 1107 and does not apply to other FDA regulations.

(b) This order is intended only to improve the internal management of the Federal Government. Nothing contained in this order shall create any right or benefit, substantive or procedural, enforceable by any party against the United States, its agencies or instrumentalities, its officers or employees, or any other person.
WILLIAM J. CLINTON
THE WHITE HOUSE,
September 30, 1999.

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Appendix D

ENLISTMENT/REENLISTMENT DOCUMENT
ARMED FORCES OF THE UNITED STATES

PRIVACY ACT STATEMENT

AUTHORITY: 5 USC 3331; 32 USC 708; 44 USC 708 and 3101; 10 USC 133, 265, 275, 504, 508, 510, 591, 672(d), 678, 837, 1007, 1071 through 1087; 1168, 1169, 1475 through 1480, 1553, 2107, 2122, 3012, 5031, 8012, 8033, 8496, and 9411; 14 USC 351 and 632; and Executive Order 9397, November 1943 (SSN).

PRINCIPAL PURPOSE(S): To record enlistment or reenlistment into the U.S. Armed Forces. This information becomes a part of the subject's military personnel records which are used to document promotion, reassignment, training, medical support, and other personnel management actions. The purpose of soliciting the SSN is for positive identification.

ROUTINE USE(S): This form becomes a part of the Service's Enlisted Master File and Field Personnel File. All uses of the form are internal to the relevant Service.

DISCLOSURE: Voluntary; however, failure to furnish personal identification information may negate the enlistment/reenlistment application.

A. ENLISTEE/REENLISTEE IDENTIFICATION DATA

1. NAME *(Last, First, Middle)*		2. SOCIAL SECURITY NUMBER			
3. HOME OF RECORD *(Street, City, State, ZIP Code)*		4. PLACE OF ENLISTMENT/REENLISTMENT *(Mil. Installation, City, State)*			
5. DATE OF ENLISTMENT/ REENLISTMENT *(YYYYMMDD)*	6. DATE OF BIRTH *(YYYYMMDD)*	7. PREV MIL SVC UPON ENL/REENLIST	YEARS	MONTHS	DAYS
		a. TOTAL ACTIVE MILITARY SERVICE			
		b. TOTAL INACTIVE MILITARY SERVICE			

B. AGREEMENTS

8. I am enlisting/reenlisting in the United States *(list branch of service)* _____ this date for _____ years and _____ weeks beginning in pay grade _____. The additional details of my enlistment/reenlistment are in Section C and Annex(es) _____.

a. FOR ENLISTMENT IN A DELAYED ENTRY/ENLISTMENT PROGRAM (DEP):

I understand that I will be ordered to active duty as a Reservist unless I report to the place shown in item 4 above by *(list date (YYYYMMDD))* _____ for enlistment in the Regular component of the United States *(list branch of service)* _____ for not less than _____ years and _____ weeks. My enlistment in the DEP is in a nonpay status. I understand that my period in the DEP is **NOT** creditable for pay purposes upon entry into a pay status. However, I also understand that this time is counted toward fulfillment of my military service obligation or commitment. I must maintain my current qualifications and keep my recruiter informed of any changes in my physical or dependency status, moral qualifications, and mailing address.

b. REMARKS: *(If none, so state.)*

c. The agreements in this section and attached annex(es) are all the promises made to me by the Government. **ANYTHING ELSE ANYONE HAS PROMISED ME IS NOT VALID AND WILL NOT BE HONORED.**

(Initials of Enlistee/Reenlistee) _____ *(Continued on reverse side.)*

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C. PARTIAL STATEMENT OF EXISTING UNITED STATES LAWS

9. FOR ALL ENLISTEES OR REENLISTEES: Many laws, regulations, and military customs will govern my conduct and require me to do things a civilian does not have to do. The following statements are not promises or guarantees of any kind. They explain some of the present laws affecting the Armed Forces which I cannot change but which Congress can change at any time.

a. My enlistment is more than an employment agreement. As a member of the Armed Forces of the United States, I will be:

(1) Required to obey all lawful orders and perform all assigned duties.

(2) Subject to separation during or at the end of my enlistment. If my behavior fails to meet acceptable military standards, I may be discharged and given a certificate for less than honorable service, which may hurt my future job opportunities and my claim for veteran's benefits.

(3) Subject to the military justice system, which means, among other things, that I may be tried by military courts-martial.

(4) Required upon order to serve in combat or other hazardous situations.

(5) Entitled to receive pay, allowances, and other benefits as provided by law and regulation.

b. Laws and regulataions that govern military personnel may change without notice to me. Such changes may affect my status, pay, allowances, benefits, and responsibilities as a member of the Armed Forces **REGARDLESS** of the provisions of this enlistment/reenlistment document.

c. In the event of war, my enlistment in the Armed Forces continues until six (6) months after the war ends, unless my enlistment is ended sooner by the President of the United States.

10. MILITARY SERVICE OBLIGATION FOR ALL MEMBERS OF THE ACTIVE AND RESERVE COMPONENTS, INCLUDING THE NATIONAL GUARD.

a. FOR ALL ENLISTEES: If this is my initial enlistment, I must serve a total of eight (8) years. Any part of that service not served on active duty must be served in a Reserve Component unless I am sooner discharged.

b. If I am a member of a Reserve Component of an Armed Force at the beginning of a period of war or national emergency declared by Congress, or if I become a member during that period, my military service may be extended without my consent until six (6) months after the end of that period of war.

c. As a member of a Reserve Component, in time of war or national emergency declared by the Congress, I may be required to serve on active duty (other than for training) for the entire period of the war or emergency and for six (6) months after its end.

d. As a member of the Ready Reserve I may be required to perform active duty or active duty for training without my consent (other than as provided in item 8 of this document) as follows:

(1) in time of national emergency declared by the President of the United States, I may be ordered to active duty (other than for training) for not more than 24 consecutive months.

(2) I may be ordered to active duty for 24 months, and my enlistment may be extended so I can complete 24 months of active duty, if:

(a) I am not assigned to, or participating satisfactorily in, a unit of the Ready Reserve; and

(b) I have not met my Reserve obligation; and

(c) I have not served on active duty for a total of 24 months.

(3) I may be ordered to perform additional active duty training for not more than 45 days if I have not fulfilled my military service obligation and fail in any year to perform the required training duty satisfactorily. If the failure occurs during the last year of my required membership in the Ready Reserve, my enlistment may be extended until I perform that additional duty, but not for more than six months.

(4) When determined by the President that it is necessary to support any operational mission, I may be ordered to active duty as prescribed by law, if I am a member of the Selected Reserve.

11. FOR ENLISTEES/REENLISTEES IN THE NAVY, MARINE CORPS, OR COAST GUARD: I understand that if I am serving on a naval vessel in foreign waters, and my enlistment expires, I will be returned to the United States for discharge as soon as possible consistent with my desires. However, if essential to the public interest, I understand that I may be retained on active duty until the vessel returns to the United States. If I am retained under these circumstances, I understand I will be discharged not later than 30 days after my return to the United States; and, that except in time of war, I will be entitled to an increase in basic pay of 25 percent from the date my enlistment expires to the date of my discharge.

12. FOR ALL MALE APPLICANTS: Completion of this form constitutes registration with the Selective Service System in accordance with the Military Selective Service Act. Incident thereto the Department of Defense may transmit my name, permanent address, military address, Social Security Number, and birthdate to the Selective Service System for recording as evidence of the registration.

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NAME OF ENLISTEE/REENLISTEE *(Last, First, Middle)*	SOCIAL SECURITY NO. OF ENLISTEE/REENLISTEE

D. CERTIFICATION AND ACCEPTANCE

13a. My acceptance for enlistment is based on the information I have given in my application for enlistment. If any of that information is false or incorrect, this enlistment may be voided or terminated administratively by the Government or I may be tried by a Federal, civilian, or military court and, if found guilty, may be punished.

I CERTIFY THAT I HAVE CAREFULLY READ THIS DOCUMENT. ANY QUESTIONS I HAD WERE EXPLAINED TO MY SATISFACTION. I FULLY UNDERSTAND THAT ONLY THOSE AGREEMENTS IN SECTION B OF THIS DOCUMENT OR RECORDED ON THE ATTACHED ANNEX(ES) WILL BE HONORED. ANY OTHER PROMISES OR GUARANTEES MADE TO ME BY ANYONE ARE WRITTEN BELOW: *(If none, X "NONE" and initial.)* ☐ **NONE** _____ *(Initials of enlistee/reenlistee)*

b. SIGNATURE OF ENLISTEE/REENLISTEE	c. DATE SIGNED *(YYYYMMDD)*

14. SERVICE REPRESENTATIVE CERTIFICATION

a. On behalf of the United States *(list branch of service)* _____, I accept this applicant for enlistment. I have witnessed the signature in item 13b to this document. I certify that I have explained that only those agreements in Section B of this form and in the attached Annex(es) will be honored, and any other promises made by any person are not effective and will not be honored.

b. NAME *(Last, First, Middle)*	c. PAY GRADE	d. UNIT/COMMAND NAME
e. SIGNATURE	f. DATE SIGNED *(YYYYMMDD)*	g. UNIT/COMMAND ADDRESS *(City, State, ZIP Code)*

E. CONFIRMATION OF ENLISTMENT OR REENLISTMENT

15. IN THE ARMED FORCES EXCEPT THE NATIONAL GUARD (ARMY OR AIR):

I, _____, do solemnly swear (or affirm) that I will support defend the Constitution of the United States against all enemies, foreign and domestic; that I will bear true faith and allegiance to the same; and that I will obey the orders of the President of the United States and the orders of the officers appointed over me, according to regulations and the Uniform Code of Military Justice. So help me God.

16. IN THE NATIONAL GUARD (ARMY OR AIR):

I, _____, do solemnly swear (or affirm) that I will support and defend the Constitution of the United States and the State of _____ against all enemies, foreign and domestic; that I will bear true faith and allegiance to the same; and that I will obey the orders of the President of the United States and the Governor of _____ and the orders of the officers appointed over me, according to law and regulations. So help me God.

17. IN THE NATIONAL GUARD (ARMY OR AIR):

I do hereby acknowledge to have voluntarily enlisted/reenlisted this _____ day of _____, _____ in the _____ National Guard and as a Reserve of the United States *(list branch of service)* _____ with membership in the _____ National Guard of the United States for a period of _____ years, _____ months, _____ days, under the conditions prescribed by law, unless sooner discharged by proper authority.

18.a. SIGNATURE OF ENLISTEE/REENLISTEE	b. DATE SIGNED *(YYYYMMDD)*

19. ENLISTMENT/REENLISTMENT OFFICER CERTIFICATION

a. The above oath was administered, subscribed, and duly sworn to (or affirmed) before me this date.

b. NAME *(Last, First, Middle)*	c. PAY GRADE	d. UNIT/COMMAND NAME
e. SIGNATURE	f. DATE SIGNED *(YYYYMMDD)*	g. UNIT/COMMAND ADDRESS *(City, State, ZIP Code)*

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NAME OF ENLISTEE/REENLISTEE *(Last, First, Middle)*	SOCIAL SECURITY NO. OF ENLISTEE/REENLISTEE

F. DISCHARGE FROM/DELAYED ENTRY/ENLISTMENT PROGRAM

20a. I request to be discharged from the Delayed Entry/Enlistment Program (DEP) and enlisted in the Regular Component of the United States *(list branch of service)* _____ for a period of _____ years and _____ weeks. No changes have been made to my enlistment options **OR** if changes were made they are recorded on Annex(es) _____ _____ which replace(s) Annex(es) _____ .

b. SIGNATURE OF DELAYED ENTRY/ENLISTMENT PROGRAM ENLISTEE	c. DATE SIGNED *(YYYYMMDD)*

G. APPROVAL AND ACCEPTANCE BY SERVICE REPRESENTATIVE

21. SERVICE REPRESENTATIVE CERTIFICATION

a. This enlistee is discharged from the Reserve Component shown in item 8 and is accepted for enlistment in the Regular Component of the United States *(list branch of service)* _____ in pay grade _____ .

b. NAME *(Last, First, Middle)*	c. PAY GRADE	d. UNIT/COMMAND NAME
e. SIGNATURE	f. DATE SIGNED *(YYYYMMDD)*	g. UNIT/COMMAND ADDRESS *(City, State, ZIP Code)*

H. CONFIRMATION OF ENLISTMENT OR REENLISTMENT

22a. IN A REGULAR COMPONENT OF THE ARMED FORCES:

I, _____ do solemnly swear (or affirm) that I will support and defend the Constitution of the United States against all enemies, foreign and domestic; that I will bear true faith and allegiance to the same; and that I will obey the orders of the President of the United States and the orders of the officers appointed over me, according to regulations and the Uniform Code of Military Justice. So help me God.

b. SIGNATURE OF ENLISTEE/REENLISTEE	b. DATE SIGNED *(YYYYMMDD)*

23. ENLISTMENT OFFICER CERTIFICATION

a. The above oath was administered, subscribed, and duly sworn to (or affirmed) before me this date.

b. NAME *(Last, First, Middle)*	c. PAY GRADE	d. UNIT/COMMAND NAME
e. SIGNATURE	f. DATE SIGNED *(YYYYMMDD)*	g. UNIT/COMMAND ADDRESS *(City, State, ZIP Code)*

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