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Should Combat Troops Be Given the Option of Refusing Investigational Drug Treatment?

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I. INTRODUCTION

While she was stationed in Iraq during Operation Desert Storm, Sergeant Carol Picou, a U.S. Army nurse, was under the orders of her field commander to take a little white pill every eight hours.1 Almost immediately, Picou began to suffer side effects from the drug. Her eyes became blurry; she drooled; she lost control of her bladder functions.2 When she skipped the pill one day to avoid these side effects, her commanding officer ordered her to take the pill, watching her as she swallowed it.3 “This is for your own protection. You need to continue . . . taking this as long as we’re in Iraq,” she reports him as saying.4 This went on for fifteen days.5

Today, Picou must wear diapers and catheterize herself eight times a day because of incontinence.6 In 1992, she was diagnosed with a suppressed autoimmune system.7 She has central and peripheral vision field disorders. Picou believes that her illnesses, in part, can be traced to the little white pills she was forced to take in Iraq.8

The pills — pyridostigmine bromide (PB) — were administered under a sharply-criticized landmark wartime emergency protocol, Interim Rule section 50.23(d), issued by the Food and Drug Administration (FDA) on December 21, 1990, only weeks before the ground war in Iraq began.9 Under this protocol, FDA allowed the Department of Defense (DOD) to compel troops to take experimental drugs without first getting their informed consent.10 Fearing the use of chemical and biological warfare by the Iraqi army, DOD sought FDA approval of the use of PB and another drug, a botulism vaccine, that DOD believed were its best chance at prophylactically protecting the troops from the effects of nerve gas attacks.11

Because these drugs had not yet received FDA approval for this use, the drugs could only be administered under an investigational new drug (IND) protocol.12 Until

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2 Id.
3 Id.
5 Id.; Bradley, supra note 4, at *2.
6 S. Rep. No. 97, supra note 1, at 22.
7 Id.; Bradley, supra note 4, at *2.
9 Id. at 52,817.
the Persian Gulf War, FDA only allowed the use of such investigational drugs with the fully informed consent of the subjects, except in narrowly-conscibed emergency situations when the patient could not communicate.13 DOD sought a waiver of this informed consent requirement, arguing that informed consent was not feasible in times of war.14 After six months of often-heated debate, FDA agreed to DOD’s demands and waived the informed consent requirement for troops in the Persian Gulf.15

In total, an estimated two-thirds of the 696,562 U.S. troops in the Persian Gulf took PB for varying periods of time.16 Approximately 8000 individuals received the botulism vaccine.17 In a Senate survey of 150 troops, over thirty percent reported some of the following significant side effects from taking the drugs: joint pain, headaches, skin problems, memory loss, and fatigue.18

Although the troops were ordered to take these drugs six years ago, Interim Rule 50.23(d) has current implications for future wars and engagements19 and for how the government views the necessity of informed consent. FDA presently is considering DOD’s proposal to make the Interim Rule permanent; FDA officials have indicated that the agency plans to make the rule permanent with few modifications.20 DOD also is seeking full FDA approval for the prophylactic use of PB and botulinum toxoid.21

This article discusses the implementation of this Interim Rule and the ethics of forced administration of investigational drugs during wartime without the troops’ informed consent. The article also offers some suggestions for ensuring that the rule is implemented only after sufficient consideration for the troops’ autonomy and health.22 Part II of this article outlines the events that led to DOD’s administering the two

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17 S. Rep. No. 97, supra note 1, at 22.
18 Id. at 46, 48, 51, 52.
19 In 1989, Judge William H. Webster, Director of the Central Intelligence Agency, testified before the Senate that at least 20 countries had chemical weapons and the trend toward chemical and biological warfare would continue “despite ongoing multilateral efforts to stop the proliferation.” Hearings on Global Spread of Chemical and Biological Weapons Before the Senate Comm. on Governmental Affairs and Perm. Subcomm. on Investigations, 101st Cong., 1st Sess. 10 (1989) (cited in Doe v. Sullivan, 938 F.2d 1370, 1377 (D.C. Cir. 1991)). In 1991, the Secretary of Defense, Dick Cheney, also recognized that the proliferation of nuclear, chemical, and biological weapons and the missile technology for long-range delivery systems would make “regional conflict increasingly destructive and lethal.” Dick Cheney, Annual Report of the Secretary of Defense to the President and Congress 3 (1991) (cited in Doe, 938 F.2d at 1377).
20 Stuart L. Nightingale, Permitting the Use of Investigational Agents for Prophylaxis/Treatment with Waiver of Informed Consent in Battlefield or Combat-Related Situations, statement at meeting of Presidential Advisory Committee Gulf War Veterans’ Illnesses 9 (Jan. 12, 1996) [hereinafter Nightingale prepared statement] (on file with author). Despite the stated intentions of FDA officials, FDA is unlikely to make the Interim Rule permanent without a public comment period and, possibly, legislative hearings. The Presidential Advisory Committee on Gulf War Veterans’ Illnesses, established by President Clinton, has recommended in its Interim Report that FDA first issue a Notice of Proposed Rule Making, revisiting several areas of change for the Rule, before making the Rule final. Interim Report, supra note 16, at 24. Additionally, the expected incoming new chairman of the Senate Veterans’ Affairs Committee has expressed an interest in the issues surrounding the Rule, which may lead to increased legislative involvement in the Rule’s fate. Interview with Jim Gottlieb, Minority Chief Counsel, Senate Comm. on Veterans’ Affairs (Oct. 23, 1996).
22 This paper does not discuss the government’s tort liability for administering the drugs under this rule. See William Brook Lafferty, Comment, The Persian Gulf War Syndrome: Rethinking Government Tort Liability, 25 Stetson L. Rev. 137 (1995) (discussion of tort liability for administering mandatory investigational drugs).
investigational drugs on a nonconsensual basis to the Persian Gulf troops. Part III discusses the Interim Rule and its implementation. Although DOD was motivated by a desire to protect the troops, the Department acted in haste and potentially jeopardized the troops' long-term health in implementing the Rule. Part IV discusses whether the decision to allow DOD to compel troops to take investigational drugs was ethical and consistent with the United States' view of the importance of informed consent as rooted in personal dignity. Finally, Part V outlines several suggestions designed to make the Interim Rule, if made permanent, more respectful of the troops' long-term health and personal dignity.

II. DEPARTMENT OF DEFENSE LOBBIES TO BYPASS INFORMED CONSENT IN THE PERSIAN GULF COMBAT

Saddam Hussein invaded Kuwait on August 2, 1990, leading to the deployment of U.S. troops in Iraq. In challenging Saddam Hussein, the United States faced an opponent with both the ability and the willingness to use chemical and, possibly, biological warfare. Although other military commentators discounted the likelihood that Hussein would use these weapons, General H. Norman Schwarzkopf took the threat of chemical and biological warfare very seriously. Schwarzkopf's plans for war included the possibility of mass casualties numbering up to 20,000 from chemical weapons.

As one element in the planned U.S. response to the threat of chemical warfare, the Army wanted to use vaccines and pretreatments — PB and botulinum toxoid — that it believed would help protect the troops from a chemical warfare attack. The use of such drugs is governed by the Federal Food, Drug, and Cosmetic Act. At the time of the Iraqi invasion, however, FDA had not approved either drug for general marketing for this use (such approval normally is granted only after sufficient proof exists to warrant that the drug is safe and effective). DOD wanted troops to take PB orally in tablet form to help ward off the effects of a nerve gas attack. PB is believed to enhance the effectiveness of two other drugs, atropine and 2-PAM, which are given as standard treatment for nerve agent poisoning. For several years, DOD had been researching the effectiveness and safety of PB under an IND approved by FDA. The known side effects of an overdosage of PB include skin rash, decreased short-term memory, loss of bladder control, seizures, and respiratory arrest. Through a series of injections with botulinum toxoid, DOD also

23 Edward Spiers, Chemical and Biological Weapons: A Study of Proliferation 107-109, 110 (1994). As early as the late 1980s the United States was aware of Iraq's capability to use chemical warfare. Id. at 110. In April 1988, the Iraqis used chemical warfare in the recapture of the Al Fao peninsula. Id. Later Iraqi troops underscored its chemical warfare ability by publicly loading and then unloading chemical warfare from combat aircraft. Id.
24 Id. at 111-13.
25 Id. at 113.
28 21 U.S.C., § 355(a), (d).
30 S. Rep. No. 97, supra note 1, at 11.
31 Nightingale prepared statement, supra note 20, at 11.
32 Staff of Senate Comm., on Veterans' Affairs, supra note 29, at 30.
wanted to vaccinate the troops from botulism, which was believed to be a deadly product of biological warfare.\textsuperscript{33} Researchers had studied botulinum toxoid since the 1970s through an IND sponsored by the Centers for Disease Control, using the drug to protect laboratory workers and others who faced exposure to botulism.\textsuperscript{34} The botulinum toxoid vaccine has the known side effects of swelling, itching, soreness at injection site, hives, general malaise, and headaches.\textsuperscript{35} 

Physicians and clinicians may use drugs that have not received full FDA approval to treat patients and provide research support for the final approval of the drugs.\textsuperscript{36} Such drugs are considered investigational products.\textsuperscript{37} FDA can approve an IND protocol after sufficient data demonstrate sufficient evidence of efficacy and a reasonable assurance of safety.\textsuperscript{38} A key condition to allowing the use of these investigational drugs, however, is that the doctor generally must first get the patient's informed consent before treatment.\textsuperscript{39} FDA authorizes the waiver of informed consent only when such consent is not "feasible."\textsuperscript{40} Until the Gulf War, FDA had waived informed consent as not feasible only when the patient faced a life-threatening emergency; the patient was unable to communicate; and time was not sufficient to obtain consent from the patient's legal representative.\textsuperscript{41} In short, FDA's interpretation of not feasible focused on the condition of the patient.

DOD, however, wanted to bypass informed consent as not feasible when troops could face combat.\textsuperscript{42} Beginning in the summer of 1990, DOD lobbied FDA to relax the informed consent requirement in military combat circumstances.\textsuperscript{43} While the Department supported informed consent in peacetime applications, DOD argued that military combat was different.\textsuperscript{44} DOD claimed that it would be unacceptable from a military standpoint to allow a soldier to refuse to undergo the investigational treatment.\textsuperscript{45} Allowing a soldier to refuse the treatment would endanger him or her, as well as those who would have to try and save his or her life, and undermine the success of the military mission.\textsuperscript{46} A DOD official wrote, "[b]ased on unalterable requirements of

\begin{footnotes}
\item[33] Id. at 127 (statement of Edward Martin, Acting Principal Ass't Sec'y of Defense, Health Affairs).
\item[34] Nightingale prepared statement, supra note 20, at 15; S. Rep. No. 97, supra note 1, at 13.
\item[35] STAFF OF SENATE COMM. ON VETERANS' AFFAIRS, supra note 29, at 266 (table providing the systemic reactions to botulinum pentavalent toxoid for the years 1970 through 1992).
\item[36] Nightingale prepared statement, supra note 20, at 5.
\item[37] 21 U.S.C. § 355(a)(i).
\item[38] STAFF OF SENATE COMM. ON VETERANS' AFFAIRS, supra note 29, at 137 (statement of Dr. Robert J. Temple, Dir., Off. of Drug Evaluation, Center for Drug Evaluation and Research (CDER), FDA).
\item[39] 21 C.F.R. § 50.23.
\item[40] Id.
\item[41] Id. Section 50.23 provides, in pertinent part:
\begin{itemize}
\item[(a)] The obtaining of informed consent shall be deemed feasible unless, before use of the test article, both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:
\begin{itemize}
\item[(1)] The human subject is confronted by a life-threatening situation necessitating the use of the test article.
\item[(2)] Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
\item[(3)] Time is not sufficient to obtain consent from the subject's legal representative.
\item[(4)] There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.
\end{itemize}
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\item[42] 55 Fed. Reg. at 52,815.
\item[44] 55 Fed. Reg. at 52,815.
\item[45] Id.
\item[46] Id.
\end{footnotes}
gational drug use and held that FDA had authority to enact the Interim Rule. The court also determined that the DAA was not directly implicated by FDA's enactment of the Interim Rule. Finally, the court held that Interim Rule's application would not violate the troops' due process rights. Neither court ruled on the reasonability of FDA's decision to allow DOD to proceed without getting the troops' informed consent.

FDA has indicated that it plans to finalize the Interim Rule, which expired one year after its enactment, making only minor modifications.

III. THE INTERIM RULE AND ITS IMPLEMENTATION: A CASE OF RECKLESS DISREGARD

A. The Interim Rule

The Interim Rule authorized FDA to determine that informed consent was not feasible and thus was not necessary, as a prerequisite to treating soldiers with investigational drugs during a "specific military operation involving combat or the immediate threat of combat." According to the Rule, the Commissioner may find that informed consent is not feasible and waive its requirement "when withholding treatment would be contrary to the best interests of military personnel and there is no available satisfactory alternative therapy.

Thus, the Rule establishes a presumption against informed consent for the military under "actual or threatened" combat circumstances when FDA and DOD conclude that withholding the treatment would not be in the troops' best interests. The Rule sets up a false dichotomy whereby FDA must decide between two artificially established alternatives: forcing troops to take drugs without first getting their informed consent or withholding the proposed treatment altogether. The Commissioner's decision regarding informed consent at this stage does not include an evaluation of whether informed consent can and should be required with the specific treatment proposed. The structure of the Rule assumes that in combat circumstances, troops cannot be given the option of refusing investigational drugs. Instead of having to rebut the presumption that informed consent is essential every time DOD wants to waive it, DOD wins at the outset by arguing that troops cannot be given the right of informed consent because they might refuse.

58 The court held that the authorizing statute was sufficiently ambiguous to allow for FDA's decision to carve out another exception to the informed consent requirement. Id. at 1382.
59 Id. at 1383. The court reasoned:

The DAA, however, limits the authority of the Department of Defense, not the authority of the Food and Drug Commissioner. Although it might be argued that the DAA restricts the authority of the Assistant Secretary of Defense to make the request anticipated by Rule 23(d), it cannot be argued that the DAA restricts the Secretary of Health and Human Services from promulgating Rule 23(d).

Id. at 1383.
60 Id. at 1383. The court conducted a balancing test, concluding that the government's interest in preventing unnecessary danger to troops and medical personnel and its interest in successfully completing the military mission were legitimate government concerns that outweighed the individual's interest in being free from experimental treatment without giving informed consent. Id. at 1383.
61 Doe I, 756 F. Supp. at 14 n.2.
62 Nightingale prepared statement, supra note 20, at 9.
64 Id.
This exception to the informed consent requirement can be triggered only by a DOD request that includes two elements. First, the request must include a written conclusion by investigators and the physician responsible for the involved military personnel that a military combat exigency exists, due to "actual or threatened" military combat, that necessitates the administration of a particular treatment to the troops, without regard to "what might be any individual’s personal preference for no treatment or for some alternative treatment." Second, the DOD request must include a statement that an institutional review board (IRB) has reviewed and approved the use of investigational drugs without informed consent. It is unclear what role the IRB actually has in this process and whether the IRB is charged with conducting an independent evaluation of the safety evidence and the potential risks and benefits of the proposed treatment, considering the likelihood that the need for the treatment will be triggered given the available military information, and weighing the seriousness of the potential harm that would result from not taking the treatment.

The Interim Rule directs the Commissioner to review the DOD request, taking into account several factors, including the extent and strength of the evidence of the drug’s safety and effectiveness for the intended use, the context in which the drug will be used, and the nature of the disease or condition for which the treatment is proposed. The Commissioner also is directed to evaluate the information that will be provided to the troops regarding the drug’s potential risks and benefits.

B. The Rule’s Implementation: A Case of Reckless Disregard

The conduct of DOD in lobbying for the Interim Rule and in administering the two investigational drugs raises serious questions about whether the Army acted in reckless disregard of the troops’ long-term health through its haste and lack of preparation for the potential chemical and biological warfare threat.

1. The Rigor of DOD’s Internal IRB is Questionable

DOD initially applied for a waiver of informed consent for a third drug, but later withdrew this application after further tests revealed serious side effects. DOD sought an IND waiver for an experimental burn cream, Multi-Shield, which was believed to hasten burn healing. The Department applied for this waiver only after its IRB approved the use of the drug, apparently satisfied with the drug’s safety and effectiveness. After filing this application, however, further animal studies indicated that the drug could have potentially serious side effects, including skin irritation so severe that
officials feared that the desire to itch would overwhelm soldiers. While the drug’s failure to receive an FDA waiver of informed consent highlights the rigor of FDA’s analysis of DOD’s request, it also highlights the potential for a DOD internal IRB to act as a mere rubber stamp for the Department’s requests.

2. Safety Concerns Exist Regarding the Use of PB

While the studies that DOD provided to FDA indicated that PB could be used safely as a pretreatment, critics later pointed out that this research ignored the drug’s effects on some populations and was inadequate to support the usage of the drug as a prophylactic for potentially long periods of time. Furthermore, DOD did not submit an Army study, completed as negotiations came to a close, that questioned PB’s effectiveness as a pretreatment.

PB has been approved by FDA since 1955 for treating myasthenia gravis, a neurological disease characterized by muscle weakness. DOD planned to treat the soldiers with a daily dosage of the drug that was fifteen percent of the daily dosage of myasthenia gravis patients. FDA officials stated that they felt that the safety of PB was established by these patients’ long-term use of the drug. This belief in the drug’s safety by analogy to the myasthenia gravis use essentially discounts the possibility of differences in the absorption of the drug by healthy patients as compared to myasthenia gravis patients. Furthermore, it is not necessarily true that a small amount of a drug is safe for healthy patients, although a much larger dosage is used by patients with a certain health condition.

DOD did not include in its PB investigational drug application an Army study that cast doubts on the drug’s effectiveness as a pretreatment, although this study was completed at the time the negotiations were going on between FDA and DOD. The study, which was conducted at the U.S. Army Medical Research Institute of Chemical

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74 Id. Later, a federal grand jury charged a scientist who had been contracted by the Army to analyze the skin lotion with performing a fraudulent demonstration of an analysis of the skin cream before FDA. *Scientist Charged With Lying to the FDA*, BOSTON GLOBE, Nov. 21, 1991, at 65.

75 S. REP. NO. 97, supra note 1, at 28-34; Public Citizen, Petition to Repeal Interim Rule 16-19 (May 7, 1996) (on file with author) [hereinafter Public Citizen Petition].

76 Public Citizen Petition, supra note 75, at 20-22.

77 Nightingale prepared statement, supra note 20, at 11.

78 Id. DOD proposed treatment was 30 milligrams three times a day for seven days; in comparison myasthenia gravis patients were treated with doses of up to 1500 milligrams a day for many years. STAFF OF SENATE COMM. ON VETERANS’ AFFAIRS, supra note 29, at 368. Several other North Atlantic Treaty Organization countries hold PB in reserve for use as a pretreatment against nerve gas attack, including the United Kingdom, Germany, The Netherlands, Belgium, Canada, Israel, and Spain. Id. at 369.


80 STAFF OF SENATE COMM. ON VETERANS’ AFFAIRS, supra note 29, at 104 (statement of Thomas J. Callender, M.D.). Dr. Callender criticized this finding of safety by analogy, saying that myasthenia patients have abnormal physiology that could account for differences in the safety of their treatment with PB from treatment of healthy patients. Id. He also stated that myasthenia patients receive other medications that could be protective of some of the side effects of PB. Id. Callender questioned the assumption that a lower dosage was necessarily safer, commenting that while large doses of insulin were safe for diabetics that even small doses of insulin can cause serious harm in nondiabetic patients. Id.

81 Id.; S. REP. NO. 97, supra note 1, at 12.

82 Public Citizen Petition, supra note 75, at 20-21; DEPARTMENT OF DEFENSE, DEPARTMENT OF DEFENSE COMMENTS ON PUBLIC CITIZEN LITIGATION GROUP’S PETITION TO REPEAL INTERIM RULE ON THE TREATMENT USE WITHOUT INFORMED CONSENT OF INVESTIGATIONAL NEW DRUGS IN MILITARY COMBAT EXIGENCES 15 (1996) (on file with author) [hereinafter DOD RESPONSE TO PUBLIC CITIZEN PETITION].
Defense at the Aberdeen Proving Ground in Maryland, indicated that when rodents were exposed to the nerve gas agents sarin or VX, instead of soman, the use of PB neutralized the effects of the two common nerve gas treatments to be used in conjunction with PB.\(^83\) The study's results are particularly important in light of the Pentagon's recent acknowledgment, after years of denials, that as many as 5000 troops were exposed to sarin at Khamsiya, when U.S. forces blew up an Iraqi ammunition dump.\(^84\) Although the Army was under a continuing duty to update FDA with new information about the drugs for which it sought a waiver of informed consent, the Army did not notify FDA of this study until it was published in 1992.\(^85\) The study, which was submitted for publication on February 11, 1991, was most likely completed in the fall of 1990.\(^86\) DOD, however, claimed that it was unaware of the study until it was published because the study was conducted under a different Army command element.\(^87\) DOD asserts this lack of knowledge although Army officials reported to FDA in January 1991 the results of two other recently completed studies, for which final reports had not yet been filed, that did not question the drug's safety or efficacy; one of these studies was conducted by an Army unit.\(^88\)

The research results submitted by DOD to FDA as evidence of PB's safety and efficacy fell short of supporting the long-term usage of PB for prophylactic use on a large and heterogeneous population.\(^89\) Virtually all of the studies submitted by DOD excluded women as subjects, although woman served as soldiers in the Gulf.\(^90\) The DOD studies also excluded men who smoked, took medication, or had abnormal blood pressure, although men with these conditions were not excluded from combat in the Gulf.\(^91\) Furthermore, critics have pointed out that the studies involved a statistically small number of subjects, focused solely on immediate reactions of the drugs, and included no follow-up to assess long-term effects.\(^92\) Finally, subjects in some of these studies suffered serious side effects following the ingestion of PB, including loss of consciousness, vision problems, and abnormal liver tests.\(^93\) One Army pilot went into respiratory arrest after taking a third dose of PB.\(^94\)


\(^85\) Nightingale prepared statement, supra note 20, at 14, 15. Under the pre-war IND protocols on PB and botulinum toxoid, DOD and the Center for Disease Control prepared annual reports for FDA on the safety and efficacy information about the drugs. Id.

\(^86\) Public Citizen Petition, supra note 82, at 21.

\(^87\) DOD RESPONSE TO PUBLIC CITIZEN PETITION, supra note 82, at 15 n.7.

\(^88\) STAFF OF SENATE COMM. ON VETERANS' AFFAIRS, supra note 29, at 385 (letter from Gregory P. Berezuk, Chief, Human Use Rev. and Reg. Affairs Off., Dep't of the Army, Off. of the Surgeon Gen., to Dir., Div. of Neuropharmacological Drug Prods., CDER, FDA (Jan. 17, 1991)).

\(^89\) S. REP. No. 97, supra note 1, at 28-32.

\(^90\) Id. at 26. One doctor, a specialist in internal medicine as well as environmental and occupational toxicology, stated that the research indicated that there are sexual differences in responses to PB. STAFF OF SENATE COMM. ON VETERANS' AFFAIRS, supra note 29, at 100, 102 (statement by Dr. Callender). Dr. Callender stated that research that excluded women as subjects posed an unwarranted risk to women in combat zones. Id.

\(^91\) S. REP. No. 97, supra note 1, at 29.

\(^92\) STAFF OF SENATE COMM. ON VETERANS' AFFAIRS, supra note 29, at 101 (Callender statement). Dr. Callender pointed out that long-term studies were essential because "it was well known that the ACHe [the enzyme acetylcholinesterase] inhibiting agents that cause permanent nerve damage typically take several weeks to months for the nerve damage to become evident." Id. at 101.

\(^93\) S. REP. No. 97, supra note 1, at 29.

\(^94\) Id.
Another flaw in the research supporting the use of PB was that the research studied PB in isolation, ignoring any possible synergistic effects of its usage in combination with exposure to other drugs or chemicals with which soldiers foreseeably would come into contact.95 A post-war animal study, conducted at Duke University Medical Center, indicated that the low-level use of PB in conjunction with exposure to chemicals found in the insecticides sprayed on troops' uniforms and insect repellents rubbed on the skin could lead to potentially serious side effects, ranging from weakness and tremors to total paralysis and death.96 A later study involving humans exposed to lower amounts of PB and pesticides found that the combination of these agents could cause subtle nerve damage, potentially resulting in fatigue, dizziness, disorientation, and muscle weakness.97 Additionally, a 1993 U.S. Department of Agriculture study conducted on cockroaches found that when PB was used simultaneously with diethylm-tolamide (DEET), an insecticide, the DEET became seven times more toxic than when used alone and the PB became four times more toxic than when used alone.98

An Israeli study also raises the possibility that ingestion of PB during wartime could have made the troops much more sensitive than usual to adverse effects of the drug on their nervous systems.99 This study theorized that battlefield stress might have allowed PB to get into the brain.

3. DOD did not Provide Information on Drugs as Required by FDA

FDA allowed DOD to bypass informed consent for the two investigational drugs contingent on DOD providing troops with information about the drugs' potential risks and benefits.100 While FDA allowed DOD to bypass soldiers' right to consent or withhold consent, the agency required that the soldiers at least be informed about what they were being compelled to take. During months of negotiations, DOD and FDA officials prepared in-depth information sheets detailing the expected benefits of the drugs, how the drugs worked, and any known side effects and contraindications for those with certain health conditions.101 DOD, however, did not provide this information as required and most troops received no information, oral or written, about the

95 Public Citizen Petition, supra note 75, at 18; STAFF OF SENATE COMM. ON VETERANS' AFFAIRS, supra note 29, at 102 (Callender statement); STAFF OF SENATE COMM. ON VETERANS' AFFAIRS, supra note 29, at 147 (post-hearing answers provided by Dr. Edward Martin, Acting Principal Ass't Sec'y of Defense, DOD).
96 Philip Hilts, Chemical Mix May be Cause of Illnesses in Gulf War, N.Y. TIMES, Apr. 17, 1996, at A17.
97 Warren E. Leary, Gulf Illness May Reflect Multiple Exposures, Report Says, N.Y. TIMES, Jan. 9, 1997, at A18. The study, conducted by researchers from the University of Texas Southwestern Medical Center in Dallas, studied the effects of PB and pesticides on Navy combat construction engineers. Id.
98 S. REP. NO. 97, supra note 1, at 32.
99 David Brown, A Theory of Chemical Interactions, N.Y. TIMES, Jan. 2, 1997, at A10. The study, conducted by scientists at the Hebrew University in Jerusalem, studied the effects of PB ingestion by a group of laboratory mice under stressed conditions. "The stressed mice needed only one-hundredth of the dose given unstressed mice to show a similar amount of pyridostigmine 'activity' in brain tissue." Id.
100 STAFF OF SENATE COMM. ON VETERANS' AFFAIRS, supra note 29, at 383 (letter from David Keasler, M.D., Comm'r of Food and Drugs, FDA, to Enrique Mendez, Jr., M.D., Ass't Sec'y for Defense, Health Affairs, DOD (Jan. 8, 1991)). In his testimony before the Presidential Advisory Committee on Gulf War Veterans' Illnesses, Dr. Stuart Nightingale, Assoc. Comm'r for Health Affairs, FDA, stated that "although informed consent was waived, giving as complete information as practicable to the troops was deemed a crucial ethical mandate and sine qua non for this distribution system to be approved." Nightingale prepared statement, supra note 20, at 8-9.
101 STAFF OF SENATE COMM. ON VETERANS' AFFAIRS, supra note 29, at 375-80 (citing DOD FIELD MANUAL 149, 151 (1990)); Nightingale prepared statement, supra note 20, at 4.
Drugs they were taking. DOD has given two conflicting explanations for not fulfilling its obligations to provide troops with these information sheets. At first, a DOD spokesman stated that the Pentagon did not provide this information to troops because they did not want Iraqi intelligence to learn that U.S. troops were prepared to defend against chemical weapons. Later, the Pentagon backtracked and issued a written statement claiming that the information on the investigational drugs’ side effects did not get to the Gulf in time.

There are several reasons why it was important to provide troops with information about the drugs they were taking. First, providing troops with knowledgeable information about their treatment accords them respect as human beings. Second, informed troops would be aware of possible side effects and on the alert for any symptoms of overdosage. Troops with health conditions that should not take PB would be able to notify their field command and possibly be exempted from taking the investigational drugs. Finally, receiving such information creates a psychological benefit, and possibly would enhance the troops’ trust that their command is acting in their best interest. By not providing troops with knowledge about what they were taking, DOD violated troops’ trust, jeopardized morale, and fostered rumors.

Army officials also failed to keep adequate medical records on the troops’ use of investigational drugs, a lapse that has led to repeated problems by Persian Gulf veterans in getting needed and appropriate follow-up medical treatment. Some field commanders were under the impression that the investigative drugs were classified as “secret” so as not to give Iraqi intelligence any information about the U.S. troops’ defensive capability. Therefore, DOD is uncertain about who took what drug.

IV. THE ETHICS OF TAKING AWAY SOLDIERS’ RIGHT TO INFORMED CONSENT

In its efforts to treat the troops with investigational drugs on an involuntary basis, DOD was motivated by two sometimes-conflicting responsibilities: 1) to protect American troops against the threat of chemical weapons, and 2) to protect the privacy of the troops. The decision to use investigational drugs on the troops raised ethical questions about the right to informed consent. The use of investigational drugs on soldiers without their consent violated the principles of respect for autonomy and the right to self-determination. The troops were not able to make an informed decision about the treatment they received, and their trust in their command was compromised.

FDA officials, who have the option of imposing sanctions on DOD for not complying with the IND requirements, told Senate officials in 1994 they would discuss the noncompliance with DOD.

FDA RESPONSE TO PUBLIC CITIZEN PETITION, supra note 82, at 13.

Additionally, several troops believe that their children’s birth defects may have been caused by their forced ingestion of PB. R. Alta Charo, Prepared Statement for the Presidential Advisory Committee on Gulf War Illnesses Meeting 12 (Jan. 1996) [hereinafter Charo prepared statement].

FDA officials, who have the option of imposing sanctions on DOD for not complying with the IND requirements, told Senate officials in 1994 they would discuss the noncompliance with DOD. STAFF OF SENATE COMM. ON VETERANS’ AFFAIRS, supra note 29, at 122 (statement of Arthur L. Caplan, Ph.D., Ctr. for Bioethics, Univ. of Pa.).
can interests and complete a successful military mission, and 2) to protect as best it could the health and safety of the troops.112 The difficult ethical question posed by the implementation of the Interim Rule is not whether DOD should have withheld the use of these investigational drugs from the troops because neither drug was approved by FDA for the war usage. Indeed, the answer to this question is that DOD should have offered these drugs because it had some evidence of the drug's safety and effectiveness. Rather, the principal question is whether FDA should have allowed the right of informed consent for treatment with investigational drugs, a right that is accorded virtually all Americans, to be taken away from the troops.113

A. Background: Importance of Informed Consent

Informed consent is a relatively recent concept that has come to be viewed, in the second half of the twentieth century, viewed as a treasured right of American patients in medical treatment and research.114 Although ill-defined, informed consent generally means that the patient must be informed about the substantial risks and benefits of any proposed treatment, and about the availability of any alternative treatment, and that the patient must consent to the treatment.115 Informed consent has evolved into more than just a mere technicality that precedes experimental treatment and research, it has become a fundamental social value judgment.116 Foremost, informed consent is rooted in the belief that society should respect each individual's autonomy and his or her right to make choices concerning medical treatment and life.117

The elevation of informed consent to a pillar value of the American medical practice reflects a transformation of the patient-doctor relationship from a paternalistic one with a “doctor-knows-best” attitude to a relationship in which the patient, along with the doctor, decides the course of treatment.118 Revelations of brutal experiments by the Nazis during World War II and American experiments on unknowing or ignorant participants, such as the Tuskegee syphilis experiments and Army experiments on troops involving mustard gas and LSD, also have solidified public and legislative support for informed consent.119

Following the medical trials at Nuremberg, the American military court issued the Nuremberg Code, which contained ten legal principles to guide experimentation on human beings.120 The Nuremberg Code has become a part of the international common law and can be applied to both civil and criminal cases in state and federal courts in the United States.121 The first principle of the Nuremberg Code provides a

112 DOD RESPONSE TO PUBLIC CITIZEN PETITION, supra note 82, at 1, 3-4.
113 21 C.F.R. § 50.23.
115 JAY KATZ, EXPERIMENTATION WITH HUMAN BEINGS 523 (1973) ("lawyers, investigators, and courts often seem to overlook the fact that it lacks specific construction and remains an ill-defined concept"); PAUL S. APPELBAUM, CHARLES W. LIDZ & ALAN MEISEL, INFORMED CONSENT 3 (1987) (discussion of different concepts of informed consent and concept's "complex lineage").
118 44 Fed. Reg. at 47,718.
119 44 Fed. Reg. at 47,713.
121 Id. at 21.
patient/subject with the right to informed consent:

The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.122

This concept of informed consent has four elements: that the patient be competent to consent, that the patient be informed, that the patient understand this information and the right to consent or withhold consent, and that any consent be voluntary.123 It is significant that although the Nuremberg Code was drafted in response to wartime circumstances, it did not contain any exceptions for military troops.

Physicians groups adopted their own alternative code to guide medical research with the World Medical Association’s Declaration of Helsinki in 1964.124 Similar to the American judges at Nuremberg, the doctors who drafted and adopted the Helsinki declaration made informed consent a central tenet of medical research.125 Unlike the Nuremberg Code, however, the Declaration of Helsinki distinguished between “clinical research in which the aim is essentially therapeutic for a patient, and clinical research the essential object of which is purely scientific and without therapeutic value the person subjected to the research.”126 In the context of the latter, written consent must be obtained. In the context of research that would be therapeutic, however, the Declaration encouraged voluntary informed consent only “if at all possible, consistent with patient psychology.”127

Despite the adoption of these two ethical codes highlighting the importance of informed consent, for the better part of the twentieth century doctors could administer investigational drugs to their unknowing patients without even hinting to them that FDA had not yet evaluated the drugs’ safety.128 While drugs could be marketed only after a determination of their safety, FDA allowed clinical research to be conducted on human subjects, usually in the context of doctor-patient individual treatment, without

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122 See Katz, supra note 115, at 305-06. See also 2 Trials of War Criminals Before the Nuremberg Military Tribunal Under Control Council Law No. 10, at 181-82 (1946-1949).
123 Annas, Glantz & Katz, supra note 120, at 7.
125 Id.
126 Id.
127 Id.
128 44 Fed. Reg. at 47,713.
any review at all. Furthermore, such research could be conducted legally without first obtaining the patients' informed consent.

While the horrors of the Nazi medical experiments dramatized the necessity of informed consent in the pure research context, it was not until the thalidomide tragedy of the 1960s that Congress acted to make informed consent a condition to the more commonplace therapeutic experimentation conducted in the United States. While the manufacturers of thalidomide were seeking FDA approval, doctors prescribed the drug to pregnant women with almost no FDA oversight. Records indicated that 2,500,000 thalidomide tablets were distributed to doctors for investigational use; at least 624 pregnant women received the drug. This tragedy sparked Senator Jacob Javits of New York to propose that doctors should inform patients of the investigational nature of drugs before prescribing them:

Let us remember that thalidomide was not administered to mental patients — at least not in the main — to people who would suffer terribly in terms of being upset if they knew they were taking a medicine which was experimental in character . . . . The drug was administered to people who could have been told, and then if they chose to take it, they would have taken it. If they did not choose to take it, they did not have to take it.

Javits spoke of the patient's right to informed consent as a right rooted in personal dignity. The Javits amendment resulted in FDA regulation that conditions use of investigational drugs in treatment or research on obtaining the subject's informed consent. This regulation requires informed consent in purely therapeutic treatment and in research that is deemed experimental because the drug has not yet passed full

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129 Id. It was only when the drug manufacturer applied for final approval that FDA reviewed how the research was conducted. Id. Until that point, FDA regulations required only that the drug be labeled "for investigational use only" and that the manufacturer keep records on how much drug was supplied and to whom. Id.

130 Id.

131 44 Fed. Reg. at 47,714. Thalidomide is a sleeping pill that was given to patients in Europe and that caused women who took the pill during pregnancy to give birth to babies with severe birth defects. See 108 Cong. Rec. 17,403-04 (1962) (reprinting News Release from FDA, U.S. Dep't of Health, Education, and Welfare (Aug. 23, 1962)).


133 Id.

134 108 Cong. Rec. 17,397 (1962). Javits' proposed amendment initially did not require that consent be obtained, although Javits and others recommended that such consent be obtained, Id.

135 Id. Senator Carroll added:

I have great confidence in our medical profession. I know the physician recognizes his ethical responsibility to the patient . . . . I know that in most cases the doctor is going to act in the interest of his patient. However, I repeat that I believe firmly every human being has a right to know whether he is being treated with experimental medicine.

Id.

FDA safety and efficacy standards. Thus legislators viewed informed consent as necessary to protect the dignity of persons involved in the normal doctor-patient relationship beyond that of the pure research setting.

The only statute specifically addressing informed consent in the military context was enacted in 1985, following revelations of the 1960s Tuskegee syphilis experiment. This experiment involved hundreds of unknowing African American men, twenty-eight of whom died after medical researchers left their syphilis untreated to study the disease’s development. The statute, section 1401(c)(1) of the DAA, requires the military to obtain troops’ informed consent before DOD performs any “research” on the troops, even if such research is intended to benefit the soldiers. The statute, however, does not define “research.” Moreover, the Army regulation on standardized treatment does not require a soldier’s consent before administering drugs or treatment. The DOD statute and Army regulation on standardized treatment therefore leave open the question of informed consent for troops in the gray area between standardized treatment and pure research.

Ethicists assert that the concept of informed consent should be applied most rigorously in the context of “research,” as opposed to during standardized medical treatment. In the context of experimentation, the risks of undergoing the investigative treatment are generally unknown, and the subject and researcher often have conflicting interests: the patient is interested in his or her health, while the researcher is interested in the integrity of the experiment. Furthermore, when the research subject is unlikely to directly benefit from the treatment, more detailed information regarding the treatment’s risks and benefits is essential to ensure that the subject truly consents.

The question of whether a particular treatment fits into the category of standard treatment or research, and thus whether informed consent is of heightened importance, continues to trouble medical and legal ethicists. In 1974, Congress directed its
newly-created National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research to consider the boundaries between research and the routine practice of medicine. In distinguishing between the two settings, the Commission, in its Belmont Report, defined medical practice as “interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success.” This definition focuses on the risk involved and the intent of the physician, stating that the purpose of medical practice is “to provide diagnosis, preventive treatment or therapy to particular individuals.” In contrast, the Commission defined research as “an activity designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge.” Thus, the purpose of research is to contribute to generalizable knowledge. The Commission stated that the fact that a procedure is “experimental” should not automatically place it in the category of research. The Commission, however, offered little guidance on how to evaluate the nature of experimental procedures, except to advocate that radically new procedures should be studied first in the formal research setting.

B. DOD's Treatment of Troops With Investigational Drugs Violated Troops' Autonomy

The right to informed consent should not be taken away from soldiers in most combat situations. Maintaining troops' right to informed consent in taking investigational drugs is essential to respecting their autonomy, as recognized by current FDA law and medical ethical canons. Military personnel deserve and need this right because of the research aspects of the wartime use of investigational drugs and because of their vulnerable legal status as the subjects of military law. Although commanders have the right to make reasonable military decisions that risk the lives of their troops, the decision to force someone to take investigational drugs is qualitatively different because of the uncertainty regarding the safety and efficacy of these drugs. In all but the most extreme combat situations, in which the country’s security is directly threatened or large numbers of war victims face death, troops should be given the right to refuse to take investigational drugs.

1. The Use of the Investigational Drugs in the Persian Gulf Was a Combination of Therapy and Research

DOD's use of the two investigational drugs on the Persian Gulf troops constituted a mixture of research and therapy. Therefore, the heightened need for informed consent in the research context should apply. Ethicist Arthur Caplan argues compellingly that the Belmont Report's definitions, focusing on the purpose of the medical

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147 Id. at 3.
148 Id.
149 Id.
150 Id.
151 Id.
152 Id. “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.” Id.
intervention, do not go far enough in determining the nature of complex settings that fall between the two extreme ends of the pure research-pure therapy continuum. DOD's administration of the two drugs was "manifestly experimental," but it also was not conducted with the "intent of generating new knowledge." DOD's treatment was experimental in that the safety and efficacy of the drugs were not sufficiently known for full FDA approval. FDA allowed their usage only because there was some evidence that the drugs would be effective and no alternative treatment was known to exist. Still, DOD did not administer the treatment with the primary intent of generating new knowledge. The drugs were given to the troops, with the decision being left to the field commanders as to when or for how long to order treatment, based on the commanders' assessment of the risk of a nerve gas attack. The treatment, although used and intended as individual therapy for the troops, also included research aspects because of the ultimate uncertainty about its safety and efficacy for the purpose for which it was utilized in the Gulf. As Caplan stated, "[t]hese agents were used in large populations for purposes other than those for which they were originally designed in circumstances under which they had never been before tried."

2. The Military Should Be Viewed as a Vulnerable Population in the Research Context

Because of their unique status, military personnel deserve even greater consideration before the right to informed consent is taken away from them. Upon entering the military, each soldier gives up many rights enjoyed by regular citizens, such as the right to civilian remedies for negligent or abusive treatment, because of governmental immunity from liability. For example, the U.S. Supreme Court held that a serviceman could not sue for damages caused by Army researchers who secretly spiked his drink with LSD to study the drug's effects on humans. The court held that his suit was barred because the injuries "arose out of or ... [were] in the course of activity incident to service." The serviceman, however, had volunteered for a study in chemical warfare, not LSD. Subsequent to the secret LSD treatments, he suffered radical personality changes that led to his discharge from the Army and the dissolution of his marriage.

Furthermore, military personnel often undergo treatment pursuant to orders supported by federal statutes and regulations, as in the Persian Gulf. As the outcome of the Doe lawsuit reveals, military authority under law is relatively immune from out-

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153 STAFF OF SENATE COMM. ON VETERANS' AFFAIRS, supra note 29, at 120-21 (Caplan statement).
154 Id. at 121.
155 Id. Caplan argues that the fact that both FDA and DOD viewed the treatment as research, the fact that both parties believed that they needed to seek waivers from prevailing informed consent requirements is further evidence that the treatment constituted research. Id. Ironically, Caplan reaches his conclusion by focusing on the intent of the investigators, while criticizing the Belmont Report's focus on investigators' intent. Id.
156 STAFF OF SENATE COMM. ON VETERANS' AFFAIRS, supra note 29, at 125 (Martin statement).
158 Id.
159 S. REP. NO. 97, supra note 1, at 44; Charo prepared statement, supra note 106, at 2.
161 Id. at 684.
162 Id. at 671.
163 Id.
164 Charo prepared statement, supra note 106, at 2.
side review due to courts' traditional stance of extreme deference to military judgment and the doctrine of separation of powers.

3. DOD's Advocates the Involuntary Treatment of Investigational Drugs for Troops in Certain Combat Situations

DOD argued that informed consent is appropriately waived in the military combat setting because the military has a duty to take all reasonable precautions to bring about the successful completion of a mission and the safe return of the forces. These duties require the military, at the very least, to offer the troops investigational treatments, provided that such treatments are supported adequately by safety and efficacy information and that no standard alternative treatments are available. The soldier surrenders up some individual rights when serving in the military in the interest of the group and the military mission as a whole. The soldier's individual rights thus are tempered by his or her status as a member of the group. The government argued that to allow a soldier to refuse the prophylactic treatment would leave the soldier exposed to potentially debilitating nerve gas attack. If such a soldier became unable to function, other soldiers would have to be diverted to save him or her, risking their lives and further undermining the success of the military mission. DOD claimed that to fulfill its two duties — to successfully complete the military mission and to protect the troops — consent is not feasible in times of war.

The department essentially was asserting that consent is not feasible under military combat circumstances because some soldiers might refuse to undergo the investigational treatment. Previously, FDA exceptions to the informed consent requirement focused on the medical condition of the patient, allowing consent to be waived in the narrow circumstances of an emergency coupled with the inability of the patient to communicate and the inability to reach the patient's legal representative for proxy consent. With the Interim Rule, however, FDA interpreted the infeasibility of informed consent to include a situation in which some of the potential patients might refuse to undergo the treatment.

The military is advocating the use of a therapeutic privilege exception — the belief that patients should get the treatment they need and that doctors can best determine what this is — to the informed consent requirement in combat circumstances. FDA's adoption of this position is surprising, considering that the agency specifically repudiated the therapeutic privilege exception in drafting the original informed consent requirements. In response to the written public commentary on the original rule, FDA quoted a paper on informed consent that had stated:

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165 DOD RESPONSE TO PUBLIC CITIZEN PETITION, supra note 82, at 1.
166 Id.
167 Id. at 10.
168 Id.
172 Id.
173 21 C.F.R. § 50.23.
174 Charo prepared statement, supra note 106, at 10-11.
Because of the great potential for abuse, e.g., the withholding of information for convenience or to assure the patient will not reject the treatment, and because the probability of success with an experimental treatment is either not known or very low, this exception should also not be permitted in the case of therapeutic experimentation . . . . In order to protect self-determination and promote rational decision-making, more, not less, information should probably be required to be disclosed in the experimental therapy situation than in the purely experimental setting with a normal volunteer.\(^{175}\)

Thus FDA specifically rejected including within the “not feasible” exception to the informed consent requirement situations in which the patient might refuse to take treatment.\(^{176}\)

4. The Forced Administration of Investigational Drugs Violates Troops’ Autonomy and Their Trust, and Should Not Be Allowed in Most Modern Combat Situations

The involuntary treatment of the troops with investigational drugs violates the spirit of the Nuremberg Code that informed consent is necessary to preserve the dignity of the human beings undergoing treatment.\(^{177}\) While the Nuremberg Code dealt only with nontherapeutic experimentation, the Code stands for the principle that informed consent is essential to ensuring that human beings are treated as human beings, and not merely as means to an end.

While military commanders make decisions that expose their troops to grave injury and even death, the military should not be allowed to compel troops to take drugs that have not been approved fully by FDA. The weapons of war increasingly are complex and unknown. The injuries or deaths suffered in past conflicts are fundamentally different from the mixture of symptoms that has left thousands of Persian Gulf soldiers in a netherland between a state of total disability and good health.\(^{178}\) With the potential for chemical and biological warfare comes an obligation for DOD to gather as much knowledge as possible about these threats and to research how to protect the troops against them. As always the case in war time, today’s troop commanders make decisions about their units that could endanger their troops’ lives. In contrast to past wars that did not involve the threat of biological and chemical warfare, however, modern troop commanders are making decisions that could affect the long-term health of the troops and possibly, the health of their families and unborn children.\(^{179}\)

Furthermore, the decision to compel troops to take investigational drugs such as PB is qualitatively different from the decision to force troops to receive approved vaccines, such as anthrax, or to use a quality-tested helmet. DOD forced the troops to


\(^{176}\) Id.

\(^{177}\) Katz, supra note 115, at 305-06; George J. Annas & Michael A. Grodin, Treating the Troops, 21 Hastings Ctr. Rep., at *9, available on LEXIS, NEWS library, ASAPII file; Bradley, supra note 4; at *6 (comment of Sen. John D. Rockefeller IV that DOD’s mandatory treatment of troops violated Nuremberg Code).


\(^{179}\) There is little scientific evidence, however, supporting the contention that troop commanders are potentially endangering the health of the troops’ unborn children and families. David Brown & Dana Priest, Report Finds No Evidence of “Gulf War Syndrome,” Wash. Post, Nov. 9, 1996, at A1.
surrender their autonomy because DOD believed that the Department knew what was best for the soldiers and the viability of the mission. DOD, however, did not have the same reasonable assurance that these drugs were indeed what was best for the troops, as it does when obligating soldiers to wear certain protective gear. Not enough information was known about the use of these drugs as prophylactics to ward off the effects of chemical or biological warfare.

Troops must surrender some rights in the interest of supporting their fellow troops and the military mission, but forcing them to take investigational drugs, in addition to undergoing the normal risks of the battlefield, is forcing soldiers to surrender too many rights. In writing about World War II soldiers, historian Paul Fussell wrote that "[they were] uniform, anonymous [.and] undifferentiated . . . [they] might as well [have been] an inert item of Government Issue, like a mess kit or a tool."180 Society’s conceptions of respect toward human beings and toward their rights when undergoing medical treatment have become more enlightened since World War II and, therefore, troops should possess rights that reflect these changed views. Every other American citizen has the right to refuse to take investigational drugs.181 Except in extreme cases, this right should not be removed from those citizens who already are sacrificing so much for their country. While soldiers agree to put their lives at risk in combat to defend their country, they still should be treated as human beings.

Finally, DOD should offer troops investigational drugs on a consensual basis to help restore troop morale. The Army has a history of conducting research on unknowing troops, from the LSD experiments to ordering hundreds of troops who lacked protective gear to stand for several hours in a field where an atomic explosion had occurred only thirty minutes before.182 Most recently, DOD violated the trust of Persian Gulf troops by not providing them with the required information about the investigational drugs they were compelled to take and by devoting insufficient resources to investigating the Persian Gulf illnesses.183 DOD also has raised the spectre of a cover-up by taking five years to reveal that troops were exposed to nerve gas, although DOD possessed the documents revealing this exposure in 1993, when Congress first posed questions about troop exposure.184

If soldiers are given the right to refuse to take investigational drugs, it is unknown how many will exercise this right and refuse the treatment. In the Persian Gulf, troops were allowed to refuse consent to the botulinum toxoid treatment and approximately 8000 soldiers still took the vaccine.185 In future wars, the military should provide troops well in advance of actual combat with the required information about a treatment’s risks and benefits and the risks of taking nothing during threatened biological and/or chemical warfare. An educational campaign with disclosure about the drugs would allow troops to make rational decisions about the particular treatments. At the very least, if soldiers do take the investigational drugs, as many were compelled to do in the Persian Gulf, these soldiers will have the psychological benefit of knowing that they were treated as human beings.

180 PAUL FUSSELL, WARTIME (1989).
181 21 C.F.R. § 50.23.
182 S. REP. NO. 97, supra note 1; at 7-8, 9-10; Schuchardt, supra note 138, at 284-85.
183 The Presidential Advisory Committee on Gulf War Veterans’ Illnesses in its draft Final Report harshly criticized DOD for conducting a “superficial investigation of possible chemical warfare agent exposures, which is unlikely to provide credible answers to veterans’ questions.” Brown & Priest, supra note 178, at A1.
184 Dana Priest & Bill McAllister, Gulf War’s Depot of Distrust; Pentagon Lagged in Noting Possible Chemical Exposure, WASH. POST, Nov. 10, 1996, at A1.
185 INTERIM REPORT, supra note 16, at 21.
A significant number of troops may decide that they do not want to take these drugs, especially considering the troops' reactions to DOD's conduct in the Persian Gulf War and the yet-unexplained Persian Gulf Syndrome. Assuming, that the investigational drugs would be effective, this will leave some troops protected from a nerve gas attack and others vulnerable to its effects. In this scenario, some troops will be diverted to try and pull these unprotected troops off the front. Depending on the number of untreated troops involved, this diversion and the illness of the untreated soldiers will tend to undermine the success of the military mission. This scenario, however, is no worse than what the military's position would be if the military did not offer any troops the investigational drug. Most fundamentally, the autonomy of troops, and of human beings in general, is important enough to risk such losses in most combat situations.

In the most extreme combat situations, the interest of serving the military mission may outweigh the autonomy of the troops, calling for the involuntary administration of investigational drugs. Modern troops generally are called on to fight and serve in limited engagements in which the security of the United States is not directly threatened, such as the Persian Gulf or Grenada engagements, or peacekeeping missions similar to Somalia. In other combat situations, however, such as World War II the troops' autonomy will be outweighed by the importance of the overriding military mission. For example, in World War II, U.S. territory in the Pacific was threatened directly, while in Europe the Nazis were engaged in mass genocide and were overthrowing the governments of several autonomous nations in an attempt to gain control of the continent. This level of direct and serious threat merits forcing the troops to take investigational drugs that have a good chance of protecting them and thus supporting the success of the military mission. Under such circumstances, the security of the nation and lives of thousands of victims of war would merit a temporary, limited waiver of the right of troops to informed consent. This type of combat situation, however, is becoming increasingly rare in the post-Cold War international global political structure. In present-day limited engagements, the risks resulting from giving troops the right to refuse investigational drugs are risks that the United States can afford to take to uphold the country's core belief in the personal dignity of human beings.

V. PROPOSAL FOR CHANGES IN INTERIM RULE

If FDA makes the Interim Rule final, as agency officials have claimed they will, several changes should be made to ensure that the health of the troops is given more consideration. The process did not work with PB. Not enough information was known about the drug's long-term effects, its safety and efficacy on different populations (including women), and its synergistic effects with other chemicals that were used in the Gulf.

First, the Rule should be redrafted to create a presumption in favor of requiring informed consent in the military context that must be overcome on a case-by-case basis. As it stands, the Rule authorizes the Commissioner to waive informed consent upon a determination that 1) withholding the investigational drugs from the troops would not be in their best interest, and 2) there is no available satisfactory...
alternative therapy. This means that the Commissioner already has accepted that the right to informed consent — a right given to all other citizens taking investigational drugs — can be ethically waived for soldiers in military combat circumstances. The rights of the soldiers would be given more consideration if the Commissioner had to balance the possibility of waiving informed consent for each request in the context of a specific combat situation against the following factors: the risks of harm to be potentially averted by the investigational treatment, the strength of the drug’s safety and efficacy information, a DOD report on the likelihood that the risk will occur, and a DOD report on the relative gravity of the military engagement’s threat to U.S. security. Additionally, more information should be gathered about the likelihood that soldiers would refuse treatment in the combat circumstance.

In the Persian Gulf, perhaps the proposed changes would have led to the informed consent requirement being waived for botulinum toxoid, a drug with a more in-depth and strong record of safety and efficacy, and not waived for PB, for which both the safety and efficacy data for the type of treatment planned in the Gulf were not as strong. In the case of PB, a redrafted Interim Rule might have led to the troops being offered the drug on a voluntary basis, after they were informed of its risks and benefits.

Second, the IRB that considers the use of these drugs without informed consent should be separate from the internal DOD bureaucracy. Military leaders have two primary functions: performing the military mission and providing for the public health of their troops. As the Interim Rule currently stands, the public health mission could too easily be eclipsed by the urgency of wartime. In the Gulf conflict, an internal IRB approved a drug, Multi-Shield, that later was proven to cause potentially serious side effects. This IRB approval raises the concern that military concerns may overpower medical viewpoints at the IRB meetings. A DOD-dominated IRB could create an atmosphere in which haste and the momentum marching toward war dominate, overpowering a careful examination and weighing of potential risks and benefits.

Therefore, the IRB should be composed of outside medical specialists who would be given access to the military studies and make a determination on the investigational drug’s safety and efficacy. These specialists would evaluate a report with conclusions by DOD officials on the urgency of the threatened military combat and the particular warfare threat that may merit investigational drug treatment. Current

189 See id. at 52,815; Eugene G. LaForet, Limits of Loyalty and Obedience: Does the Military Physician Serve Two Masters, in ETHICS AND NATIONAL DEFENSE 101 (James C. Gaston et al. eds. 1993) (author argues that when physician’s duty to military bureaucracy and its mission come in conflict with ethical duty and duty to patient that physician should resort to his or her informed conscience).
190 Interview with Jim Gottlieb, Minority Chief Counsel, Committee on Veterans’ Affairs, U.S. Senate, Washington, D.C. (Oct. 23, 1996). See also LaForet, supra note 189, at 104-10.
191 The minutes of DOD’s IRB meetings relating to the three proposed drugs were not available to give a clearer idea of the rigor of these boards’ analyses.
192 This suggestion also was proposed by R. Alta Charo. Charo prepared statement, supra note 106, at 13-14, Harold Edgar & David Jonathan Rothman, The Institutional Review Board and Beyond: Future Challenges to the Ethics of Human Experimentation, MILBANK Q. 489, Dec. 1, 1995, at *15, available in 1995 WL 12381760. The authors advocate for increased regulations governing IRBs and increased influence of outsiders on these boards. In the context of government-sponsored research, they argue that the need for external voices is even more important to ensure that such research remains within the bounds of ethical research. Id. While this would involve some complications, such as granting outsiders security clearances, the commitment to extra-institutional review could surmount these obstacles. Id.
federal regulations require that IRBs such as these must have at least five members, one of whom must be an outsider to the organization.\(^{193}\) A greater proportion of outsiders is needed to ensure that the critical outside viewpoint is heard.

While the Interim Rule provides that FDA also will conduct its review of safety and efficacy findings, the pressures to approve the DOD request in the time of war may undermine the strength of this FDA review.\(^{194}\) Furthermore, FDA is reviewing what DOD assembled for it, thereby missing the chance to evaluate other completed studies that DOD left out.\(^{195}\) An IRB with a stronger outside presence may help to ensure that FDA is presented with a more objective and complete evaluation of the proposed investigational drugs.

Third, FDA should require studies on the drug’s synergistic effects with other chemicals with which troops foreseeably could come into contact.\(^{196}\) As the threat of war increasingly involves the risk of chemical and biological warfare, soldiers are being exposed to a cocktail of chemicals on the battlefield. The stakes for these soldiers’ long-term health are much higher than were those facing the soldiers of wars of the past. With this reality comes an increased responsibility to protect the soldiers’ long-term health. Although a soldier going into combat faces the very real possibility that he could lose his life in combat, the military and FDA should do all they can to ensure that a surviving soldier should not have to face the possibility that his or her progeny will face other long-term health problems. A study on the safety of these investigational drugs taken in combination with other drugs or chemicals would help protect soldiers’ long-term health.

V. Conclusion

The current version of Interim Rule section 50.23 undervalues the personal autonomy and dignity of soldiers called on to defend the United States, and instead treats these soldiers as tools of war. In lobbying for and implementing the FDA waivers of informed consent during the Persian Gulf War, DOD exhibited haste and a singular focus on its war mission that potentially jeopardized the soldiers’ long-term health. Additionally, DOD’s actions constituted a violation of soldiers’ trust in their commanders, adding to the sad history of treating soldiers as human guinea pigs.

In allowing informed consent to be waived when treating soldiers with investigational drugs, the Interim Rule violates the spirit, if not the letter, of the Nuremberg Code and the prevailing legislative value system that holds informed consent to be an integral principle of medical research and investigational therapy. The autonomy of the soldier regarding these investigational drugs, which have uncertain safety and efficacy results, should not be trammeled in the interest of ensuring a successful military mission, except in the most extreme combat situations. Modern soldiers most often will face combat in limited military engagements that do not involve a direct threat to U.S. security. In such engagements, the soldiers’ right to informed consent

\(^{193}\) 45 C.F.R. § 46.107(a), (d) (1996).

\(^{194}\) Despite these pressures, FDA caught the problems with Multi-Shield and did not approve this application in the Persian Gulf War.

\(^{195}\) Public Citizen Petition, supra note 75, at 20, 21.

\(^{196}\) In its Final Report, the Presidential Advisory Committee on Gulf War Veterans’ Illnesses also stressed the need to commit federal funds for scientific studies about the synergistic effects of PB and other chemicals and agents to which troops would be exposed. PRESIDENTIAL ADVISORY COMMITTEE ON GULF WAR VETERANS’ ILLNESSES, FINAL REPORT 117 (1997) (on file with author).
should be preserved to uphold the belief in informed consent as integral to personal dignity. Therefore, the Interim Rule should not be made permanent.

If FDA does make the Interim Rule permanent, however, the Rule should be modified so that DOD must overcome a presumption of informed consent in the military context for each proposed investigational drug treatment to be used in specific combat situations. The IRB that must evaluate the drug's use without informed consent should be separated from the DOD bureaucracy and its institutional pressures. The IRB reviewing the use of investigational drugs in combat instead should be composed of independent medical specialists. Finally, the modified rule should mandate that FDA review safety and efficacy studies on the synergistic effects of the proposed investigational drug along with other chemicals to which the troops foreseeably would be exposed in combat.