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ANTHRAX VACCINE AS A COMPONENT OF THE STRATEGIC NATIONAL STOCKPILE: A DILEMMA FOR HOMELAND SECURITY

by

Thomas L. Rempfer

December 2009

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The author explains how past problems with the Defense Department anthrax vaccine currently affect Department of Homeland Security and Department of Health and Human Service policy. The departments included the BioThrax® anthrax vaccine in the Strategic National Stockpile following the 2001 anthrax letter attacks. According to the Federal Bureau of Investigation, the vaccine's "failing" status possibly motivated the letter attacks to create demand for the vaccine.

This thesis explores the Department of Defense's troubled experience with the vaccine through four methodologies. The multiprism methodological approach of "quadrangulation" serves to "box" in past safety, efficacy, regulatory, and legal problems. A literature review demonstrates an evolving shift in critiques of the vaccine that parallels policy pronouncements. A case study tool offers a chronological review of the anthrax vaccine to evaluate causal events precipitating the anthrax letter attacks in 2001. A program evaluation includes process tracing through quantitative, qualitative, summative, and formative reviews. Finally, a gap analysis aids in explaining continued reliance on the old vaccine technology.

To conclude, the thesis recommendations encourage formulation of a Presidential Study and Policy Directive process to reassess the vaccine, while suggesting alternative Department of Homeland Security policy courses of action centered on antibiotics and new technologies.

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ANTHRAX VACCINE AS A COMPONENT OF THE STRATEGIC NATIONAL STOCKPILE: A DILEMMA FOR HOMELAND SECURITY

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ABSTRACT

The author[1] explains how past problems with the Defense Department anthrax vaccine currently affect Department of Homeland Security and Department of Health and Human Services policy. The departments included the BioThrax® anthrax vaccine in the Strategic National Stockpile following the 2001 anthrax letter attacks. According to the Federal Bureau of Investigation, the vaccine's "failing" status possibly motivated the letter attacks to create demand for the vaccine.

This thesis explores the Department of Defense's troubled experience with the vaccine through four methodologies. The multiprism methodological approach of "quadrangulation" serves to "box" in past safety, efficacy, regulatory, and legal problems. A literature review demonstrates an evolving shift in critiques of the vaccine, which parallels policy pronouncements. A case study tool offers a chronological review of the anthrax vaccine to evaluate causal events precipitating the anthrax letter attacks in 2001. A program evaluation includes process tracing through quantitative, qualitative, summative, and formative reviews. Finally, a gap analysis aids in explaining continued reliance on the old vaccine technology.

To conclude, the thesis recommendations encourage formulation of a Presidential Study and Policy Directive process to reassess the vaccine, while suggesting alternative Department of Homeland Security policy courses of actions centered on antibiotics and new technologies.

---

[1] Lieutenant Colonel Thomas Rempfer is a distinguished academic and military graduate from the U.S. Air Force Academy and prepared this thesis as a graduation requirement for the Master of Arts Program with the Naval Postgraduate School's Center for Homeland Defense and Security. He is an Air Force Command pilot, experienced in F-16s, F-117s, A-10s, and MQ-1s. His prior service included membership on the U.S. Air Force Cyberspace Task Force, as well as flight safety and operational risk management duties. LtCol Rempfer has testified twice before Congress regarding the anthrax vaccine issue. Senior White House Office and DoD officials enlisted his expertise. He may be contacted at trempfer@aol.com.

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LIST OF ACRONYMS AND ABBREVIATIONS

ACHRE	Advisory Committee on Human Radiation Experiments
ACIP	Advisory Committee on Immunization Practices
AFBCMR	Air Force Board for Correction of Military Records
AVA	Anthrax Vaccine Adsorbed
AVIP	Anthrax Vaccine Immunization Program
BDC	Biodefense Commission
BDS	Biohazard Detection System
BLA	Biologic License Amendment
BMBL	Biosafety in Microbiological and Biomedical Laboratories
BPRP	Biological Personnel Reliability Program
BSAT	Biological Select Agents and Toxins
BSL	Biosafety level
BTRA	Bioterrorism Risk Assessment
BTWC	Biological and Toxin Weapons Convention
BW	Biological Warfare or Biological Weapons
CAAF	Court of Appeals for the Armed Forces
CB	Chemical and Biological
CBER	Center for Biologics, Evaluation, and Research
CBMS	Chemical Biological Mass Spectrometer
CBRN	chemical, biological, radiological, and nuclear
CDC	Centers for Disease Control
CDFAIT	Canadian Department of Foreign Affairs and International Trade
CF	Canadian Forces
cGMP's	Current Good Manufacturing Practices
CIA	Central Intelligence Agency
CIDRAP	Center for Infectious Disease Research and Policy
CJCS	Chairman of the Joint Chiefs
CNS	Center for Nonproliferation Studies
CPG	Compliance Policy Guidance
CRS	Congressional Research Service
CSS	Center for Security Studies
DHHS	Department of Health and Human Services (U.S.)
DHS	Department of Homeland Security (U.S.)
DND	Department of National Defence (Canada)
DoD	Department of Defense (U.S.)
DOE	Department of Energy (U.S.)
DOJ	Department of Justice (U.S.)
DOS	Department of State (U.S.)
DVA	Department of Veterans Affairs (U.S.)

EBS	Emergent BioSolutions
EO	Executive Order
EUA	Emergency Use Authorization
FAS	Federation of American Scientists
FBI	Federal Bureau of Investigation
FBO	Federal Budget Office
FDA	Food and Drug Administration
FDCA	Food Drug and Cosmetics Act
FEMA	Federal Emergency Management Agency
FR	Final Rule
GAO	Government Accountability Office (U.S.)
HASC	House Armed Services Committee
HR	House Report
HSAC	Homeland Security Advisory Council
HSPD	Homeland Security Presidential Directives
IC	Intelligence Community
IDF	Israeli Defense Force
IMA	Israel Medical Association
IND	Investigational New Drug
IOM	Institute of Medicine
JAMA	Journal of the American Medical Association
JPOBD	Joint Project Office for Biological Defense
MBPI	Michigan Biologic Products Institute
MDPH	Michigan Department of Public Health
MEHPA	Model Emergency Health Powers Act
MIIS	Monterey Institute of International Studies
MILVAX	Military Vaccine Agency
MMRS	Metropolitan Medical Response System
MOD	Ministry of Defence (United Kingdom)
MPOD	Medical Plans and Operations Division
NALC	National Association of Letter Carriers
NAS	National Academies of Science
NIH	National Institutes of Health
NOIR	Notice of Intent to Revoke
NRC	National Research Council
NSIAD	National Security and International Affairs Division

PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PODs	points of dispensing
POTUS	President of the United States
PPD	Presidential Policy Directive
PR	Proposed Rule
PREP	Public Readiness and Emergency Preparedness
PSD	Presidential Study Directive
QnA	Question and Answer
RAC-GWVI	Research Advisory Committee on Gulf War Veterans' Illnesses
RFP	Request for Proposal
rPA	Recombinant Protective Antigen
RSS	Receiving, staging, storage
SAIC	Scientific Applications International Corporation
SASC	Senate Armed Services Committee
SNS	Strategic National Stockpile
SOTUA	State of the Union Address
TPER	Terrorism Preparedness and Emergency Response
U.K.	United Kingdom
UN	United Nations
UNMOVIC	UN Monitoring, Verification and Inspection Commission
UPMC	University of Pittsburgh Medical Center
USAF	United States Air Force
USAMRIID	U.S. Army Medical Research Institute for Infectious Diseases
USAMRMC	U.S. Army Medical Research and Materiel Command
USD	Undersecretary of Defense
USMC	United States Marine Corps
VHA	Veterans Health Administration
WHO	White House Office
WMD	Weapons of Mass Destruction

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EXECUTIVE SUMMARY

The Department of Homeland Security faces a vital challenge in charting fiscally practical and legally prudent policy to protect Americans. An important aspect of the Department's duty includes the application of fundamental checks and balances with Departmental partners when selecting biodefense countermeasures in accordance with legal and regulatory standards. The following thesis project reveals a probable analysis deficit by the government when endorsing the Defense Department's anthrax vaccine as a citizen-wide biodefense countermeasure for the Strategic National Stockpile. Synthesizing the complex history of the Department of Defense's intimate involvement in the early development and past promotion of the vaccine requires a diligence to objectivity. The resulting intellectually independent lens enables an evaluation process where checks and balances prevail over politics to ensure a future national biodefense policy capable of withstanding scrutiny.

The genesis of this thesis began in the summer of 2008 when the Federal Bureau of Investigation revealed the motive for the anthrax letter attacks of 2001. According to investigators, the "failing" status of the vaccine program preceded the attacks and served as the possible motive for the crimes. The perpetrator sought to revive confidence in the inoculation. Following the government's revelations, thesis research efforts endeavored to incorporate varied academic means of reviewing the anthrax vaccine from a historical context. Therefore, the thesis analyzes why the Defense Department initiative was failing prior to 2001, the mechanisms behind its revival afterward, and the depth of governmental reflection on the past problems after federal legal authorities officially connected the vaccine to the letter attacker's motive. What at face value appears as a well-intentioned attempt to protect the citizenry of the United States from a seemingly viable biological threat, and with a reputable remedy, ultimately evolves into a disquieting story about violations of the law, altered scientific assessments, and failed oversight that warrant renewed evaluation.

In the case of the anthrax vaccine, a picture emerges about a vaccine invented, patented, licensed, procured, altered, and mandated for decades almost exclusively by the military for a captive audience—soldiers. Critiqued as inadequate by military scientists, the Pentagon pursued a replacement vaccine as early as 1985, to no avail. Faced with an assumed imminent threat in 1990, on the eve of the first Persian Gulf War, the military accelerated and

altered the vaccine's manufacturing process, but without proper regulatory approvals. The Pentagon mandated the vaccine for deployed troops, with many later reporting unexplained illnesses. The post–Gulf War era included attempts at Food and Drug Administration oversight through notices of intent to revoke the manufacturer's license, belated approvals of 1990s manufacturing changes, plant renovations, and generally critical reviews of the vaccine in scientific literature. Upon the expulsion of United Nations weapons inspectors from Iraq in 1997, the armed forces initiated a mandatory immunization policy for all its personnel. The renewed use of the vaccine spawned legislative inquiry and conclusions about the vaccine's illegal mandatory use and experimental status, later confirmed by federal courts. The controversy and regulatory hurdles left the military's use of the vaccine stalled until reinvigorated by the deaths of Americans from the anthrax letter attacks. Since the attacks, over $1 billion in allocations for the vaccine accompanied nearly $60 billion for biodefense. Now the same vaccine, recommended for replacement 25 years earlier, enjoys sole source procurement status and product liability protection, despite a dubious regulatory history.

The circumstances behind the apparent willful blindness of government officials regarding the vaccine, and the anthrax immunization program's controversial resuscitation, warrant review through multiple techniques. In order to accomplish this task, the following thesis modifies the concept of "methodological triangulation" to scrutinize the timeline of events from four angles. The resulting methodological "quadrangulation" begins with a literature review. Significantly, the thesis claims and arguments actually reiterate the original critical conclusions previously held by Defense Department officials about the vaccine's inadequate status. The thesis methodologies continue with a case study, a program evaluation, and a gap analysis to highlight problematic oversight. While the violations of law and the troubling alteration of the scientific and regulatory record documented in the four methodologies serve as the premise of the thesis, other unresolved vaccine issues pertaining to Gulf War Illness, manufacturing deviations, and increases in vaccine potency warrant further analysis, particularly given the reactionary stockpiling of the vaccine for civilians.

To conclude, the thesis recommends a Presidential Study and Presidential Policy Directive process to resurvey judgments by the Department of Homeland Security. This course of action ensures the due diligence and meticulous review required by commonsense and the law for current and future countermeasures in America's biodefense toolbox.

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I. INTRODUCTION

A. PROBLEM STATEMENT AND BACKGROUND

1. Problem Statement

Documented problems with anthrax vaccine adsorbed (AVA, also known as BioThrax®) reveal historic regulatory and oversight gaps that affect national counter-bioterrorism policy. Laws promulgated by the U.S. Congress and edicts by the President of the U.S. in the form of Homeland Security presidential directives (HSPDs) appoint the Secretary of the Department of Homeland Security (DHS) as the principal official for management of domestic bioterrorism events (President of the United States [POTUS], 2003b).[2] The DHS, Department of Defense (DoD), and Department of Health and Human Services (DHHS) each possesses authority under HSPDs 8, 10, 18, and 21 to determine and review bioterrorism countermeasures based upon preparedness and response directives issued by the president (POTUS, 2003c; POTUS, 2004; POTUS, 2007a; POTUS, 2007b). The BioThrax® anthrax vaccine currently plays a central role in both biological warfare and bioterrorism defense policies. The delta between the past critical governmental reviews of the vaccine, compared to recent accelerated procurement following the anthrax letter attacks, dictates a comprehensive reevaluation. The conclusion of this reassessment process may render the current vaccine unnecessary as a complement to the Strategic National Stockpile (SNS), based upon the proven efficacy of antibiotics and pending the development of a satisfactory immunization.

2. Background

Anthrax as a disease results from bacterial infection due to toxins released by spores of *Bacillus anthracis*. The disease manifests itself through different routes of exposure. Skin infection, or cutaneous anthrax, leads to fatality rates of up to 20% absent antibiotics or <1% with antibiotic treatment. In rare cases, the ingestion of anthrax and subsequent gastrointestinal infection poses a fatality risk of between 25%–60%. The most

[2] The Homeland Security Act of 2002 was promulgated under Public Law 107-296.

lethal exposure relates to inhalation anthrax, sometimes referred to as pulmonary or inhaled anthrax, with a fatality risk of up to 89% if left untreated (Centers for Disease Control [CDC], 2000). A clinical study, sponsored by the DoD from 1954–1959, executed by Dr. Philip Brachman, explored the safety and efficacy of an earlier version of the currently stockpiled anthrax vaccine. The study appeared to demonstrate vaccine efficaciousness for cutaneous anthrax, but uncertainty prevailed for the next fifty years regarding effectiveness for inhalation anthrax (Brachman, Gold, Plotkin, Fekety, Werrin, & Ingraham, 1962). Regardless, in late 1997, the DoD announced plans to commence mandatory vaccinations with the vaccine to guard against inhalation anthrax anticipated in the battlefield environment from an aerosolized threat (United States Department of Defense [DoD], 1997b). By mid-1998, the DoD announced completion of a comprehensive review and launched the mandatory anthrax vaccine immunization program (AVIP) (DoD, 1998).

Controversy over the current anthrax vaccine first surfaced during Dr. Brachman's 1957 clinical trial in Manchester, New Hampshire. Four workers died in the first inhalation anthrax "epidemic" in a century (Belluck, 2001; Plotkin, 1960). By 1965, U.S. Army scientists had patented the current anthrax vaccine (Wright & Milton, 1965). The first license application occurred in 1966 (Elengold, 2000a; Elengold, 2000b). Though the government granted a license, during the process regulators noted a failure to submit the required "scientific evidence for efficacy of the vaccine" (see Appendix 1) (Pittman, 1969a, p. 1; Pittman, 1969b). The CDC specifically challenged the licensing application at that time due to the absence of proper data and noted "no controlled evaluation studies" (see Appendix 1) (Kokko, 1969, p. 2).

The DoD also recognized problems with the anthrax vaccine as early as 1985 through a request for proposal (RFP) for a new anthrax vaccine. The RFP stated, "There is an operational requirement to develop a safe and effective product which will protect US troops against exposure from virulent strains of *Bacillus anthracis*." The RFP added, "There is no vaccine in current use which will safely and effectively protect military personnel against exposure to this hazardous bacterial agent." The historic candor of the RFP document also clarified that the current vaccine is, "highly reactogenic [reactive],

requires multiple boosters to maintain immunity and may not be protective against all strains of the anthrax *bacillus*" (see Appendix 2) (DoD, 1985, p. 4).

Also in 1985, a Food and Drug Administration (FDA) advisory panel published a proposed rule in the *Federal Register* in order to finalize the anthrax vaccine's license. The proposed rule noted that the "efficacy against inhalation anthrax is not well documented," and that "no meaningful assessment of its value against inhalation anthrax is possible due to its low incidence" (United States Food and Drug Administration [FDA], 1985). The FDA delayed publication of a final rule and order for anthrax vaccine for 20 years until federal courts ruled in 2005 that mandatory use of the vaccine was illegal absent a finalized license (FDA, 2005). At present, the CDC does not generally recommend anthrax vaccine as a prophylaxis for anthrax infection. Instead, the CDC encourages the use of antibiotics, such as penicillin, ciprofloxacin, and doxycycline, as the "first line of defense" for anthrax infection (CDC, 2001; CDC, 2002; CDC, 2000).

Adding to the licensing peculiarities, the Government Accountability Office (GAO) reported that the manufacturer "did not notify FDA of a number of changes made in the manufacturing process in the early 1990s and no specific studies were undertaken to confirm that vaccine quality was not affected." GAO added that the "ingredients used to make vaccine were changed from the original vaccine," and that "prior to the time of licensing, no human efficacy testing of the … vaccine was performed" (United States Government Accountability Office [GAO], 2001b, p. 3). A congressional report evaluating the military's controversial mandate of the vaccine determined that the DoD program violated FDA regulations due to the vaccine's known "investigational" testing status. The report recommended that "while an improved vaccine is being developed, use of the current anthrax vaccine for force protection against biological warfare should be considered experimental and undertaken only pursuant to FDA regulations governing investigational testing for a new indication" (United States House of Representatives [HR] (HR 106-556), 2000, p. 4).

The Federal Bureau of Investigation (FBI) associated testing irregularities with the existing vaccine to the 2001 anthrax letter attacks. The FBI alleged a U.S. Army scientist's motive stemmed from the fact that the "anthrax vaccine he was working on

was failing" due to potency problems, which the scientist was responsible for resolving. The scientist worried in the time frame preceding the letter attacks, "I think the **** is about to hit the fan … bigtime. The final lot … isn't passing the potency test, and now there's nothing to back it up. Plus, the control vaccine isn't working … It's just a fine mess" (Federal Bureau of Investigation [FBI], 2008, pp. 12–15). Subsequent to the attacks, federal court Judge Emmet G. Sullivan ruled in *Doe v. Rumsfeld*, a legal challenge to the DoD anthrax vaccine mandate (*Doe v. Rumsfeld*, 2003, 2004, 2007). The court declared the DoD program illegal, specifically in violation of 10 U.S.C. § 1107 based on the same "investigational" findings articulated earlier by the Congress (*Doe v. Rumsfeld*, 2004, p. 40).[3] The illegal status of the vaccine's mandatory use persisted until the FDA finalized the license and approved the product for use against inhaled anthrax (FDA, 2005b). Regarding the propriety of the new license, a federal court chose to "not substitute its own judgment when the FDA made no clear" (*Doe v. Von Eschenbach*, 2008, p. 20).[4]

Despite the arguably controversial history, the government also approved the vaccine's altered manufacturing process in 2002 (FDA, 2002a), in addition to the final licensing order in 2005 (FDA, 2005b). On the heels of the August 2008 FBI revelations, the DHHS also announced on September 30, 2008 the procurement of up to 14.5 million additional doses of anthrax vaccine for the SNS at a cost of $404 million (Federal Budget Office [FBO], 2008). The DHHS cited 41 U.S.C. § 253, which authorizes "noncompetitive procedures" for sole source procurement, to justify continued inclusion of the vaccine in the SNS. The contract recipient, Emergent BioSolutions, specifically Emergent BioDefense Operations of Lansing, Michigan, held previous contracts with both the DoD and the DHHS to supply the government with anthrax vaccine. Over $1.2 billion in contracts occurred after the anthrax letter attacks (FBO, 2004; FBO, 2005;

[3] October 17, 1998, was the effective date of the 1998 amendment to 10 U.S.C. § 1107(f)(1). The amendment provided, "In the case of the administration of an investigational new drug or a drug unapproved for its applied use to a member of the armed forces in connection with the member's participation in a particular military operation, the requirement that the member provide prior consent to receive the drug in accordance with the prior consent requirement imposed under section 505(i)(4) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355 (i)(4)) may be waived only by the President.

[4] Note: Upon further judicial review, U.S. courts to date continue to "defer to the FDA's judgment" on the aptness of the new license (*Rempfer v. Sharfstein*, 2009, p. 13–14).

FBO, 2007; FBO, 2008), attacks designed to rekindle vaccine demand according to the FBI. To date, the DoD inoculation program has impacted over 2.3 million U.S. armed forces personnel with more than 9 million doses of vaccine (DoD, 2009b). These figures pale in comparison to the potential magnitude of inoculations for the larger civilian population.

An important additional problem for analysis involves reviewing the government's failure to reevaluate reliance on anthrax vaccine following the FBI's revelations. The problematic analysis requires a review of the implications of stockpiling a known antiquated product for the American people. The stockpiling appears to contradict previous accepted assessments that the "United States has developed an anthrax vaccine for use by military personnel, but there is no vaccine available for civilian use" (Wyatt, 2000, p. 66). This assessment about the vaccine's inapplicability for civilian use likely relates to ill-suited applications for emergency response based on a five-dose protocol over 18 months. Other experts on the vaccine believe the "constraints on the present method of manufacturing argue strongly against procuring large amounts for civilian use," particularly due to its inability to be "efficiently delivered to large populations" (Russell, 1999; Russell, 2007, p. S71).

A successful investigation of the aforementioned problems allows a methodical determination of future national public health strategy for the general populace. If policy conclusions lead to a replacement of the old anthrax vaccine, the analysis then asks leaders to determine how to efficiently apportion future valuable research and limited resources toward the necessary development of "new vaccines, especially against anthrax" (Hamburg, 1999), as well as examining the potential benefits of relying on protections from CDC-recommended antibiotics.

B. RESEARCH QUESTIONS

Based on the aforementioned background, one primary and three subordinate research questions materialized at the outset of the thesis research.

1. Primary Question

Does an analysis of anthrax vaccine as a complement to the SNS reveal historic controversial scientific, regulatory, legislative, judicial, and ethical issues and concerns?

2. Sub-Questions

Is procurement and stockpiling of the current anthrax vaccine wasteful if the product proves unviable as a course of action for prophylaxis of anthrax in an emergency scenario?

What countermeasure alternatives exist beyond the current anthrax vaccine, and what policy options exist in the absence of this current, yet old anthrax vaccine technology?

What mechanisms for oversight exist for the procurement of the current anthrax vaccine or require formulation in the pursuit of future alternative countermeasures?

C. RESEARCH ARGUMENT

1. Summary of Claims

In addressing the questions, the central research claim for the thesis argues that the existing anthrax vaccine deserves reevaluation as a component of the SNS in light of the controversial scientific, regulatory, legislative, judicial, and ethical issues discovered. The claim asserts that the procurement of anthrax vaccine is indeed wasteful, while alternatives with fewer liabilities already exist. The claim finds support through copious examples where the government fails to apply regulatory and legal standards, appears deficient in analyzing the vaccine's problems, seemingly ceases corrective processes in reaction to the anthrax letter attacks, delays the synthesis of alternative countermeasures, and apparently suffers bias when evaluating the anthrax vaccine landscape. If compelled by presentation of the argument, DHS officials should recommend that the DHHS expedite the development of a new vaccine and stockpile proven efficacious and recommended antibiotic treatments for the SNS in the interim. The argument, or claim, boils down to the demand for good government and the vision to anticipate how future generations will judge policymakers' past decisions. In the case of this thesis, we find

significant inconsistencies, misrepresentations, and omissions in the DoD experience with the anthrax vaccine. Expectantly, the DHS review will discover those same issues as they reevaluate the DoD program and model future SNS acquisition strategies.

The thesis relies principally on past claims and recommendations by top governmental leaders, executive agencies, and judicial bodies. Their supportive conclusions, and those of DoD scientists, essentially echo the same argument presented herein. The argument of the present thesis and claim turns out to be indistinguishable from that of the DoD position prior to the 1998 policy announcements to mandate anthrax vaccine (Cohen, 1998b). The evidence for the thesis and claims originates primarily from DoD documents and governmental scientific accounts, adding weight to the merits or warrants of the argument. As a result, the thesis argument's conclusion asks the government to resurvey its present policy by reflecting earnestly on its former position. The previous official DoD position, and the position advocated by the research argument in this thesis, advised officials to use the vaccine at a "minimum level" (Chu & Aldridge, 2001). Ultimately, the argument's claims and sub-claims merely intend to remind policymakers of those recommendations. By informing the government of these previous conclusions, we place the subsequent omissions, misrepresentations, and violations in perspective. The resulting conclusions may assist the current or next administration to demonstrate prudence when expending future taxpayer resources on safe, effective, and modern products that address the threat, versus presenting a façade by relying on those known to be inadequate and unsatisfactory.

2. Warrants

The thesis claim's warrants, or reasons, involve complex regulatory, scientific, legal, and legislative landscapes that document historic government awareness about the safety, efficacy, and legality of problems with the old, currently stockpiled, anthrax vaccine technology. Unhealthy centralized decision-making processes, and extralegal regulatory mistakes by executive departments, provide the background leading up to the pivotal 2001 anthrax letter attacks. The FBI's conclusions in 2008 that a DoD scientist's motive in those attacks rested on concern over the vaccine's "failing" status adds

important perspective as well regarding regulatory and scientific problems (FBI, 2008, p. 15). Concerning the regulatory and scientific processes, the FDA found that the DoD participated directly in a role "similar to a manufacturer" (FDA, 2002b, p. 8). Federal courts also ruled that the DoD anthrax vaccine program violated the law based on regulatory errors (*Doe v. Rumsfeld*, 2004, p. 40). Cumulatively, these warrants reinforce the merits for the argument that subsequent expenditures for the vaccine in the SNS require review.

3. Evidence

Evidence supporting the argument is derived primarily from historic and critical DoD, congressional, and scientific assessments about the vaccine. This evidence described the unsatisfactory and undefined nature of the product and problems related to efficacy. FBI evidence about scientific frustrations over vaccine potency problems in particular contributed to the motive for the anthrax letter attacks. Such evidence provides perspective to better understand the DoD's awareness of the need for a new vaccine as early as 1985. These facts also help explain why the CDC recommends antibiotics to protect against the most deadly inhaled form of the disease in lieu of anthrax vaccine. Evidence of DoD consensus on the problems exists in multiple documents, including internal recommendations to minimize use of the vaccine prior to the anthrax letter attacks, along with advice to procure antibiotics and develop coherent doctrinal processes to deal with such threats in the future. Finally, the limitations with the product's inoculation protocol, requiring five doses over 18 months, provides compelling evidence when realistically analyzing the vaccine's compatibility as a bioterrorism prophylaxis in the SNS for the general population under emergency exigencies. While cost effectiveness also weighs in favor of antibiotic prophylaxis, the best evidence for the argument includes corroborative government findings across five decades where the DoD effectively made the same arguments presented in this thesis.

Overall, the debate over the contents of the SNS involves many tentacles of evidence. The overarching argument to exclude the current anthrax vaccine from the stockpile relies on a series of claims based on this evidence. They include the fact that the

U.S. Army patented, altered, experimented with, mismanaged the licensing of, and perpetuated the use of a documented inadequate anthrax vaccine. After the anthrax letter attacks the subsequently confirmed illegal and experimental mandate on the troops evolved into reactionary stockpiling of the same product for the SNS to defend citizens against bioterrorism. The outwardly laudable goal of protecting soldiers and citizens with anthrax vaccine ultimately demands the multiple methodology analysis of this thesis in order to test the claim of wastefulness by procuring a recognized unsatisfactory immunization when recommended antibiotics protect civilians.

The thesis reviews the methodologies utilized to more fully disclose and analyze this evidence after addressing the anticipated challenges to the research techniques.

4. Anticipated Challenges

Anticipated challenges to the claim, reasons, and arguments lie in the fact that the issue remains highly controversial, particularly given the noted lapses and conflicts within the DoD, FDA, and executive branch collectively. The argument spotlights those breaches in an effort to protect the DHS from adopting, or potentially assisting in closing, the programmatic gaps. The thesis attempts to surmount institutional or bureaucratic barriers to digesting its findings and recommendations by addressing the problem through the inherent authorities of the DHS and DHHS under HSPDs 8, 10, 18, and 21. Those directives obligate the DHS and DHHS to manage the composition of the SNS and to assess the bioterrorism threat. Stopping or redirecting the inertia of significant past and ongoing appropriations poses a challenge. Therefore, the HSPDs provide a methodical means to reevaluate past policy process errors, reflect on previous expert recommendations, and review legal rulings regarding the vaccine.

The encouragement for review presents a main anticipated challenge as well. Notwithstanding the critical judicial and legislative branch reviews, the outgoing executive branch appeared to ignore the logical requirement to review past anthrax vaccine decisions following the letter attacks. Instead, the administration expended over $57 billion (Clark, 2009) on biodefense and over $1 billion on anthrax vaccine since the 2001 anthrax letter attacks (FBO, 2004; FBO, 2005; FBO, 2007; FBO, 2008). Therefore,

in the face of reactionary expenditures, and expanded use of anthrax vaccine outside DoD, the core argument for the thesis objectively hinges not only on past rulings and opinions, but also on the truth in the fine print of reports currently utilized to justify the program.

However, claims of omissions, misrepresentations, or misinterpretations do not provide sufficient reason to exclude anthrax vaccine from the Strategic National Stockpile. Instead, the exclusions of data and misconstrued analysis only provide important perspective and context when making the argument to the larger audience, in particular lawmakers and public servants charged with the responsibility to provide the best available protections for their soldiers against the threat of biowarfare and for their citizens against the threat of bioterrorism. Instead of portraying potential distortions as the central claim, the evidence standard required for a dispassionate and objective thesis argument alternatively attempts to highlight government assessments of the vaccine before the DoD altered the message.

Therefore, the methodical analysis must make the case dispassionately, primarily through analysis of past official government findings, as well as through the most recent FBI revelations. This method ensures process transparency and the prudent allocation of future resources toward research and development of modern vaccines and the stockpiling of CDC recommended antibiotics. Such a conclusion comports with the documentary record and prior governmental official positions revealed through the multimethod analysis. The thesis outlines the multiprism approach in the next section on methodologies.

D. METHODOLOGY

To address the research questions the following thesis project incorporates a "quadrangulation" technique that utilizes four research methodologies: literature review, case study, program evaluation, and gap analysis. The multiprism approach begins by evaluating peer-reviewed and published literature sources, which enumerate an evolving record on safety, efficacy, regulatory, and legal issues. A methodological triangulation continues by employing the three additional research methods: case study, program

evaluation, and gap analysis. The methodological "quadrangulation" of the thesis effectively "boxes in," and takes a snapshot of, the root facts to ensure that future policy decisions benefit from the historical patterns discovered.[5]

1. Literature Review

The first methodology tackled in the thesis revolves around the available literature on anthrax vaccine. The review of the writings on anthrax vaccine summarizes published sources and synthesizes a pattern, or shift, in the literature around the 1998 time frame. At that time, the DoD announced plans for mandatory immunization of the armed forces. Literature was generally negative about the vaccine prior to this point, but it shifts circa 1998 to an overall pro-vaccine stance. The highly politicized atmosphere surrounding the DoD mandatory inoculations helps explain the evolution of the literature during a time frame when the United States attempted to assure its citizens that it could protect the troops in the Middle East in the midst of weapons-of-mass-destruction (WMD) verification problems with the Iraq regime. Alternatively, changes to the vaccine's manufacturing process, potentially improving the vaccine, might also explain a shift in professional assessments. The preponderance of supportive literature on anthrax vaccine emanates primarily from government and military sources. Civilian reviews generally commented on the vaccine negatively both before and after the 1998 time frame. Interesting to note, much of the literature surrounding the vaccine appears to emanate from a small group of government-affiliated scientists. Those authors continue to chronicle the vaccine reviews to this day. Their reviews similarly shifted over time from generally negative during the pre-policy mandate time frame to generally positive in the post-policy pronouncement era.

2. Case Study

The case study methodology allows pertinent issue analysis regarding the fundamental research question. The primary question explores the timeline of decision-

[5] A certain degree of duplicative, yet unique, explanation of the factual background supporting the claims and arguments appears in each individual chapter or methodology. This technique allows any given methodological approach to stand on its own merit.

making processes leading to the inclusion of anthrax vaccine as a complement to the composition of the SNS. The case study traces specific relevant processes through an event and causal-factor analysis. Timeline tracing reveals multifaceted problems across lengthy time frames, as well as the complex causal processes involved. The timeline analysis and illustration directly support a subsequent event and causal-factor relationship illustration documenting root causes, contributing causes, direct causes, and problematic events. Using an event-cause metric, the case study breaks down the institutional actors involved and analyzes their participation in anthrax vaccine programmatic processes over time.

The case study identifies anthrax vaccine use by the government to be an outlier or deviant case, one generally atypical in the administration of military medicine or public health policy. Due to the unacceptability of such deviations, the case study serves as a timely and valuable means of analyzing the current expansion of the anthrax vaccine's use in the realm of civilian public-health policy. Throughout the case study, methodical process tracing serves as an instrumental tool in order to reveal recurring themes as the thesis formulates causal hypotheses about the problematic events. As well, Chapter VI, Recommendations, represents a continuation of the case study by offering future courses of action and corrective actions to address the potentially corrosive trends revealed throughout thesis process tracing.

Overall, the sequence of events, and the actors involved or absent, assists in drawing causal connections. By leveraging the case study of the DoD anthrax vaccine experience, the thesis objectively derives a causal theory about the effectiveness of past policy by the DoD in order to extrapolate success or failure against future potential policy challenges faced by the DHS and the DHHS as those departments incorporate the anthrax vaccine in the SNS.

3. Program Evaluation

Following the case study, a program evaluation methodology serves to summatively and quantitatively evaluate DoD experiences with the old anthrax vaccine. Quantitative performance metrics include documenting acceptance of the program by

military members, as well as chronicling adverse reaction rates incurred (United States Department of Veterans Affairs, Research Advisory Committee on Gulf War Veterans' Illnesses [DVA-RACGWVI], 2008, pp. 8, 125, 127). Government reports and studies primarily provide the data points. Additionally, the use of a formative and qualitative evaluation attempts to evaluate ongoing efforts to procure anthrax vaccine for the SNS and the administration of the Metropolitan Medical Response System (MMRS) (United States Department of Homeland Security [DHS], 2008a). The evolving nature of the policy regarding anthrax vaccine, particularly with a new president, DHHS Secretary, and FDA commissioner, dictates a formative evaluation as a natural means for current policymakers to anticipate and consider modification of governmental initiatives as future events warrant. The thesis research provides a balanced collection of lessons learned from the Pentagon experience with soldiers' ethical objections (Pica-Branco & Hudak, 2008, p. 2), as well as medical community recommendations (Centers for Disease Control, Advisory Committee on Immunization Practices [CDC-ACIP], 2008, p. 97).

The program evaluation documents several recent reports that suggest stockpile alternatives and omit reference to the current anthrax vaccine altogether (Graham & Talent, 2008, pp. xviii, 32, 33, 109). Program-effectiveness lessons captured from the DoD experience with anthrax vaccine provide instructive generalizations for assessing expanded use of the vaccine by other governmental departments, as well as recommendations for improving strategies to procure alternative proven countermeasures for U.S. citizens. As with the case-study research method, use of process tracing and process evaluation within the program-evaluation methodology allows the project to explore both retrospective (summative) and anticipatory (formative) generalizations and recommendations regarding the mechanisms involved. The evaluation incorporates the unique experiences surrounding implementation of the DoD anthrax vaccine program, with the relevant frameworks of analysis involving executive department regulatory activities, legislative oversight and judicial review.

Implementation evaluation permeates the thesis, providing an opportunity for process tracing to compare the "theory of action," or plan for success, behind military and civilian anthrax vaccine programs, versus the realities encountered when faced with legal,

regulatory, and legislative oversight. Ultimately, conclusions derived from an evaluation of the DoD program translate directly to potential problems with implementing a similar program for the American public writ large. The public is in effect the target audience for the policymakers, who in turn are the target audience of this thesis.

4. Gap Analysis

The last research methodology, gap analysis, serves as a direct lead-in to the research conclusions and recommendations of the thesis. By defining the present state, and the inherited program problems, we have the ability to clearly outline the future desired target state, as well as to identify gaps and their causes.

The gap analysis aspect of the research methodology remains the most important element for reflection leading into the corrective process to ensure that we understand the conditions and potential systemic problems that created the current state. The analysis identifies past opportunities to close the gap, as well as explanations for the failures and success to do so.

The gap analysis concludes by evaluating essential trust issues required for repair of the current program and formulation of future programs. The concluding recommendations are intended to guide future policy in a direction free from adoption of problematic policy precedents, while ensuring that American citizens remain protected by proven countermeasures.

II. LITERATURE REVIEW

A literary review for the anthrax vaccine revealed a distinct disparity between pre-1998 writings versus those sponsored primarily by the DoD thereafter. The DHS decision-making process regarding the anthrax-vaccine component of the SNS should take note of the pivotal period when the shift or delta in the literary record began—with DoD Secretary William Cohen's announcement of the mandatory anthrax vaccine immunization program in 1998 (Cohen, 1998b). In addition to the pre- versus post-1998 writings, literary subcategories worthy of analysis include scientific literature, government reports, judicial rulings, and literature exploring the SNS.

A. PRE-1998

1. Scientific Evaluations

Early scientific literature negatively reviewed the safety and efficacy of the current anthrax vaccine used by the U.S. government. Literature chronicling the vaccine first surfaced following an anthrax epidemic in Manchester, New Hampshire, in 1957, which resulted in four deaths due to inhalation anthrax infection (Belluck, 2001). Coincidently, the U.S. Army conducted an anthrax vaccine field trial (experiment) at the Manchester wool-sorting mill collocated with the epidemic (Schumm, Nazarinia, & Bosch, 2009, p. 597). Dr. Phillip Brachman published a study in 1962 discussing the field trial. He specifically noted the vaccine's effectiveness against cutaneous (skin) infection. He wrote, however, that "when inhalation anthrax is considered, the limited experience with this form of the disease makes the data less significant in showing effectiveness of the vaccine" (Brachman et al., 1962, p. 642). *American Journal of Pathology* articles also evaluated the inhalation (pulmonary or lung) illnesses from the 1957 DoD field trial, reporting approximately a 50% survival rate without vaccination (Albrink & Goodlow, 1959; Albrink & Goodlow, 1960).

The American Journal of Medicine also chronicled the 1957 anthrax epidemic through author Dr. Stanley Plotkin, Dr. Brachman's co-investigator during the field trial. Like Brachman, Dr. Plotkin remained rooted in the anthrax-vaccine literary history for

many years to come (Plotkin, S., Brachman, P., Utell, M., Bumford, F., and Atchison, M., 1960). A *Bacteriological Review* article by Brachman corroborated the reasonable survival rate against inhaled infection without treatment when detailing an investigation supported by a U.S. Army Biological Center, Fort Detrick contract (Brachman, Kaufmann, & Dalldorf, 1966). Years later, DoD scientist Dr. Bruce Ivins, the alleged perpetrator of the anthrax letter attacks (FBI, 2008), confirmed for a memo written by U.S. Army Col. Arthur Friedlander, a researcher at the U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID), that "no data on MDPH-PA [anthrax vaccine] efficacy in humans" existed with respect to inhalation anthrax (Ivins, 1992, p. 2). MDPH referred to the Michigan Department of Public Health, a quasi-state entity managing anthrax vaccine as a surrogate for the DoD. Dr. Ivins published similar conclusions in a *Clinical Immunology Newsletter* (Ivins, 1988, p. 30–32). In another journal, Dr. Ivins described the current anthrax vaccine's "drawbacks, including the need for frequent boosters, the apparent inability to protect adequately against certain strains of *B. anthracis*, and occasional local reactogenicity" (Ivins et al., 1988, pp. 12–19). Still other Army scientists described the product as an "experimental," "limited use vaccine" (Takafuji & Russell, 1990, p.156).

Expanding on the work of Dr. Brachman, Ivins, and others, articles in *Medical Microbiology and Immunology* and *Vaccines* discussed the "vaccine resistant" Ames strain (used in the 2001 bioterrorism crimes). The articles advanced the call for a "second generation anthrax vaccine," one "containing only essential ingredients and producing effective levels of protection with a single or, at worst, two doses" and one which "produces no side reactions" (e.g., Turnbull, 1991; Turnbull, Leppla, Broster, Quinn & Melling, 1988, p. 535). Several of the same scientists, such as Dr. Brachman and Dr. Friedlander, with Dr. Plotkin as the editor, authored additional chapters in *Vaccines* over the next decade, continuing to describe the "unsatisfactory" nature of the current product due to its unknown purity, undefined nature, undesirable constituents, and problematic efficacy issues (Brachman & Friedlander, 1994; Brachman & Friedlander, 1998, pp. 629–636).

Early literature up to the 1998 time frame exhibits a straightforward awareness of the anthrax vaccine's problems in the safety, efficacy, legality, and regulatory realms. Post-1998 scientific literature does not appear to exhibit the same unembellished critique. Another important aspect of the early literature and studies includes the evidence of high survival rates without treatment, as opposed to the post-1998 message, which appears to exaggerate a "lethal threat" (Cragin, 1999) without anthrax vaccine as a form of protection.

2. Government Reports

In addition to scientific literature in the 1980s and 1990s, government reports also acknowledged the problems with the current anthrax vaccine. In 1985, the DoD attempted to solicit a new vaccine. The DoD request stated, "There is an operational requirement to develop a safe and effective product which will protect US troops against exposure from virulent strains of *Bacillus anthracis*." The proposal added, "There is no vaccine in current use which will safely and effectively protect military personnel against exposure to this hazardous bacterial agent." The request clarified that the current vaccine is, "highly reactogenic, requires multiple boosters to maintain immunity and may not be protective against all strains of the anthrax *bacillus*" (see Appendix 2) (DoD, 1985, p. 4). The RFP coincided in 1985 with publication of an FDA proposed rule to finalize the anthrax vaccine's license, which cited similar efficacy inadequacies. The proposed rule noted the "efficacy against inhalation anthrax is not well documented," and that "no meaningful assessment of its value against inhalation anthrax is possible due to its low incidence" (FDA, 1985, p. 51058). Shortly thereafter, just before the first Persian Gulf War, then-Senator William Cohen held membership on the Government Affairs Committee. In 1989, the U.S. Army briefed that committee on the limitations of the current anthrax vaccine to protect against the aerosolized anthrax, or the inhaled route of exposure expected on a battlefield:

> Current vaccines, particularly the anthrax vaccine, do not readily lend themselves to use in mass troop immunization for a variety of reasons: the requirement in many cases for multiple immunizations to accomplish protective immunity, a higher than desirable rate of reactogenicity, and, in

some cases, lack of strong enough efficacy against infection by the aerosol route of exposure (United States Senate, 1989).

In 1994, a Senate committee report analyzing anthrax vaccine employment during Desert Storm came to the same conclusion. The report found, "the vaccine's effectiveness against inhaled anthrax is unknown," and therefore should be "considered investigational when used as a protection against biological warfare." The committee added a concern about "safety, particularly when given to thousands of soldiers in conjunction with other vaccines," finding the data "not well established." The Senate concluded, "Anthrax vaccine should continue to be considered as a potential cause for undiagnosed illnesses in Persian Gulf military personnel" (United States Senate, 1994, p. 35). The DoD Joint Project Office for Biological Defense (JPOBD) also recognized anthrax vaccine as "not licensed for a biological defense indication," based on the fact that efficacy remained unproven (see Appendix 3) (United States Department of Defense, Joint Project Office for Biological Defense [DoD-JPOBD], 1997, p. 5.5). As a result, the DoD applied to the FDA for a use, or labeling "indication," for "inhalation anthrax" in 1996 (see Appendix 4) (Myers, 1996). The DoD and the manufacturer collaborated by updating the FDA application in 1998 for this same indication (see Appendix 5) (DoD, 1999b, p. 1).

Based on the written evidence prior to 1998, the anthrax vaccine received generally unfavorable governmental, military, and scientific reviews, with recommendations for limited use based on lack of known efficacy and safety. The assessments existed prior to the politically charged mandatory use of the anthrax vaccine (Cohen, 1998a; Cohen, 1998b; DoD, 1997a). The shift in policy to mandate the vaccine during the 1998 time frame coincided with a subsequent change in the scientific and governmental reviews of the vaccine, primarily those emanating from DoD.

B. POST-1998

1. Scientific Evaluations

With the announcement of the DoD anthrax vaccine program in 1998, the conclusions in the literature appeared to change. Beginning with a *JAMA* article in 1999, most subsequent DoD-authored literature generally supported the vaccine as "safe,"

"effective," and "FDA licensed" to treat anthrax infection against diverse strains, regardless of the route of exposure: cutaneous, gastrointestinal, or inhaled (Friedlander, Pittman, & Parker, 1999, pp. 2104–2106). The authors included three U.S. Army scientists, Col. Arthur M. Friedlander, Col. Phillip R. Pittman, and Col. Gerald W. Parker. An additional *JAMA* article by Dr. Thomas V. Inglesby, with familiar co-authors such as Friedlander, Parker, and Russell, provided an endorsement of the vaccine, finding it "likely that the vaccine would be safe and effective" (Inglesby, Henderson, & Bartlett, 1999, p. 1742). Inglesby reiterated the safe and effective status of anthrax vaccine in a 2002 *JAMA* article (Inglesby, O'Toole, Henderson, & Bartlett, 2002, pp. 2244, 2248).

Another example of the scientific and medical reversal of opinion, published in the *Air Power Journal* by a Deputy Assistant in the DoD for Chemical and Biological Defense, provides a "tutorial on anthrax, the predominant bioweapon threat," and a "clear rationale for our needing a viable vaccination defense" (Davis & Johnson-Winegar, 2000, p. 15). A DoD pharmacist joined the intellectual discussion in the same time frame, writing several pro-anthrax-vaccine articles. He assured the reader that the vaccine could be "prescribed with the confidence commensurate with dozens of human safety studies and experience in 1.8 million recent vaccinees" (Grabenstein, 2008, p. 134). Dr. Stanley Plotkin, the co-researcher involved with Dr. Brachman in the 1957 DoD anthrax trial and epidemic study, "invited" the article as the section editor for the *Clinical Infectious Diseases Journal*. The "million recent vaccinees" referred to by Grabenstein were soldiers, mandated to take the vaccine partially due to the Institute of Medicine (IOM) report, which was funded by the DoD (Institute of Medicine [IOM], 2002, p. II). The report cleared the way for FDA approval of the Biologic License Application (BLA) for anthrax vaccine (FDA, 2002a). The report and approval also enabled the DoD to restart the mandatory anthrax vaccine program upon resolution of FDA-discovered quality-control deficiencies and the earlier "notice of intent to revoke" the manufacturer license (see Appendix 6) (FDA, 1997). Notably, the IOM report found the vaccine "sufficiently safe and effective for use," though "far from optimal," and advised that a "new vaccine, developed according to more modern principles of vaccinology, is urgently needed"

(IOM, 2002, p. 208). A 2000 IOM report also determined, "there is a paucity of published peer-reviewed literature on the safety of the anthrax vaccine" (IOM, 2000, p. 6).

The familiar core group of government scientists, and those involved with the original clinical trial, Dr. Brachman, Colonel Friedlander, Colonel Grabenstein, with Dr. Plotkin again serving as the editor, published a recent update on the anthrax vaccine for a chapter in *Vaccines*. This time, citing the FDA's conclusion and the IOM report to demonstrate efficacy for inhalation anthrax, the scientists acknowledged the fact that "there have been no controlled clinical trials in humans of the efficacy of the currently licensed U.S. vaccine." They provided the caveat that "the differences between the U.S. licensed vaccine and the PA-based vaccine used in the Brachman et al. study are minor from a regulatory perspective"[6] (Brachman et al., 2008, p. 119). Both the IOM and the FDA partially cite the Brachman study as evidence for the efficacy of the vaccine for inhaled anthrax, whereas the scientists in turn cite those entities to affirm efficacy.

Scientists outside the DoD predominantly came to contrary conclusions. Those academics challenged the IOM report, asserting that the "Institute of Medicine ignored evidence of several recent research studies from three different nations that have implicated vaccines, often including anthrax vaccine, in the epidemiology of Gulf War illnesses" (Schumm, Webb, Jurich & Bollman, 2002). Others published reports of gastrointestinal adverse reactions. One article found that overall "reactions reported following anthrax vaccine was higher for every reaction analyzed in comparison to the adult vaccine control groups" (Geier & Geier, 2004, p. 762). In September of 2006, the Geier team also delivered a presentation sponsored by VaxGen Corp., a company later purchased by Emergent BioSolutions, the maker of BioThrax®. The Geier team determined that the "anthrax vaccine is causing massive damage" and revealed research showing that the vaccine "is associated with a series of serious adverse events that can significantly impact multiple organ systems within the body, and result in permanent disability" (Geier & Geier, 2006, slide 33). The same group found significant "joint related adverse reactions" (Geier & Geier, 2002, p. 217).

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[6] "PA" refers to protective antigen, one of the proteins in *Bacillus anthracis* (FDA, 2002a, p.2).

The *Journal of Emergency Medicine* listed "lymphocytic vasculitis associated with the anthrax vaccine," or immune-related vascular inflammation (Muniz, 2003, p. 271). Another physician detailed in the *American Journal of Epidemiology* a "small observed association" of "birth defects among infants born to women who received anthrax vaccine in pregnancy" (Ryan, Smith, Sevick, Honner, Loach, Moore, 2008, p. 434). A doctor from Kansas State University, Dr. Walter Schumm, published research results in *Psychological Reports*, indicating "adverse long-term health outcomes as a result of anthrax vaccination" (Schumm, Reppert, Jurich, Bollman, Webb, Castelo, 2002, p. 649). Dr. Schumm also defended an editorial in the *British Medical Journal,* charging, "at least three major studies in England, Canada, and the United States had found problems with the anthrax or other vaccines among military veterans" (Schumm, 2004, p. 978). Dr. Schumm, and a civilian practitioner, Dr. Meryl Nass, also discovered correlations between reactions to anthrax vaccine and optic neuritis (Nass, 2006; Schumm, 2007).

Additionally, work by Dr. Schumm published in *Medical Veritas* exposed additional findings that warrant further research. Dr. Schumm's research included mathematical models correlating the 1957 anthrax vaccine clinical field trial to a biological warfare anthrax attack on civilians (Schumm & Webb, 2005, p. 331). He discovered changes in the health of veterans from the first Persian Gulf War (Schumm, Jurich, Web, Bollman, Reppert & Castelo, 2007, p. 1414), and posed questions about the statistical legitimacy of using Dr. Brachman's study to establish the efficacy of the anthrax vaccine (Schumm, 2005a, p. 342). He also questioned human rights violations related to the 1957 human anthrax vaccine trials (Schumm, 2005b, p. 343), as well as the long-term safety of anthrax vaccine (Schumm, Jurich, Bollman, Webb & Castelo, 2005, p. 348). Dr. Schumm challenged what he viewed as the biased nature of the regulatory process in an article titled "FDA's acceptance of Brachman's 1950s anthrax research: Good politics? Maybe. Good science? No" (Schumm & Nass, 2006, p. 747–752). Beyond Dr. Schumm and Dr. Nass's extensive work, additional critical reviews discovered "hypersensitivity pneumonitis following anthrax vaccination," warning physicians to be attentive to "vaccine related complications" (Timmer, Amundson, & Malone, 2002,

p. 744). Other publications confirmed that the U.S. Army investigated anthrax vaccine as a possible cause of hypersensitivity pneumonitis after anthrax vaccination (Oransky, 2003, p. 543).

In summary, while some literature began to minimize problems with the anthrax vaccine post-1998, the conclusions in DoD-sponsored literature generally stand in stark contrast to both pre-1998 scientific documentation and non-DoD post-1998 reviews of the vaccine. Coincidentally, the "stark divergence of the medical community's assessment of the safety and efficacy of AVA [anthrax vaccine] occurred at exactly the same time as the AVIP was announced" (Dingle, 2001). A reasonable conclusion materializes, based on the coincidental timing of the literature shift, that some medical literature experienced biases due to the mandatory anthrax vaccine program.

2. Government Reports

Based perhaps on the inconsistencies documented in the abovementioned scientific literature, the United States House of Representatives held a series of hearings from 1999 to 2000 after the DoD launched mandatory inoculations.[7] Ultimately, the House of Representatives published a report with findings that deemed the anthrax vaccine program investigational and in violation of FDA regulations. The final report form the House Government Reform Committee, titled "Unproven Force Protection," recommended that use of the "current anthrax vaccine for force protection against biological warfare should be considered experimental and undertaken only pursuant to FDA regulations governing investigational testing for a new indication" (HR 106-556, 2000, pp. 4, 52). The Senate held limited hearings. The legislative body withheld a formative, critical position regarding the anthrax vaccine, as occurred with the earlier

[7] Multiple hearing reports published by the Government Printing Office (GPO) for the U.S. Congress are available. See, e.g., United States House of Representatives [HR], Committee on Government Reform (HR 106-130) 1999e; HR, Committee on Veterans' Affairs, Subcommittee on Health and Subcommittee on Oversight and Investigations (HR 106-28) 1999; HR 106-102 1999; HR, Committee on Government Reform, Subcommittee on National Security, Veterans Affairs, and International Relations (HR 106-131) 1999d; HR, Committee on Government Reform, Subcommittee on National Security, Veterans Affairs, and International Relations (HR 106-17) 1999a; HR, Committee on Government Reform (HR 106-249) 2000; HR, Committee on Government Reform, Subcommittee on National Security, Veterans Affairs, and International Relations (HR 106-26) 1999b; HR, Committee on Government Reform, Subcommittee on National Security, Veterans Affairs, and International Relations (HR 106-36) 1999c; HR, Committee on Armed Services (HR 106-62) 2000).

Senate Veteran's Committee Report (United States Senate, 1994; United States Senate, Armed Services Committee, 2000). That earlier report occurred after the first Persian Gulf War, but before the mandatory DoD anthrax vaccine immunization program.

Government Accountability Office (GAO) reports, often previewed in the congressional hearings, marked the most voluminous governmental research post-1998. The GAO persistently provided critical reviews of the vaccine program. Alternatively, the Congressional Research Service (CRS) remained effectively mute on the issue. GAO confirmed the "long-term safety of the vaccine has not yet been studied"; that "ingredients used to make vaccine were changed from the original vaccine," and that "prior to the time of licensing, no human efficacy testing of the MDPH vaccine was performed" (United States Government Accountability Office, National Security and International Affairs Division [GAO-NSIAD], 1999a, p.2–3). Twenty additional GAO reports worthy of further analysis found similarly critical conclusions concerning safety and efficacy.[8]

An early GAO report of testimony to the Senate Committee on Veterans' Affairs documented the vaccine as "licensed by the Food and Drug Administration," and reported that it "has been routinely administered to populations at risk for several years" (GAO-NSIAD, 1998, p. 3). Later revelations ultimately debunked both assertions. For example, the lack of a final FDA license resulted in court injunctions and orders to finalize the vaccine license (*Doe v. Rumsfeld*, 2003; *Doe v. Rumsfeld*, 2004; *Doe v. Rumsfeld*, 2007). Moreover, the U.S. Army admitted that "we did not intend to mislead or confuse people" when apologizing for overstating use as "widespread" (Funk, 1999). Subsequent GAO reports were consistently critical, to include an important discovery documented in a report involving the alteration of the vaccine with unapproved manufacturing changes (GAO, 2001b, p. 3–4). The FDA indifferently characterized the DoD role in this phenomenon when describing "DoD's continuous involvement with, and

[8] Multiple reports critical of the anthrax program were published by the GPO for the GAO. See GAO-NSIAD, 1999d; GAO-NSIAD, 1999g; GAO-NSIAD, 2000a; GAO-NSIAD, 2000b; GAO -NSIAD, 1999e; GAO-NSIAD, 1999f; GAO-NSIAD, 1999a; GAO-NSIAD, 1999b; GAO-NSIAD, 1999c; GAO, 2001a; GAO, 2000b; GAO, 2000a; GAO, 2001c; GAO, 2002a; GAO, 2002b; GAO, 2006; GAO, 2007a; GAO, 2007b; GAO, 2008; GAO, 2007c; GAO, 2007d).

intimate knowledge of, the formulation and manufacturing processes of all of these versions of the anthrax vaccine" (FDA, 2002b, p. 8). The FDA ultimately cited the DoD's involvement to justify the finalized license rule for anthrax vaccine in 2005. The anthrax vaccine finally received an FDA licensing 20 years after the 1985 proposed rule (FDA, 2005b, p. 75180-98), fifty years after the vaccine's advent, but only after the courts had ruled the mandatory DoD program illegal and "investigational" absent a license (*Doe v. Rumsfeld*, 2004, p. 40). In effect, the government requested and responded to public comments about the proposed license and then completed the paperwork by adding the controversial indication for inhalation anthrax. Despite the apparent FDA acquiescence to the DoD's central role, a consistently less-than-laudatory theme permeates the majority of the GAO reports following the 1998 potential policy-driven shift in the literature.

Rounding out post-1998 governmental review, the CDC effectively recommended antibiotics, such as penicillin, ciprofloxacin, and doxycycline, as the treatment for anthrax infection instead of the vaccine (CDC, 2001; CDC, 2002; CDC, 2000). According to the CDC, anthrax vaccine remains "not recommended for routine pre-event anthrax vaccination," notwithstanding a DHS and DHHS declaration of an "anthrax emergency" through the year 2015 (Centers for Infectious Disease Research and Police [CIDRAP], 2008). In contrast, DHS confirmation that, "there is not currently a domestic emergency involving anthrax," that "there is not currently a heightened risk of an anthrax attack," and that there is "no credible information indicating an imminent threat of an attack involving *Bacillus anthracis*." Regardless, the DHHS indeed declared an "anthrax emergency" extending "through December 31, 2015" (Chertoff, 2008; United States Department of Health and Human Services [DHHS], 2008b). Recently, proposed guidance reveals DHS recommendations for protective measures "during the first week following a wide-area anthrax attack." The DHS proposal recommends "personal protective equipment and decontamination and hygiene procedures," while clarifying that post-exposure use of the old anthrax vaccine requires the vetting of emergency use authorizations or investigational new drug approvals (DHS, 2009d, p. 55246).

Table 1 summarizes highlights of the transformation in the scientific and government assessments of the anthrax vaccine detailed thus far in the literature review.

Ultimately, the pre- and post-1998 conclusion chasm captured in the preceding literature review requires consideration, along with the fact that later favorable literature originates from, or was sponsored by, the DoD.

Critical Reviews Pre-Policy Morph to 'Safe and Effective' Rhetoric Post-Policy	
Pre-policy	**Post-policy**
"There is no vaccine in current use which will safely and effectively protect military personnel" (see Appendix 2) (DoD, 1985, p. 4)	From DoD informational Web site: "The anthrax vaccine is safe and effective" (DoD, 2009b)
"Efficacy against inhalation anthrax is not well documented," & "no meaningful assessment of its value against inhalation anthrax is possible due to its low incidence" (FDA, 1985, p. 51058)	"AVA [anthrax vaccine] is effective against B. anthracis strains that are dependent upon the anthrax toxin as a mechanism of virulence, regardless of the route of exposure" (FDA, 2005b, p. 75183)
"When inhalation anthrax is considered, the limited experience with this form of the disease makes the data less significant in showing effectiveness of the vaccine" (Brachman et al., 1962, p. 642)	"The US Food & Drug Administration independently affirmed that anthrax vaccine adsorbed prevents anthrax regardless of route of exposure" (Brachman et al., 2008, p. 119)
"No data on MDPH-PA [anthrax vaccine] efficacy in humans" existed (Ivins, 1992, p. 2)	"Likely that the vaccine would be safe and effective" (Inglesby et al., 1999, p. 1742)
FDA issued a "Notice of intent to revoke" the manufacturer license (FDA, 1997)	"Safe," "effective" and "FDA licensed" (Friedlander et al., 1999, pp. 2104–06)
Early IOM letter report: "There is a paucity of published peer-reviewed literature on the safety of the anthrax vaccine" (IOM, 2000, p. 6)	"Sufficiently safe and effective for use," though "far from optimal," and advised that a "new vaccine, developed according to more modern principles of vaccinology, is urgently needed" (IOM, 2002, p. 208)
DoD applied for a licensing approval for use against "inhalation anthrax" (see Appendix 5) (DoD, 1999b, p.1)	"The vaccine is safe, effective, FDA-licensed and essential" (Cragin, 1999)
DoD scientists described the vaccine as an "experimental," "limited use vaccine" (Takafuji & Russell, 1990, p.156)	"Vaccine currently being administered to the US armed forces has been used safely for 30 years and has passed extensive testing by the FDA" (Davis & Johnson-Winegar, 2000)
"Current vaccines, particularly the anthrax vaccine, do not readily lend themselves to use in mass troop immunization for a	"The US vaccine is licensed to prevent anthrax, regardless of the route of exposure. Its dosing schedule is

variety of reasons: the requirement in many cases for multiple immunizations to accomplish protective immunity, a higher than desirable rate of reactogenicity, and, in some cases, lack of strong enough efficacy against infection by the aerosol route of exposure" (United States Senate, 1989)	cumbersome and somewhat painful (shortcomings that may be resolved by ongoing clinical studies). It can be prescribed with the confidence commensurate with dozens of human safety studies and experience in 1.8 million recent vaccinees (Grabenstein, 2008, p. 134)
Anthrax vaccine "drawbacks, including the need for frequent boosters, the apparent inability to protect adequately against certain strains of B. anthracis, and occasional local reactogenicity" (Ivins, 1988)	"The current anthrax vaccine is a licensed vaccine and has been demonstrated to be clinically safe and effective for preventing inhalation anthrax after exposure to anthrax spores" (Hersack, 2002, p. 123)
Brachman, et al: "unsatisfactory" nature of the current product due to its unknown purity, undefined nature, undesirable constituents and efficacy issues (Brachman & Friedlander, 1994; Brachman & Friedlander, 1998, pp. 629–36)	Brachman, et al: "AVA as licensed is an effective vaccine for the protection of humans against anthrax, including inhalation anthrax, caused by all known or plausible engineered strains of B. anthracis" (Brachman et al., 2008, p. 119)
Army Surgeon General Ronald Blanck Senate briefing: "Therefore, its safety, particularly when given to thousands of soldiers in conjunction with other vaccines, is not well established. Anthrax vaccine should continue to be considered as a potential cause for undiagnosed illnesses in Persian Gulf military personnel because many of the support troops received anthrax vaccine, and because the DoD believes that the incidence of undiagnosed illnesses in support troops may be higher than that in combat troops" (United States Senate, 1994, p. 35, fn. 143)	Army Surgeon General Ronald Blanck Opinion Editorial: *Army Times*: "Ignore the Paranoiacs; the Vaccine is Safe" (Blanck, 1999) Congressional Testimony: "The threat is real," (HR, Committee on Government Reform, Subcommittee on National Security, Veterans Affairs, and International Relations, 1999, p. 14); "If they are not vaccinated, they will inevitably die" (HR, Committee on Armed Services, 1999, p. 27)

Table 1. Dichotomies in the Literary Record

Within the review of the literature, an interesting note also discovered lies in the fact that the DoD informational Web site (DoD, 2009b) serves for news, policy, and as an archive of medical publications. Largely, the archive includes only literature supportive

of the institutional position, versus the less-than-favorable literature covered within this review. An additional note worth mentioning is the fact that the DoD placed the 1985 Proposed Rule on their Web sites in a transcribed form, versus the original, stating "All the sections that discuss anthrax vaccine are reprinted in their entirety." The DoD actually appeared to transcribe all sections except for the key "Proposed" aspect of the ruling (FDA, 1985, p. 1). This fact was not lost on the judicial review process by the federal courts where the never-finalized Proposed Rule led directly to preliminary (*Doe v. Rumsfeld*, 2003) and permanent injunctions (*Doe v. Rumsfeld*, 2004) that found the DoD mandate of the vaccine in violation of the law. The recasting of the scientific and medical evidence, and the significant legal implications of the omissions, make the historical literature review even more important.

Overall, the DoD's and the FDA's documented pattern of reinterpreting the spirit and specifics of the medical and scientific appraisals for the anthrax vaccine in the post-1998 era potentially represents an outlier case compared to the standards imposed on other pharmaceuticals. Oversight functions of Congress, the GAO, and the courts, as illustrated by the next section, partially provided a check and balance for the literature. Additionally, the CDC effectively maintained resolute recommendations centering on post-exposure use of antibiotics over the vaccine (CDC, 2000; CDC 2001; CDC, 2002; CDC, 2008; CDC-ACIP, 2008).

C. JUDICIAL REVIEW

Judicial review may ultimately serve as a means of adjudicating some finality in the literature by providing final decisions about continued reliance on BioThrax® for the SNS. The judicial record rendered the anthrax vaccine "investigational" and the program "illegal" due to a lack of licensing and an absence of approval for use against inhalation anthrax (*Doe v. Rumsfeld*, 2004, pp. 40–41). Court rulings resulted in a preliminary injunction in December 2003 (*Doe v. Rumsfeld*, 2003), followed by a permanent injunction on summary judgment in October 2004 (*Doe v. Rumsfeld*, 2004). Though the rulings were not overturned, the military criminal courts system put forth an alternative ruling from the Court of Appeals of the Armed Forces (*United States v. Kisala*, 2006). A

critique of judicial review process became part of one of the rulings where a court found the depth of other rulings lacking. The court wrote:

> Taken as a whole, Judge Sullivan's decisions in *Doe v. Rumsfeld* conclude that, prior to the FDA's December 2005 rulemaking, it was a violation of federal law for military personnel to be subjected to involuntary AVA inoculation because the vaccine was neither the subject of a presidential waiver nor licensed for use against inhalation anthrax. … Other courts have affirmed the legality of pre-2005 orders subjecting military personnel to involuntary anthrax vaccination, although they did so without giving detailed consideration to the implications of the FDA's licensing requirements (*Rempfer v. U.S. Dep't of Air Force Bd.*, 2008, pp. 18-19).

Ultimately, additional federal court decisions affirmed the earlier rulings requiring proper licensure, but did not question the new licensure for the vaccine. Those subsequent judicial opinions deferred to the FDA's scientific expertise on the issues (*Doe v. Von Eschenbach*, 2008).[9] As part of the legal analysis of the literature, academic papers explored the anthrax vaccine program and the pivotal informed-consent rights that soldiers and citizens enjoy when it comes to vaccines (Miller, R., 2002). Other academic efforts highlighted the complex legal issues involved with ongoing litigation, while also concluding that the essential element of trust was missing with the anthrax program and required restoration (Lynch, 2003, p. 78–80). The judicial literature review remains incomplete due to the ongoing nature of the controversy, but court rulings to date document the impervious past illegality of the mandatory anthrax vaccine program up until the 2005 licensure of the vaccine. Judicial reviews reveal that when the federal courts looked deeply into the issue they discovered illegal conduct upon "detailed consideration" (*Rempfer v. U.S. Dep't of Air Force Bd.*, 2008, pp. 18–19).

D. STRATEGIC NATIONAL STOCKPILE

Limited SNS policy literature exists. The CDC informed the U.S. public in a report on terrorism preparedness and emergency response (TPER) about the inclusion of "vaccines and antibiotics to prevent and treat anthrax" (CDC, 2009, pp. 20, 33). A report from the GAO also provided recommendations to preclude waste of BioThrax® through

[9] Note: Court deference to FDA also affirmed as recently as 2009 (*Rempfer v. Sharfstein*, 2009).

a joint DoD-DHHS "single integrated inventory system" (GAO, 2007c, p. 26). Today, DoD utilizes stockpiled anthrax vaccine under a collaborative agreement with the DHHS (CDC, n.d.). The DHHS plans to distribute the anthrax vaccine in the event of an anticipated or actual anthrax emergency occurrence from CDC's SNS via the Federal Emergency Management Agency's (FEMA) Metropolitan Medical Response System (MMRS). Receiving, staging, storage (RSS) and points of dispensing (PODs) nodes allow delivery of prepackaged antibiotics and anthrax vaccine if required. The MMRS program evolved after the 1996 Tokyo mass-transit attacks with sarin gas by Aum Shinrikyo. During the same time frame, the bombing of the Alfred P. Murrah Building in Oklahoma City intensified preparatory efforts (DHS, 2008a).

DHS shares responsibility for the SNS, and Presidential Directives task the DHS with annual product content review (POTUS, 2007b). As mentioned, along with the GAO reports, a CRS report reviewed policy and procurement issues related to the SNS, including a cursory review of legal, safety, and sole-source procurement problems with the current anthrax vaccine versus a next-generation vaccine (Congressional Research Service, 2007, p. 13). Examination of BioShield Act legislation (Public Law 108–276, 2004), a law to provide "medical countermeasures protecting Americans against a chemical, biological, radiological, or nuclear (CBRN) attack," makes no mention of anthrax vaccine (POTUS, 2004). Additionally, a thorough review of other presidential sources reveals early 2002 references to anthrax vaccine in the National Strategy for Homeland Security (NSHS) and the State of the Union Address (POTUS, 2002a; DHS, 2002, pp. 1, 44). Yet by the 2007 NSHS (DHS, 2007), in a 2008 "Biodefense for the 21st Century" speech, the president omitted mention of the current anthrax vaccine, instead replacing BioThrax® with procurement announcements for "75 million doses of a second generation anthrax vaccine" (POTUS, 2008b).

Although the governmental literature appears to deemphasize the anthrax vaccine, and even omit mention of it as time goes on, the DHHS continues to procure the vaccine for the SNS. The de-emphasis may be due to the fact that the FBI deemed a U.S. Army scientist's motive for the letter attack crimes related to the anthrax vaccine's "failing" status in 2001 (FBI, 2008, pp. 12–15). But, considering the government procured over $1

billion worth of BioThrax® since the anthrax letter attacks of 2001 (FBO, 2004; FBO, 2005; FBO, 2007; FBO, 2008),[10] the disappearing act of anthrax vaccine from official National Strategies remains significant when contrasted against continued appropriations for the countermeasure. Additionally, the fading away of the earlier pronouncements of the anthrax threat contrast with the current, more evenhanded, assessments (GAO-NSIAD, 2000a, p. 1). Indeed, the GAO confirmed as early as 1999 that "the nature and magnitude of the military threat of biological warfare (BW) has not changed since 1990, both in terms of the number of countries suspected of developing BW capability, the types of BW agents they possess, and their ability to weaponize and deliver those BW agents" (GAO-NSIAD, 1999a, p. 2).

Overall, the inconsistencies between the threat pronouncements and the expenditures dictate scrutiny regarding continued procurement. Future policy regarding the SNS, based on the DHS's statutory oversight, requires an intellectually forthright review of past inconsistencies within the literature in order to ensure credible and transparent government practices in the budget-constrained years ahead. The DHS's task to provide the best countermeasures based on reliable threat assessments requires a candid process, one free of literary dichotomies and gaps.

E. SUMMARY OF THE LITERATURE REVIEW

In conclusion, the literature demonstrates that the courts, Congress, and the GAO in particular remain steadfast in maintaining the continuity of the literature, while literature emanating from the DoD or other government entities changed its position on the vaccine, apparently to coincide with changes in policy. As a result, the more "spotty" literature emanates from the DoD following the 1998 policy pronouncements for the mandatory anthrax-vaccine program. Ultimately, the DoD funded (IOM, 2002, p. II) efforts by the IOM to endorse the vaccine's safety and efficacy, in contrast to years of alternative critical assessments. The IOM's qualification that a "new vaccine … is

[10] On September 30, 2008, the DHHS procured $404 million worth of BioThrax® for use in the Strategic National Stockpile (SNS). At the end of FY 2007, the DHHS procured $448 million. The DoD procured $245 million in 2003. The DoD's original purchase price per dose rose from $2.26 to its current level of $29.91, a 1,235% increase, although "the contractual price per dose was expected to decrease as production quantities increased."

urgently needed" appeared contradictory to policy resumptions (IOM, 2002, p. 208). A similarly inconsistent, circular argument by the IOM and the FDA involved referencing Dr. Brachman's study to justify efficacy for inhalation anthrax. Even Dr. Brachman does not appear to take this leap himself. Instead, he acknowledges the absence of a required field trial for the old anthrax vaccine and in turn cites the FDA and the IOM as the basis for documenting the current vaccine's efficacy against inhalation anthrax (Brachman et al., 2008, p. 119).

Overall, as Dr. Brachman's work demonstrates to this day, the majority of pro-anthrax vaccine literature emanates from a small group of military and government scientists, many whom have been involved with the vaccine for decades. In the case of Dr. Brachman and Dr. Plotkin, participation in the scientific record on anthrax vaccine stretches back to the 1950s, not only with repetitious updates to articles, but through editorial contributions in medical journals. In comparison, most authors from the civilian medical community remain relatively constant in their critical assessments, or mute in other cases based on nonexposure to the subject matter. Potential expanded civilian exposure to the old anthrax vaccine through the SNS might change the current literary reality of the small core cadre of military and government scientists manufacturing most of the literature related to the vaccine.

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III. CASE STUDY

As discussed in the previous section on methodology, the following case study carefully analyzes the DoD experience with anthrax vaccine, revealing a deviant or outlier program and product. Evaluating the lengthy timeline and causal chain of events helps to place the deviations in perspective. Tracing programmatic processes across time assists the case study's attempt to derive and explain the causal connections of the various conditions and subsequent problematic events outlined. The thesis focuses on two "emergency occurrences" related to anthrax vaccine as the premise to begin the study. The first involved the 2001 anthrax letter attacks, and the second relates to the DHHS declaration of an anthrax emergency in 2008. The DHHS declaration extends through 2015 under the auspices of the Public Readiness and Emergency Preparedness (PREP) Act (DHHS, 2005; DHHS, 2008b).

According to government guidelines, "emergency occurrences" necessitate investigations using formal analytical models (United States Department of Energy [DOE], 1992). Federal guidelines propose root-cause analysis to identify program deficiencies and corrective actions. Preventing recurrences protects the public. In the case of this analysis, we focus on the public's health. The five phases of analysis include Phase I, data collection; Phase II, assessment; Phase III, corrective actions; Phase IV, inform; and finally, Phase V, follow-up. This chapter's case study specifically reviews the development of Phase I, data collection, and Phase II, assessment. Phase III, corrective actions; Phase IV, inform; and finally, Phase V, follow-up, are each addressed in the recommendations of the next chapter.

A. PHASE I - DATA COLLECTION

The "emergency occurrence" under investigation in this case study involves the anthrax letter attacks of 2001. Clearly, the anthrax letter attacks negatively affected the entire nation. The attacks qualify as an emergency occurrence worthy of analysis given that they represented the nation's first anthrax related bioterrorism event in U.S. history. In accordance with the governmental guidelines, the Amerithrax (FBI, 2008)

investigation by the FBI allowed for initial data collection. Congressional and GAO reports detailed in Chapter II's literature review contributed as well. In accordance with the recommendations in the following chapter, consequential data collection by the DoD, the DHS, the DHHS and the Department of Justice (DOJ) should necessarily recommence a comprehensive Phase I data collection upon adoption of the suggestions outlined in this thesis.

B. PHASE II – ASSESSMENT

1. Identify the Problem

According to government guidance, we must analyze and identify causal factors, specifically the root, contributing, and direct causes of any emergency occurrence in order to evaluate preceding or succeeding problematic events (DOE, 1992, p. 7–9). The first step in the assessment phase dictates identification of the root problem. Fortunately, the FBI Amerithrax investigation highlighted the root facts after several years of investigation, and therefore FBI findings serve as a foundation for the assessment phase. The lone U.S. Army scientist employing weaponized anthrax through the mail can be identified as a conceivable root cause of the problem. In essence, a DoD scientist's involvement with the anthrax vaccine, and his related criminal actions, clearly fell outside the normal arenas of expertise, although the emergency occurrence would not have occurred absent DoD level involvement, security lapses, and history with anthrax vaccine.

The root cause, DoD involvement with anthrax vaccine, if corrected, should preclude recurrences of the emergency event. The FDA previously acknowledged these root access issues by documenting "DoD's continuous involvement with, and intimate knowledge of, the formulation and manufacturing processes of all of these versions of the anthrax vaccine" (FDA, 2002b, p. 8). Identification of DoD involvement as a root cause does not imply involvement itself equated to violations of the law or regulation. Instead, the ensuing analysis identifies subsequent violations of the law as contributing causes. The root cause of DoD involvement only served as the crux of the problem. In turn, the U.S. Army scientist's anthrax letter attacks served as the direct cause, a highly significant

one considering the government appears to ignore the implications of the crime's possible motive related to inherent "failings" of the vaccine. The root and direct causes consequently present a window to view the associated proximate or contributing causes, as well as the subsequent problematic events.

2. Determine the Significance of the Problem

The significance of a trusted military scientist turning his expertise and government resources into a weapon to murder American citizens cannot be understated. Documented problems with the government program emerging as a factor possibly motivating a scientist's crime only adds to the significance. The government's acknowledgment of the connection between anthrax vaccine program troubles and the crimes stands incongruously against the government's reluctance to reflect on these revelations with respect to current policy. The government's apparent failure to analyze the events and synthesize modifications to biodefense policy and SNS priorities represents the most significant of the resultant problematic events.

The FBI released emails documenting the scientist's frame of mind on August 6, 2008. The U.S. Attorney for the District of Columbia, Jeffrey Taylor, revealed that Dr. Bruce Ivins, a scientist at Fort Detrick's USAMRIID, was the "sole suspect" in the letter attacks. The FBI concluded, "Dr. Ivins was the only person responsible for these attacks." The motive included the fact that Dr. Ivins "was facing a difficult time professionally in the summer and fall of 2001 because an anthrax vaccine he was working on was failing." Mr. Taylor stated that the "possible motive is his concern about the end of the vaccination program … and one theory is that by launching these attacks, he creates a situation, a scenario, where people all of a sudden realize the need to have this vaccine." According to FBI affidavits chronicling e-mails by Dr. Ivins, the scientist wrote, "Unfortunately, since the BioPort people aren't scientists, the task of solving their problem has fallen on us." Ultimately, the apparent use of the letter attacks to help resolve production problems potentially led to the "scenario" to solve the "mess" (FBI, 2008, p. 12–15).

Understandably, the DoD, unaware that the attacks were being perpetrated by an insider, then leveraged the tragic "scenario" to justify the belated licensure of the anthrax

vaccine. The DoD capitalized on the "situation" stating, "The anthrax attacks in October 2001 illustrated the risk of an unprotected population in an environment contaminated with a biological warfare agent" (Keys & Taylor, 2005). The DoD also used the attacks to rationalize resumption of the suspended anthrax vaccine immunization program (AVIP), officially posting references to the "22 cases of anthrax resulted from attacks with anthrax spores" (DoD, 2009c, p. 4). As the FBI confirmed, the FDA "had suspended further production" because the "same vaccine was having problems in the production phase" (FBI, 2008, p. 15). Defense Web sites document the 2001 problems, stating, "DoD ordered a series of three temporary slowdowns of the AVIP, until additional FDA-approved vaccine became available." Congressional members previously queried DoD officials regarding these slowdowns and the availability of the vaccine based on invalidating FDA inspections. Representative Christopher Shays asked Deputy Secretary of Defense Rudy De Leon and Deputy Assistant Secretary of Defense for Chemical and Biological Defense Anna Johnson-Winegar, "Didn't the FDA make it clear that they would not approve any more from this old plant and that they needed to upgrade it?" Dr. Winegar responded, "Yes." Deputy Secretary De Leon replied, "Correct" (HR, Committee on Armed Services, Military Personnel Subcommittee (HR 106-62, 2000, p. 63). The DoD acknowledged that the "supply was restored in January 2002, with FDA approval of renovations by BioPort Corporation of its facilities and processes" (Military Vaccine Agency [MILVAX], 2005, p. 3–4). The perpetrator's e-mails in September of 2001 confirmed that there were "no approved lots currently available." Failed potency tests previously prevented FDA approval. The scientist wrote, "Apparently Gore (and maybe even Bush) is considering making the anthrax vaccine for the military voluntary, or even stopping the program." The scientist knew that if the vaccine "isn't passing the potency test," the program would end. He detailed the implications, stating, "If it doesn't pass, then there are no more lots to test, and the program will come to a halt. That's bad for everyone concerned, including us."

FBI analysis also documented that Dr. Ivins directly worked on the vaccine's problematic potency testing from 2000 to 2001 in his duties for the Anthrax Potency Integrated Product Team. The DoD awarded Dr. Ivins the highest honor for "getting the

anthrax vaccine back into production" (FBI, 2008, pp. 12–15). USAMRIID documented how Dr. Ivins worked to get "the anthrax vaccine back into production … to determine where the problems were and resolve them so the vaccine would pass the potency test" (United States Army Medical Research and Materiel Command [USAMRMC], 2003, p. 14). Dr. Ivins said at the time, "Awards are nice. But the real satisfaction is knowing the vaccine is back on-line" (Vander Linden, 2003). In conclusion, well-documented anthrax vaccine production problems related to DoD involvement in the manufacturing process (root cause) possibly motivated an Army scientist to launch the anthrax attacks (emergency occurrence) in order to restore confidence in the anthrax vaccine (direct cause). The scientist's actions led to FDA validation of the anthrax vaccine's manufacturing process, resumption of the DoD anthrax vaccine program, relaxation of regulatory oversight, and significant expansion of anthrax vaccine procurement (problematic events). This causal chain qualifies as highly significant due to the nature of the crimes, processes, and actors involved.

Perhaps more disconcerting in the event and causal factor analysis, we discover that inquiry and oversight into the core problems apparently evaporated after the crimes occurred throughout all levels of the government, prolonging these problematic events. DHS endorsement of further expansions to the vaccine's stockpiling in the DHHS SNS illustrates the final problematic, but correctable, event. Specific examples of abandoned oversight and inquiry reside in the next section, detailing the event timeline of the root cause analysis. Ideas on correcting such events with renewed oversight appear in the next chapter's recommendations as suggested future courses of action.

3. Identify the Problem's Causes and Conditions

A time-tested government-advocated analysis offers six methods for determining the causes and conditions surrounding a problem (DOE, 1992, p. 9–14). The thesis exercises the "Events and Causal Factor Analysis" tool due to multifaceted problems across lengthy time frames and the complex causal processes involved. Normally, the serious nature of an occurrence dictates use of "all applicable analytical models" for root cause analysis. The complex aspects of the anthrax letter attacks and problems related to

the anthrax vaccine issue dictate use of all alternative tools in a successive formal governmental analysis. The "change analysis tool" allows discovery of organizational behavior breakdowns. Procedural and administrative problems require the "barrier analysis tool." Personnel problems call for the "human performance evaluation method." Thorough analysis of all phases of the problematic occurrences, as well as causes and corrective actions, might utilize the "Kepner-Tregoe model" (DOE, 1992, p. 10, Fig. 2). Subsequent government-directed inquiry should accomplish the more comprehensive reviews. This thesis focuses only on the Events and Causal Factor Analysis.

a. Events and Causal Factor Relationships

Establishing an illustration of causal factor relationships and relevant chains of events serves as the first step in the Events and Causal Factor Analysis (DOE, 1992, p. 12, Fig. 3). Figure 1 reflects an illustration of a framework for this causal analysis.

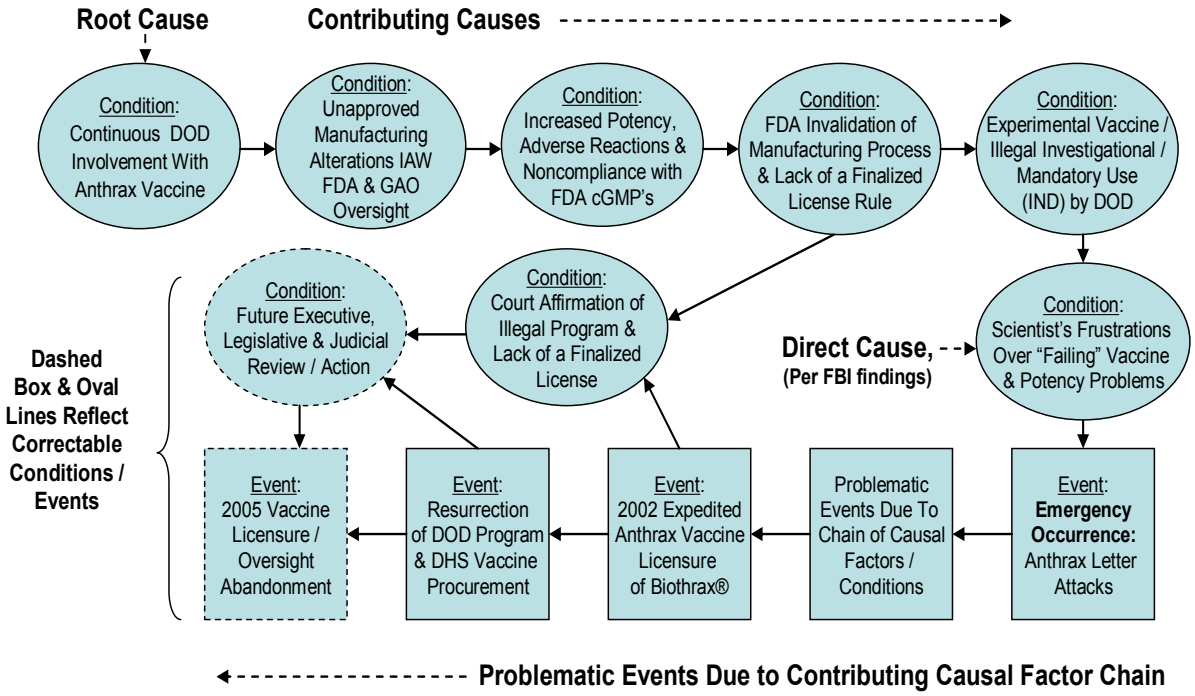

Figure 1. Events and Causal Factor Relationships Illustration

The circles represent the "conditions" precipitating the root cause (continuous DoD involvement), the contributing causes (regulatory, medical, and legal complications), and the direct causes (the U.S. Army scientist's frustrations over the "failing" status of the vaccine and its potency problems). The squares represent the "events," including the emergency occurrence (the anthrax letter attacks) and the subsequent problematic events (the potential relaxation of regulatory controls that allowed for the resumption of the DoD program and anthrax vaccine procurement expansion in the SNS).

The Events and Causal Factor Relationships illustration documents the root cause for the problem. The illustration portrays continuous involvement in anthrax vaccine manufacturing by the DoD as the core cause. The DoD's seemingly under regulated involvement precipitated the contributing causes. These contributing conditions included safety questions, efficacy issues, lack of a finalized licensure for anthrax vaccine, unapproved alterations to the anthrax vaccine manufacturing process leading to potency problems and adverse reactions, and finally, the illegal experimental use of anthrax vaccine for inhaled anthrax. The direct cause, Dr. Ivins's letter attacks, occurred to some extent due to each of these root and contributing causes. Each of these causes in turn precipitated the problematic events, which included expedited anthrax vaccine licensure, resumption of the DoD anthrax vaccine immunization program, DHS and DHHS anthrax vaccine procurement, and the apparent abandonment of inquiry and oversight. The regulatory problems, for the purposes of the case-study assessment phase serve as "conditions," or an "as-found state," which could present "adverse safety, health, quality assurance, security, operational, or environmental implications." The regulatory deviations frustrating the scientist fit the programmatic "conditions," errors or anomalies that, when identified but left uncorrected, potentially lead to a "Causal Factor Chain" (DOE, 1992, p. 9). In this case, the regulatory conditions, based on multiple contributing causes, apparently motivated the anthrax letter attacks. As the FBI surmised, the scientist "creates a situation, a scenario, where people all of a sudden realize the need to have this vaccine" (FBI, 2008, pp. 12–15), thus generating a "cause and effect sequence" (DOE, 1992, p. 9). In effect, the primary problematic event, the letter attacks, scared the

government and the FDA into a subsequent event in the causal factor chain. Thus, the FDA approved the anthrax vaccine manufacturing process potentially despite the known regulatory problems. The DoD then leveraged the attacks in the next problematic event by resurrecting the anthrax vaccine program, literally making a reality of the attacker's motive. Significantly, the DoD subsequently rewarded the scientist for repairing the problems underlying the motive for his crime. Throughout the event and cause factor chain, Dr. Ivins effectively participated firsthand in the root, contributing, and direct causes of the problematic events.

As the illustration suggests, the root cause of the illegal activities related to anthrax vaccine directly or indirectly lies in continuous involvement by DoD personnel. Consequent "contributing causes" or "conditions" resulting from this involvement included reports of high adverse reaction rates and safety problems, perhaps due to increased potency; increased potency, potentially due to unapproved manufacturing changes; failure to finalize the vaccine's license; and illegal use of the vaccine for an unapproved purpose due to unproven efficacy. Tolerance of the extralegal occurrences, or conditions, precipitated the direct cause and subsequent problematic events—offensive use of weaponized anthrax spores against American citizens in a scenario that resuscitated the DoD anthrax vaccine program and spurred SNS procurement. A lack of oversight regarding DoD involvement in turn continued the causal chain with further problematic events including vaccine licensure by the FDA and the appearance of abandonment of previous critical inquiry at all levels of government.

The case study analysis moves forward with a more detailed Events and Causal Factor Analysis timeline. Each chronological example places a historical perspective on the depth of DoD involvement in the anthrax vaccine (root cause) leading up to, and following, the anthrax letter attacks (direct cause). The historical review traces myriad processes and provides perspective on the vaccine's safety problems, illegal experimental use, unapproved manufacturing alterations, and the nonfinalized license (all contributing causes). Following the Events and Causal Factor Analysis timeline, the thesis further details the problematic events in the remaining thesis methodologies: a

program evaluation in Chapter IV, a gap analysis in Chapter V, and a proposal for future courses of action and recommendations in Chapter VI.

b. Event and Causal Factor Analysis: Timeline

The following detailed event and causal factor chain analysis divides chronologically across three time frames. The first, the 1950s to 1980s, involved the development of root causes. The second time frame, the 1990s to late 2001, became the contributory cause years. Finally, following the anthrax letter attacks in 2001, the problematic events began in the post-emergency occurrence years. Figure 2 illustrates these three separate timelines and illuminates the root cause, contributory cause, and problematic event years.

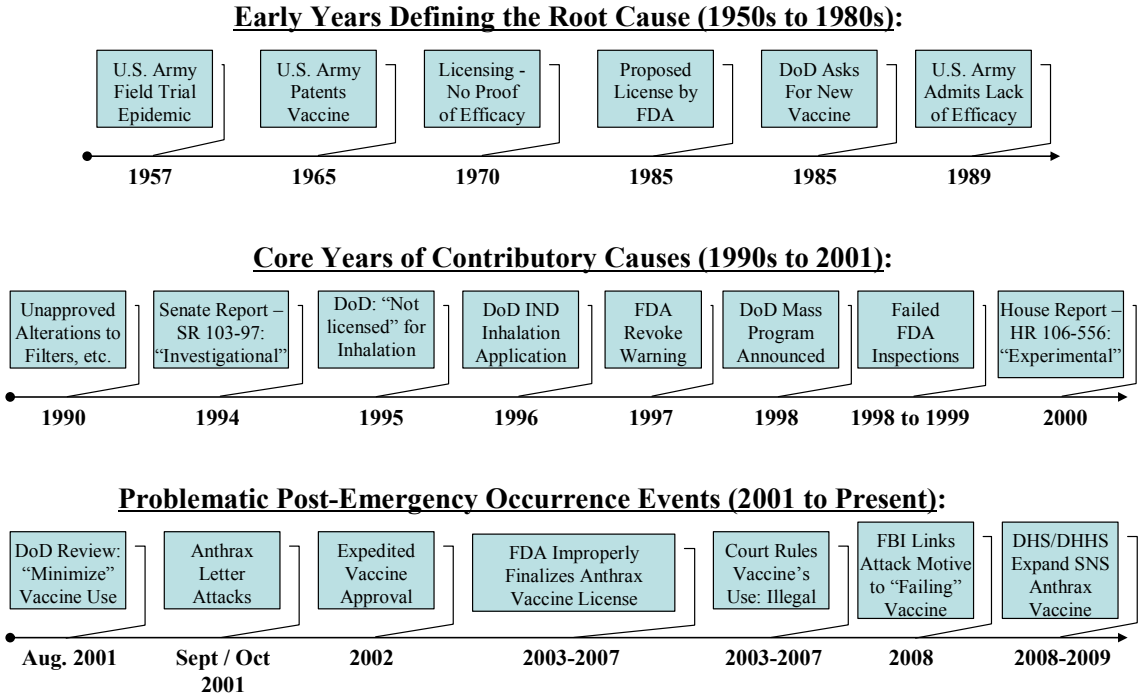

Figure 2. Timeline Illustration of Causes and Events

(1). Early Years Defining the Root Cause (1950s to 1980s). Beginning in January of 1955, at a wool mill in Manchester, New Hampshire, the anthrax vaccine developed by the U.S. Army Chemical Corps underwent a field trial. In the summer of 1957, an unexpected outbreak of inhalational anthrax occurred, killing four

Americans (Belluck, 2001).[11] DoD researchers, Dr. Brachman and Dr. Plotkin, characterized the outbreak as the first inhalation anthrax epidemic in a century for the United States (Brachman et al., 1966; Brachman, Plotkin, Bumford & Atchison, 1960; Plotkin, 1960). By 1962, as an amendment to the Food Drug and Cosmetics Act (FDCA), the Harris-Kefauver Act added the legal requirement for proof of effectiveness for all vaccine licenses (FDA, 1962). The "efficacy" requirement for a "well-controlled" field trial would later become pivotal in the anthrax vaccine legal debate. In 1965, the U.S. Army patented the vaccine used in the 1957 epidemic (Wright & Milton, 1965). Initially, the DoD contracted with Merck, Sharpe, & Dohme for vaccine production (FDA, 2005b, pp. 75180, 75192). Later, the state of Michigan's plant, MDPH, applied for a license on April 14, 1966 for the U.S. Army (Elengold, 2000b).

Curiously, the licensing data did not include the Manchester, New Hampshire mill epidemic, instead using a Talladega, Alabama test for efficacy justification. On February 6, 1969, government regulators questioned the data, writing, "The lack of cases of anthrax in an uncontrolled population of approximately 600 persons in the Talladega mill can hardly be accepted as scientific evidence for efficacy of the vaccine" (see Appendix 1) (Pittman, 1969a). The CDC challenged the license application stating, "There have been no controlled evaluation studies with the Michigan anthrax product as was done by Dr. Phillip Brachman" (see Appendix 1) (Kokko, 1969, p. 2). In summary, the manufacturer did not submit Dr. Brachman's study data used to justify the vaccine today. Despite the questions over efficacy, the government recommended licensure, but provided a caveat, writing, "It was noted also that clinical data establishing efficacy of the product had not been submitted." The recommendation commented that the license application appeared complete, "except the results of an adequately controlled

[11] The first "epidemic" of inhalational anthrax in the past 150 years occurred in Manchester, New Hampshire, while the U.S. Army conducted the original anthrax vaccine clinical trial. Dr. Phillip Brachman's observations at the time found insufficient proof for the efficacy of the vaccine for inhalation anthrax (Brachman et al., 1966; Brachman et al., 1962; Brachman & Friedlander, 1994; Brachman & Friedlander, 1998). The historic study became central to the later court cases. Based on the IOM report and subsequent license in 2006, Brachman, et al., in the 2008 medical textbook *Vaccines*, cite the proven efficacy of the vaccine. In the latest text, Brachman's chapter on anthrax vaccine states, "There have been no controlled clinical trials in humans of the efficacy of the currently licensed U.S. vaccine, although the differences between the U.S. licensed vaccine and the PA-based vaccine used in the Brachman et al. study are minor from a regulatory perspective" (Brachman, Friedlander, & Grabenstein, 2008, p. 119).

clinical investigation that establishes efficacy" (see Appendix 1) (Pittman, 1969a). Therefore, the anthrax vaccine apparently received licensure at the time "without conclusive evidence of efficacy" (see Appendix 1) (Pittman, 1969b). The National Institute of Health (NIH), which regulated biologics (vaccines) prior to the FDA's assumption of these responsibilities in 1972, licensed anthrax vaccine on November 2, 1970 (FDA, 2005b, p. 75193). Many years went by, and the vaccine's extremely limited use by scientists in military laboratories allowed this first regulatory oversight condition, a contributing cause, to go unnoticed.

DoD awareness of the problems presumably resulted in the solicitation for a new anthrax vaccine through a formal procurement request in 1985. The proposal stated, "There is an operational requirement to develop a safe and effective product which will protect U.S. troops against exposure from virulent strains of *Bacillus anthracis*." The request explained, "There is no vaccine in current use which will safely and effectively protect military personnel against exposure to this hazardous bacterial agent" (see Appendix 2) (DoD, 1985, p. 4). The DoD clarified, "a licensed vaccine against anthrax … is currently available for human use.... The vaccine is, however, highly reactogenic, requires multiple boosters to maintain immunity and may not be protective against all strains of the anthrax *bacillus*." The same year the anthrax vaccine issue also reemerged on the FDA's radar in the form of a Proposed Rule in the *Federal Register* to finalize the current vaccine's license. The Proposed Rule, published on December 13, 1985, noted the "efficacy against inhalation anthrax is not well documented," and that "the vaccine manufactured by the Michigan Department of Public Health has not been employed in a controlled field trial." The Proposed Rule referenced the U.S. Army's Manchester, New Hampshire 1957 vaccine study by Dr. Brachman, which the FDA leverages today to justify licensure of the current anthrax vaccine (FDA, 2005). The government's Advisory Panel that formulated the Proposed Rule stated, "Brachman

employed a similar vaccine," but clarified, "No meaningful assessment of its value against inhalation anthrax is possible due to its low incidence"[12] (FDA, 1985, p. 51058).

The Proposed Rule languished without finalization for another twenty years, conceivably due to the lack of proper efficacy data. In the ensuing years, the DoD continued to highlight the vaccine's inadequacies. In a 1989 letter to Senator John Glenn, the DoD gave the situation report:

> Current vaccines, particularly the anthrax vaccine, do not readily lend themselves to use in mass troop immunization. [DoD's reasons included] … higher than desirable rate of reactogenicity, and, in some cases, lack of strong enough efficacy against infection by the aerosol route of exposure. (United States Senate, 1989, p. 480)[13]

In nontechnical language, the vaccine made soldiers sick and did not work well enough. The question and answers also clearly explain the understandable goal of the DoD to acquire a satisfactory vaccine based on the logistics limitations related to antibiotic therapies.

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[12] The "proposed" rule aspect of the Federal Register entry is omitted from the DoD transcribed version on its anthrax vaccine Web site. The fact that the rule was proposed, yet never finalized for 20 more years, until December 19, 2005, became the basis for the federal court rulings determining the vaccine mandate violated the law. The original 1985 Federal Register "Proposed Rule" is available on request from the author: tlrempfe@nps.edu.

[13] Excerpt: Question 14—"The 1986 DoD report on the Biological Defense Program states that as a result of the neglect of the program in the 1970s, the U.S. cannot adequately defend itself against 'conventional' biological agents such as anthrax. Do you agree with that assessment? If therapies in the form of vaccines and antibiotics are available for treating anthrax, how do you explain DoD's assessment that the U.S. cannot adequately defend its service personnel against anthrax?" Answer: "The assessment in the 1986 report is accurate. Current vaccines, particularly the anthrax vaccine, do not readily lend themselves to use in mass troop immunization for a variety of reasons: the requirement in many cases for multiple immunizations to accomplish protective immunity, a higher than desirable rate of reactogenicity, and, in some cases, lack of strong enough efficacy against infection by the aerosol route of exposure. Antibiotics could not be delivered fast enough to mass treatment in the event of a BW attack with anthrax. Such an attack, most likely in the form of an aerosol, would cause pulmonary anthrax, which is difficult to diagnose and has an extremely rapid time course leading to death. Current efforts in vaccine development are directed to addressing the deficiencies in existing vaccines outlined above."

(2). Core Years of Contributory Causes (1990s to 2001). U.S. Army physicians at the time acknowledged the vaccine as a "limited use vaccine ... unlicensed experimental vaccine" (Takafuji & Russell, p. 156).[14] These revelations, just prior to the first Persian Gulf War, reflect incongruously with the subsequent 1990 use of the vaccine by the DoD as fully licensed. Additionally, the anthrax vaccine producer at the time, MDPH, reengineered its production capabilities in the early 1990 time frame to provide anthrax for the conflict in the Middle East. DoD officials were involved to some extent with changes to the vaccine manufacturing process. Changes occurred to the filtration and fermentation systems, as well as the sterilization procedures and chill tanks. The manufacturer or the DoD notified the FDA about some of these changes after the fact. The FDA was unaware of several alterations until congressional and GAO inquiries brought the lack of approvals to the FDA's attention in 2000 (GAO, 2001b). DoD involvement in the manufacturing changes to an unknown degree is apparent from a review of declassified Medical Plans and Operations Division (MPOD) chronology documents. Segments of the record reveal the DoD referenced a "need for an additional fermentor," which DoD officials documented had ultimately been "installed" (DoD, 1996, items 47, 52). FDA officials discovered changes to fermentors based on the manufacturer's forthrightness. FDA records show the company was reminded that the alterations constituted "a major change and should be submitted in the form of an Establishment License Amendment which should include validation data" (Devine, 1990). Later mid-1990 fermentor alterations failed to garner approval until 1999. Specifically, the GAO recording of the regulatory missteps reveal that the pre-Gulf War early 1990s filter changes were never reported until the GAO brought them to FDA's attention. The FDA approved those changes in July 2001 (GAO, 2001b, pp. 4, 5, nn. 8–10).

After the first Persian Gulf conflict, due to concerns over Gulf War illness, the FDA initiated a series of inspections of the anthrax vaccine manufacturer in Michigan. The FDA inspections resulted in findings of "significant deviations" from

[14] The authors, Colonel Takafuji and Russell, worked for the Office of the U.S. Army Surgeon General.

current good manufacturing practices (cGMP's) (FDA, 1997; FDA, 1998). During this time frame, ownership of the anthrax vaccine manufacturing facility transferred from the state of Michigan to a private company known as Michigan Biologic Products Institute (MBPI), and later to BioPort Corporation. BioPort later rebranded itself as Emergent BioSolutions. Transfers of ownership did not halt FDA oversight. The FDA transmitted a letter of concern on December 22, 1993, followed by a warning letter dated August 31, 1995. Warning letters as FDA enforcement actions "are issued only for violations of regulatory significance." Ultimately, the FDA filed a Notice of Intent to Revoke (NOIR) the manufacturer's license on March 11, 1997 (FDA, 1997). The notice led to inspections in 1998 and 1999 finding the manufacturing process: "not validated" (see Appendix 6) (FDA, 1998). The FDA "Inspectional Observations" specifically noted on line 1 that the "manufacturing process for anthrax vaccine is not validated."

Legislative inquiry also ensued. Citing February 1994 testimony by Army Surgeon General Ronald Blanck, the Senate Veteran Affairs Committee determined a possible link between the anthrax vaccine and the maladies associated with Gulf War illness. The Surgeon General's testimony conceded, "Anthrax vaccine should continue to be considered as a potential cause for undiagnosed illnesses in Persian Gulf military personnel" (United States Senate, 1994, p. 35, n. 143). The Committee concluded, "The vaccine's effectiveness against inhaled anthrax is unknown." The Senate staff report described anthrax as a "biological weapon," assessing "it is likely to be aerosolized and thus inhaled. Therefore, the efficacy of the vaccine against biological warfare is unknown." The Committee determined, "The vaccine should therefore be considered investigational when used as a protection against biological warfare" (United States Senate, 1994, p. 15). Fort Detrick scientists also critically evaluated the vaccine in a 1999 version of the medical text *Vaccines,* writing, "The current vaccine against anthrax is unsatisfactory for several reasons." The scientists documented that the "degree of purity is unknown." They detailed the potency problems and noted that the "undefined nature of the vaccine and the presence of constituents that may be undesirable may account for the level of reactogenicity observed." Finally, the scientists found that "there

is also evidence in experimental animals that the vaccine may be less effective against some strains of anthrax" (Brachman & Friedlander, 1994, p. 737).

During this time, from the mid-1980s to the mid-1990s, the DoD appeared to assess the anthrax vaccine's limitations in a methodical and scientifically forthright manner, precluding the later conditions leading to the problematic events. A high point in the methodical, process-oriented approach occurred in the 1996 time frame when questions about the vaccine led to a critical internal DoD acquisitions review when weighing the issues of efficacy, safety, legality, and product reliability (Graham, 1996).[15] Ultimately, a study contracted to Scientific Applications International Corporation (SAIC) pursued a plan to obtain proper FDA approval for the anthrax vaccine for inhalation anthrax expected from aerosolized exposure in wartime. SAIC's conclusions stated, "This vaccine is not licensed for aerosol exposure expected in a biological warfare environment" (Johnson-Winegar, 1995). The DoD office seeking the review, the JPOBD, acknowledged the nature of the meeting in formally transcribed meeting minutes later obtained via congressional subpoena. The minutes detailed that a "meeting was held on 20 Oct 1995 to discuss the process for modifying the MDPH anthrax vaccine license to … expand the indication to include protection against aerosol challenge of spores." In discussing the previous clinical trials, the Defense Department working group

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[15] The background on the military debate over biodefense doctrine included an article from the *Washington Post* titled "Military Chiefs Back Anthrax Inoculations, Initiative Would Affect All of Nation's Forces." Internal DoD debate in the 1996 time frame over how to protect troops revealed the doctrinal debate and departures represented by mandatory force-wide inoculations.

Excerpts: "Reversing earlier opposition, the nation's military chiefs have endorsed a plan to vaccinate all U.S. forces against anthrax." … "The about-face by senior commanders removes the principal obstacle to the plan and reflects heightened Pentagon concern about the prospect of biological attack." … "Military leaders initially were dubious about the need for the anthrax vaccine." … "In addition, some commanders thought that the United States could deter an enemy from launching an anthrax attack simply by threatening massive retaliation—an approach that worked in the Persian Gulf War." … "But some senior civilian Defense Department officials, who ardently support the vaccination plan, ultimately convinced the military leaders." … " 'The whole area of biological warfare was one not very familiar to the chiefs,' a senior defense official said" … "It's been a gradual process for the military to recognize the seriousness of the threat and understand the kind of protection that vaccination provides." … "Military leaders also raised questions about safety of the anthrax vaccine given speculation that some of the 'Gulf War Syndrome' maladies suffered by U.S. troops may have been caused by one or a combination of several vaccines administered." … "Senior defense officials, eager to institute a broad vaccination program, departed from normal departmental practice this spring and organized two meetings that included vice chiefs of the Army, Navy, Air Force and Marine Corps and civilian experts" … "The meetings were unusual in that we were starting at the top instead of trying to staff an issue, from the bottom up" (Graham, 1996).

acknowledged, "there was insufficient data to demonstrate protection against inhalation disease" (see Appendix 3) (DoD-JPOBD, 1995).

Ultimately, a complicated internal process promulgated an Investigational New Drug (IND) application to the FDA by the manufacturer in 1996. The DoD's USAMRIID held responsibility for the clinical trial to test for new indications based on an indication for "inhalation anthrax," as well as a change in route of administration and the schedule of dosage. A federal court later noted that the application stated, "The ultimate purpose of this IND is to obtain a specific indication for inhalation anthrax and a reduced vaccination schedule" (see Appendix 4) (Myers, 1996; *Doe v. Rumsfeld*, 2003, p. 25). Updated applications were filed after the DoD announced its mandatory program (see Appendix 5) (DoD, 1999b). DoD meeting minutes confirmed the awareness of the need for FDA approval for the vaccine's use for inhalation anthrax prior to commencement of any large-scale vaccinations (see Appendix 3) (DoD-JPOBD, 1995).

The official record also uncovered a less methodical, more expedient, parallel, informal political appeal directly to the FDA by the DoD outside the realms of formal regulatory processes. A letter to the FDA Commissioner documented the DoD goal. The letter stated, "We wish to obtain an indication for protection against inhalation anthrax." The letter added, "DoD has long interpreted the scope of the license to include inhalation exposure, including that which would occur in a biological warfare context" (Joseph, 1997). Subsequent responsive letters by the FDA acquiesced to the personal communications and circumvented the ongoing regulatory process. The FDA informal response stated, "While there is a paucity of data regarding the effectiveness of Anthrax Vaccine for prevention of inhalation anthrax, the current package insert *does not preclude* this use" (Friedman, 1997). Courts later captured the "does not preclude"[16] double negative nature of the terminology in affirming that the anthrax vaccine lacked approval for such a purpose at the time (*Doe v. Rumsfeld*, 2004, p. 24). The CDC also

[16] *Doe v. Rumsfeld*, 297 F. Supp. 2d 119 (D.D.C. 2003). "The apparent change in position from the December 1985 proposed rule and the use of a double negative (i.e. "it is not inconsistent"), fail to persuade this Court that the view expressed in the 1997 letter is the FDA's formal opinion," *Doe v. Rumsfeld*, 2004, p. 24.

weighed in through an Advisory Committee in public comments, confirming, "We do not have specific information on the efficacy of the existing vaccine for the prevention of inhalational anthrax and we probably never will"[17] (Bussey, 2000). To the outside observer, including the court, political attempts to shortcut the regulatory processes epitomized the contributory events during this time frame.

A Defense Secretary–mandated "independent" expert review also revealed apparently more politically than scientifically oriented efforts to make the vaccine program appear properly approved. The DoD utilized review recommendations by Dr. Gerard Burrow of Yale University. Dr. Burrow determined, "The anthrax vaccine appears to be safe and offers the best available protection against wild-type anthrax as a biological warfare agent" (Burrow, 1998). Later, the expert placed his recommendations in perspective when asked to testify about the program and his review. In a letter to Congress, Dr. Burrow explained, "I was very clear that I had no expertise in Anthrax and they were very clear they were looking for a general oversight of the vaccination program." Dr. Burrow clarified in telephone interviews for congressional investigators that "he has little experience with vaccines," and his "charge" included a "general review" aimed at "communication strategies" (HR 106-556, 2000, pp. 17–18). The information campaign paralleled the political approval efforts, versus a regulatory compliant scientific review.

Simultaneously, the actual risks for the recipients of the vaccine, and the corresponding lack of legal responsibility for the manufacturer, resulted in a DoD indemnification to protect from liability associated with mass inoculations of the troops. Indemnification documents revealed the language omitted from the public communications such as, "The obligation assumed by MBPI under this contract involves unusually hazardous risks associated with the potential for adverse reactions in some recipients and the possibility that the desired immunological effect will not be obtained

[17] Quote by Dr. David Ashford, co-author of a December 2000 CDC Advisory Committee on Immunization Practices regarding use of the anthrax vaccine. The report was referenced by the Centers for Disease Control: Use of Anthrax Vaccine in the United States, Recommendations of the Advisory Committee on Immunization Practices (CDC, 2000).

by all recipients" (see Appendix 7) (Caldera, 1998).[18] In other words, the behind-the-scenes legal cover provided to the manufacturer defied the public messages of safety and efficacy. The ultimately successful efforts at political circumvention of the normal regulatory and legal processes marked a turning point where the DoD's "continuous involvement" set in motion a slippery slope of contributing causes which would ultimately lead to violations of the law.

Aside from the informal memo from the FDA employee, the FDA actually stood firm in 1998, not joining the DoD contributing cause actions. The DoD's new message to the troops of proven vaccine safety and efficacy contrasted with the FDA's regulatory oversight. The FDA repeatedly found in 1998 and 1999 that "the manufacturing process for the production of Anthrax Vaccine Adsorbed is not validated" (see Appendix 6) (FDA, 1998, p. 1, ln. 1). The lack of validation for the manufacturer led to the suspension of the anthrax vaccine program. The FDA investigations also revealed potency problems related to the vaccine that Dr. Ivins attempted to solve but apparently did not until after the letter attacks (FBI, 2008; FDA, 1997; GAO, 2001b; Little, 1998; USAMRMC, 2003; Vander Linden, 2003, p. 12). Congressional investigators also obtained documents through congressional subpoenas that showed the DoD knew as early as May 1998 that vaccine potency testing was "all over the board." Documents confirmed that DoD officials and the manufacturer suspended testing to preclude reporting these results to the FDA (see Appendix 8) (Little, 1998). The DoD originally made successful supplemental testing of the vaccine a prerequisite for launching mandatory mass immunizations (MILVAX, 2005).[19] Based on the problems with the supplemental testing, one DoD official wrote:

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[18] The DoD Indemnification history for anthrax vaccine is also available in Congressional Report 106-556 (HR, 2000, p. 13).

[19] "On December 15, 1997, Defense Secretary William Cohen announced a plan to immunize military personnel against anthrax, contingent on four conditions: (1) supplemental testing of vaccine lots in the stockpile to assure potency, purity, sterility, and safety, consistent with Food and Drug Administration (FDA) standards; (2) approval of the Services' implementation plans for execution and communication; (3) implementation of a system for fully tracking anthrax vaccinations; and (4) review of the health and medical aspects of the program by an independent expert (former dean of medicine of Yale University and member of the prestigious National Academy of Sciences)" (MILVAX, 2005, p. 3).

> I'm not prepared to defend going forward with the SECDEF's plan if I can't be reasonably sure there will be vaccine available to continue any force immunization. … I will forward a recommendation through BG Doesburg to the SECDEF to either delay the immunization of the force or recommend that the action be terminated because of confidence that the manufacturer will be able to meet vaccine dose requirements is in question (DoD-JPOBD, 1999).

Ultimately, a report by the congressional House of Representatives Government Reform Committee published on the anthrax vaccine, titled "Unproven Force Protection," determined that the DoD program violated FDA regulations due to the vaccine's "investigational" status. The report recommended, "While an improved vaccine is being developed, use of the current anthrax vaccine for force protection against biological warfare should be considered experimental and undertaken only pursuant to FDA regulations governing investigational testing for a new indication" (HR 106-556, 2000, p. 4).[20] Congressional investigations also revealed DoD awareness that the "potency test required for the present vaccine has not been well correlated to efficacy in humans and it is doubtful that it can be" (HR 106-556, 2000, p. 62. fn. 269). GAO reports also confirmed that the "long-term safety of the vaccine has not yet been studied;" the "vaccine and the manufacturing process were changed;" the "ingredients used to make vaccine were changed from the original vaccine," and "prior to the time of licensing, no human efficacy testing of the MDPH vaccine was performed" (GAO, 1999a, p. 1–3). As discussed previously, all these problems led to the "failing" status of the DoD immunization program and motivated the U.S. Army anthrax vaccine scientist to commit the anthrax letter attacks later in 2001. In this case, the positive contributing cause of FDA, congressional and GAO oversight effectively led to the direct cause of the attacks.

Adding to the pressure on those implementing the anthrax vaccine program, the political leadership of presidential candidates at the time mirrored the congressional oversight. Presidential candidate George W. Bush stated, "I don't feel the administration's anthrax immunization program has taken into account the effect of this

[20] Excerpts from the "Findings in Brief" stated, "Efficacy of the vaccine against biological warfare is uncertain. The vaccine was approved for protection against cutaneous (under the skin) infection in an occupational setting, not for use as mass protection against weaponized, aerosolized anthrax" (HR 106-556, 2000, p. 4).

program on the soldiers in our military and their families … Under my administration, soldiers and their families will be taken into consideration" (U.S. Medicine, 2000; Katz, 2001, p. 1855, fn. 133). Candidate Senator John McCain also weighed in saying, "I think that there should be a pause. I think that they have not done the job in educating the members of the military, and I would pause and I would get the best scientific and medical people together and make a better argument than they've made" (Marelius, 2000). Al Gore joined the call, explaining, "Based on the concerns I have heard, from military personnel directly, I think we are justified in taking a closer look—I think that some increased sensitivity to the kinds of questions that are being raised is needed" (Sobieraj, 2000). Beyond the political candidates, additional inquiries from Democratic leaders Senator Tom Daschle and Representative Dick Gephardt expressed their "interest in and concern about reports regarding the Pentagon's continued use of an anthrax vaccine." The Democratic leaders wrote Rumsfeld on June 21, 2001 questioning the "safety and effectiveness of the anthrax vaccination" and queried the Defense Secretary about the "punishments already meted out" (Daschle & Gephardt, 2001).

Even state involvement resulted in the Connecticut Attorney General, Richard Blumenthal, investigating the program. The state's top lawmaker sent inquiries in 2001 to the DoD and the FDA recommending that the federal government "cease and desist" its illegal administration of the anthrax vaccine immunization program. The Attorney General frankly stated, "In effect, the military is forcing its personnel to serve as human guinea pigs for an unlicensed drug that has not been proven to be safe or effective." He captured the fact that previously the DoD actually concurred at one time about the experimental nature of the vaccine. He therefore questioned why:

> Suddenly in 1997, DoD and the FDA, with no change in the facts or the law, reversed themselves and with the stroke of a pen wiped out the protections afforded our members of the Armed Services by clearing the way for DoD's mandatory mass inoculations (Blumenthal, 2001).

The state Attorney General called upon the DoD and the FDA to "cease and desist from their illegal conduct and to abandon plans for Anthrax Vaccine inoculation of the Armed Forces." He specifically commented on the informal memo by the FDA, which he claimed, "Wiped out ten years of DoD analysis and 25 years of FDA

law designed to protect the safety and well being of the citizens of the United States." The Attorney General asserted that, "Mandatory vaccination of troops with a biologic product not licensed for its current use violates the Federal Food, Drug and Cosmetic Act and 10 U.S.C. § 1107" (Blumenthal, 2001). Years later, federal courts echoed these very arguments in the injunctions against the vaccine program (*Doe v. Rumsfeld*, 2003; *Doe v. Rumsfeld*, 2004; *Doe v. Rumsfeld*, 2007). The Attorney General later provided an amicus curiae (friend of the court) brief opposing the DoD's attempt to vacate the original federal court injunctive decisions. In the end, a federal appeals court declined to vacate or overturn the lower court rulings (*Doe v. Rumsfeld*, 2007).

Top government advisors also reacted to the questions and concerns. Based on research materials delivered to the White House on March 22, 2001, pertaining to Gulf War illness, presidential Senior Advisor Karl Rove tasked DoD Undersecretaries of Defense (USD) Dr. David Chu and Edward Aldridge to review the "political problems" associated with the anthrax vaccine and Gulf War illness (see Appendix 9) (Rove, 2001).[21] Veteran's advocate H. Ross Perot energized Rove, and the undersecretaries promptly studied the controversy and presented recommendations to Defense Secretary Donald Rumsfeld on August 10, 2001. The undersecretaries recommended an effective halt to the anthrax vaccine program. Highlights of the undersecretaries' recommendations included continuing the program only "at a minimum level." They advocated implementing "an acquisition strategy to purchase additional bio-detectors and stockpiles of antibiotics to augment force protection in the absence of an anthrax vaccine." They suggested that the Defense Secretary develop a "coherent institutional process to assess and prioritize biological threats and approve the use of associated countermeasures." Finally, they recommended the development of a "national long-range vaccine that will address the full range of requirements of the DoD, DHHS, and other stakeholders" (see Appendix 10) (Chu & Aldridge, 2001).[22]

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[21] Reported in the *New York Daily News* in an article titled "Anthrax mailer feared his life's work was doomed, prosecutors say." The article references presidential Senior Advisor Karl Rove's memo to Deputy Secretary of Defense Paul Wolfowitz (Meek, 2008).

[22] Reported in the *Washington Post* in an article titled "Demand Growing for Anthrax Vaccine, Fear of Bioterrorism Attack Spurs Requests for Controversial Shot." The article references the Chu and Aldridge memo to Secretary of Defense Rumsfeld (R. Weiss, 2001).

The chairman of the Joint Chiefs (CJCS), General Henry H. Shelton, responded to the Defense Secretary review on August 30, 2001. General Shelton reaffirmed that "Service and combatant commanders are unanimous in their continued support for the military requirement to vaccinate our forces against anthrax, and view the vaccine as the centerpiece of our defense against the most likely biological threat agent" (Shelton, 2001).[23] Placing General Shelton's appeal in perspective, at the time the DoD anthrax vaccine immunization program had exhausted FDA-approved vaccine due to potency testing problems. The DoD "centerpiece" program was "failing" according to the FBI, using a vaccine from a manufacturer invalidated by the FDA since 1998. In line with General Shelton's disagreement with the internal DoD undersecretaries' conclusions, DoD officials had previously similarly rebuffed congressional cautions and conclusions. Regarding the congressional report that previously found the program in violation of FDA regulations, and the vaccine's use experimental, DoD officials appeared to consistently express their disagreement and disappointment with conclusions that challenged the anthrax vaccine policy (Quigley, Bailey & West, 2000).

Clearly, the months preceding the anthrax letter attacks in 2001 marked high stakes. The DoD immunization program had exhausted its supply of approved vaccine based on FDA license revocation warnings and unwillingness to validate the anthrax vaccine manufacturing process (FDA, 1997; FDA, 1998). Top administration officials recognized anthrax vaccine and Gulf War illness as "political problems" (Rove, 2001) and essentially recommended courses of action similar to the positions that earlier DoD leadership, and DoD's historic documents, had held prior to 1998. Those civilian leaders, and their recommendations, recognized and methodically dealt with the problems associated with the anthrax vaccine forthrightly prior to the 2001 letter attack emergency events. After the emergency occurrence, the earlier systematic civilian oversight apparently gave way to the policy inertia created by the attacks and instead facilitated more problematic events.

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[23] Reported in the *Washington Post* in an article titled "Demand Growing for Anthrax Vaccine, Fear of Bioterrorism Attack Spurs Requests for Controversial Shot." The article references Shelton's memo to Rumsfeld, prepared by LTG John P. Abizaid, Director J-5 (Weiss, 2001).

(3). Post Emergency Occurrence Events (2001 to Present). The FDA invalidation of the anthrax vaccine manufacturer quickly reversed, and the resulting program "slowdowns" ceased, after the anthrax letter attacks. The FDA expedited approval of the manufacturing process (MILVAX, 2005, pp. 3–4). Prior to the attacks the DoD "involvement," the identified root cause in this analysis, contrasted with FDA and congressional oversight. Both FDA and congressional oversight effectively served as contributing causes to the emergency occurrence of the later anthrax letter attacks. After the attacks, though, the FDA's causal contribution transformed from one that helped contribute to the first problematic event of the attacks based on haphazard oversight to one that contributed to the resultant problematic events. Examples of the resultant problematic events include the vaccine's expedited approvals, expanded procurement for the SNS, and diminished oversight by the FDA. While seeds of the FDA's transformation began with the Friedman memo in 1997 to the DoD (Friedman, 1997), the agency fully adopted, and even championed, the DoD's position from a regulatory perspective after the anthrax letter attack emergency occurrence.

The GAO also concluded key investigations pertaining to the unapproved alterations of the anthrax vaccine manufacturing process during this pivotal time frame. A 2001 report by GAO confirmed, "DoD found up to a hundredfold increase in the protective antigen [potency] levels in lots produced after the filter change that year." The GAO also reported on a 1994 medical journal article, which "hypothesized that the filter change altered the composition of the vaccine by increasing the level of protective antigen in the finished product." GAO found that DoD scientists attributed the increases to the "change in the filter" (GAO, 2001b, p. 5). Dr. Ivins, the presumed anthrax murderer, authored the 1994 article (GAO, 2001b, p. 5, fn. 12).[24] The GAO also confirmed that "any changes to the manufacturing [process] that have the potential to affect the safety, purity, or potency of a biologic must be submitted and approved … prior to implementation" (GAO, 2001b, p. 4, fn. 9). The GAO found that the "FDA reviewed and accepted the data and approved the filter changes in July 2001." Awareness

[24] The GAO report cited Dr. B.E. Ivens [sic] and referenced the Ivins et al. article titled, "Efficacy of a Standard Human Anthrax Vaccine Against *Bacillus anthracis* Spore Challenge in Guinea Pigs," published in *Vaccines* (Ivins, Fellows, & Nelson, 1994, pp. 872–74).

of the manufacturing alterations occurred only after the GAO reported them to the FDA (GAO, 2001b, p. 4).[25] The DoD acknowledged the advanced requirement for such approvals (DoD, 2009c, p. 46),[26] though according to the GAO report, none occurred for over ten years after the original manufacturing alterations. The lapses could have rendered the vaccine "adulterated" during the interim time frame in accordance with Federal Food Drug and Cosmetic Act requirements pertaining to potency, manufacturing changes, and noncompliance with current good manufacturing practices (21 U.S.C. §351, 1997). The GAO report also alluded to the timing of the manufacturing changes potentially impacting veterans' health stating, "Published and unpublished data on anthrax vaccine use during the Gulf War and since 1998 show a significantly greater incidence of … adverse reactions" (GAO, 2001b, p. 6). Over the years, each of 16 follow-on GAO reports assessed critical findings, adding credence to the contributing causes of vaccine safety concerns, potency problems, and unapproved manufacturing alterations by the DoD.

After the anthrax letter attacks by the scientist involved with many of these anomalies, the root, contributing, and direct causes resulted in the problematic events. The anthrax letter attacks silenced high-level government inquiry by the fall of 2001, despite the fact that the government quickly determined that the anthrax attacks

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[25] "Because we could find no evidence in BioPort or FDA records that the filter changes had been reported to FDA, we contacted FDA officials in December 2000 to discuss the filter changes. They told us that they had not been notified and were not aware of changes to any filters used to produce anthrax vaccine. In February 2001, FDA wrote to BioPort, raising questions about the changes to the filters. In April 2001, BioPort submitted documentation, primarily in-process tests and lot release data, to FDA to demonstrate that the filter changes had not had a significant impact on vaccine quality. FDA reviewed and accepted the data and approved the filter changes in July 2001" (GAO, 2001b, p. 4).

[26] The DoD's acknowledgment of licensing amendments for major manufacturing changes stated: "Emergent BioSolutions ceased manufacturing to renovate its vaccine production facility in February 1998. When the manufacturing process or equipment in a renovated facility or establishment differs materially, from that in the former facility or establishment (CFR 21.314.70), a Biologics License Application (BLA) Supplement must be submitted for Agency approval before production can be resumed. Emergent BioSolutions' BLA Supplement consisted of many parts. Included in the BLA supplement were data validating an updated potency test, process validation test results, and information concerning the qualification and testing of three fermentation systems, raw material quality and acceptance criteria and updated procedures for operating the new facility" (DoD, 2009c, p. 46).

originated from "domestic" sources.[27] No apparent investigation of the reason why the product was "failing" occurred. Instead, the government rapidly approved anthrax vaccine in response to the manufactured emergency occurrence. The GAO also documented the IOM and the National Academy of Sciences (NAS) joining as contributing cause actors as well. According to the GAO, initially the IOM reviewed anthrax vaccine potency and efficacy writing, "The licensed anthrax vaccine has several additional disadvantages." The IOM explained to the GAO that the "amount of protective antigen in the vaccine varies from lot to lot, because the manufacturing process cannot precisely quantify the antigen" (GAO-NSIAD, 1999c, p. 10). The IOM added, "There is some evidence that the current anthrax vaccine may have diminished efficacy against certain virulent strains of anthrax" GAO, 2006, p. 16). At first glance, it appears that the IOM's DoD sponsored report in 2002 endorsed the safety and efficacy. Yet, the truth in the fine print actually stated, "Despite recent FDA approval of the license … relying on AVA and the current specifications for its use is far from satisfactory. There is a need for research toward the development of a different and better anthrax vaccine" (IOM, 2002, p. 15). The earlier March 2000 IOM findings, inserted in the final appendix of the 2002 IOM report, also included the statement, "There is a paucity of published peer-reviewed literature on the safety of the anthrax vaccine." Though the IOM explicitly avoided judging the propriety of past FDA regulatory approval processes, the record also shows the IOM studies' primary author, Dr. Lois Joellenbeck, indeed had previously inquired of the DHHS and FDA about the anthrax vaccine manufacturing changes. Dr. Joellenbeck received a reply one year prior to publication of the IOM report referencing the manufacturer's requirement to report the filter changes. Dr. Ivins described the filtration changes in a 1994 journal article (Ivins et al., 1994). The GAO reported Dr. Ivins's article and the unapproved manufacturing alterations in a report shortly after the letter attacks (GAO, 2001b). In contrast, the IOM's reticence to explore the filter changes may lie with the FDA's assertion that it was unaware of evidence showing a detrimental effect on the

[27] During a White House press briefing a reporter asked if the U.S. Army laboratories at Fort Detrick were the source, and Ari Fleischer responded, "All indications are that the source of the anthrax is domestic. And I can't give you any more specific information than that. That's part of what the FBI is actively reviewing. And I just can't go beyond that" (Fleischer, 2002).

vaccine. Regardless, both the GAO analysis and FDA requirements confirmed that any such changes require approval prior to implementation and only after proving the absence of deleterious impact (GAO, 2001b, p. 4, fn. 8–9).[28]

Overall, the IOM's causal contributions to the problematic event of oversight breakdowns appear as either inept or willfully blind. No logical explanation exists to clarify why the IOM failed to investigate the central issue of manufacturing changes. If the IOM had analyzed the regulatory and medical implication of the manufacturing changes, the report could have potentially revealed "show stoppers" for the anthrax vaccine program. Though the IOM and NAS possess no statutory authority in the regulatory realm, the FDA ultimately leveraged IOM's report to justify licensure. In turn, the courts accepted the IOM analysis. Dr. Brachman even used the report to imply substantiation of the vaccine's efficacy against inhalation anthrax for his own study. In comparison, the DoD's participation in the manufacturing changes and its scientists' studies suggesting significant potency changes, as well as the manufacturer's overt failure to comply with FDA rules, traverse into the regulatory noncompliance realm, one both the FDA and the IOM ultimately used, or potentially abused, their discretion to not pursue.

Beyond political inquiries, internal reviews and government reports, a parallel path of judicial review from the courts commenced after the 2001 letter attacks, based on mounting concern over the contributing causes. Citizens filed a formal petition highlighting the manufacturing changes and investigational status of the vaccine in accordance with the requirements of the Food, Drug and Cosmetics Act (Dingle et al., 2001).[29] The petition later served as a cited foundation and basis for the preliminary

[28] "When implementing changes in manufacturing, the manufacturer is required to submit evidence, using available technology appropriate to the product, that provides assurance that the change does not adversely effect the identity, strength, quality, purity, and potency of the product (21 CFR § 601.12). The specific evidence required is determined by the FDA review team assigned to evaluate this change. In the case of a filter change, FDA would have required the manufacturer to show by available and appropriate technology, that AVA [anthrax vaccine adsorbed] manufactured using a new filter was comparable to the AVA using the previously approved filter" (Clifford, 2001, p. 1).

[29] FDA citizen petitions are authorized under 21 U.S.C. § 10.30, and the referenced petition was filed as Docket # 01P-0471 (Dingle et al., 2001) on the same day that the anthrax vaccine manufacturer filed its request for expedited approval of its manufacturing process.

injunction by the D.C. federal district court in December 2003. That injunction temporarily halted the program (*Doe v. Rumsfeld*, 2003, p. 7). The court deemed the anthrax vaccine "an investigational drug and a drug being used for an unapproved purpose. As a result of this status, the DoD is in violation of 10 U.S.C. § 1107, Executive Order 13139, and DoD Directive 6200.2" (*Doe v. Rumsfeld*, 2004, p. 32). The court cited the "Citizen Petition," confirming that the proposed rule for the anthrax vaccine license in the "*Federal Register* has never been finalized" (*Doe v. Rumsfeld*, 2004, p. 4). In the opinion, the judge addressed the DoD's political maneuvering, finding the "personal opinions of FDA officials as expressed in a series of letters are not entitled to any particular deference" (*Doe v. Rumsfeld*, 2004, p. 24). Instead, the court upheld the notion that "the right to bodily integrity and the importance of complying with legal requirements … are among the highest public policy concerns one could articulate" (*Doe v. Rumsfeld*, 2004, p. 30). The judge concluded, "The women and men of our armed forces put their lives on the line every day to preserve and safeguard the freedoms that all Americans cherish and enjoy" (*Doe v. Rumsfeld*, 2004, p. 33). The judge addressed the DoD's contention that the vaccine was properly licensed opining, "the documents submitted to this Court under seal suggest otherwise." The judge added that the "statements made by DoD officials suggest that the agency itself has, at some point at least, considered AVA [anthrax vaccine] experimental with respect to inhalation anthrax." The ruling held, "The Court would be remiss to conclude that the original license included inhalation anthrax." The court concluded, "The DoD's administration of the inoculation without consent of those vaccinated amounts to arbitrary action" (*Doe v. Rumsfeld*, 2004, pp. 28–29). The court essentially addressed the root and contributing causal conditions leading up to the core problematic event, the emergency occurrence of the anthrax letter attacks.

After the letter attacks, the conditions created by the crime produced an imperative for anthrax vaccine. The FDA initially made the vaccine available, only to be halted by the aforementioned judicial review in late 2003. At that point, the FDA hurriedly filed a "final rule" for anthrax vaccine one week after the court injunction. The court, unwilling to join as a contributing cause to the problematic

oversight events, reviewed the new license and ordered a permanent injunction in October 2004 on summary judgment.[30] The court again affirmed the anthrax vaccine as "an investigational drug being used for an unapproved purpose," and that the "involuntary anthrax vaccination program, as applied to all persons, is rendered illegal absent informed consent or a Presidential waiver (*Doe v. Rumsfeld*, 2004, pp. 12, 40). The court clarified the proper procedures for the FDA and the DoD for ordering the troops to submit to experimental inoculations:

> If the Executive branch determines that this is truly an exigent situation, then obtaining a presidential waiver would be an expeditious end to this controversy. ... Absent an informed consent or presidential waiver, the United States cannot demand that members of the armed forces also serve as guinea pigs for experimental drugs (*Doe v. Rumsfeld*, 2003, pp. 31, 33).

In response to the ruling, the FDA continued the causal event chain by licensing the vaccine again two years later, in December 2005, after following the court-directed rule-making procedures. The new FDA licensure in the *Federal Register* referenced the potency questions and multiple efficacy studies by Dr. Ivins, the direct cause of and the actor who had committed the emergency occurrence letter attacks (FDA, 2005b, p. 75183). Ultimately, the DoD and the FDA, through an appeal spearheaded by the DOJ, moved the court to vacate or overturn the 2003 and 2004 injunctions. Where the DOJ appeared to exonerate the causal contributions by the DoD and FDA, the federal appeals court declined to do so, instead mooting the case in 2006 based on the FDA's licensing.[31] By 2007 the courts affirmed that the anthrax vaccine immunization program was "not substantially justified" prior to the FDA licensure and requisite rule making (*Doe v. Rumsfeld*, 2007). The Court ultimately granted "prevailing party" status for the

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[30] "Summary judgment" means "there are no genuine issues of material fact and the moving party is entitled to judgment as a matter of law" (*Doe v. Rumsfeld*, 2004, p. 16).

[31] See *Doe v. Rumsfeld*, 127 Federal Appendix 327 (D.C. Cir. 2006), cited in 538 F. Supp. 2d 200 (D.D.C. 2008) (*Rempfer v. U.S. Dep't of Air Force Bd.*, 2008, p. 8).

plaintiffs against defendants DoD and FDA.[32] As recently as 2008, another federal court upheld the prior court ruling in an opinion regarding correction of records. The court affirmed the "undisturbed factual and legal findings" of the previous ruling and clarified that:

> Prior to the FDA's December 2005 rulemaking, it was a violation of federal law for military personnel to be subjected to involuntary AVA [anthrax vaccine] inoculation because the vaccine was neither the subject of a presidential waiver nor licensed for use against inhalation anthrax (*Rempfer v. U.S. Dep't of Air Force Bd*., 2008, pp. 18–19).

Despite the action by the courts and the revelations by the FBI, the "controversial" (CRS, 2007) anthrax vaccine and the mandatory DoD program appear to survive as vigilantly as anthrax spores themselves. While Defense Secretary Rumsfeld acknowledged, "Things have not been going swimmingly," he also expressed the DoD intention that they were "going to try and save it"[33] (DoD, 2001). The creation of "a scenario where people all of a sudden realize the need to have this vaccine" (see Appendix 11) (FBI, 2008, pp. 12–15) succeeded beyond all expectations based on the revival of the DoD anthrax program and SNS procurement.

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[32] The ultimate status of the *Doe v. Rumsfeld* litigation cost the U.S. taxpayers considerable sums of money when the attorneys were reimbursed for their professional contributions and successful litigation as the "prevailing party" based on the Administrative Procedures Act and the Equal Access for Justice Act. The court's conclusion determined: "The Court concludes that plaintiffs are entitled to fees and costs for litigating this action, including on appeal, because plaintiffs are the prevailing party and the government's position was not substantially justified" (*Doe v. Rumsfeld*, 2007).

[33] DefenseLink News transcript excerpt of a DoD News briefing by Secretary Rumsfeld and Gen. Myers, answering questions about the status of the anthrax vaccine:

Q: "Mr. Secretary, I wonder if you can give us an update on the Pentagon's anthrax vaccine program? The sole manufacturer in Michigan hasn't produced vaccine for quite some time, and it could be months before they can start producing again. You have a minimal amount of vaccine, and you're only doing a certain number of troops, small numbers of troops. And finally, last week there was a petition sent to FDA by military officers, and others, calling for them to pull the license and destroy the stockpiles of the vaccine. Can this program be saved, do you think, or are you going to look at alternatives to the vaccine?"

A: (Sec. Rumsfeld) "We're going to try and save it. There have been other efforts that have failed over a period of years. And it may or may not be savable, but I met this morning with Pete Aldridge and David Chu, and we discussed this at some length. And they or their representatives are going to be meeting with people from HHS and Secretary Thompson's office and try to fashion some sort of an arrangement whereby we give one more crack at getting the job done with that outfit. It's the only outfit that—in this country that has anything underway, and it's not very well underway, as you point out. We're trying to fashion a way that the—it's a combination of things, but they have not been approved by the FDA, as I understand it. They do not have what looks to be—well, I shouldn't be characterizing a private entity that way, but things have not been going swimmingly for them. And what we're trying to do is figure out a way where we might get some help so that they might improve their performance" (DoD, 2001).

Some contend that following the attacks the U.S. government "spent extravagantly and wastefully on a perishable (and, as it happened, utterly unnecessary) anthrax vaccine." The "overblown" reaction to the anthrax attacks cost $5 billion, or "$1 billion for every fatality inflicted by the terrorist." According to renowned terrorism expert Bruce Hoffman, the attacks proved "quite effective at unnerving an entire nation" (Mueller, 2006, pp. 32, 31, 149), not to mention successfully rekindling the anthrax vaccine program and additional procurements for the SNS. After the 2008 federal law enforcement revelations about the connections between the anthrax attacks and the vaccine, the DHS Secretary confirmed, "There is not currently a heightened risk of an anthrax attack," and reported "no credible information indicating an imminent threat of an attack involving *Bacillus anthracis*" (Chertoff, 2008, p. 1). Regardless, the government declared an "anthrax emergency" (DHHS, 2008b) through 2015 in order to provide product liability protection for the manufacturer, and it simultaneously purchased vast additional quantities of the old controversial anthrax vaccine for the SNS (FBO, 2004; FBO, 2005; FBO, 2007; FBO, 2008).[34]

C. SUMMARY OF THE CASE STUDY

For argument sake, future analysts could contend the less than satisfactory vaccine more appropriately served as the root cause, although this thesis reaffirms the central role of the DoD in those factors as a de facto manufacturer for the vaccine. As Figure 1 depicts, the root cause of continuous DoD involvement with the anthrax vaccine created an environment lacking apparent adherence to the normal scientific and regulatory processes. The process breakdowns appear to demonstrate causal connections to unapproved manufacturing changes and in turn the increased adverse reactions, testing problems, and ultimately increased regulatory oversight due to noncompliance. In addition, the resulting "failing" status of the DoD anthrax vaccine program possibly served as the primary stated motive according to the FBI and precipitated the direct cause, the anthrax letter attack emergency occurrence perpetrated by the frustrated Army

[34] Since the anthrax letter attacks almost $57 billion (Clark, 2009) has been allocated for biodefense, with over $1.2 billion spent on anthrax vaccine procurement (FBO, 2004; FBO, 2005; FBO, 2007; FBO, 2008).

scientist. The subsequent causal chain of problematic events found FDA oversight potentially curtailed or expedited with the validation of the vaccine's previously noncompliant manufacturing process in January 2002 and the 20-year overdue finalization of the vaccine vaccine's license in 2005. Prospective relaxation of regulatory controls allowed the DoD anthrax vaccine program to get back on track. Approvals also allowed for significant expansions in procurement by the DHS and DHHS for the SNS.

The preceding case study timeline demonstrates that many government officials yielded to, or collaborated in, the identified contributing causes and causal events. In comparison, some courts and the GAO resisted acquiescing to the inertia to disregard the known problems inherent with the vaccine. As well, the FBI's eventual illumination of the anthrax attacker's motive highlighted an opportunity to resurvey the problematic events accurately. The timeline reveals the motive of anthrax letter attacks, to revive the "failing" anthrax vaccine program, synchronized with institutional DoD efforts to save the program. The FDA joined the resumption effort after the problematic letter attack event, thereby joining the root, contributing, and direct causes, while facilitating the subsequent problematic events related to failed oversight.

The present thesis reminds readers of the DoD and FDA official positions in the years preceding the DoD's troubled employment of the vaccine and the letter attacks. Both entities critically evaluated the vaccine or invalidated its use. This analysis contends that the emergency occurrence itself potentially provides insufficient weight to overcome the earlier deficiencies. Moreover, disturbingly missing from the case study timeline is an intellectually honest attempt after the letter attack emergency occurrence to make the connection to the anthrax vaccine, something it took the FBI almost seven years to report. Equally alarming, the failure of the U.S. government to analyze the causal chain and problematic events after the FBI revelations in August of 2008 warrants future executive, legislative, and judicial level review. Instead, to date the government has dramatically increased anthrax vaccine purchases and declared an "anthrax emergency" to provide product liability protection for the manufacturer in actions certain to generate critical review in the years to come.

The foregoing analysis illustrates how continuous DoD involvement with the anthrax vaccine evolved. The DoD's contributions to violations of FDA law progressed from participating in illegally changing the vaccine to violating soldiers' health rights with an experimental product based on its known investigational status. Illegally employing an immunization that lacked a finalized FDA license then degenerated into the exceedingly more egregious crimes of the letter attacks by a lone, rogue actor in an effort to successfully save and expand the vaccine program. The next chapter of this thesis offers a program evaluation to further explore the quantitative, qualitative, and summative facets of the DoD anthrax vaccine experience, as well as a formative review to analyze the vaccine's current state. A subsequent gap analysis chapter presents plausible explanations for the problematic events, violations of the law, and breaches of normal governmental conduct outlined in this chapter. Chapter VI, Recommendations, offers the final steps of the case study with suggested future courses of action and corrective measures. The DHS may find the corrective measures fundamentally necessary in order to reinstitute oversight in the realm of bioterrorism countermeasure development and procurement for the SNS.

IV. PROGRAM EVALUATION

The program evaluation attempts to summarize quantitatively measurable factors such as the safety and efficacy of the anthrax vaccine, as well as technological aspects and alternatives. Qualitative analysis follows in order to review regulatory mechanisms designed to ensure the quality of biologic products, as well as to evaluate intelligence issues related to the threat. Summative breakdowns include historical doctrinal issues, comparative government approaches to biodefense policy, and an examination of biosecurity matters. Finally, a formative approach offers a glimpse of the current state and future directions for the anthrax vaccine in light of executive, judicial, and legislative review mechanisms. The entire program evaluation provides process tracing to compare the "theory of action," or original plan for success behind military and civilian anthrax vaccine programs, as opposed to the thesis's retrospective analysis of the realities encountered.

A. QUANTITATIVE ANALYSIS

The quantitative portion of the program evaluation includes the quantifiable issues related to the anthrax vaccine. We begin by discussing historic safety assessments, followed by efficacy evaluations, and finally we analyze the current anthrax vaccine as compared to alternative technologies.

1. Safety

Prior to DoD's anthrax vaccine immunization program, the immunization "was rarely used," considered "investigational," and deemed as "a potential cause for undiagnosed illnesses in Persian Gulf military personnel" (United States Senate, 1994, p. 35). A later congressional report found the DoD mandatory inoculation program "heavy handed," suffering from "one-sided informational materials," and determined this "only fuel suspicions the program understates adverse reaction risks in order to magnify the relative, admittedly marginal, benefits of the vaccine." The report concluded the vaccine status as "experimental" (HR 106-556, 2000, pp. 2, 4). Other government and U.S. Army scientists critically evaluated the vaccine writing, "The current vaccine

against anthrax is unsatisfactory for several reasons," including highlighting the fact that the "degree of purity is unknown." They detailed that the "undefined nature of the vaccine and the presence of constituents that may be undesirable may account for the level of reactogenicity observed" (Brachman & Friedlander, 1994; Brachman & Friedlander, 1998, p. 636).

Additional oversight reports cited Pentagon studies acknowledging that up to 35% of soldiers had adverse reactions to the anthrax vaccine, and that 6% of recipients reported serious complications after vaccination (CRS, 2007, pp. 12–14). The military studies caused authorities to raise the previously low adverse reaction rates, changing warnings listed on the officially approved product labeling (FDA, 2002a, p. 6). The courts also noted that the "product insert, which originally stated that the adverse reaction rate to the vaccine was 0.2 percent, was recently revised to reflect an adverse reaction rate between 5.0 percent and 35.0 percent (*Doe v. Rumsfeld*, 2003, p. 7). Earlier the GAO had found, "The systemic reaction rate reported through the survey represents a level more than a hundred times higher than the 0.2 percent published in the product insert." The GAO commented, "We were unable to determine why the AVIP reaction rates so exceeded the product insert rates for the vaccine as approved in 1970" (GAO, 2002a, p. 5). Despite the changes to the product label, due to the higher adverse reaction rates, the military continued to insist on the safety of the vaccine, while the GAO persistently disclosed that "a significantly large number of vaccine recipients reported experiencing adverse events" (GAO, 2002a, p. 23). Government oversight reports confirmed that the long-term safety of the vaccine remained undetermined, while raising questions about ingredient alterations and problems with human efficacy testing of the vaccine (GAO-NSIAD, 1999a, pp. 2–3). Recent Department of Veterans Affairs Research Advisory Committee on Gulf War Veterans' Illnesses scientific findings and recommendations validated concerns that "studies have indicated that the current anthrax vaccine is associated with high rates of acute adverse reactions" (DVA-RACGWVI, 2008, p. 125). Though the report ostensibly dismissed anthrax vaccine as a possible cause of veterans' illnesses, the study acknowledged the need for further research to "analyze associations between Gulf War illness and individual vaccines," and to evaluate "diagnosed diseases

in personnel known to have received the anthrax vaccine" (DVA-RACGWVI, 2008, p. 127). Other esteemed medical professionals, such as Dr. Vinh Cam, who served on the Presidential Special Oversight Board for DoD Investigations of Gulf War Chemical and Biological Incidents, objected to that board's conclusion. The doctor provided dissenting remarks to the panel due to the fact that she believed that the committee had manufactured a stress theory to dismiss Gulf War illness (Cam, 2000). Ross Perot testified to Congress with the same concerns about the "stress team" and a concerted government effort to dismiss the maladies associated with the first Persian Gulf War with diverting allegations related to "stress theories" (HR 107–137, 2002).

An early IOM report corroborated the need for more data, stating, "There is a paucity of published peer-reviewed literature on the safety of the anthrax vaccine" (IOM, 2002, p. 259). A later IOM report included additional findings that the "current anthrax vaccine is difficult to standardize, is incompletely characterized, and is relatively reactogenic [reactive]." The Institute acknowledged the "long and challenging" dose regimen, and determined a "new vaccine, developed according to more modern principles of vaccinology, is urgently needed" (IOM, 2002, pp. 200, 208). The conclusions comport with pre-2001 cautions from a former Commander of the U.S. Army Medical Research and Development Command at Fort Detrick concerning multiple doses and purification issues, which "argue strongly against procuring large amounts for civilian use" (Russell, 1999, p. 643). This concept of "multiple inoculations" presenting the "difficulties of implementing an anthrax vaccination program" stands as a constant theme from the earliest evaluations of the vaccine. These conclusions repeatedly led to the call for an "improved vaccine" which would "prove more potent," and therefore would call for "a less strenuous immunization schedule" (Brachman et al., 1962, p. 643).

Independent civilian medical and scientific community assessments consistently conflicted as well with the continuous DoD position that the vaccine was "safe" after the department began mass mandatory inoculations in 1998 (Cohen, 1998b; DoD, 2009b). Reports of resulting problems included gastrointestinal adverse reactions (Geier & Geier, 2004, p. 762), joint problems (Geier & Geier, 2002, p. 217), lymphocytic vasculitis issues (Muniz, 2003, p. 271), and potential birth defects in infants of females vaccinated during

pregnancy (Ryan et al., 2008, p. 434). Other researchers specifically noted a "significant association" for U.S. veterans from the first Persian Gulf War subjected to anthrax vaccine and declines in health (Schumm et al., 2002; Schumm, 2007, p. 649). Another safety issue involved a rash of hypersensitivity pneumonitis cases following anthrax vaccination (Oransky, 2003; Timmer et al., 2002, p. 543).

Beyond the historic military assessments, legislative critiques, and oversight conclusions, military members spoke out despite the "politically sensitive" nature of deviating from the mantra of vaccine safety. A military health care advocate from Dover Air Force Base in Delaware specifically reported a swath of adverse reactions (Rovet, 1999). The FDA documented several of the severe adverse reaction cases as a part of the license review in 2005 (Levine, 2005). Meeting transcripts related to those illnesses found a DoD physician addressing this particular "pocket" of sickness at the First Annual Department of Defense Conference for Biological Warfare Defense Immunizations. The doctor confirmed that the Dover Air Force Base cohort attributed their illnesses to the anthrax vaccine. The doctor discussed the difficultly in assessing the safety impact of the vaccine since most of the aircrew had not "gone in to see anybody because they are afraid of being grounded." Regarding the illnesses, the doctor captured the propensity for negative attribution bias by military physicians saying, "One of the docs I talked to said it couldn't be anthrax." The doctor commented on the difficulty of making such assumptions and concluded, "There are things that as I get older, as an immunologist, I am humbled ever more about the things we don't understand … I think we cannot make a presumption; we should just report and then the cards fall where they may" (Engler, 1999, pp. 15–16).

Clearly, questions over the safety of the anthrax vaccine still exist. The government's most prominent IOM appraisal of the vaccine upholds it merely as "reasonably safe," but with an important quantifying "caveat that the studies reviewed were carried out in populations of healthy adults only" (IOM, 2002). Unfortunately, use of the vaccine through the SNS would not enjoy distribution to only a strictly healthy adult population. Overall, the tepid "reasonably safe" endorsement does not appear to

match up to the DoD script touting the vaccination as a "very safe force protection measure" and the initiative as an "extremely successful program" (DoD, 1999a).

2. Efficacy

The scientific history on efficacy contravenes the DoD assertion that an "anthrax attack is fatal if you are not inoculated" (HR, Committee on Armed Services, 1999, p. 22). Therefore, since this contention is not actually true, a policy predicated on the "unequivocal" need to "take these steps," the mass inoculation of the armed forces, warrants review at a minimum (HR, Committee on Armed Services, 1999, p. 43). Additionally, the earliest assessments of the current vaccine documented significant survival rates without vaccination, even due to inhalation anthrax (Albrink & Goodlow, 1959; Albrink & Goodlow, 1960; Brachman et al., 1966). While the statistical analysis of the data from the original clinical trial indicates vaccine efficacy in protecting against cutaneous anthrax infections, "when inhalation anthrax is considered, the limited experience with this form of the disease makes the data less significant in showing effectiveness of the vaccine" (Brachman et al., 1962, p. 642). As a result, the first FDA proposed rule noted the "efficacy against inhalation anthrax is not well documented," and that "no meaningful assessment of its value against inhalation anthrax is possible due to its low incidence" (FDA, 1985, pp. 51058–59). Each of these facts casts doubt on the repeated imperatives by officials who promoted the vaccine.

Legislative inquiry appeared to uphold this conclusion. A Senate Report analyzed post–Desert Storm use of the vaccine concluding, "The vaccine's effectiveness against inhaled anthrax is unknown," and that the vaccine was "considered investigational when used as a protection against biological warfare." The committee added a concern that the vaccine's "safety, particularly when given to thousands of soldiers in conjunction with other vaccines, is not well established." It concluded, "Anthrax vaccine should continue to be considered as a potential cause for undiagnosed illnesses in Persian Gulf military personnel" (United States Senate, 1994, p. 35). The DoD JPOBD also recognized the anthrax vaccine as "not licensed for a biological defense indication" based on the fact that efficacy remained unproven (see Appendix 3) (DoD-JPOBD, 1997, p. 5.5). The DoD

scientist suspected of the anthrax attacks, Dr. Ivins, confirmed for a memo by fellow U.S. Army scientist Colonel Arthur Friedlander that "no data on MDPH-PA efficacy in humans" existed, and he published the same conclusions. Dr. Ivins chronicled the vaccine's "drawbacks, including the need for frequent boosters, the apparent inability to protect adequately against certain strains of *B. anthracis*, and occasional local reactogenicity" (Ivins, 1988; Ivins, 1992; Ivins et al., 1988). Other military medical professionals repeated their official assessment that the "actual efficacy for the prevention of inhalation anthrax [was] not known but presumed, based on existing data for prevention of disease (e.g., primate data)" (Engler, 1999, p. 1 & slide). Early scientists involved with the original clinical trials added concerns about effectiveness issues dependent on strains encountered. Dr. Brachman found, "There is also evidence in experimental animals that the vaccine may be less effective against some strains of anthrax" (Brachman & Friedlander, 1998, p. 636). The GAO's multiple studies of the vaccine also uniformly reported problems with DoD immunizations, finding scientists could "not provide information to determine its effectiveness against inhalation anthrax" except in animals, but that the "level of protection varied for different species and the results cannot be extrapolated to humans" (GAO-NSIAD, 1999d, p. 2). As a result, Army scientists' early appraisals of the vaccine deemed it as an "experimental limited use vaccine" (Takafuji & Russell, 1990).

Drs. Brachman, Friedlander, and Grabenstein updated their review of the current immunization used by the military and stockpiled in the SNS in the 2008 edition of *Vaccines*. The scientists acknowledge the current anthrax vaccine license is based on a "less potent" but "similar" vaccine. They added that the "strain differed slightly," as did the manufacturing process. The vaccine used as a basis for licensure exhibited no implicit proof of efficacy for inhaled anthrax. The scientists explained, "No isolated assessment of the effectiveness of the vaccine against inhalational anthrax could be made because there were too few cases, although the only inhalational cases observed occurred in non-vaccinated individuals" (Brachman et al., 2008, p. 119). In maintaining the vaccine's proof of efficacy through "various animal models and routes of challenge," they disclosed that no clinical field trial had occurred for the current licensed product. Instead,

the researchers cited a "comprehensive, peer-reviewed evaluation by the National Academy of Sciences" [IOM], as well as FDA affirmations of the current vaccine's efficacy "regardless of route of exposure." According to the IOM:

> The committee finds that the available evidence from studies with humans and animals, coupled with reasonable assumptions of analogy, shows that AVA [anthrax vaccine] as licensed is an effective vaccine for the protection of humans against anthrax, including inhalation anthrax, caused by all known or plausible engineered strains of B. anthracis (Brachman et al., 2008).

It remains interesting to note that the Brachman study does not explicitly contend either efficacy for inhalation anthrax, or efficacy against all strains but instead appears to rely on the FDA's and the IOM's findings. Reasonably, these assertions emerge as a leap for the scientists when their previous scientific assessments contradicted FDA and IOM judgments. In an early edition of *Vaccines,* Drs. Brachman and Friedlander asserted, based on "evidence in experimental animals," that the vaccine "may be less effective against some strains of anthrax" (Brachman & Friedlander, 1994). In another publication they found that "when inhalation anthrax is considered, the limited experience with this form of the disease makes the data less significant in showing effectiveness of the vaccine" (Brachman et al., 1962, p. 642). In the 1998 edition of *Vaccines,* they described the "unsatisfactory" nature of the current product due to its unknown purity, undefined nature, undesirable constituents, and efficacy issues (Brachman & Friedlander, 1994; Brachman & Friedlander, 1998, pp. 629–636). For the unobserving reader to realize Dr. Brachman's contention of efficacy cites FDA and IOM, and that those entities in turn previously cited Brachman's study, seems less than seriously scientific and methodical taken as a whole. The scientists provided the caveat about the "differences between the U.S. licensed vaccine and the PA-based vaccine used in the Brachman et al study." They also contended that the lack of a field study and differences were "minor from a regulatory perspective" (Brachman et al., 2008, p. 119). To the contrary, this thesis contends that the circular attribution of efficacy for inhalation and against all strains based on FDA and IOM pronouncements warrants attention.

An overall review of efficacy points out that a bioterrorism scenario most likely necessitates the employment of the vaccine after an event. Unlike with armed forces personnel a pre-exposure vaccination is not practical. Therefore, the fact that the "safety and efficacy of BioThrax® in a post-exposure setting has not been established" also emerges as an important factor for first responders contemplating use of the vaccine from the SNS (FDA, 2002a, p. 3).[35]

3. Technology

A logical aspect of the program evaluation involves an analysis of the alternative technological solutions available to decision makers in their effort to create robust capabilities in the biological response arena. The analysis begins with considering the directive driving the need to procure protections and the technological problems posed by anthrax in the SNS (CDC, n.d.). Use of the vaccine falls under the "preparedness" pillar of Homeland Security Presidential Directive 8, and pertains to the "equipment" to "respond to, and recover from major events" (POTUS, 2003c). Based on the foregoing critiques of anthrax vaccine as a valid biological prophylaxis alternative, more modern strategies and alternate technologies may equate to more coherent, credible, and efficient solutions for the preparedness pillar.

Behind the scenes of DoD laboratories, top scientists knew the current anthrax suffered from seemingly irrevocable problems. The DoD documented the outdated technology as "not ideal." The DoD wrote about the fact that the vaccine was "developed in the 1950s and 1960s" prior to "advances in biotechnology and genetic engineering," which could now "enable improvements in the vaccine that allow fewer doses or use of highly purified protective antigen" (HR 106-556, 2000, p. 48). To date an improved vaccine remains elusively on the drawing boards, and therefore the government stockpiles the established vaccine, BioThrax® (CDC, 2000, p. 5). Invented and patented by the U.S. Army in 1965 (Wright & Milton, 1965, p. 1), problems were foreseen years ago and led to congressional calls for the DoD to "accelerate research and testing on a second-generation, recombinant anthrax vaccine" (HR 106-556, 2000, p. 47). The DoD

[35] The 2008 package insert reiterates a lack of approval in a post-exposure setting (FDA, 2008b, p. 1).

itself acknowledged the need in the department's 1985 proposal soliciting an improved product. The DoD proposal expressed the "operational requirement to develop a safe and effective product which will protect US troops against exposure from virulent strains of *Bacillus anthracis*." The DoD confirmed, "There is no vaccine in current use which will safely and effectively protect military personnel against exposure to this hazardous bacterial agent." The DoD acknowledged that the vaccine was "highly reactogenic, requires multiple boosters to maintain immunity and may not be protective against all strains of anthrax *bacillus*" (see Appendix 2) (DoD, 1985, p. 4). Technological barriers aside, the concerns about "Gulf War Syndrome and Anthrax Vaccine" as "political problems" troubled leaders in the top offices of government (see Appendix 9) (Rove, 2001). The DoD reviews recommended minimizing use of the old anthrax vaccine and procurement of technological alternatives, including "bio-detectors and stockpiles of antibiotics to augment force protection in the absence of an anthrax vaccine" (see Appendix 10) (Chu & Aldridge, 2001).

Despite long-term recognition of technological problems, and the calls for a new vaccine by top government officials, others held tightly to the old vaccine as "the centerpiece of our defense against the most likely biological threat" (Shelton, 2001). Such proclamations by non-scientists conflicted with the fact that use of the vaccine at the time was effectively halted due to an FDA-imposed Notice of Intent to Revoke the manufacturer's license based on manufacturing deviations (see Appendix 6) (FDA, 1997). In the end, the anthrax letter attacks successfully rekindled demand for the technologically questionable vaccine and resulted in an expedited validation of the previously deviant manufacturing process. The FBI revealed that the motive for the anthrax letter attacks related to anthrax vaccine potency testing problems, and the desire to create "a scenario where people all of a sudden realize the need to have this vaccine" in order to revive the "failing" program (see Appendix 11) (FBI, 2008, pp. 12–15). Of course, the attacks, the subsequent approval of the vaccine, the restoration of the DoD program and the expansion to the SNS by means of DHS endorsement did not resolve the technological troubles. These pivotal events highlight the problems confronted while attempting to pursue a coherent procurement policy for biodefense. Although the

development of a new vaccine continued, the DoD capitalized on the "scenario" to justify continued use of the anthrax vaccine stating, "The anthrax attacks in October 2001 illustrated the risk of an unprotected population in an environment contaminated with a biological warfare agent" (Keys & Taylor, 2005). The DoD partially justified resumption of the suspended anthrax vaccine immunization program by referencing the cases of anthrax that "resulted from attacks with anthrax spores" (DoD, 2009a). The momentum for a return to use of the old known inadequate technology flourished, with both the DoD and DHHS procuring over $1.2 billion in the years that followed (FBO, 2004; FBO, 2005; FBO, 2007; FBO, 2008).

Notwithstanding the historical realities, technology offers more alternatives than the original anthrax vaccine. More financially efficient options range from not reacting to what might be a minimal threat, based on the technological limitations of an adversary, to investing in other layers of defense preparedness and response. Biodetection technologies exist, as do alternative methods of protection. Pointing out the deficiencies in considering the current anthrax vaccine as a "centerpiece" for biodefense presents an opportunity to highlight potential avenues to create savings for the U.S. taxpayer when compared to the ten-fold increases in price for the countermeasure over the past decade (GAO-NSIAD, 2000a, p. 3). The old anthrax vaccine technology price increased contrasted with the GAO's reported expectation that the price would decrease as production increased (GAO T-NSIAD, 1999b, p. 4). The GAO also identified additional cost-efficiency issues related to anthrax vaccine's use in the SNS, including inevitable expiration of the product that would waste "over $100 million per year." To address this problem the GAO recommended a single inventory system, which both the DoD and DHHS adopted. The GAO also questioned the government's intention to use expired vaccine because this practice violated FDA rules and would "undermine public confidence since the vaccine's potency could not be guaranteed" (GAO, 2007c, pp. 2, 5).

In the face of the technological hurdles on the part of the U.S. with the old anthrax vaccine, and in fielding a new vaccine, an important awareness of adversary technological limitations warrants discussion. The GAO questioned whether terrorist entities could "overcome the major technological and operational challenges to

effectively and successfully weaponize and deliver a biological warfare agent to cause mass casualties" (GAO, 2002b, p. 3). A practical example from a United Nations Monitoring, Verification, and Inspection Commission (UNMOVIC) report confirmed technological barriers prohibited Iraq from successfully producing a "dry agent" for distribution in anthrax weapons (United Nations, 2007, p. 1156). A recent Weapons of Mass Destruction (WMD) committee report, sponsored by Congress, continued to generically deem the threat significant due to the "biotechnology revolution … raising the specter of a modern day plague, spawned from a back room or garage anywhere in the world (Weapons of Mass Destruction Commission [WMD], 2005, p. 502). Countering this scenario, a scientist, Dr. Milton Leitenberg, described the reality of "unsuccessful attempts to procure, produce and disperse anthrax" by the Aum Shinrikyo group. He added that al-Qaida was also "unsuccessful" in their objective to "obtain anthrax and to prepare a facility in which to do microbiological work." Dr. Leitenberg reminds us that the 2001 "Amerithrax" letter attacks remain the only successful "distribution of a high-quality dry-powder preparation." Yet, as the FBI determined, this single data point originated from inside the U.S. biodefense community (Leitenberg, 2005, p. 22). Dr. Leitenberg also placed the threat in perspective with a statement by terrorist Al-Zawahiri about how Defense Secretary William Cohen "drew our attention" in his 1997 television warning (DoD, 1997a) with a five-pound bag of sugar to simulate anthrax. The photo in Figure 3 captures Secretary Cohen's television performance. In contrast, Dr. Leitenberg described the threat as "greatly exaggerated" (Leitenberg, 2005, p. 35). The GAO remains one of the few watchdog agencies to quantify the "attendant publicity" lavished on the threat by DoD leaders (GAO, 2002b, p. 3). Ultimately, the GAO leveraged the DoD's estimates to place the debate in perspective. The GAO wrote, "In the context of the conventional battlefield, the nature and magnitude of the military BW threat has not changed materially since 1990 in terms of the number of countries suspected of developing BW capability, the types of BW agents they possess, or their ability to weaponize and deliver BW agents" (GAO, 2002a, p. 3).

In Figure 3, Defense Secretary William Cohen holds a five-pound bag of sugar to show the amount of the biological weapon anthrax that could destroy half the population of Washington, D.C.

Figure 3. Defense Secretary Cohen and the Five-Pound Bag of Sugar[36]

Conservatively conceding to the prospect of the threat, the WMD Commission report alluded to moving away from a "reactive biological weapons posture," while funding other strategies and alternative technologies, such as those recommended by DoD undersecretaries in 2001 (WMD, 2005, p. 508). Proactive strategies include fielding the next-generation recombinant Protective Antigen (rPA) vaccine. The IOM found the old anthrax vaccine was "far from optimal," and that a "new vaccine, developed according to more modern principles of vaccinology, is urgently needed." The IOM repeated previous findings that the current "anthrax vaccine is difficult to standardize, is incompletely characterized, and is relatively reactogenic … and the dose schedule is long and challenging," and determined that an "anthrax vaccine free of these drawbacks is needed, and such improvements are feasible" (IOM, 2002, pp. 207, 208). In an attempt to

[36] Secretary of Defense Cohen later described this event as "crowning moment"—"We have chemical and biological weapons that can be used as terrorist devices. If you may recall, one of my crowning moments on television was to hold up a five-pound bag of sugar, and say, 'Imagine that this is filled not with Domino's sugar but with Anthrax, and properly released, it could in fact destroy a city the size of Washington, D.C., and eliminate about 80 percent of its population, with a small five-pound bag.' And there are tons of this available in many parts of the world" (Cohen, 2000).

overcome the current vaccine's limits, scientists such as Drs. Brachman, Friedlander and Grabenstein all acknowledged the "ideal anthrax vaccine would be more completely defined and less reactogenic, and able to produce long-lasting immunity within 30 days" (Brachman et al., 2008, p. 123). As well, Nareen Abboud, Ph.D. from Albert Einstein College of Medicine, recently revealed the identification of protein fragments that might translate into new technologies for an anthrax vaccine causing "fewer side effects than the current vaccine." The Albert Einstein College research attempts to overcome the "significant limitations" of the present vaccine caused by the "extraneous protein material that triggers the adverse reactions" (Abboud, 2009).The rPA vaccine is expected to move in this positive direction by resolving these problems. Legislative reports concurred with the advantages that a new product offers in terms of a "more consistently characterized … PA content" versus the old anthrax vaccine. The superior consistency equates to a "more uniform level of protection" (HR 106-556, 2000, p. 48). According to research by the Congressional Research Service, DHHS officials believe the rPA vaccine "will address many of the shortcomings of … anthrax vaccine adsorbed [AVA]." According to the CRS, the past problems involved federal court injunctions that "ordered the DoD to stop mandatory vaccinations pending FDA review." The CRS also documented that "AVA vaccine cost per dose is twice the cost per dose of rPA." The CRS highlighted another alternative, ABthrax, "an antibody-based treatment that works in a manner similar to anti-venom treatments for snake bites." Still another alternative therapy includes the Anthrax Immune Globulin, which involves collecting and using the blood of recipients of the anthrax vaccine as an "antibody based therapeutic." The high costs associated with both ABthrax and an Immune Globulin alternative led the CRS to assess their value most practically for post-exposure treatments (CRS, 2007, p. 12–14). An additional antibody-based product, Valortim, uses a "fully monoclonal antibody" and appears to be safe and "well tolerated." The advantages earned the product "fast-track and orphan drug designations from the U.S. Food and Drug Administration" (OneMedPlace, 2009). Costs allocated for buying alternative technologies all at once is prohibitive. Fortunately, at least in regards to natural or weaponized anthrax, the CDC confirms that antibiotics, such as penicillin, ciprofloxacin, and doxycycline, remain the

preferred proven "first line of defense" for treatment of inhaled, cutaneous, and gastrointestinal anthrax in lieu of the old anthrax vaccine (CDC, 2001; CDC, 2002; CDC, 2000; HR, Committee on Homeland Security, Subcommittee on Emerging Threats, Cybersecurity and Science and Technology (HR 110-23), 2007, p. 48–50).

Other non-reactive strategies include biological detection systems. If prevention fails, or policies change, detection systems may warn of a biological threat, as well as promote accelerated treatment. One means of identifying pathogens before citizens or soldiers become ill utilizes antibodies to identify pathogens (Frauenfelder, 2003). Others employ "strips" which react to specific biotoxins, including anthrax (Alexeter Technologies, n.d.). Micro electro-mechanical systems, or "MEMS," present another option to detect biohazards through nanotechnologies (CombiMatrix, n.d.) as would be the case with the Joint Biological Point Detection System (JBPDS) (General Dynamics, n.d.) and the Chemical Biological Mass Spectrometer (CBMS) (DOE, n.d.). The U.S. Postal Service also purchased the Biohazard Detection System (BDS) (National Association of Letter Carriers [NALC], 2008) for mail screening. JBPDS, CBMS, and BDS all employ varying techniques from spectral analysis to DNA detection technologies. Overall, biodetection processes involve tradeoffs between "sensitivity, specificity and speed of detection" (Mason, 2005). Experts maintain sensitivity and specificity emerge as inversely proportional, and speed reigns paramount in any response and treatment contingency. Future procurement decisions must prudently weigh these factors in addition to their costs.

A recent report by the congressional Commission on the Prevention of Weapons of Mass Destruction Proliferation and Terrorism recommended "oral antibiotics" for the anthrax threat, as well as "new classes of antibiotics" against "genetically modified" anthrax. Additionally, the report called upon the next president to "enhance the nation's capabilities for rapid response to prevent biological attacks from inflicting mass casualties," and cautioned us to the reality that biological activities, equipment, and technology can be used for good as well as harm." The commission sagely reminded us that the "globalization of the life sciences and technology has created new risks of misuse by states and terrorists," but it significantly omitted any reference to the old anthrax

vaccine in its report (Graham & Talent, 2008, pp. xviii, 32, 33, 109). Fresh oversight reports such as these, and the preceding review of the current anthrax vaccine option, balanced against alternative technologies, provides data points for consideration when weighing the future composition of the SNS. Future cost-benefit analysis by the DHS may support the elimination, or halt the replenishment, of the old anthrax vaccine technology from the SNS based on the significant problems documented in the above analysis. The vaccine's documented "unsatisfactory" status and lengthy protocol, weighed against the proven efficacy of promptly applied antibiotics, supports at a minimum reviewing the nation's preparedness approach.

The United States possesses the resources to harness top-tier technologies, as the DoD proposed as early as 1985, and remains prepared to address the threat through the efficacy of antibiotics in the interim. Resorting to stockpiling of the old anthrax vaccine as a means to "appear" prepared may prove unnecessary and wasteful, while violating the confidence of the American people.

B. QUALITATIVE ANALYSIS

The qualitative portion of the program evaluation reviews more detailed aspects of the vaccine's regulatory history than covered previously. The qualitative aspect of program evaluation also reviews intelligence estimates and the vaccine's ability to address the threat of *bacillus anthracis*.

1. Regulatory

Evaluating the anthrax vaccine requires an analysis of the overarching regulatory scheme. Evaluation of the quality of a vaccine, related to purity, potency, sterility, and stability, falls under the auspices of the FDA. The U.S. experience with drug regulation began with the Food and Drugs Act in 1906. The revised Federal Food, Drug, and Cosmetic Act of 1938 (FDCA) responded to the disastrous experience of an elixir that killed over 100 citizens. The 1938 legislation effectively added proof of safety as a requirement for new drugs. The next major milestone involved the Harris-Kefauver amendments to the FDCA in 1962. A disaster in Europe motivated the law because of thalidomide that caused birth defects when used for a previously unapproved purpose.

This legislation marked the requirement for manufacturers to demonstrate drug effectiveness (FDA, 1962). As previously discussed, the safety and efficacy of vaccines, or biologics, also fell under FDA control by 1972. Revamping of the regulatory scheme clarified FDA's mission to "protect the public health as it may be impaired by drugs."[37] Simultaneously 21 C.F.R. § 601.25 codified the procedures for review of drug safety, effectiveness, and labeling. As a result, FDA mandates required that the agency review and finalize the licenses of existing vaccines. The 1970 licensure of anthrax vaccine compelled the FDA to certify the anthrax vaccine license under its own letterhead. Although the FDA proposed such a license in 1985 (FDA, 1985), the agency did not effectively finalize the license order until 2005 and only in response to court orders to do so (FDA, 2005b). Following this pivotal early 1970s transition in vaccine regulation and FDA history, the anthrax inoculation languished in a questionable nonfinalized state. This oversight of oversight exemplifies the vaccine's procedural conundrums.

The historic involvement of the DoD with the anthrax vaccine further complicated the regulatory equation. The involvement began with the DoD's patenting of the vaccine in 1965 (Wright & Milton, 1965). The product's clinical trial for the DoD by Dr. Brachman occurred from 1954 to 1959. The resulting inhalation anthrax "epidemic" in 1957 killed four workers at the Arms Mill in Manchester, New Hampshire (Brachman et al., 1966; Brachman et al., 1960; Plotkin, 1960). A state entity in Michigan then applied for a license in 1966 for the U.S. Army. That licensing data did not include Brachman clinical trial data but instead listed a Talladega, Alabama, test meant to justify proof of efficacy. On February 6, 1969, regulators questioned the data, writing, "The lack of cases of anthrax in an uncontrolled population of approximately 600 persons in the Talladega mill can hardly be accepted as scientific evidence for efficacy of the vaccine" (see Appendix 1) (Pittman, 1969a). The CDC challenged the license application, stating, "There have been no controlled evaluation studies with the Michigan anthrax product as was done by Dr. Phillip Brachman" (see Appendix 1) (Kokko, 1969, p. 2). The previously responsible regulatory entity, the National Institutes of Health (NIH), licensed

[37] 21 C.F.R. § 601.25 was codified in 37 Federal Register 16679 and cited in the 2004 ruling on summary judgment and permanent injunction that required the FDA to finalize the anthrax vaccine license (*Doe v. Rumsfeld*, 2004).

the vaccine in 1970, but explicitly noted the lack of resolution on the efficacy data issue. Government public health officers specifically noted that "clinical data establishing efficacy of the product had not been submitted," but granted the license pending submission of "the results of an adequately controlled clinical investigation that establishes efficacy" (see Appendix 1) (Pittman, 1969a; Pittman, 1969b).

Many years passed before the FDA proposed a ruling to finalize the anthrax vaccine's license in 1985. That proposed license rule cited efficacy inadequacies with respect to inhalational anthrax effectiveness in particular. The proposed rule became a final order in the *Federal Register* twenty years later under court order (*Doe v. Rumsfeld*, 2004). A 2001 citizen petition filed under Title 21 precipitated the legal process for the belated 2005 licensure. The petition specifically identified that the "December 1985 proposal … had not been finalized" (FDA, 2005b, p. 75182). When the FDA did license the product, the agency added an indication for inhalation anthrax to the approval. The court had dissected the inconsistencies of the FDA's "contradicting" an advisory panel's earlier 1985 position regarding insufficient evidence of efficacy cited in the Brachman study absent a final license specifying route of exposure, cutaneous versus inhalation exposure (*Doe v. Rumsfeld*, 2003, p. 7). Once the FDA published this final ruling, the courts doubly deferred to FDA's "scientific judgment" on the reliability of the Brachman study to provide proof of efficacy for inhaled anthrax and with regard to the FDA's contention that it could prove the vaccine versions remained sufficiently similar despite multiple manufacturing changes (*Rempfer v. Sharfstein*, 2009). The "considerable deference" exponentially granted to the FDA meant that the agency successfully avoided answering questions about why the Brachman study had not been submitted in the 1960s to justify efficacy, or how the FDA resolved the vaccine's potency problems and "failing" status that preceded the anthrax letter attacks (*Rempfer v. Sharfstein*, 2009, pp. 13–14). The court granted the FDA similar deference on the issue of approving the potentially "adulterating" manufacturing changes ten years after the fact (21 U.S.C. §351, 1997). With respect to the question of whether or not the vaccine was "similar," after multiple alterations and without additional clinical trials, the FDA weighed in by granting the DoD status as a de facto manufacturer. The FDA's verdict that "DoD's continuous

involvement" and the department's "intimate knowledge of … all of these versions of the anthrax vaccine" meant that the vaccine current product compared adequately to the "original DoD vaccine" (FDA, 2002b, p. 8).

Previously, the GAO had highlighted specific differences between vaccine versions, including changes in the "manufacturing process," the "strain," the quantity or "yield of the protective antigen," and finally the "ingredients used to make vaccine" (GAO-NSIAD, 1999a, p. 3). The GAO added to these known differences with a report titled "Anthrax Vaccine Changes to the Manufacturing Process" (GAO, 2001b, pp. 6–7). The manufacturer "did not notify FDA of several changes to the manufacturing process in the early 1990s, and no specific studies were done to confirm that vaccine quality was not affected." The GAO cited that "FDA inspections found several deficiencies, many of which were not corrected in a timely manner." The GAO revealed potential "potency" problems resulting from the unreported alterations. Moreover, according to DoD studies, the changes may have contributed to a "hundredfold increase in the protective antigen levels in lots produced after the filter change that year." The GAO reported, "DoD researchers, referencing the earlier study, hypothesized that the filter change altered the composition of the vaccine by increasing the level of protective antigen in the finished product" (GAO, 2001b, p. 5). The watchdog group quoted FDA rules requiring "any changes to the manufacturing that have the potential to affect the safety, purity, or potency of a biologic must be submitted and approved by CBER [Center for Biologics Evaluation and Research] prior to implementation" (GAO, 2001b, pp. 2, 4, fn. 9). Potentially unprecedented in regulatory history, the FDA approved the changes after the GAO reported them and over a decade after implementation. The GAO found that the "FDA reviewed and accepted the data and approved the filter changes in July 2001" (GAO, 2001b, p. 4). The IOM review of the anthrax vaccine explained that the "modifications were undertaken to incorporate more modern technology into the manufacturing process and to increase assurance of the consistency of the final product," but it passed on evaluating the propriety of the modifications or the regulatory process. The IOM concluded that the vaccine "remains a relatively crude vaccine by current standards" (IOM, 2002, p. 200).

Beyond the regulatory controversy over proper approvals, the FDA had previously served the manufacturer with notices of deviating from quality control standards (see Appendix 6) (FDA, 1997). In addition to the explicit notice of license revocation, the FDA's inspection reports noted the "manufacturing process for Anthrax Vaccine is not validated" in 1998 and 1999 (see Appendix 6) (FDA, 1998). The deviant status meant that FDA compliance policies supported nonapproval of contracts for anthrax vaccine. Technically, this policy also supported "disapproval of any pending drug marketing application," such as the request for approval for using the vaccine against inhalation anthrax (FDA, 1981). The regulatory problems appeared to weigh heavily on the mind of the U.S. Army scientist suspected of mailing the 2001 anthrax letters. E-mails released by the FBI revealed admissions that the vaccine "isn't passing the potency test." The scientist's e-mail stated, "If it doesn't pass … the program will come to a halt" (FBI, 2008). Eventually the anthrax letter attacks effectively reset the regulatory circuit breakers, because the anthrax vaccine manufacturing process received expedited approval soon after the crimes (FDA, 2002a). The government documented the bioterrorism architect's role in the problematic potency testing prior to the attacks and then rewarded him for sequentially resolving the potency problems (see Appendix 11) (FBI, 2008, p. 15). Despite the known and potentially unresolved pre-2001 problems, the letter attacks succeeded in reversing the suspected cancellation of the Defense Department's mandatory program due to the manufacturer's FDA noncompliance. In addition, by early 2002 the manufacturer had evidently overcome the earlier regulatory impediments. The vaccine's use resumed within DoD and significantly expanded with additional SNS stockpiling contracts.

The FDA continued to work with the manufacturer in recent years to surmount additional known deficiencies such as the cumbersome dosage requirement. The FDA reduced the approved doses to five over 18 months, and altered the accepted route of administration, in an attempt to minimize "adverse events." Though "routine immunization is not recommended," and the lengthy protocol seems incompatible with emergency response, the regulatory changes gained approval in late 2008 (FDA, 2008b). Additional license modifications, sanctioned in early 2009, extended the shelf life of

BioThrax® from three to four years, and garnered added revenues of approximately $30 million for the manufacturer due to existing contractual provisions covering prior deliveries to the SNS (Emergent BioSolutions [EBS], 2009). On the issue of shelf life and efficacy, e-mails released by the late U.S. Army scientist from Fort Detrick, Dr. Bruce E. Ivins, appeared to contradict FDA's extensions. Dr. Ivins's emails revealed potency data from animal tests that demonstrated significant survival rate decreases over time. Whereas anywhere from 11 to 15 of 16 guinea pigs survived with fresh vaccine in its first six months of shelf life, the survival rate when challenged with anthrax spores dropped to 8, or one-half, with one-year-old vaccine and 5, or one-third, with 2.5-year-old product. Dr. Ivins's data did not extrapolate out to four years to determine if the survival rates declined further (Ivins, 2000, p. 31). The FDA approval of shelf life extensions may have overlooked these scientific observations by Dr. Ivins. However, the FDA published three of Dr. Ivins's efficacy studies in the *Federal Register* for the new anthrax vaccine licensing vetted in 2005. The FDA cited Dr. Ivins's studies from animal models and Dr. Brachman's in humans to "support the conclusion that [anthrax vaccine] is effective (FDA, 2005b, p. 75183, fn. p. 75197). The conclusions conflicted with FDA's 1985 assessments precluding approval for inhalation anthrax based on Dr. Brachman's 1962 analysis that confirmed "too few cases to evaluate the vaccine's efficacy for the prevention of inhalational disease" (Brachman et al., 1962; FDA, 1985, p. 51058). The FDA scientific judgments relied on IOM findings that the studies, "coupled with reasonable assumptions of analogy" proved the vaccine worked against inhalational anthrax for "any known or plausible engineered strains" (IOM, 2002, p. 10). Reliance on the IOM as a regulatory arbiter appears unprecedented in FDA history, and "reasonable assumptions of analogy," appear to be nonexistent in the legal frameworks guiding FDA law.

Of note, Dr. Brachman, in subsequent literature evaluating the anthrax vaccine, never personally maintains vaccine efficaciousness against inhaled anthrax (Brachman et al., 2008). Though Brachman's original studies remain the basis for the FDA's 2005 basis of efficacy and licensure of the vaccine, the scientist verified his own professional assessment shortly after the anthrax letter attacks. Dr. Brachman wrote, "Although five

cases of inhalational anthrax occurred in one of the field trial mills …, the results were not statistically significant in view of the small number of events to address the efficacy of the vaccine in preventing inhalation anthrax" (Brachman, 2002, p. 984). Dr. Brachman and the other scientists almost exclusively involved with the vaccine's literary history attempt to differentiate the original experimental PA-based vaccine from the present vaccine (Brachman et al., 2008, p. 119). However, this contention appears to conflict with the FDA's assertion that the vaccine is "similar" to the original version to justify licensure (FDA, 2005b, p. 75184). This may provide perspective as to why the scientists do not assert that the current vaccine is efficacious against inhalation anthrax, instead deferring to the FDA's and the IOM's judgment on the matter. As previously noted, the FDA justifies its logic based on the FDA's comparability guidance (FDA, 1996). It asserts that the DoD was "involved in developing the three versions of the anthrax vaccine and had knowledge of the manufacturing processes of each version." They conclude, "DoD is thus similar to a manufacturer that made manufacturing changes to its product as contemplated by FDA's Comparability Guidance" (FDA, 2002b, p. 8). Notably, the changes occurred prior to the mid-1990s when FDA "contemplated" and published the comparability guidance (FDA, 1996). In addition, the FDA appears to leverage its regulatory discretion, selectively choosing which guidance the agency enforces. In contrast to allowing FDA comparability policy guidance to substantiate the vaccine's approval, even though these standards postdated the vaccine's manufacturing changes, the FDA disregarded enforcement of its own compliance policy guidance when addressing "the issuance of a *warning* letter or initiation of other regulatory action." According to that FDA guidance, such regulatory departures "must be accompanied by disapproval of any pending drug marketing application," and a "government contract for a product produced under the same deficiencies" must face disapproval (FDA, 1981). Yet in the case of the anthrax vaccine, the FDA maintains that compliance policy guidance "is not a regulation and thus does not legally bind FDA" (FDA, 2002b, p. 16).

Beyond the FDA's apparent qualitative regulatory shortcuts, the common theme of DoD involvement in these processes precipitated unapproved changes and "accelerated procurement actions," according to declassified documents. Those documents revealed

that DoD decisions related to the manufacturing alterations "were no longer 'medical' in origin; rather were political, social, and military/operational" (DoD, 1996).[38] Reasonably, although DoD involvement impacted the regulatory process by the FDA, that department's "operational" objectives should not today hamper due diligence on behalf of the DHS in reviewing SNS composition. Though the FDA worked with the DoD to overcome the regulatory hurdles, the DHS must consider the practical reality of using the same product during an emergency occurrence on American citizens. Such cautions for the DHS are particularly relevant since the FDA confirms, "routine immunization is not recommended," that a "patient's medical immunization history should be reviewed for possible vaccine sensitivities," and that the "law prohibits dispensing without a prescription." Based on these facts, and the lengthy dosage series, the lack of approval for use of the vaccine in a post-bioterrorism incident scenario through the SNS appears highly problematic (FDA, 2002a, pp. 3, 6, 7).

Overall, a thorough evaluation of the regulatory experience with anthrax vaccine undoubtedly assists the DHS as the department charts the future of the current use of anthrax vaccine in the SNS, as well as with the formulation of follow-on programs. Although much of the documented regulatory landscape falls in the past, the DHS needs to digest the background prior to employing the anthrax vaccine through the SNS in response to a bioterrorism emergency occurrence.

2. Intelligence and Threat Assessments

Reevaluation of DHS endorsement for anthrax vaccine inclusion in the SNS requires an evaluation of past and current threat assessments. This portion of the thesis outlines why historic threat estimates may not warrant continued reliance on BioThrax® use as a threat mitigation tool. Conflicting evidence pertaining to the vaccine's safety and efficacy covered previously in the thesis, coupled with the remote conceivability of a viable threat, supports reappraisal of the anthrax vaccine's feasibility as a sound countermeasure alternative. As well, the validity of using the vaccine after an attack

[38] See the reference materials for detailed document analysis in order to help explain the DoD intimate involvement in the first Persian Gulf War time frame and to better understand how military and operational imperatives potentially outflanked regulatory requirements and the law (DoD, 1996).

weighs importantly in this debate based on the inefficacy of an onerous five-dose regimen across 18 months. Scientists, such as Dr. Ivins and Dr. Friedlander from the U.S. Army Ft. Detrick laboratory, understood the current vaccine proved inadequate and unnecessary outside of a bioterrorism or biowarfare environment. The scientists affirmed the need for a new vaccine to address the remote threat of deliberately dispersed anthrax:

> The only reason to develop a new vaccine is to protect against disease arising as a result of the intentional release of B. anthracis spores by a bioterrorist or in warfare, because the incidence of human disease, particularly inhalational anthrax, is extraordinarily low (Schumm et al., 2009, p. 597, fn. 44).[39]

Therefore, while in agreement as to any anthrax vaccine's purpose, resurveying current policy requires recognition of previous known inadequacies of the old anthrax vaccine in addressing this threat. The DoD acknowledged problems by 1985 when outlining the department's "operational requirement to develop a safe and effective product which will protect US troops against exposure from virulent strains of *Bacillus anthracis*." The DoD confirmed it had "no vaccine in current use which will safely and effectively protect military personnel against exposure to this hazardous bacterial agent" (see Appendix 2) (DoD, 1985, p. 4). Fort Detrick scientists also acknowledged the product as an "experimental limited use vaccine" (Takafuji & Russell, 1990, p. 156). Congressional reports corroborated "investigational" status with concerns about the vaccine's connections as "a potential cause for undiagnosed illnesses in Persian Gulf military personnel" (United States Senate, 1994, p. 35). Others determined the "current anthrax vaccine for force protection against biological warfare should be considered experimental" (HR 106-556, 2000, p. 4, 52). Therefore, the fact remains that the government and its scientists previously determined the inability of the vaccine to mitigate the threat. Regardless of the inconsistencies inherent in government conclusions compared to present procurement policy almost 25 years later, the threat itself deserves evaluation.

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[39] Reasons for employing an anthrax vaccine cite Friedlander, A., Welkos, S., and Ivins, B. in an article titled "Anthrax Vaccines," *Current Topics in Microbiology and Immunology* (2002), p. 50.

Since 1990, and prior to the 1998 anthrax vaccine immunization program announcements by DoD (Cohen, 1998b), the GAO reported that "according to DoD … the nature and magnitude of the anthrax threat has been stable since 1990" (GAO, 2002a, p. 3, 9). Despite this assessment, many levels of the government emphasized the threat of anthrax after the 1998 initiation of the anthrax vaccine program, and especially after the 2001 letter attacks. Examples included the DHS National Strategy for Homeland Security (DHS, 2002, pp. 1, 44) and the President's State of the Union Address (POTUS, 2002a). Later, warnings waned entirely from the 2007 DHS Strategy (DHS, 2007) and the more recent State of the Union addresses. Most recently, the DHS Secretary announced, "There is not currently a domestic emergency involving anthrax," adding "there is not currently a heightened risk of an anthrax attack," and finally that there is "no credible information indicating an imminent threat of an attack involving *Bacillus anthracis*" (Chertoff, 2008, p. 1). Conversely, the DHHS declared an "anthrax emergency" (DHHS, 2008b) through 2015 based on the "significant potential for a domestic emergency," although this maneuver likely related to product liability indemnification (DHHS, 2005).[40]

Additional assessments emerged from the WMD Commission Report. The congressionally sponsored report cited the five deaths from the 2001 anthrax letter attack, and an excess of $1 billion in cleanup costs. The report deemed the threat "deeply troubling," documenting weaponized anthrax program evidence from both Iraq and the former Soviet Union. Most importantly, the commission captured the need for "resources" to apply to "funding new intelligence collection strategies" and alluded to the CDC's calls for the "need to move upstream from the event" and away from a "reactive biological weapons posture" (WMD, 2005, pp. 34, 81–82, 284, 501–508, p. 533, fn. 1, 4, 5). Similar less reactive and more "resilient" strategies appear to be gaining ground with the new administration (DHS, 2009c; Napolitano, 2009; Ramo, 2009, pp. 173–199).

Another relevant intelligence resource evaluating the threat included Dr. Mark Lowenthal, former Assistant Director for the Central Intelligence Agency's division of

[40] According to the 2005 Public Readiness and Emergency Preparedness Act, the "Declaration [is] pursuant to section 319F-3 of the Public Health Service Act (42 U.S.C. §247d-6d) to provide targeted liability protections for anthrax countermeasures based on a credible risk that the threat of exposure to *Bacillus anthracis* and the resulting disease constitutes a public health emergency" (DHHS, 2005).

Analysis and Production, and former Vice Chair for Evaluation on the National Intelligence Council. He aptly points out "major shifts in U.S. nonproliferation policy" and a resulting heightened attention to biological weapons after the letter attacks. Lowenthal identified the difficulty "to detect this type of attack in advance or to stop it once under way," and the health dimension, meaning the need to "differentiate between natural occurrences and terrorism" (Lowenthal, 2006, pp. 239, 242, 247).

Another assessment worthy of mention includes a compendium by the United Nations Monitoring, Verification, and Inspection Commission, UNMOVIC. The commission confirmed the intended threat of weaponized anthrax from Iraq prior to the first Persian Gulf War. Iraq apparently eventually dismantled its biological warfare program because it suffered technological hurdles in fielding dry anthrax (United Nations, 2007, pp. 788, 890, 896, 976–77, 1153). Capabilities aside, other anonymous reports by U.S. counterterrorism officials highlighted the nefarious intentions of potential terrorists articulated in a video by an "al Qaeda recruiter threatening to smuggle a biological weapon into the United States via tunnels under the Mexico border." Officials also verified, "There is no credible information that al Qaeda has acquired the capabilities to carry out a mass biological attack although its members have clearly sought the expertise" (Carter, 2009).

In addition to threat assessments and reports of bona fide intentions to acquire anthrax, actual threat occurrences require review. According to the Monterey WMD Terrorism Database, between 1992 and \September 2009, a total of 13 anthrax "incidents" and 498 "hoaxes" occurred in the U.S. (Monterey WMD Terrorism Database [Monterey], 2009). The actual employment events primarily involved the 2001 FBI "Amerithrax" case. Additionally, antibiotics, not vaccine, significantly mitigated the death rate. As a result, the CDC recommends antibiotics to combat inhalation anthrax (CDC, 2001; CDC, 2002; CDC, 2000). The GAO also analyzed over 400 hoaxes in a report shortly after the letter attacks. The report reiterated the earlier GAO efforts, effectively challenging the DoD increased-threat assessments necessitating the anthrax vaccine immunization program. The report chronicled anthrax vaccine immunization program troubles and "attendant publicity" by DoD leaders, with added questioning of

whether terrorists could "overcome the major technological and operational challenges to effectively and successfully [weaponize] and deliver a biological warfare agent" (GAO, 2002b, p. 3).

In fairness, some evaluations continue to suggest, "If an aerosolized B. anthracis bioterror attack does occur, a combination of vaccination and antibiotic therapy provided the most health benefit at the lowest cost." But even that study concludes that "until the individual probability of exposure reaches about 1 in 200, adverse effects of the vaccine outweigh potential benefit" (Fowler, Sanders, Bravata, Nouri, Gastwirth & Peterson, 2005, p. 608). Considering that 13 actual events, documented over more than 25 years, created 22 illness and five deaths (DoD, 2009c, p. 4), for a present population of over 300 million, the "probability of exposure" vastly outweighs consideration of anthrax vaccine when considering its "adverse effects."

The final evaluation of the threat remains uncertain. The facts of the matter show that the first anthrax epidemic for the United States in the twentieth century, during the 1950s Army vaccine clinical trial, killed four citizens. The second epidemic, inflicted by the U.S. Army scientist, killed five Americans in 2001. Nine deaths across fifty years, when considering that prompt medical treatment with antibiotics may have saved all those lives, presents the possibility that anthrax vaccine procurement belies present DHS themes of resiliency and efficiency. The entire reevaluation process takes on added importance when assessing the origins of the threat and the commensurate problematic proximate issues associated with the old vaccine as a countermeasure.

C. SUMMATIVE ANALYSIS

The summative account of the anthrax vaccine is an important aspect of a program evaluation from a historic perspective. Reflection on historic doctrinal debates, comparative policies of allied nations, and background of biosecurity issues will aid the DHS in better understanding how these core issues relate to their present and future Homeland Security Presidential Directive responsibilities regarding the SNS.

1. Doctrinal Review

Following the September 11, 2001 tragedies and the anthrax letter attacks a group of American scientists gathered in Washington, D.C. to explore the fundamental question of whether or not science and technology could combat terrorism, and bioterrorism in particular. One of those scientists, Dr. Simon Levin of Princeton University, concluded, "We could build up stocks of every known vaccine on the planet … but it wouldn't matter. [An enemy] could just engineer something we had never seen before." Interviews related to Dr. Levin's experiences captured his conclusion about the complexities in countering "an adaptive enemy." Dr. Levin believed, "Whatever you [the U.S.] did, they [the enemy] still had an ability to think around it and surprise you." He added, "There was a limit to how much you could prepare" (Ramo, 2009, p. 42–44). Dr. Levin's quandary defines the doctrinal dilemma the U.S. faces when responding to the threat of bioterrorism (DHS) or biological warfare (DoD).

Evaluating biological threat response requires a review of past doctrinal viewpoints. For many years, "the moral ambiguity and legal uncertainty concerning the use of chemical/biological (CB) weapons" resulted in a "CB taboo" (Krickus, 1986, pp. 410, 422). Essentially, the nation's strategic position relied on the credible willingness to resort to massive retaliation in the event that a traditional state actor resorted to the use of biological weapons. Though partially inhibited due to the uncertain nature of this type of abhorrent warfare, doctrine also calls for a "rigorous and dispassionate analysis of the military implications" of such weapons (Krickus, 1986, p. 410). Therefore, retracing doctrinal history, in an attempt to rigorously analyze bioterrorism and biowarfare implications, requires reflection on past protocols. Examples of such treaties and decrees include the 1972 Biological Weapons Convention and President Richard Nixon's 1969 decree to renounce first use and limit research to defensive measures (Biological and Toxin Weapons Committee [BTWC], 1975).

Strategic doctrinal approaches alter over time. The Weinberger and Powell doctrines of limited force appear most methodical and conservative. In 1984, Secretary of Defense Caspar Weinberger discussed the uses of military power at the National Press Club in Washington, D.C. Secretary Weinberger articulated six tests, or conditions, for

the employment of military power. First, the United States would not employ forces in combat overseas unless deemed vital to national interests. Second, employment required the clear intention of winning. Third, the use of military power required clearly defined political-military objectives. Fourth, a continual reassessment of those objectives remained paramount. Fifth, the use of force required the support of the American people and their elected representatives in Congress. Finally, sixth, the United States considered the commitment of forces to combat strictly as a last resort (Weinberger, 2004). Those doctrinal approaches preceded the most recent George W. Bush administration's preemptive war doctrine. Execution of President Bush's preemptive war approach in the latest Persian Gulf War hinged on questionable intelligence (ABC News, 2008; Hersh, 2003; United States Senate, Intelligence Committee, 2008). The Bush doctrine set a course of pursuing wars of choice, preemptive wars, based on a new paradigm of terrorist tactics that would likely employ asymmetric threats. The U.S. National Security Council's 2002 *National Security Strategy* communicated the nation's intention to "exercise our right of self defense by acting preemptively against such terrorists." The intended goal was "to forestall or prevent such hostile acts by our adversaries," where the United States would "if necessary, act preemptively" (POTUS, 2002b).

Defensive posturing by DoD officials with vaccines paralleled the shift to a preemptive war doctrine based on the use of preemptive countermeasures against asymmetric WMD threats such as anthrax. The logic of force-wide immunizations stated that "by protecting against anthrax and other top priority BW threats, the vaccines also serve as a deterrent (see Appendix 3) (DoD-JPOBD, 1995, p. 5). This example of a doctrinal argument for the current anthrax vaccine's role in biodefense precipitated the DoD's mandatory anthrax vaccine immunization program. A *Washington Post* article captured the controversial nature of the DoD mandate, one that represented a new direction despite "earlier opposition." The article stated, "Military leaders initially were dubious about the need for the anthrax vaccine," revealing an inverted policy process "starting at the top instead of trying to staff an issue from the bottom up" (Graham, 1996). The upside-down decision-making process resulted in conceivably politically driven policy choices. Potential politicization at the program's genesis potentially

resulted in a lack of the normal vetting process associated with important doctrinal decisions.

Beyond the viability of the threat, covered in detail in the previous qualitative analysis section on intelligence, considerable debate existed as to the doctrinal rationale for force-wide inoculations. The outgoing administration recognized the "problems" associated with the anthrax vaccine when George W. Bush took office. His appointees undertook an immediate review. A memo from Karl Rove, Senior Advisor to the President, to Deputy Secretary of Defense Paul Wolfowitz (see Appendix 9) (Rove, 2001) resulted in recommendations from DoD undersecretaries Dr. David Chu and Edward Aldridge to Defense Secretary Donald Rumsfeld. They advocated continuing the program at a "minimum level," while purchasing "bio-detectors and stockpiles of antibiotics to augment force protection in the absence of an anthrax vaccine," and suggested a "comprehensive review of doctrinal positions." The officials recommended development of a "coherent institutional process to assess and prioritize biological threats and approve the use of associated countermeasures," while also calling for a "national long-range vaccine" (see Appendix 10) (Chu & Aldridge, 2001). In response, the chairman of the Joint Chiefs of Staff challenged the recommendations by insisting to Secretary Rumsfeld that the vaccine was "the centerpiece of our defense against the most likely biological threat agent" (Shelton, 2001). At the time, the program in effect was halted due to a Food and Drug Administration (FDA) imposed Notice of Intent to Revoke the manufacturer's license for prior deviations (see Appendix 6) (FDA, 1997). The "heated battle" was captured in news articles (Weiss, 2001), and the internal review became known recently due to FBI revelations. The FBI found the "failing" status of the anthrax vaccine motivated the anthrax letter attacks to create the "scenario where people all of a sudden realize the need to have this vaccine" (FBI, 2008, pp. 12–15; Meek, 2008).

From a doctrinal perspective, adding to the pressures motivating the anthrax letter attacks, congressional reports also documented questions about the "necessity of the program." The legislative analysis asked, regarding mandatory inoculation programs against anthrax, "whether it betrays a lack of confidence in deterrence and other force

protection elements." The report also pondered whether "a vaccine program makes anthrax attack more, not less, likely" (HR 106-556, 2000, p. 15, fn. 83). The congressional account simplified the DoD objective to "provide the best armor against biological dangers," and the belief that the "armor is immunization'' (HR 106-556, 2000, p. 23, fn. 118). The report also distinguished "an important difference between the physical body armor worn in battle, which can be removed, and medical prophylaxis, which cannot." Some service members commented, ''The body armor that our Department of Defense refers to is perceived by many service members as 'tin foil armor' '' (HR 106-556, 2000, p. 23, fn. 119). According to the report an important doctrinal issued that was raised implicated the possibility that "primary reliance on medical intervention may also undermine confidence in other elements of the force protection hierarchy." The vital resultant question asked in testimonials was whether or not the vaccine could " 'create a facade of force protection' provoking an adversary to even more lethal chem/bio or conventional attack" (HR 106-556, 2000, p. 23, fn. 120). Harkening back to the contention that the "foundations of force protection rely on a credible willingness to use force," witnesses question whether or not "abandoning this time tested doctrine and emphasizing the inevitability of biological attack to advocate a defensive anthrax vaccination policy may inadvertently result in legitimizing biological warfare" (HR 106-556, 2000, p. 23 fn. 121). The congressional account concluded that while the DoD anthrax mandate was "well-intentioned," it represented an "over-broad response to the anthrax threat," and constituted a "doctrinal departure overemphasizing the role of pre-exposure medical intervention in force protection" (HR 106-556, 2000, p. 17).

The examination of the evolution of doctrinal debate suggests that one challenge the United States faces as a nation includes the potential "doctrinal departure" represented by preemptive biodefense doctrines related to bioterrorism and biowarfare. The doctrinal departure results in expensive, reactive attempts to counter the incalculable risks. The reluctance by DoD leaders to address thoughtful questions posed by some military members seems to perpetuate groupthink and silence rational objections. The threat to security involves the possibility that groupthink about threats and protections

silenced a rational debate over doctrine. The dysfunctions of groupthink also apply as do the myriad processes involved in the proper approval of biologic products as covered in this section and the previous qualitative evaluation section. A thorough, renewed doctrinal review offers the possibility that a DHS evaluation of homeland security policy would serve to ensure sound and efficient biodefense doctrinal policy versus preemptive, nonresilient, reactionary, and wasteful strategies.

2. Comparative Policy Review

A comparative policy review begins by presenting a summary of accords related to biowarfare and by providing contrasting policies on biological prophylaxis for citizens or soldiers. This approach presents another interesting aspect of the multimethodological quadrangulation in order to understand the issues better. Biodefense policy benefits from dissecting allied biological defense strategies, both their successes and controversies. The comparative analysis reviews two fundamental arenas in the biological weapons (BW) debate: Biological and Toxin Weapons Convention (BTWC) adherence and biodefense strategies, with a specific focus on anthrax vaccination. The review discovers a correlation for the nations adopting and internalizing BTWC language against the proliferation of biological weapons and their commensurate avoidance of mandatory biological prophylaxis strategies. For other nations, mandates for anthrax inoculations created significant controversy over time.

For example, Canada suffered an initial controversy over its mandatory program until cancelling the mandate. Two other nations, the United Kingdom (U.K.) and France, enjoyed a relatively controversy-free experience with their nation's biological defense strategies. Both countries readily accept the tenets of the BTWC. Other countries, such as Israel, reflect a rare example of countries with a nonparticipation status in the biological weapons protocol, along with a recent controversy related to anthrax vaccine experimentation. Russia, an original depository government for the BTWC, along with the United States and the U.K., remains "hesitant" as signatory of BTWC protocol, while simultaneously mandating biological defense prophylaxis on their armed forces. A

concluding thought in the subsection on comparative analysis adds perspective on the "hesitant" Russian experience, but not as a specific allied case study.

The analysis illustrates that signatory status by nations such as the U.K., Canada, and France may directly translate to the perception by other nations that those respective countries' national defense policies are not threatening or destabilizing. Similarly, these nations' lack of mandatory biological defense programs and prophylaxis policies may present more stabilizing influences on the international community and more efficient, less costly strategies to the nations themselves. To the contrary, the policies of the U.S. and Israel, with their ongoing controversial internal biological prophylaxis program challenges, and withdrawal or nonsignatory status to the BTWC, may create destabilizing influences vis-à-vis the international community. The approaches also carry significant costs in lost credibility as well as currency. The comparative government policy approach allows U.S. policymakers to reflect on the comparative successes, and lack of controversies, in the collective experiences of allied nations as our leaders contemplate future policy vectors.

a. Background

The changing face of warfare, driven by man's ability to harness technologies for destructive means, caused pause within the international community before and after World War I. A series of treaties and conventions, the significance of which should not be lost in present times, resulted in important doctrinal commitments against offensive uses of chemical and biological weapons. As touched upon in the program evaluation chapter's doctrinal review, academics coined the term "CB taboo" (or Chemical-Biological Taboo) to describe this abhorrent form of warfare (Krickus, 1986). To codify the CB taboo, even before the twentieth century, leaders within the international community signed on to the Hague Convention, with the express purpose of establishing laws of war to prohibit the use of projectiles to disperse asphyxiating gases or chemical weapons (Hague Convention, 1899). Following World War I, the Geneva Protocol of 1925 specifically added bacteriological materials to the list of weapons outlawed in warfare (United Nations, 1925). The U.S. complied with the spirit of these

protocols during World War II, though the Cold-War era that followed resulted in significant escalation of biological weapons research, both offensive and defensive. This period culminated with a presidential directive in 1969 by Richard Nixon to stem BW escalation. The president's National Security Decision Memorandum 35 (NSDM-35) specifically directed the destruction of all offensive biological weapon stockpiles (POTUS, 1969). By 1970, with NSDM-44, President Nixon reaffirmed commitments prohibiting offensive use of biological weapons, and committed to exclusively defense-oriented research, such as development of immunizations as a prophylaxis against biological toxins (POTUS, 1970). By 1972, the United States formally signed the Convention on the Prohibition of the Development, Production, and Stockpiling of Biological Weapons (BTWC, 1975). The convention codified the U.S. presidential national security memoranda into international agreements. The treaty, ratified by 1975, prohibited stockpiling of biological agents intended for any purpose other than peaceful prophylactic development. By the turn of the twenty-first century, the United States in particular expressed concerns about compliance and verification elements of the BTWC. The United States effectively withdrew from the protocol just prior to the anthrax letter attacks pending future agreements related to verification and monitoring in subsequent BTWC negotiations (BTWC, 1975).[41]

Independent academic analysis adds perspective to the controversial U.S. withdrawal from the BTWC Protocol in early 2001. A report by the Center for Nonproliferation Studies (CNS) at the Monterey Institute of International Studies (MIIS) detailed U.S. concerns over the protocol's potential to compromise biodefense research, as well as proprietary industry secrets (Tucker, 2001). The United States framed the temporary withdrawal from the protocol as an objection to the protocol's ineffectiveness in halting proliferation and as effectively compromising biodefense. As a depository government for the BTWC, the international community remains concerned about U.S. "opposition against the establishment of a monitoring and verification mechanism"

[41] Initial reports reveal that the new administration of President Obama similarly expresses concerns about the verification mechanisms of the BTWC but supports increased international cooperation to prevent proliferation of WMDs (Landler, 2009; Sheridan, 2009).

(Bonin, 2007, p. 227). By 2006, the United States had resumed participation in the BTWC process, with well-articulated reservations about the protocol's limitations on restricting proliferation, particularly amongst nonstate actors. The year 2011 marks the next scheduled review of the protocol (United States Department of State [DOS], 2006).

b. Case #1: U.S. Policy as a Baseline for Comparison

The aforementioned background provides a glimpse of the U.S. and international experience with BW accords leading up to the domestic bioterrorism events of the 2001, the anthrax letter attacks. Notably, those attacks emanated from a lone actor within the U.S. military biodefense complex, motivated, according to federal investigators, by a desire to salvage the "failing" mandatory DoD anthrax vaccine program by creating "a scenario where people all of a sudden realize the need to have this vaccine" (FBI, 2008, pp. 12–15). Although mandatory inoculations currently only apply to members affiliated with the armed forces, despite the "critical shortcomings in the U.S. anthrax vaccine program," some recommend that the government "assume direct production of anthrax vaccine" and the "development of a capacity capable of preemptive immunization of the public against anthrax" (Weiss, Weiss, & Weiss, 2007). The prudence and potential success of such plans appear to disagree with empirical data points. For example, with respect to the anthrax letter attacks of 2001 and contaminated postal service centers, an "overwhelming majority of postal workers elected not to be vaccinated" due to disagreement amongst public health professionals on the necessity of the vaccine and workers' fears of being "guinea pigs" (United Press International [UPI], 2009).

Just prior to the anthrax letter attacks top government officials investigated their soldiers' concerns regarding "Gulf War Syndrome and Anthrax Vaccine" as "political problems" (see Appendix 9) (Rove, 2001). DoD reviews of the vaccine program, and recommendations to reduce use to "minimum level" (see Appendix 10) (Chu & Aldridge, 2001), conceivably helped motivate the attacks against the backdrop of

military officials insisting that the vaccine served as the "centerpiece"[42] of U.S. biodefense. In the midst of the postal workers' rejection of the vaccine, and DoD troubles, Defense Secretary Donald Rumsfeld expressed hesitation when answering questions about the anthrax vaccine program saying, "things have not been going swimmingly" (DoD, 2001). The Defense Secretary had several reasons to justify this concern. After all, "military leaders initially were dubious about the need for the anthrax vaccine" (Graham, 1996). Moreover, "according to DoD," the "nature and magnitude of the anthrax threat has been stable since 1990" (GAO, 2002a, pp. 3, 9). In addition, the DoD was forced to slow, halt, and relaunch mandatory military inoculations from 1998 through 2002 due to production problems.

Indeed, the U.S. Defense Department appeared to be swimming against the stream based on internal acknowledgements that they possessed "no vaccine in current use which will safely and effectively protect military personnel" (see Appendix 2) (DoD, 1985, p. 4). Further, some military researchers and congressional reports concurred that the anthrax vaccine was "experimental" (Takafuji & Russell, 1990, p. 156; HR 106-556, 2000, p. 4, 52). Despite this tide of problems, the U.S. DoD persisted in emphasizing the need for the anthrax vaccine mandate (Shelton, 2001). Attempts to swim against that tide continue to reveal contradictions when the U.S. government accedes that "there is not currently a heightened risk," and "no credible information indicating an imminent threat of an attack involving *Bacillus anthracis*" (Chertoff, 2008, p. 1). Regardless, the government simultaneously imposed an "anthrax emergency" (DHHS, 2008b) through 2015 to provide liability immunities for the manufacturer (DHHS, 2005).

From the international perspective, allies may observe these past events with trepidation, just as they likely did when witnessing the United States withdrawal from the BTWC in the midst of the ongoing controversies surrounding an anthrax vaccine and prior to the domestic anthrax bioterrorism attack. The chain of events necessitates a comparative policy review of other allied nations. The inconsistencies

[42] Chairman of the Joint Chiefs, General Henry H. Shelton, held tightly to the anthrax vaccine as "the centerpiece of our defense against the most likely biological threat" (Shelton, 2001).

presented regarding U.S. adherence to past protocols, and the problems associated with the anthrax vaccine as a biodefense countermeasure, render the issues ripe for comparison through foreign case studies.

c. Case #2: Canada

Canada maintains a firm commitment to the Geneva Protocol, as well as to the BTWC (Canadian Department of Foreign Affairs and International Trade [CDFAIT], 2008). Beyond mere participation and signatory status, Canadian disarmament representatives from the nation's Department of Foreign Affairs and International Trade (DFAIT) worked diligently as members of an ad hoc committee to develop a "legally binding instrument," or LBI, in order to strengthen the BTWC through compliance mechanisms (BTWC, 2006). The goal for transparency in the process, as recommended by Canada and the ad hoc committee for legal enforcement, appears to be partially responsible for the U.S. reluctance to share burgeoning advances in biotechnology.

Beyond Canada's internalization of the value of the BTWC process, its own very brief experience with mandating the U.S. anthrax vaccine for its soldiers presented important revelations about the integrity of the program and the status of the vaccine. A solider that refused to accept the anthrax vaccine, Sergeant Michael Kipling, ultimately had all charges dropped on appeal in 2002. The Canadian military halted the court martial of Sergeant Kipling, finding administration of the vaccine in violation of the Canadian Charter of Rights and Freedoms. The Canadian military continues to reserve the right to mandate biological defense inoculations, following proper risk analysis and "balancing of the rights of the individual" (Department of National Defence (Canada) [DND], 2002). The balancing of rights gained momentary consideration during early debate over use of anthrax vaccine in the United States when top DoD officials reminded Pentagon colleagues that "soldiers are citizens first" (see Appendix 3) (DoD-JPOBD, 1995, p. 3).

In this particular Canadian court martial, the minutes of proceedings (Prober, 2000) captured U.S. Army Colonel Arthur Friedlander testifying for the prosecution. During the original March 2000 court martial, Colonel Friedlander testified

that he was unaware of U.S. government licensing applications to obtain approval for the vaccine's use against the inhaled form of the anthrax. The aerosolized form of the threat might occur on the battlefield, causing inhalation anthrax infection. The DoD knew the use of the vaccine for inhaled anthrax required a licensing application, an IND. The application meant that the vaccine was indeed experimental for use against biological warfare. This experimental status rendered the vaccine illegal to mandate in the United States absent a presidential order or simply allowing soldiers their informed consent. U.S. courts ruled on the experimental and illegal status of the vaccine several years after the Canadian forces determined that the mandatory vaccination program violated Sgt. Kipling's rights and freedoms (*Doe v. Rumsfeld*, 2003; *Doe v. Rumsfeld*, 2004; *Doe v. Rumsfeld*, 2007). Colonel Friedlander also served as an anthrax vaccine scientist at Fort Detrick, Maryland. The assertion by this Fort Detrick scientist that he was "not aware" of the purpose of the anthrax vaccine's IND application for anthrax vaccine appeared to belie the facts (Prober, 2000). The U.S. Army participated in preparation of the IND submission for filing by the manufacturer in 1996, as well as the application's update in 1999 (see Appendix 5) (DoD, 1999b). Additionally, Colonel Friedlander was directly involved in joint FDA-DoD meetings related to the original application and its updates (see Appendixes 3–5) (DoD, 1999b; DoD-JPOBD, 1995, p. 3).[43] The officer specifically briefed the reasons for the IND application, including the FDA license amendment's intent to add an "indication," or use, as a biological defense against inhalation anthrax. This was the nature of the questioning in the Kipling case.[44] Concerning the application, U.S. federal court accounts also disclosed, "While the government states that the inhalation anthrax aspect of the IND is no longer active, the documents submitted to this Court under seal suggest otherwise (*Doe v. Rumsfeld*, 2003, p. 28, fn. 7). The

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[43] The meeting attendee list for the Investigational New Drug (IND), #BB-IND 6847, update meeting included Col Art Friedlander, USAMRIID, Room 1A09, Building 29B, 1300 hours, December 15, 1998; FDA Form 1571 includes block 7, "indications" for the Investigational New Drug Application as "Inhalation Anthrax."

[44] Sergeant Michael Kipling's Canadian Forces (CF) court martial proceedings transcript excerpt:

CF Defense counsel: "If I'm going to suggest to you, sir, that the drug was licensed for cutaneous anthrax only and that there has been a subsequent amendment for coverage for inhalation anthrax, would you agree with me or disagree with me?"

U.S. Army Officer, Col/Dr. Friedlander: "I'm not aware of that."

inconsistencies and testimonial inaccuracies reflected poorly on the integrity of the anthrax vaccine program, and likely weighed in the Canadian Force's decision ultimately not to sanction its soldier for refusing to accept the U.S. vaccine.

The Canadian Forces also departed from U.S. policy direction during the latest conflict in Afghanistan. A news report quoted a Canadian Forces medical representative acknowledging that Canada did not follow the U.S.'s lead in mandating anthrax vaccine inoculations. The Canadians stated, "At this point in time, we are not requiring our people to have anthrax vaccinations nor are we considering it" (Moore, 2007). The article disclosed that the U.S. Food and Drug Administration "declared the anthrax vaccine safe and effective," in 2005 after the earlier safety and efficacy concerns and licensing problems. This subsequent regulatory action allowed resumption of the U.S. mandatory program after the anthrax letter crimes. U.S. military leaders also leveraged those attacks as justification for resumption of the shots (DoD, 2009a; Keys & Taylor, 2005). In contrast, according to the article, the Canadian Forces maintained that the anthrax threat in Afghanistan was an insufficient justification for mandatory vaccinations (Moore, 2007).

The Canadian Forces do not possess an independently manufactured anthrax vaccine. For whatever reason, whether lack of confidence in the U.S. product or lack of concurrence about the threat, the Canadians have opted to avoid the less resilient path of reacting to the threat preemptively in mandating a problematic vaccine. It is possible that the Canadians' additional experiences working on the ad hoc committee for the BTWC gave their nation added perspective on the doctrinal issues related to the threat, i.e., the pros and cons to pursuing singular disease specific defensive countermeasures against a potentially diverse array of BW threats.

d. Case #3: United Kingdom

The U.K. also serves as an unwavering signatory of the BTWC. Like Canada, the U.K. never pursued an offensive biological weapons capability. On the other hand, they do possess an organic defensive biological prophylaxis program. However, the U.K.'s armed forces chose not to mandate anthrax vaccine on their troops based on the

significant historic controversies with the U.S. anthrax vaccine program, as well as their own attempts with inoculations during the first Persian Gulf War (United Kingdom, Ministry of Defence [UK-MOD], 2007). One recent report revealed that over 150,000 troops (mostly U.S.) received these inoculations during the 1990 Middle East conflict and that "recent studies have indicated that the current anthrax vaccine is associated with high rates of acute adverse reactions." The study added that the "anthrax vaccine is highly reactogenic [reactive]" (DVA-RACGWVI, 2008, pp. 8, 125, 225). British medical journal articles in the years since the conflict's use of anthrax vaccine to mitigate the anticipated threat of aerosolized anthrax by Iraqi dictator Saddam Hussein reported that "vaccination against biological warfare and multiple routine vaccinations were associated with the … multi-symptom syndrome" from the Gulf War (Unwin, Blatchley, Coker, Ferry, Hotopf, & Hull, 1999, pp. 169–178). The U.S. GAO reported similar findings upon analyzing medical data related to the U.K.'s first Persian Gulf War cohort. The GAO stated, "Several studies in the U.S. and the U.K. now show a relationship between anthrax vaccine and Gulf War syndrome" (GAO, 2002a, pp. 25–26).

Based on these conclusions the U.K. initiated a "Voluntary Immunization Program Against Anthrax" (UK-MOD, 2007) for the conflicts in Iraq and Afghanistan (Bonin, 2007, p. 206). Analysis of the response to the voluntary anthrax program by almost 6,000 U.K. soldiers showed that 72% of those who accepted anthrax vaccination reported "adverse health." The studies' authors assessed the "reported side effects were related to whether acceptance of vaccination was perceived to be informed" (Murphy, Hull, Horn, Jones, Marteau, & Hotopf, 2007, pp. 3109–14). Discussion of the study determined that an important missing element in the program was "trust," i.e., many "respondents made it clear that they did not trust MoD [Ministry of Defense] on this issue." The analysis concluded that soldiers continued to believe they were "coerced into accepting the vaccine," even under the voluntary program, and that the MoD was "'covering up'" evidence that the vaccine was in fact harmful" (Murphy et al., 2007, p. 3113). Coincidentally, medical reports about the U.S. mandatory program during the same time frame also found that the majority of soldiers surveyed questioned the ethics of the program, as well as the safety and efficacy of the anthrax vaccine (Pica-Branco &

Hudak, 2008, pp. 429–33). Curiously, both studies insisted that more education would solve the fundamental concerns of trust in the countermeasure, with the medical community implementing the program. No analysis of the doctrinal necessity, programmatic integrity, or threat estimation controversy apparently existed in the research.

e. Case #4: France

France provides an interesting example of a nation missing in recent years from the biological weapon debate. Considering France was the "depository" government of the earlier Geneva Protocol (United Nations, 1925), it is interesting to note that France's primary concern with the BTWC is its potential to weaken the Geneva Protocol. It specifically cites concern about the BTWC's insufficient controls. As a result, France promulgated legislation on the domestic level to prohibit biological weapons, in addition to their BTWC signatory status (Federation of American Scientists [FAS], 2008).

In terms of biological weapon prophylaxis, France maintains a program of "strategic stockpiling of vaccines, antibiotics, and antidotes" (Bonin, 2007, p. 73). In the first Persian Gulf War, this ally implemented alternative policies based on differing assessments of the threat. France did not assess a valid biological warfare threat, but did assess a possible chemical threat. Therefore, the French military concentrated on protective gear and anti-nerve agents, but did not distribute biological warfare countermeasures (GAO, 2001a, pp. 6, 10, 19). Of the more than 25,000 troops deployed, the only ones subjected to biological warfare vaccines were those stationed alongside U.S. troops. The French reported no cases of Gulf War syndrome per se, but reveal that the "lower rate of illnesses reported by French Gulf War veterans does not point unambiguously to any particular cause." As such, the "differences in French veterans' experience," such as not supplying "troops with medical countermeasures against exposure to biological warfare agents" warrants review when compared to the U.S. or U.K. experience (GAO, 2001a, pp. 22, 23, fn. 19).

Beyond the suspected illnesses caused by the vaccination policies, and regardless of whether threat-based assessments solely drove French protective posture,

France's military does not suffer the "recruitment, retention, readiness, and morale" problems that the alternative U.S. policies created and continue to pose (Corrigan, 2001, p. 40). As a result, French experiences provide valuable comparisons for this analysis.

f. Case #5: Israel

A final case worthy of analysis includes the Israeli experience. Israel does not participate in the BTWC, and it encountered significant controversy related to its military anthrax vaccine experiments. In fact, a government-appointed expert panel reviewing the circumstances related to its anthrax vaccine experiments recently discovered "grave ethical failures" (Teibel, 2009). Soldiers uninformed of the risks reported classic Gulf War syndrome illnesses such as "headaches, dizziness and skin, respiratory and digestive problems." The news report of the panel's assessment detailed "no clear justification for the experiment," and alleged "seriously flawed" methodologies in the protocols for the vaccine tests.

Another article explained that the government-sponsored Israel Medical Association (IMA) report investigating the "Omer-2" experiment found that the study set out to determine the efficacy of an anthrax vaccine on over 700 Israeli Defense Force (IDF) soldiers. While the details about who ordered the experiment, and suspicions of foreign influence, remain unclear, the IDF apparently proceeded with the experiment without proper approvals for the testing or the production of the anthrax vaccine. According to the article, top governmental officials appeared to be aware of the experiment. The IMA report found that the experiments evidently deviated from the requirements of the Helsinki Accords,[45] and appeared unnecessary. Israel already possessed a stock of anthrax vaccine, raising additional concerns that the experimentation resulted from "external pressure" (Melman, 2009a). An alternative opinion article insisted that the experiment was necessary, that it was conducted in accordance with all medical protocols, and argued that its approval emanated from both Prime Ministers Yitzhak Rabin and his successor, Shimon Peres (Eldad, 2009).

[45] The Helsinki Accords, signed by 35 nations in 1975, guarantee basic protections and respect for human rights, of which the right not to be subjected to medical experimentation is included (Melman, 2009a; Eldad, 2009).

An additional article documenting the experimentation controversy reported that the military accepted "full responsibility" for the anthrax vaccine experiment. The commentary revealed, "A quarter of participants were given an American version of the vaccine" (Lappin, 2009). Those reports also divulged that the United States paid Israel upwards of $200 million to fund the experiments (Melman, 2009b). Elements of the IMA report remain redacted, and assessments about which vaccine made the troops sick are undetermined. Conceivably, the IDF's haphazard implementation of the clinical trials, allegedly outside medical or ethical standards, and their use of the problematic American vaccine and funding provides valuable lessons learned for the future of Israel's biological defense efforts, as well as those of the U.S.

g. Analysis:

Reviewing the case study synopsis in Table 2 may assist the United States in modifying its traditional posture of threat emphasis. Observers could reasonably perceive threat posturing as embellishment in order to justify the U.S. biowarfare countermeasures-centric policy. Reviewing comparative countermeasure policy postures allows a dispassionate and measured approach. Consequential reductions in threat emphasis, seen by some as threat embellishment, may also preclude unauthorized offensive releases, as represented by the 2001 anthrax letter attacks by a nonstate actor. Table 2 reviews the positions of the several nations discussed previously regarding their participation in the BTWC and their stance on mandatory or voluntary biological defensive countermeasure policies.

The first column summarizes signatory status to the 1972 BTWC (Bonin, 2007, p. 29). The second column attempts a best estimate of the voluntary or mandatory status of biological defense vaccination for a given country's military or first responders, using anthrax vaccine as a basis when applicable. The International Biodefense Handbook, published by the Center for Security Studies (CSS) at the Swiss Federal Institute of Technology in Zurich subjected four of the countries listed below to analysis. Additional countries, Canada and Israel, are included as primary allies and in line with the contents of the preceding comparative government analysis. The thesis analysis adds

Russia for a supplementary perspective, particularly due to this nation's recent "hesitancy" with the verification protocols established at the BTWC's fifth conference in 2001 (Bonin, 2007, p. 358).

On one side of the spectrum of nations signing on to the BTWC, we find countries such as the U.K. and Canada that do not pursue offensive capabilities. They also do not force biological prophylaxis on their soldiers or citizens based on the historic controversies and doctrinal dilemmas such policies pose. In the middle, we find countries such as France and Israel quietly abstaining from the BTWC process and policies altogether. On the other extreme, we find the United States as a signatory of the BTWC but also suffering from documented unauthorized offensive releases of biological agents emanating from the operations under the purview of permissible defensive programs.

As Table 2 depicts, the United States stands alone amid allied nations as the only one that compels its armed forces, and potentially its citizenry, to submit to defensive biological weapon prophylaxis.

Country/Policy	**BTWC**	**Voluntary BW Shots?**
U.S. (Bonin, 2007, p. 227, 358)	Signatory, but rejected fifth conference verification and monitoring protocol in 2001	Mandatory DoD policy, with past legal and regulatory problems, plus history of 2001 attacks
Canada (Prober 2000; DND, 2002)	Signatory, plus active ad hoc Committee member	Voluntary, declaring the U.S. anthrax vaccine in violation of Canadian Human Rights Charter
U.K. (Bonin, 2007, p. 181)	Signatory	Voluntary
France: (Bonin, 2007, p. 51)	Signatory	Not assessed as imminent threat (GAO, 2001a, pp. 6, 10, 19)

Israel: (Melman, 2009a; Melman, 2009b; Eldad, 2009; Lappin, 2009)	Non-signatory	Past experimentation problems using U.S. anthrax vaccine
Russia: (Bonin, 2007, p. 111, 121, 358)	Signatory, but hesitant over verification protocols in 2001	Presumed mandatory, with prophylactic measures for armed forces

Table 2. BTWC and Countermeasure Policies

A hypothetical output resulting from the comparisons includes the correlation or coincidence that "hesitancy," "rejection" or nonsignatory status of the BTWC, primarily with respect to the verification and monitoring aspects of the protocol, corresponds to mandatory BW vaccination programs in those countries. The correlation of mandatory BW defensive vaccination programs, and reluctance toward or rejection of the BTWC tenets, may prove destabilizing and dangerous in the international arena. As detailed in the handbook, European Community partners appear reluctant to accept at face value the U.S. reasons for withdrawal from the protocol. The U.S. ambassador to the convention argued that the protocol "runs the risk of providing a proliferator or terrorist with a roadmap to exploit our vulnerabilities … [and] would endanger not only the [U.S. biotechnology] industry." The allied responses seemed disappointed with the U.S.-centric approach, versus a global commitment of compliance. Without naming the United States, the report suggested that intelligence reports suspected some of the nations analyzed in the study of violating the tenets of the BTWC (Bonin, 2007, p. 358–59).

Current events may actually demonstrate progress, at least in the realm of securing domestic biodefense laboratories from security lapses. Recently DHS Secretary Janet Napolitano visited Kansas State University with the express purpose of checking on the progress of a $450 million lab meant to develop vaccines for biological threats (Associated Press, 2009a). Simultaneously the U.S. Army's lab, USAMRIID, at Fort Detrick halted research activities in order to review the security of its pathogens based on inventory anomalies (Hernandez, 2009a). By the time the inventory finished, the Army had discovered significantly more egregious problems beyond the original encephalitis

discrepancies (Hernandez, 2009b; Associated Press, 2009b). Ultimately, the Army discovered over 9,200 previously undocumented biological samples (Palk, 2009). While disturbing, the events demonstrate a diligent attempt by the U.S. to tighten security, as well as a potential emphasis to shift biodefense research responsibilities away from USAMRIID's umbrella of military control. We address these issues in the program evaluation's subsequent summative subsection on biosurety.

h. Conclusion

In the balancing of hard and soft power international dynamics with respect to biodefense research, U.S. credibility arguably falls into question due to the controversial attempts to create and promote defensive countermeasures. Attempts to "save" the vaccine as a countermeasure in particular directly resulted in the unauthorized release of anthrax by a nonstate actor of a pathogen that the international protocols forbid. This marks the dilemma for the United States and the challenge for the new administration—to find the right balance in devising future national courses of action to regain credibility in the realm of biodefense, while ensuring that attempts to protect citizens and soldiers do not destabilize this delicate regime of arms control further.

On the issue of biodefense with the anthrax vaccine in particular, the United States lacks credibility upon critical analysis. Due to FBI findings, court rulings, and the contradictory nature of DoD documentation, conduct from elements within the U.S. biodefense apparatus potentially violated U.S. law, presidential directives and international accords. Adding to the milieu, U.S. delays in refinement of the verification protocols for the BTWC protocol based on concern over the proliferation of these very capabilities by nonstate actors remain controversial. The reputation and credibility of the United States in this important sphere of international law apparently stands at risk with our allies and the BTWC cosigners. This risk may find mitigation through a humble and thorough analysis of domestic activities and allied nation policies. The analysis may lead to modification of current U.S. positions in the best interest of policy credibility and a more stabilized biological warfare arena.

Ultimately, the costs to credibility are severe if allies perceive U.S. policies and practices as an obstacle and a destabilizing influence in the international sphere of BW and the BTWC. Domestically as well, the United States must seriously weigh the potential for another rogue offensive release of anthrax or other deadly toxins. For our citizens and soldiers the negative externalities related to illnesses resulting from the very countermeasures meant to protect them may also outweigh perceived advantages. In the end, the dangers of doctrinal departures and experimentation in the defensive biological arena may render these efforts imprudent without proper controls, and prohibitive if failures of those controls further destabilize the arms-control regime.

3. Biosecurity

The thesis addresses biosecurity in order to summarize guidelines and evaluate the scope of high containment laboratories that secure pathogens such as anthrax. The National Institutes of Health (NIH) and the CDC promulgated the Biosafety in Microbiological and Biomedical Laboratories (BMBL) guidelines to accomplish the security task (GAO, 2009, p. 2). Both the DoD and the DHS operate biosafety level 4 (BSL-4) laboratories, but a vast majority of the biodefense activity, often involving the aerosolization of agents for animal challenge studies, occurs at the BSL-3 level (GAO, 2009, p. 10). BSL-3 high containment laboratories deal with agents transmitted in an aerosol form, such as those that U.S. citizens might encounter due to bioterrorism. BSL-3 containment operations guard toxins that cause "potentially lethal infection" and "pose a high individual risk of life-threatening disease." BSL-4 facilities specifically apply to agents where a vaccine or therapeutic remedy does not exist (GAO, 2009, p. 5). Because the United States possesses multiple remedies against anthrax, the government categorizes this pathogen for containment in BSL-3 labs (GAO, 2009, p. 3). Additionally, agent categorization finds anthrax in the BSL-3 category due to its high transmissibility and the fact that it "would cause high mortality and social disruption, require special public health preparedness, and present the greatest bioterrorism danger" (GAO, 2007a, p. 4). Presently, no singularly identified governmental body maintains accountability for both BSL-3 and BSL-4 laboratories in the U.S. (GAO, 2008, p. 7). The DHS BSL-3 labs documented in government reports include the National Biodefense Analysis and

Countermeasures Center at Fort Detrick, Maryland, and the planned National Bio and Agro-Defense Facility (GAO, 2008, p. 12). The DHS BSL research facility locations also carry a BSL-4 rating, essentially dealing with pathogens for which there is no known countermeasure (GAO, 2009, p. 10, 12).

Government reports evaluate the 2001 anthrax letter attacks as one of the incidents that demonstrate the security risks at high containment laboratories. A GAO report specifically refers to the second round of letters mailed to U.S. senators Thomas Daschle and Patrick Leahy. The "Amerithrax" case marked the first anthrax bioterrorism event in U.S. history. The attacks killed five Americans and infected 22 citizens. The first round of letters arrived at NBC News, the *New York Post*, and *National Enquirer* offices, specifically American Media, Inc., in Boca Raton, Florida. The first letters, postmarked September 18, 2001, and the second set of mailings, dated October 9, 2001, contained highly virulent anthrax powder. The contamination of postal workers in particular occurred due to cross contamination of letter processing through mail sorters. The FBI suspects that the spores originated from the Fort Detrick BSL-4 lab. According to the government report, the Fort Detrick U.S. Army scientist suspected of the crimes committed suicide. The FBI believed that the scientist possessed the knowledge, capability, and access to the equipment required to weaponize dry powdered anthrax although normally the scientist only handled wet anthrax spores for animal challenge laboratory experiments (GAO, 2009, pp. 36–39, fn. 37–39). According to the report and the FBI, at the time of the fall 2001 security breach at Fort Detrick, "Ivins was under pressure at work to assist a private company that had lost its FDA approval to produce an anthrax vaccine the Army needed for U.S. troops" (GAO, 2009, p. 39).

The GAO documented two lessons learned related to the crimes. First, that "an ill-intentioned insider can pose a risk not only by passing on confidential information but also by removing dangerous material from a high-containment laboratory." Second, the GAO contends the impossibility of the task to maintain "completely effective inventory control of biological material with currently available technologies." The GAO also determined that "no one can conclusively determine what motivated his actions," referring to Dr. Ivins as the perpetrator (GAO, 2009, p. 39). Slightly out of character for

the GAO, the oversight office stops short of thoroughly evaluating the security implications of the FBI's possible stated motive—the "failing" status of the anthrax vaccine. Instead, the GAO uncharacteristically appears dismissive about the statistical probability of a repeat occurrence based on this singular known data point across 60 years. The GAO also points out that some experts in handling select agents worry about "highly intrusive personnel reliability programs, which rely on profiling to identify insider threats" due to the negative morale impact. They cite the National Science Advisory Board for Biosecurity which believes "there is little evidence that personnel reliability measures are effective or have predictive value in identifying individuals who may pose an insider threat" and that the board recommends against "promulgation of a formal, national personnel reliability program [as] unnecessary at this time." In spite of these recommendations, the DoD took action with DoD Directive 5210.88, "Safeguarding Biological Select Agents and Toxins" (BSAT), as well as DoD Instruction 5210.89, "Minimum Security Standards for Safeguarding Select Agents and Toxins." These directives emphasized security requirements, without consideration to morale, and reaffirmed the need for the Biological Personnel Reliability Program (BPRP). The Congress also proactively passed legislation, including the USA Patriot Act and the Bioterrorism Preparedness and Response Act of 2002, in order to increase security and ensure that select agents do not fall into the wrong hands (GAO, 2009, pp. 40–42, fn. 45).

Completing at least four reports on related issues, the GAO provided executive-level recommendation for the National Security Advisor, in collaboration with the DHS, the DHHS, and the DoD, to determine a single entity accountable for the biosecurity and containment effort, while developing technologies to counter unauthorized proliferation or misuse (GAO, 2002b; GAO, 2007a; GAO, 2008; GAO, 2009, pp. 68–69). Possible additional emphasis items for the nation's national security leaders involve distinguishing between what this thesis refers to as "impermeable deterrents" and "semi-permeable deterrents." The GAO reports and legislation appear to address primarily semi-permeable deterrence through personnel reliability, which are "softer" programs as compared to the impermeable deterrents, such as gates, guards, and hardened security measures. The softer programs, relying on team work and requiring "two-man control," found use in the

military when dealing with dangerous substances such as nuclear material. The National Research Council recently made security suggestions including "two-man control" or two-person controls (National Research Council [NRC], 2009, p. 101). Even the teamwork approach with two-or-more-person chains of custody reflects semi-permeable deterrents or solutions. The semi-permeable deterrents only work based on "surety," known as biosurety, or the reliability of the team members. Multidisciplined teams, while essential to ensure the sage storage and use of pathogens, cannot replace guns, gates and guards for a "multilayered" biosecurity umbrella.

D. FORMATIVE ANALYSIS

The formative analysis phase closes out the program evaluation and offers an opportunity to leverage lessons learned from past events and processes related to the anthrax vaccine and apply them to current and future policy decisions by the DHS. The formative issues provide a means to anticipate future events based on the current state, as well as to foresee how the various arenas of executive, judicial, and legislative review may shape the policy during and beyond the current administration.

1. Current State

The current anthrax vaccine stockpiled in the SNS originates from government-funded state of the art manufacturing facilities and equipment, despite the acknowledged crude formulation of the vaccine. As well, today the manufacturer enjoys significant advantages with a recently approved reduced vaccination schedule and shelf life extensions, despite the past scientific uncertainties about the vaccine in general and pending submissions related to these improvements. In addition to previous government sponsored renovations and extraordinary financial support, the manufacturer enjoys sole source contracts with the government and product liability protections (GAO-NSIAD, 1999b, pp. 1–5).

The initial chapters of this thesis framed these current state realties by applying the fundamental research questions through the context of the vaccine's historic scientific, regulatory, and legal problems. Throughout this chapter's program evaluation, the thesis synthesized that history against the laws and regulations for products such as

anthrax vaccine. As revealed in the regulatory subsection, an analysis of the government's selectively choosing comparative policy guidance over compliance policy guidance when evaluating unapproved manufacturing changes, does not represent an ideally synthesized current state. Moreover, disregarding investigational new drug laws and rule-making procedures when evaluating experimental indications, or uses, for the vaccine bodes ill for the FDA's and the DoD's essential respect for the controlling rules of law. Violations of those laws is a matter of fact, not debate.

Extrapolating on the aforementioned analysis, the following formative subsection further evaluates additional executive, judicial, and legislative landscapes in order to anticipate the future courses of action offered in the recommendations chapter. Digesting the full breadth of arguments and history presented may help the DHS and the government to ensure current and future policies, programs, and procurements for the American people to uphold the highest standards.

2. Executive Review

Executive review revolves around oversight actions by the president and officers in the executive branch departments. Evaluating executive level actions related to the approval of investigational drug products sets the stage for additional policy actions pertaining to the procurement of bioterrorism countermeasures. Highlights related to the DoD experience with anthrax vaccine serve as an important steppingstone to the policy frameworks impacting American citizens. Examples of executive branch mechanisms for ordering the use of investigational biowarfare and bioterrorism countermeasures include:

a. Executive Order (EO) 13139: Improving health protection of military personnel participating in particular military operations (POTUS, 1999).

b. DoD Directive 6200.2: Use of investigational new drugs for force health protection (DoD, 2000).

c. Emergency Use Authorization (EUA) by the Food and Drug Administration: Authorization of emergency use of anthrax vaccine adsorbed for prevention of

inhalation anthrax by individuals at heightened risk of exposure due to attack with anthrax (FDA, 2005a).

The 1999 presidential enactment of EO 13139 effectively reiterated the requirements of U.S. law, 10 USC § 1107, formalized the previous year by Congress. The violation of that law was cited in rulings finding the DoD mandatory anthrax vaccine program illegal absent a finalized FDA licensure (10 U.S.C. §1107, 1998; *Doe v. Rumsfeld*, 2003; *Doe v. Rumsfeld*, 2004; *Doe v. Rumsfeld*, 2007; *Rempfer v. U.S. Dep't of Air Force Bd*., 2008). The DoD directive articulated the same requirements. Court rulings cited violations of this directive as well. The issues remain highly relevant to American citizens. In the case of the anthrax vaccine, explicit violations of the law occurred. The succeeding EO and DoD directives spelled out the same demands that "before administering an investigational drug to members of the Armed Forces, the Department of Defense (DoD) must obtain informed consent from each individual" (POTUS, 1999, p. 3). Over the course of the legal machinations over anthrax vaccine, the DHHS sponsored legislation for a new mechanism to allow use of countermeasures. This Emergency Use Authorization, or EUA, in effect provided the same informed consent protections for recipients as did the executive order and the DoD directive. The first implementation of an EUA occurred in 2005 as a means of continuing to provide anthrax vaccine "for prevention of inhalation anthrax by individuals at heightened risk of exposure due to attack with anthrax" (Chu, 2005). The FDA updated the EUA prior to the vaccine's licensing in 2005 to "authorize the use of an unapproved medical product or an unapproved use of an approved medical product during a declared emergency involving a heightened risk of attack on the public or U.S. military forces." The EUA specifically afforded military personnel a refusal option, which guaranteed that "individuals who refuse anthrax vaccination will not be punished." The EUA also ensured that both military and civilian personnel would not be "considered non-deployable or processed for separation based on refusal of anthrax vaccination" (FDA, 2005a, pp. 44657–60). Discussion of EUA implementation also emerged most recently with the H1N1 pandemic fears.

Several executive-level strategy pronouncements preceded the EO and EUA legal maneuverings in parallel with the court ordered halt to mandatory shots. Examples included:

d. 2002 and 2003 State of the Union addresses (POTUS, 2002a; POTUS, 2003a).

e. 2002 and 2007 National Strategies for Homeland Security (DHS, 2002; DHS, 2007).

The evolution of these executive actions demonstrated the seriousness of attention to the threat of anthrax and the vaccine on the nation's radar scope, with the issue rising to the highest offices in the land. The later State of the Union address in 2007 omitted mention of anthrax vaccine altogether, as did the 2007 National Strategy for Homeland Security and the report by the Commission for the Prevention of Weapons of Mass Destruction Proliferation and Terrorism (Graham & Talent, 2008). Comparable inconsistencies in the executive-level message existed with other recent pronouncements by the executives in both the DHS and DHHS:

f. DHS Secretary memo on the threat of anthrax (Chertoff, 2008).

g. DHHS Secretary declaration of an "anthrax emergency" through 2015 (DHHS, 2008b).

One DHS executive message confirmed that "there is not currently a heightened risk of an anthrax attack" and "no credible information indicating an imminent threat of an attack." Alternatively, the DHHS directives declared an anthrax emergency in order to provide product liability protection for the manufacturer. DHHS simultaneously announced significant additional procurements. The prevention pillars articulated in Homeland Security presidential directives (HSPD) (DHS, 2008b) and the BioShield legislation (DHHS, 2008a) potentially drove such decisions. Some of these executive level directives included:

h. HSPD-8, National Preparedness (POTUS, 2003c).

i. HSPD-10, Biodefense for the 21st Century (POTUS, 2004).

j. HSPD-18, Medical Countermeasures against Weapons of Mass Destruction (POTUS, 2007a).

k. HSPD-21, Public Health and Medical Preparedness (POTUS, 2007b).

Under the HSPDs, the DoD and the DHS share oversight responsibility for the "composition" of products included in the SNS. The directives require a biannual review, thus allowing the new president and executive-branch officers the opportunity to examine the technological assumptions behind continued procurement of the old anthrax vaccine. If the conclusions mirror the analysis and evaluation present in this thesis, prioritization of alternative technologies for the SNS and proactive detection devices deserve increased consideration. In addition, the new DHHS Secretary should review and consider rescission of the October 2008 aforementioned "anthrax emergency" PREP Act declaration providing liability protection to manufacturers. Raising future declaration authority to the level of the president warrants consideration. The Project BioShield initiative and a sage affirmation by President Bush supported overall attention to the issues. President Bush avowed, "We refuse to remain idle when modern technology might be turned against us" (DHHS, 2008a). Of course, this is precisely what occurred with the 2001 anthrax letter attacks.

The executive level HSPDs also dictate the development of Material Threat Determinations and an "unclassified briefing for non-health professionals that clearly outlines the scope of the risks to public health posed by relevant threats and catastrophic health events (including attacks involving weapons of mass destruction)." Research for this thesis could not locate such a product from the DHS. The HSPDs also require a process for extensive strategic level "all-CBRN [chemical, biological, radiological and nuclear] risk assessment," as well as DHS reporting requirements to the President, with updates every two years (POTUS, 2007b). The continual emphasis on facilitation of collaboration and "coordination across the intelligence community," including the DOJ Office of the Attorney General and the law enforcement community, stand as extremely healthy prerequisites (POTUS, 2007a). Finally, HSPD obliges the DHHS to coordinate with the DHS on a "priority-setting process" for the acquisition of medical

countermeasures and other critical medical materiel for the SNS in order to guarantee "transparent and risk-informed" decision-making.

The brief formative review of executive-level authorities related to bioterrorism countermeasure procurement sets the stage for the next "annual review of SNS composition," the first by the new administration. This process will permit analysis and modification as suggested in this thesis. Each of these executive actions holds judicial relevance. Therefore, the next section provides additional perspective on unique aspects of the judiciary's role in the anthrax vaccine experience.

3. Judicial Review

Based on the documentary record showing the DoD acknowledged the anthrax vaccine lacked approval for use against inhaled infection anticipated in a biological warfare environment, a group of anonymous members of the armed forces brought legal action under the Administrative Procedures Act in 2003 (see Appendixes 2–5) (DoD, 1985; DoD, 1999b; DoD-JPOBD, 1997; Myers, 1996). Citing violations of 10 U.S.C. § 1107, the D.C. district court granted a preliminary injunction in December of 2003 (*Doe v. Rumsfeld*, 2003) and a permanent injunction in 2004 (*Doe v. Rumsfeld*, 2004, p. 40). Between the injunctions, the FDA attempted to finalize the 1985 proposed anthrax vaccine license rule to include the indication, or use, for "inhalation anthrax." The permanent injunction vacated that attempted license ruling and directed the FDA to properly process a final order in accordance with the rule-making requirements under the Administrative Procedure Act, 5 U.S.C. § 553. The government appealed the ruling, while also filing a renewed proposed order, seeking comment from the public, in December 2004. Effectively the court ordered the FDA to seek public comment on the new final license order since the scope of the ruling exceeded that which the agency had previously proposed but never finalized in 1985, i.e., the inclusion of inhalation anthrax as an approved use of the vaccine. The FDA published a new final order on December 19, 2005. The D.C. court of appeals declined to vacate or overturn the lower court rulings and determined that the final order mooted the appeal. Ultimately, that stage of judicial review terminated with the following determination: "The Court concludes that plaintiffs

are entitled to fees and costs for litigating this action, including on appeal, because plaintiffs are the prevailing party and the government's position was not substantially justified" (*Doe v. Rumsfeld*, 2007).

Based on the December 2005 FDA final order, the DoD resumed the mandatory anthrax vaccine program for service members in October 2006. Revival of the program led to a new round of judicial review to scrutinize the propriety of the 2005 final order. The D.C. district and appellate courts dismissed the legal efforts in February 2008 and September 2009 respectively, upholding the propriety of the 2005 FDA anthrax vaccine court-ordered licensure. The ruling stated the obligation to "defer to the FDA's judgment that [anthrax vaccine] is effective regardless of the route of exposure," i.e., including inhalation anthrax. In addition, concerning the reliability of the Brachman study to provide proof of efficacy despite the manufacturing changes, the three-judge panel found this decision by FDA to be "a scientific judgment by the FDA to which we owe considerable deference." On both issues the court "grant[ed] the premise but reject[ed] the conclusion" of the arguments based on the high legal bar in questioning the discretion of a federal regulatory agency (*Rempfer v. Sharfstein,* 2009; Lowe, 2009; Pickler, 2009, pp. 13–14).

Additional legal filings related to attempts to secure record corrections for soldiers previously punished over the mandatory anthrax vaccine program prior to the 2005 FDA licensure. A case addressing these concerns verified the "undisturbed factual and legal findings" declaring the DoD program unlawful prior to the FDA final order. The ruling upheld that "prior to the FDA's December 2005 rulemaking, it was a violation of federal law for military personnel to be subjected to involuntary AVA inoculation because the vaccine was neither the subject of a presidential waiver nor licensed for use against inhalation anthrax" (*Rempfer v. U.S. Dep't of Air Force Bd.,* 2008, pp. 18–19). The ruling addressed earlier cases stating, "Other courts have affirmed the legality of pre-2005 orders subjecting military personnel to involuntary anthrax vaccination, although they did so without giving detailed consideration to the implications of the FDA's licensing requirements" (*Rempfer v. U.S. Dep't of Air Force Bd.,* p. 19). Although not cited, the Court of Appeals for the Armed Forces (CAAF) (*U.S. v. Kisala,* 2006) had

previously upheld the legality of the anthrax vaccine mandate, although it did not explore the depths of the issues as vetted in the D.C. district and appellate courts litigation. The military court determined that the service members had failed to demonstrate that FDA licensing interpretations suffered any fatal flaws since the FDA never revoked the anthrax vaccine license.[46] Therefore, the military appeals court found that the soldiers could not overcome the "presumption of lawfulness" granted to the military order to mandate the vaccine. The DoD's favorable military appeals court ruling followed the civilian orders for the FDA to finalize the anthrax vaccine proposed license rule and order and the subsequent licensing by the FDA. The military court's apparent blindness to the prior rulings declaring the vaccine program illegal possibly exemplify intentional efforts to ignore the facts or simply a failure to comprehend the implications of the law and civilian judicial control over the military.

Another case in point in the litigation history involved *O'Neil v. Secretary of the Navy,* litigated in the Western District of Pennsylvania. The court found the vaccine program properly approved in the 1999 through 2001 time frame.[47] The *O'Neil* case highlighted the carefully phrased language choices by the testifying DoD officials. Testimony by the anthrax vaccine program manager for the Department of the Navy addressed a question by the judge related to the FDA license. The officer answered the judge that the "anthrax vaccine is *not* being used in a manner that is *inconsistent* with its approval by the Food & Drug Administration." The officer had previously attended a conference earlier that year where DoD officials acknowledged "the actual efficacy for the prevention of inhalational anthrax [was] not known" (Engler, 1999). The language choice by the officer to the judge was reminiscent of the FDA informal opinions provided to the DoD in 1997 when the department asked about the vaccine's approval for inhaled anthrax. The courts later noted that the FDA responded, "I believe your interpretation is *not inconsistent* with the current label" (Friedman, 1997; *Doe v. Rumsfeld*, 2003, p. 7). The court determined that this "apparent change in position from the December 1985

[46] *U.S. v. Kisala* occurred in the context of a criminal proceeding, as opposed to the civil court proceedings under the jurisdiction of the D.C. federal district court (*Doe v. Rumsfeld*, 2007).

[47] *O'Neil v. Secretary of the Navy*, 76 F. Supp. 2d 641 (W.D. Pa. 1999).

proposed rule and the cryptic use of a double negative (i.e. 'it is not inconsistent'), fail to persuade this Court that the view expressed in the 1997 letter is the FDA's formal opinion." Absent a "formal opinion vis-à-vis AVA's investigational status" the court rejected the "inconsistencies" and pointed out that the FDA "did not do the in-depth analysis as would be appropriate to make that kind of a determination or to contradict the opinion it expressed concerning the Bachman study in 1985" (*Doe v. Rumsfeld*, 2003, pp. 24–25). The court found that the "term 'investigational' … is at the heart of the dispute" (*Doe v. Rumsfeld*, 2003, p. 23–24). The court summarized this logic:

> At bottom, this inquiry turns on whether the FDA has made a final decision on the investigational status of AVA; and if not (1) whether the 1996 IND application establishes the vaccine's status as an investigational drug and (2) whether the DoD is using AVA in a manner inconsistent with its license and intended use (*Doe v. Rumsfeld*, 2003, p. 22).

The preliminary injunction, later affirmed by higher courts, called attention to orders, directives, and laws "enacted to protect soldiers from involuntarily serving as 'guinea pigs' in a mass use of investigational medicine (*Doe v. Rumsfeld*, 2003, p. 29). Because the administrative record before the court was "devoid of an FDA decision on the investigational status" of anthrax vaccine, the court determined that anthrax vaccine was indeed "an investigational drug." The court determined that the anthrax vaccine was "a drug being used for an unapproved purpose," and therefore found the DoD "in violation of 10 U.S.C. § 1107, Executive Order 13139, and DoD Directive 6200.2 (*Doe v. Rumsfeld*, 2003, p. 32).

Another often-cited case to espouse the legality of the anthrax vaccine mandate involved *Mazares v. Department of the Navy*, which concluded in 2002. The *Mazares* case occurred before Judge Sullivan's rulings on *Doe v. Rumsfeld* in the D.C. district court and without challenging the legality of the order based on the absence of a finalized anthrax vaccine license ruling (*Mazares v. Dep't of the Navy* [*Mazares*], 2002). Another legal case relevant to civilian use of the vaccine involved a merchant mariner with a suspected disability due to anthrax or smallpox vaccines. That case, *Francis v. Maersk*, resulted in a settlement reported in the range of $2 million (*Francis v. Maersk*, 2004; Nass, 2007, p. 1512, fn. 21). Settlements of this magnitude, potentially paid by U.S.

taxpayers based on indemnification and product liability protections, warrant consideration as the government evaluates wider use of the vaccine on the civilian population. In contrast to consideration of civilian use of the vaccine, service members face a Supreme Court precedent legal bar precluding suit in tort cases based on the Feres doctrine for injuries suffered incident to service.[48] Alternatively, according to the Department of Veterans Affairs, service members qualify for disability ratings if "evidence establishes that an individual suffers from a disabling condition as a result of administration of an anthrax vaccination" (McClain, 2002).[49] Either way, indemnification and liability costs for civilian injuries or disability claims by service members could impose potentially significant costs on the government.

An additional interesting aspect of judicial review over anthrax vaccine surfaced in a different 2003 district court case in Colorado. That case dealt with a U.S. Army soldier's anthrax vaccine refusal. While dismissing the case the lower court noted:

> It is important for the parties and the public to understand exactly what the Court is ruling. The Court is not passing on the merits of the anthrax program. The plaintiff has raised significant questions about that program. If the Court were reviewing the program, the Court would be very concerned about the question that the plaintiff has raised. Title 10 United States Code Section 1107 provides that whenever the Secretary of Defense requests a member of the armed forces to receive an investigational new drug, the Secretary must provide a member with notice about the investigational nature of the drug and require the member's consent prior to administration ... There have been no tests showing that the vaccine is effective at protecting human beings from exposure to inhalation anthrax,

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[48] *Feres v. United States*, 340 U.S. 135 (1950). The *Feres* court determined that service members receive comprehensive compensatory relief if injured during their service in the form of disability pay. The court also determined that service members suing the government they serve could have a deleterious impact on military order and discipline.

[49] "QUESTION PRESENTED: Whether a former member of the Army Reserve who received two anthrax inoculations during inactive duty training and who alleges suffering from chronic fatigue and chronic Lyme-like disease as a result of these inoculations may be considered to have been disabled by an injury in determining whether the member incurred disability due to active service.

Held: If evidence establishes that an individual suffers from a disabling condition as a result of administration of an anthrax vaccination during inactive duty training, the individual may be considered disabled by an "injury" incurred during such training as the term is used in 38 U.S.C. § 101 (24), which defines "active military, naval, or air service" to include any period of inactive duty training during which the individual was disabled or died from an injury incurred or aggravated in the line of duty. Consequently, such an individual may be found to have incurred disability in active military, naval, or air service for purposes of disability compensation under 38 U.S.C. § 1110 or 1131" (McClain, 2002).

> although animal studies by the Army exist. The Court will not substitute its opinion for that of the Army, but it will not review the matter. And its ruling today should not be understood as an approval of what the military is doing in this case. The military will be held accountable to the public if it is using its own soldiers as guinea pigs to determine whether the anthrax vaccine has long-term health consequences and whether it protects against airborne anthrax. Those decisions, are, as I said, decisions that are committed to the Executive Branch of the Government. The Court neither approves nor disapproves of those decisions, because it is not the function of the Court to do that. Those decisions will be debated, and ultimately the Executive Branch will be held accountable to the public for those decisions. And that is the way the system of government works. (*Barber v. U.S. Army,* 2003, pp. 16–17). [50]

In this case, the court chose not to interfere with the DoD program, but specified it was "not passing on the merits of the anthrax program." Similar to the case dealing with the propriety of the final 2005 licensing of the anthrax vaccine, where the court granted "considerable deference" to the FDA, the court deferred to the military. Other courts similarly acquiesced to the DoD's commonly accepted jurisdiction over internal affaires.[51] Language demonstrating judicial deference in such matters is found in the following cases:

a. *United States v. Stanley,* 483 U.S. 669 (1987), noted that lawsuits "would call into question military discipline and decision making would itself require judicial inquiry into, and hence intrusion upon, military matters."

b. *Chappell v. Wallace,* 462 U.S. 296 (1983), affirmed that the "Courts are ill equipped to determine the impact upon discipline that any particular intrusion upon military authority might have."

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[50] The district court ruled in *Barber* on February, 2, 2003, writing, "The issues in this case are beyond the purview of the federal judiciary and … the Court must decline review because the Department of Defense has wide latitude over military personnel decisions. ... The courts have little competence in the complex decisions as to the control of a military force, and such professional military judgments are more properly subject to civilian control of the Legislative and Executive Branches."

[51] Cases of judicial deference include *United States v. Brown*, 348 U.S. 110, 112 (1954); *United States v. Muniz*, 374 U.S. 150, 162 (1963); *Mindes v. Seaman*, 453 F. 2d 197 (5th Cir. 1971); and *Parker v. Levy*, 417 U.S. 733, 743–44 (1974).

c. *Brown v. Glines,* 444 U.S. 348 (1980), asserted, "Both Congress and this Court have found that the special character of the military requires civilian authorities to accord military commanders some flexibility in dealing with matters that affect internal discipline and morale."

d. *Gilligan v. Morgan,* 413 U.S. 1 (1973), upheld that "complex subtle, and professional decisions as to the composition, training, equipping and control of a military force are essentially professional military judgments, subject always to civilian control."

As the last case cited above references, the matters in dispute within the DoD are "subject always to civilian control of the Legislative and Executive Branches," and ultimately the same exists for the FDA. Since the legal status of the anthrax vaccine and the government's anthrax vaccine programs may face additional judicial review, if legislative and executive control fails, a worthwhile examination of potential use of the product involves mandatory inoculation policies for civilians. While some states possess the authority to mandate inoculations, the federal government does not currently possess such broad power. The Public Health Service Act allows the federal government to pass regulations necessary "to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the States or possessions, or from one State or possession into any other State or possession." While the states hold primary authority to protect the health of the public, including enactment of mandatory vaccination policies, federal government jurisdiction remains limited to supporting the states and enforcing quarantine policies (42 U.S.C. § 264; Welborn, 2005, p. 5). As emphasized in this thesis, the requirement for the products stockpiled to undergo proper review reigns as essential to ensure that countermeasures provided by the federal government to the states warrant inclusion in mandatory state public health vaccination policies. Equally, federal quarantine policies and state mandatory vaccination policies must withstand public legal scrutiny after the fact. The federal government, under a grant to Johns Hopkins Bloomberg School of Public Health and Georgetown University, proposed a Model Emergency Health Powers Act (MEHPA) to assist states in responding rapidly to public health threats and emergency occurrences (Johns Hopkins Bloomberg School of Public Health, 2001; Mientka, 2001a). It remains important to note that the

threat of anthrax does not pose a "communicable" human-to-human risk as addressed above under the auspices of the Public Health Service Act. Instead, throughout the various analysis methodologies this thesis encourages readers to differentiate "person-to-person transmission" from "noncommunicable infectious diseases" (Hamburg, 1999). In the case of anthrax, we deal with a noncommunicable infectious disease, treatable with antibiotics, and without risk of human-to-human exposure.

Overall, the judicial review process captures an important aspect of the anthrax vaccine experience regarding checks and balances, civilian control of the military, and executive agency responses to this process. At times DoD officials reacted adversely when questioned about the federal judicial review. One reporter asked a DoD political appointee doctor if the federal judge was "factually wrong when he said that the vaccine is still in investigational drug." The official, DoD Assistant Secretary of Defense for Health Affairs Dr. William Winkenwerder, responded, "Absolutely" (Winkenwerder, 2003). Within one week, the FDA filed a final rule in the federal register to finalize the proposed ruling first published in 1985. This allowed a lifting of the federal court injunction. In an official posting on the resumption of the program Dr. Winkenwerder expressed hope that the "inflammatory and inaccurate statements the litigation has spawned can be clearly put to rest" (Winkenwerder, n.d.). Later court rulings placed the responses in perspective. Ultimately, the court granted service members "prevailing party" status based on the illegal nature of the program due to the previously unfinalized license (*Doe v. Rumsfeld*, 2007). The DoD's reaction provides instructive lessons on how the DHS, or other federal executive agencies, respond to challenges of the legal suitability of bioterrorism countermeasures in the future. Government officials' digestion of the outcomes of these oversight processes seems as important as the checks and balances themselves. When courts do rule, a process exists to appeal those findings. Just as the regulatory scheme related to the anthrax vaccine took years to sort out, ultimately the judicial review process and the laws will control the legacy of anthrax vaccine. The process of ensuring that checks and balances prevail over politics is long and arduous, but a fair one over time.

The judicial review process related to anthrax vaccine summarized above is tightly interwoven with the legislative process and the formulation of the laws of the land. The next formative section of the program evaluation chapter covers aspects of the legislative review processes in relation to the anthrax vaccine.

4. Legislative Review

Legislative review, while seemingly unproductive in the near term due to political dynamics, proves far from futile. Controversial issues may stall due to lack of consensus, but progress results over time from the process and its byproducts. In the case of the anthrax vaccine controversy, congressional and GAO reports provide a wealth of perspective. The Congress allows national figures such as Ross Perot to express his concerns about the old anthrax vaccine and Gulf War illness. Congressional testimony also allows the voices of the privates and the sergeants to be heard (HR 107–137, 2002, p. 83; Cam, 2000; DVA-RACGWI, 2008; Schumm et al., 2007). The laws promulgated by Congress provide guidance for executive implementation of programs, as well as the instruments for judicial review.

Congress often legislates to fix problems after the fact. A valuable formative impact serves as the benefit. Historic government-influenced medical controversies, such as the Tuskegee experimentation with syphilis, radiation testing, and Agent Orange exposure serve as seminal examples (Advisory Committee on Human Radiation Experiments [ACHRE], 1995; Clinton, 1997; DVA, n.d.). Because the executive, judicial, and legislative actions interlace, guiding laws are included with significant legislative events as detailed below:

a. 10 USC § 1107, a law pertaining to requirements for informed consent, titled "Notice of use of an investigational new drug or a drug unapproved for its applied use (10 U.S.C. § 1107, 1998).

b. BioShield Act[52] (HR 110-23, 2007; Public Law 108–276, 2004; CRS-, 2007; DHHS, 2008a; POTUS, 2008a).

[52] The BioShield Act of 2004, promulgated under Public Law 108-276, evolved from the 2002 Public Health Security and Bioterrorism Preparedness and Response Act, and is pursuant to § 564 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 360bbb-3).

c. Public Readiness and Emergency Preparedness Act (PREP) Act[53] (DHHS, 2005).

d. Senate Hearing confirming lack of sufficient efficacy of anthrax vaccine for aerosol exposure, titled "Global Spread of Chemical and Biological Weapons" (United States Senate, 1989).

e. Senate Report, deeming anthrax vaccine "investigational," titled "Is military research hazardous to veterans' health?: Lessons spanning half a century" (United States Senate, 1994).

f. Senate Resolution seeking an expression of the "sense of the Senate" regarding anthrax, and requesting reconsideration of the mandatory program (United States Senate, 2003).

g. House Report, citing anthrax vaccine as "experimental," titled "Unproven Force Protection" (HR 106-556, 2000).

h. House Resolution to prohibit the DoD from mandating anthrax immunizations, and to correct the records of service members previously punished for refusing to take these vaccines (United States House of Representatives resolution [HR 5166], 2004).

i. Hearings supportive or neutral of the DoD anthrax vaccine program (HR 106-28, 1999; HR, Committee on Armed Services, 1999; HR, Committee on Armed Services, 2000; United States Senate, Armed Services Committee, 2000).

j. Hearings critical of the DoD anthrax vaccine program (HR 106-17, 1999a; HR, Committee on Government Reform (HR 106-130), 1999e; HR 106-102, 1999; HR, Committee on Government Reform (HR 106-131), 1999d; HR, Committee on Government Reform (HR 106-249), 2000; HR, Committee on Government Reform (HR 106-26), 1999b; HR, Committee on Government Reform (HR 106-36), 1999c; HR, Committee on Government Reform (HR 107–137), 2002).

[53] The PREP Act, promulgated under Public Law 109-148, is pursuant to § 319F-3(b) of the Public Health Service Act (42 U.S.C. § 247d-6d).

k. A single GAO report favorably evaluated the DoD anthrax vaccine program (GAO-NSIAD, 1998).

l. GAO reports generally critical of the DoD anthrax vaccine program (GAO-NSIAD, 1999d; GAO-NSIAD, 1999g; GAO-NSIAD, 2000a; GAO-NSIAD, 2000b; GAO-NSIAD, 1999e; GAO-NSIAD, 1999f; GAO-NSIAD, 1999a; GAO-NSIAD, 1999b; GAO-NSIAD, 1999c; GAO, 2001a; GAO, 2000b; GAO, 2000a; GAO, 2001b; GAO, 2001c; GAO, 2002a; GAO, 2002b; GAO, 2006; GAO, 2007b; GAO, 2007d).

The legislative inquiry process, while illustrative of a lack of consensus, also demonstrates that the vast majority of the congressional reports and initiatives generally questioned the DoD anthrax vaccine program. The supportive hearings, as opposed to those critical of the vaccine, appeared to fall across committee versus party lines. Alternatively, the GAO reports almost unanimously criticized the DoD's anthrax vaccine experience, albeit for one report published at the outset of the program. The houses of Congress seemed similarly split in their opinions on the anthrax vaccine, with the majority of inquiry emerging from the House Government Reform Committee. That committee also published the sole program committee report in the House of Representatives after almost one dozen hearings. The conclusions of the House's "Unproven Force Protection" report mirrored conclusions by a Senate staff report the previous decade, preceding the anthrax force-wide mandatory anthrax vaccine program. Both reports deemed the vaccine either "investigational" or "experimental" (HR 106-556, 2000; United States Senate, 1994). Both the Senate and the House proposed resolutions to halt mandatory immunizations (United States Senate, 2003; HR 5166, 2004). Both resolutions asked for record corrections for soldiers for prior punishments meted out, well prior to the federal court illegality rulings, but neither garnered consensus among congressional colleagues.

As part of the legislative process, some lawmakers, such as Representatives Christopher Shays of Connecticut and Dan Burton of Indiana, vociferously advocated soldiers' health rights. Representative Shays, as the chairperson for the Committee on Government Reform, published the sole committee report on the issue, "Unproven Force

Protection" (HR 106-556, 2000). In contrast, Congressman Steve Buyer of Indiana provided comments in congressional hearings regarding the vaccine's approval:

> If the anthrax is actually placed on your skin, then it is FDA approved. If it is airborne through air assault, it is not FDA approved … See how people get confused. It is FDA approved for one type but not for the other. (HR 106-28, 1999, p. 57)

Congressman Buyer also served as a reservist. He added to his testimony, stating, "But as a soldier, if I am going into the theater and I know they are going to drop anthrax on me, give me the vaccine. You know, give me the vaccine" (HR 106-28, 1999, p. 57). In another hearing Representative Buyer took exception to the attention the vaccine issue received (HR, Committee on Armed Services, 1999, p. 128). Significantly, the issues at play with the DoD anthrax vaccine controversy centered on laws pertaining to FDA approvals and revolved around the legally prescribed health rights afforded by the Congress of the United States for service members of all ranks and occupations. While the Congressmen acknowledged that anthrax exposure from "airborne … assault" was "not FDA approved," echoing the conclusions of a later report (HR 106-556, 2000), the Congress failed to call for enforcement of the laws that the legislative body had enacted regarding informed consent for experimental products.

As a case in point, demonstrating the ongoing oversight by congressional officials, DHHS Secretary Kathleen Sebelius recently responded to an inquiry from Representative Gabrielle Giffords of Arizona. While referencing the 2008 Commission on the Prevention of WMD Proliferation and Terrorism, the DHHS Secretary ignored the fact that the report omitted reference to the current anthrax vaccine (Sebelius, 2009, p. 1; Graham, 2008). Similarly the update to that report details initiatives by the DHHS Biomedical Advanced Research and Development Authority (BARDA) to develop a new anthrax vaccine in citing the "development and stockpiling of the eight biodefense requirements laid out in HHS's Public Health Emergency Medical Countermeasures Enterprise" (PHEMCE) (Graham & Talent, 2009, p. 11). The DHHS response also specifically allayed congressional concerns about the current anthrax vaccine by reaffirming that while "vaccines are a key component of our strategy, antimicrobials are the first line of defense to protect the nation following an anthrax attack." The letter

confirmed the unapproved nature of utilizing the current anthrax vaccine after an anthrax attack without an Emergency Use Authorization, as well as BARDA's objective to "award" a decision on the next generation anthrax vaccine "before the end of 2009." The official DHHS response by the new administration's officials effectively avoided countering the concerns relayed about the current anthrax vaccine but instead cited the IOM report's recommendation about the urgent need for a new anthrax vaccine and BARDA's corresponding efforts (Sebelius, 2009, pp. 1–3).

Congress's examination, like the parallel judicial and executive processes, exemplifies the formative nature of how the checks and balances continue. The continuum of the legislative inquiry process serves as an important pattern for current or future lawmakers to consider. The earliest hearings reveal DoD endorsement of the fundamental premise of this thesis through a letter from Assistant Secretary of Defense Robert B. Barker to Chairman of the Senate Governmental Affairs Committee Senator John Glenn. Senate Report 101-744, an analysis of the global spread of chemical and biological weapons, included an assessment of the anthrax vaccine by DoD officials at the time that affirmed a "higher than desirable rate of reactogenicity [adverse reactions]." The report added concerns about instances of a "lack of strong enough efficacy against infection by the aerosol route of exposure [inhalation anthrax]" (United States Senate, 1989, p. 474). Senate Report 103-97, chronicling "military research hazardous to veterans' health" and "lessons spanning half a century," replicated the pattern (United States Senate, 1994) as did the House Report, "Unproven Force Protection," in citing anthrax vaccine as "experimental" (HR 106-556, 2000). At first glance, legislative review may appear stymied by a lack of consensus, but a formative review conclusion suggests that future legislators, as with syphilis experimentation, radiation hazards, and Agent Orange, will resolve much of the divisiveness. The legislative process, though seemingly the most political due to difficulties in gaining consensus, ultimately emerges as a powerful instrument for checks and balances once the parties reach consensus.

Summarizing the formative analysis within the program evaluation, the checks and balances designed by the founders sagely offer a healthy tension to ensure that we provide the best products to the American people through the SNS. While the political

process remains a healthy aspect of the American form of government, the DHS must guard vigilantly to guarantee the political process does not have a "corrupting influence upon science in the biodefence arena," one which subjugates the "truth, ethical practices and justice to a subordinate position" (Schumm et al., 2009, p. 597).

E. SUMMARY OF THE PROGRAM EVALUATION

The preceding program evaluation involved significant process tracing, starting with a quantitative analysis of safety, efficacy, and technological measurements related to the anthrax vaccine. The subsequent qualitative analysis reviewed regulatory constructs and intelligence forecasts regarding the threat, intended to guarantee quality protective products based on superior predictions by the intelligence community. The summative evaluation analyzed past doctrinal aspects of the program, in addition to a glimpse of how comparative governments approach biological prophylaxis. The formative evaluation sought to analyze anthrax vaccine from the lens of executive, judicial, and legislative review. Those avenues serve as the long-term arbiter for the propriety of the anthrax vaccine and potentially for successful redress by those potentially impacted by its ill effects. The stark realities highlighted throughout the program evaluation continue to reveal controversial themes of shifts in professional judgments about the vaccine. The continuum of program evaluation serves as essential for reviewing a product not originally recommended for widespread use. The chasm between a lack of historic endorsement and commensurate programmatic troubles compares incongruously to recent expanded sole source countermeasure procurement of the vaccine. Therefore, the thesis requires one final methodology in order to help explain the "gap" between the recognition of past problems versus the current increased utilization of the vaccine.

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V. GAP ANALYSIS

The following gap analysis provides explanations derived from social psychological, business strategy, political, and multi-disciplinary viewpoints. The explanations provide perspective on the inconsistencies between past medical and policy recommendations, when the government agreed on the unsatisfactory status of the current anthrax vaccine, as compared to current policy using the same vaccine 25 years later as a principal component of the SNS.

A. GAP EXPLANATIONS

Until the late 1990s, the collective wisdom of government and medical communities concluded that the long-established anthrax vaccine required replacement. To this day calls for a new vaccine persist. While most concur that "there are critical shortcomings in the US anthrax vaccine program" (Weiss et al., 2007), the continued reliance on a product long held as inadequate defines the "gap."

The pivotal 2001 anthrax letter attacks occurred at the very time when the gap had almost closed. Afterward, the DoD seized upon the crime by the lone bioterroism actor to emphasize the authentic risk that anthrax poses to combat forces (Keys & Taylor, 2005; DoD, 2009c, p. 4). Since the inside source of the anthrax letter attack, and its motive to "save" the anthrax program, were not revealed until 2008, the DoD made the case that "the threat is real" based on the five deaths in 2001 (FBI, 2008, pp. 12–15; DoD, 2009a). The sequence of events allowed the gap to widen, with DHS endorsement and DHHS procurement of significant additional quantities of the vaccine for the SNS. At that juncture, the previous review of the anthrax vaccine evaporated and analysis of the breaches escaped final examination and action to "minimize" its use (Chu & Aldridge, 2001). Many military members, and perhaps other Americans as well in the years to come, find difficulty in accepting a corresponding shift in rhetoric and promotion of a countermeasure, which even the DoD previously critiqued.

The Army Times Publishing Company published a cover story during the early years of the George W. Bush administration (Miller, 2001) depicting the gap between

what the government espoused compared to what service members discovered in readily available medical literature and government reports. Published in all four of their military papers, the article, titled "What the government doesn't want you to know about anthrax vaccine," included a cover story with an illustration of a hand covering up discomforting facts about the vaccine. The Army Times Publishing Company laid out the facts on the front page, perhaps with the objective that senior leaders of the military and government could better understand the gaps created by the mantra of those who sold the anthrax vaccine program to the troops. Figure 4 illustrates the controversial anthrax vaccine issue as depicted on the front pages of the *Marine Times*, the *Army Times*, the *Navy Times*, and the *Air Force Times*.

Figure 4. Army Times Publishing Company, "Shots In The Dark"

1. Social Psychology Methodology Explains the "Gap"

The social psychology methodology helps explain the "gap," or the holes in logic perpetuating the stockpiling of a known unsatisfactory product for the SNS by the DHS and the DHHS. The story behind the currently licensed anthrax vaccine reveals an intriguing aspect of Homeland and National Security from a psychological and sociological lens. A thorough review of the anthrax vaccine issue, viewed through the earlier literature review, case study and program evaluation multiprism methodologies, unveiled numerous problematic tentacles. Whether literary dichotomies, technological limitations, risk management questions, possible fiscal irresponsibility, or problematic medical, scientific, regulatory, and legal processes, each examination offers unique perspectives.

In the case of the psychological aspects, disclosure of intricate interactions and relationships helps us to deconstruct, and therefore better understand, continued support for procurement of the vaccine by the DHS today. The social psychology methodology assists us on the journey of discovering how "good people can be induced, seduced, and initiated into behaving in evil ways" (Zimbardo, 2007, p. 211). In this case, the DoD procured an experimental vaccine, with known problems, and illegally ordered the vaccine's use on soldiers under the threat of punishment when many entities within the institution knew that the vaccine suffered significant limitations and the mandate violated the nation's laws. Social psychologists studied such a phenomenon where, "with numbing regularity, good people were seen to knuckle under the demands of authority and perform actions that were callous and severe" (Milgram, 1974, p. 123).

Today, although the FDA finalized the vaccine license, the DHS authorizes the same documented less-than-ideal product for citizens in emergencies. Despite government risk assessment awareness that the anthrax letter attacks "demonstrated [a] low correlation between environmental exposure and infection risk" (NRC, 2008), earlier projections of up to 13,000 fatalities appeared to propel a continuation of policy and procurements (DHS, 2009b). A logical question is why, particularly when simple antibiotics remain the recommended "first line of defense" for anthrax infection (HR,

Committee on Homeland Security, 2007, p. 48–50).[54] This contradictory scenario requires the use of psychological and sociological methodologies to help explain the questions about the human behaviors and motivations that lie at the root of these questions.

Psychology offers a means of better understanding why military and government leaders continued to procure the old known "unsatisfactory" (Brachman & Friedlander, 1998, p. 636) and "inadequate" (FDA, 1997; IOM, 2000; Schumm, 2004) anthrax vaccine. The methodology offers a means for interpretation of the human behaviors involved, as well as an opportunity to derive lessons. The hermeneutic of psychology allows an evaluation of the ethical breaches associated with the anthrax vaccine, beyond individual sociopathic deviations, and instead permits a focusing on the institutional and situational contexts. To accomplish this objective for the social psychology section of the gap analysis chapter, we explore a sampling of several cognitive concepts, such as confirmation bias, probability neglect, availability heuristic, negativity bias, and social identity theory in order to provide perspective on the human behaviors that transcend the legal violations.

a. Confirmation Bias

The first cognitive concept involves that of "confirmation bias," or the ability of humans to confirm what they want to believe or rationalize, while discounting evidence to the contrary. Nazi atrocities demonstrate the strength of collective confirmation bias as one of the strongest forces in human nature, particularly when combined with societal acceptance (Weiner, 2008). When placed into the context of the anthrax vaccine issue, military leaders needed a countermeasure to protect their troops

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[54] Government officials testifying about the primacy of antibiotics and antimicrobials to address the anthrax threat, while also emphasizing the need for a next generation anthrax vaccine:

Mr. PARKER. Well, first, I just want to say that antibiotics are the first line of defense and we do have a very significant stockpile of antibiotics and that is the first line of defense.

Dr. FAUCI. The best approach towards anthrax is antimicrobial therapy.

Mr. PARKER. We need to continue to develop and procure a second generation vaccine. But we also need to look forward to that third generation that has better characteristics that make it more deployable in an emergency, in a disaster situation. So we need that balanced approach for anthrax vaccines (HR, Committee on Homeland Security, 2007, p. 48–50).

against a biological threat, and therefore when presented with evidence "partial to existing beliefs" (Nickerson, 1998) and needs, the utility of contradictory information was not entertained. In the case of the DoD anthrax vaccine program, the mantra that the vaccine was "safe, effective, FDA-licensed and essential" (Cragin, 1999) did not allow room "to be tolerant of the beliefs or opinions of others" (Nickerson, 1998, p. 1328).

The tendency to "look for evidence that is directly supportive of hypotheses" became the modus operandi of the DoD, while simultaneously "embarrassing" alternative hypotheses with maligning bylines such as "ignore the paranoiacs; the vaccine is safe" (Blanck, 1999; Nickerson, 1998). In the armed forces "simply being aware of the confirmation bias—of its pervasiveness and of the many guises in which it appears" (Nickerson, 1998)—ultimately did not comport with the requirement for good order, and therefore those pointing out inconsistencies, regardless of their veracity, were disciplined. One military officer testified about the "stark divergence of the medical community's assessment of the safety and efficacy" of the vaccine, and the coincidence that this phenomenon occurred at the same time the DoD program began (Dingle, 2001). The officer was one of hundreds of soldiers removed from their service positions when unwilling to salute smartly in the face of confirmation bias.

b. Probability Neglect

Another directly applicable cognitive concept includes probability neglect, where people "subjectively overestimate the probability of highly undesirable but objectively rare outcomes." Obviously, with an anthrax attack, "intense negative emotions are involved," and our "attention is captured by the dreaded outcome," regardless of the "relatively small chance of the threat actually occurring." Such probability neglect "is an important contributor to sustaining disproportionate fears of terrorism," (Breckenridge & Zimbardo, 2007, p. 122), in this case that of anthrax based on attacks fomented by an Army scientist to perpetuate his vaccine program. Government scientists for years recognized that a "bioterrorist event is low probability and high consequence," and also recognized that "new and better drugs for treatment or

prophylaxis, and new vaccines, especially against anthrax and smallpox, are needed" (Hamburg, 1999). The Army scientist, aware of the calls for a new vaccine, thus overcame the low probability component of probability neglect to surmount both the problems with his product and the statistical improbability of an anthrax epidemic.

c. Availability Heuristic

Experts in psychology also describe the notion of the availability heuristic, or a "tendency of people to assign a higher perceived probability (or risk) to vivid, easily imagined (available) events" (Breckenridge & Zimbardo, 2007, p. 121). For years military and government proponents of the anthrax vaccine claimed that "the threat is real" (Cohen, 1998a; Cohen, 1998b; HR, Committee on Government Reform, 1999; DoD, 2009a, pp. 14–17). The anthrax letter attacks of 2001 not only overcame probability neglect but also created the data point to make the availability heuristic a reality. The attacks, which paralyzed the nation at a time when immense residual fear existed due to the World Trade Center tragedy, demonstrated the power of the "base rate fallacy" due to the "weight [of] recent, easily imagined, and highly arousing events" (Breckenridge & Zimbardo, 2007, p. 35). Government leaders then leveraged the commonly related "affect heuristic to make judgments," with fear facilitating "decision making and risk appraisals." In other words, the attacks directly affected present policy and procurement decisions because "ordinary people use their feelings to estimate risk" (Breckenridge & Zimbardo, 2007, p. 121).

The attacks, and resultant paranoia, affected over $57 billion in biodefense expenditures (Clark, 2009; Drogin, 2009; FBO, 2004; FBO, 2005; FBO, 2007; FBO, 2008). The availability heuristic also became evident in post-facto scientific studies generated to justify the vaccine. The IOM documented the creation of the new science. Prior to 2001, there were "only a few published peer-reviewed studies examining the safety of the anthrax vaccine in humans." Independent expert reviews found a "paucity of published peer-reviewed literature on the safety of the anthrax vaccine"[55] (IOM, 2000,

[55] According to the Institute of Medicine, "The committee located only one randomized peer-reviewed study of the type of anthrax vaccine used in the United States" (IOM, 2002, pp. 257, 259).

pp. 257, 259). Presently though, "twenty safety studies of various types [had] been performed to assess anthrax vaccine," (DoD, 2009c, p. 31). The sudden availability of new medical literature, supportive of the vaccine, assisted in validating policy. Ultimately, when a "substantial number of service members disagreed with issues regarding the ethics, safety, and efficacy" of the vaccine, the rationalized conclusion was that an increased availability of "enhanced training and education" (Pica-Branco & Hudak, 2008, pp. 429–33) would solve the problem.

As a parallel to the education and information campaigns, the vaccine manufacturer also ensured the "availability" of over $5 million to pay lobbyists to remind lawmakers about the vividness of the threat, which potentially influenced decision-making in Washington (Associated Press, 2008; Willman, 2007).

d. Negativity Bias

Experts have also found that "human beings are much more powerfully influenced by negative than positive information" (Breckenridge & Zimbardo, 2007, p. 122). Within the anthrax vaccine quandary a fascinating psychological dilemma appears where negativity bias manifests itself in multidimensional forms of fear. Contrasting fears exist from fear of the immunization to fear of the threat. In addition, "military service members fear reprisal if they refuse to participate" (Pica-Branco & Hudak, 2008, p. 431). The negativity of the threat to create fear was exemplified by the Defense Secretary's waving a five-pound bag of sugar in 1997, pretending that it was anthrax, and insisting that it would kill 50% of Washington's population[56] (DoD, 1997a; also illustrated in Figure 3). Top government officials also emphasized that the "anthrax attacks in October 2001 illustrated the risk" (Keys & Taylor, 2005), while others warned of the uniformly lethal, "unequivocal," and "incontrovertible" nature of the threat to justify the vaccine (HR, Committee on Armed Services, 1999, p. 56).

Threat fears aside, military leaders attempted to counter soldiers' concerns about vaccine safety problems with negativity tactics. For example, a top general

[56] Defense Secretary William Cohen held up a five-pound bag of sugar on TV to show the amount of the biological weapon anthrax that could destroy half the population of Washington, D.C. (DoD, 1997a).

humiliated soldiers by stating that soldiers opposed to the vaccine "are petrified that their penis is going to fall off" (Bacevich, 2000, p. 225). Other top generals negatively framed concerns over the vaccine as "fear of immunization" (HR, Committee on Government Reform, 1999, pp. 15–17) by "refuseniks." In other words, they equated professional questions about the vaccine to cowardice by troublemakers "who don't want to be in the military" (HR, Committee on Armed Services, 1999, pp. 33). Both negativity bias tactics successfully diverted attention away from legitimate medical, legal, and regulatory problems. Concerned soldiers were discharged, and just when the vaccine program was about to be stopped by a new administration, the anthrax letter attacks created a new spiral of negativity.

As a result, the DoD revived and expanded the vaccination program, ostensibly confirming that the Congress, the people, and the media were swayed by "threatening" forecasts, possibly because "negative information is more contagious and 'stickier' than positive information" (Weiner, 2008). The people's fears[57] effectively succumbed to negativity bias, versus positive reflection on the fact that "antibiotics alone, without the vaccine, are effective in killing anthrax bacteria" (HR, Committee on Homeland Security, 2007, p. 17).

e. Social Identity Theory

Concepts from social psychology may also assist us in understanding "in–group bias," which supports institutionalized policy directions (Bongar, Brown, Beutler, Breckenridge, & Zimbardo, 2007, pp. 358, 363). Social identity theory in particular provides a commonsense explanation of a member's desire to belong to any organization.[58] Manifestations of the desire to belong include examples such as the fact

[57] For additional references where fear and negativity was used to justify and perpetuate the anthrax vaccine program, see, e.g., Allison, 2002; Business Wire, 2007; Charatan, 2000; Clark, 2009; Corrigan, 2001; Drogin, 2009; Eberhart, 2001a; Eberhart, 2001b; FDA, 2005b; GAO, 2000a; Graham, 1996; Grossman, 2000; Leitenberg, 2005; Mason, 2005; Mayo Clinic, 2009; Meek, 2008; Melman, 2009a; Melman, 2009b; Milbank, 2005; Stemp-Morlock, 2006; Teibel, 2009; UPI, 2009; Weiss, 2001.

[58] Western society emphasizes the need for a "positive and distinct" identity, and in a more global context some would suggest that "authenticity" in identity is also important. In the military context, though, only the "positive" identity attribute is required for success and in-group inclusion. Military service may in fact more narrowly shun both distinctiveness and authenticity in identity due to the need for the good order and discipline of the team (Moghaddam, 2006, pp. 27, 41).

that "many service members are afraid to report health problems associated with the vaccine for fear of being labeled as troublemakers" (Grossman, 2000). Further, opposition to the vaccine consistently found DoD leaders, the in-group, flanking "refuseniks" with accusations of failing to be a part of the "team effort" (HR, Committee on Armed Services, 1999). From the highest offices, the message was clear: "Soldiers, sailors, airmen and Marines fight in teams and they need to know that all team members are protected from anthrax" (Cragin, 1999).

As a result, those concerned about vaccine "adverse events," or illnesses, faced "the risk of being labeled as a malingerer" (IOM, 2002, pp. 102, 108). All the while, government reports reported that "a new vaccine, developed according to more modern principles of vaccinology, is urgently needed," that the current product is "far from satisfactory," and acknowledged the immunization as "relatively crude vaccine by current standards" (IOM, 2002, pp. 20–21, 199–200). With respect to the military dynamics at play, esteemed social psychologist Dr. Stanley Milgram identified these very social identity concepts writing, "The soldier does not wish to appear a coward, disloyal, or un-American. The situation has been so defined that he can see himself as patriotic, courageous, and manly only through compliance" (Milgram, 1974, p. 182). The in-group knew the playbook, and apparently pitted the sociological realities against the ethical choices troops must make in order to evoke obedience and belong to the in-group.

f. "Bad Apples" or "Bad Barrel"?

The pursuit of an explanation brings us to a relevant military analysis of the abuses at Abu Ghraib. The prisoner abuse controversy from America's earlier experience in Iraq highlighted perceptions regarding the institutional nature of the "psychological causes behind such disturbing metamorphoses" where people collectively commit wrongs. Without judging the case of the Abu Ghraib controversy, this analysis merely adopts the "premise that ordinary people, even good ones, can be seduced, recruited, initiated into behaving in evil ways under the sway of powerful systematic and situational forces" (Zimbardo, 2007, p. 443). The study of Abu Ghraib helps us to place the idiosyncratic social behaviors in perspective by altering the common notion of a "bad

apple." More apropos is the prospect of a "bad barrel," or "the idea that the social setting and the system contaminate the individual, rather than the other way around." The "bad barrel" concept acknowledges the potentially "corrosive influence of powerful situational forces" (Zimbardo, 2007; Zimbardo, 2009, forward).

Reflecting on the Stanford prison experiment and Dr. Zimbardo's "bad barrel" metaphor as it relates to the anthrax vaccine program, we discover the possibility of DoD leaders being "caught up in the crucible of social forces" (Zimbardo, 2007, p. 211). In contrast, concerned soldiers served as the situational subjects and, when noncompliant, found themselves labeled as "bad apples." In line with a "truism in psychology," an obedience-oriented military culture and a command-influence environment, dictating the mandatory vaccination policy emerged as a situational level "bad barrel" (Zimbardo, 2006; Zimbardo, 2009, pp. 18, 20–21) based on the program's illegalities. Like the perception of situational missteps at Abu Ghraib, the anthrax vaccine dilemma potentially "represents the triumph of a mindless dispositional view" (Zimbardo, 2006, pp. 21–22). Indeed, the DoD levied disparagement and adverse actions against individual "bad apples" for not wanting to submit to a problematic vaccine and for refusing to participate in what turned out to be an illegal order. After the fact, the courts ruled the vaccine to be unlicensed, experimental, and illegal as some troops had originally cautioned. As with perceptions regarding the controversial attempts to extract accountability for Abu Ghraib, responsibility for the problems with the anthrax vaccine ultimately only occurred at the bottom rung of the chain of command. In effect, the institutional nature of the anthrax vaccine program fulfilled the "bad barrel" role, whereas the top leaders potentially and unwittingly served as the "bad barrel makers" (Zimbardo, 2009).

Following the federal court injunctions, neither the program nor the leaders faced accountability for the violations. Top DoD leaders, the original "makers" of both the anthrax vaccine and the mandatory policy, also constructed the mandate as a "Commander's program," effectively cancelling doctors and the Hippocratic Oath out of the equation (Chu, 2005, p. 3). Reducing the medical doctor's role as an "ingredient" in the barrel complemented the "situationist recipe for behavioral transformations"

(Zimbardo, 2005, pp. 26–28). The "Commander's program" emphasis dissected the medical professionals out of the operation. In doing so, the DoD effectively cut off military doctors from performing their intended duty to serve as the "bad barrel" vaccine industry regulators.

g. Closing the Psychological Gap

Globalization and asymmetric warfare place the nation in a predicament for the near future. Bioterrorism as a form of asymmetric warfare exemplifies this conundrum, as evidenced by the 2001 anthrax letter attacks. While some suggest "irresponsible coverage" by the media could "lead to chaos," this thesis demonstrates that the government itself shares responsibility for setting the tone of the nation's reaction to such events. An article written in 2000 and prior to the letter attacks embellished the threat, saying, but not citing, that "50 kilograms of anthrax released from an airplane could create a lethal cloud of anthrax spores that would extend more than 20 kilometers downwind." The author added, parenthetically referencing a congressional source, that "130,000 to three million deaths could occur following the release of 100 kilograms of aerosolized anthrax over Washington, DC" (Wyatt, 2000, p. 63, 66). Yet government reports concluded, "Reactions to anthrax episodes were strongly conditioned—and exaggerated—by their occurrence so soon after September 11" (IOM, 2002, p.2). Confirmation bias, probability neglect, availability heuristics, and negativity bias all appear to apply. Ironically, in the case of the anthrax attacks, it was the government that hyped the threat to justify use of the vaccine before and after the attacks, and it was a government scientist that committed the terrorist attack to revive use of the vaccine when the program was about to fail. Regardless of the contributing bias and motives for the hype or the attacks, "the policy of self-policing and accurate, responsible reporting must be followed in the event of a bioterrorist attack and the time to prepare for such reporting is now" (Wyatt, 2000, p.66).

Overcoming biases and surmounting the "evil of inaction" (Zimbardo, 2005, p. 42) presents a challenge. Recently, a government report related to WMD recommended "whistleblower mechanisms" (Graham & Talent, 2008, p. 31). Others

advocate "integrity system heroes" where a dimension of humility exists in an environment that facilitates expressions of minority opinion. This environment replaces egocentrism with sociocentrism in order to overcome the "root causes" of inherent situational evils over time. "Chronicity" is a term used by Dr. Zimbardo to describe the healing power of time (Zimbardo, 2007; Zimbardo, 2009, p. 466). Historic examples of chronicity include presidential apologies for syphilis testing after 50 years (Clinton, 1997), radiation testing 40 years after the fact (ACHRE, 1995), and government acknowledgment about the toxic effects of Agent Orange (DVA, n.d.). Notwithstanding the inherent injustices created due to untimely corrections, man's dispositional ability to correct evil through the remedy of reflection serves as a belated counterweight to situational evils (Zimbardo, 2005, pp. 47, 210). Along with time, societies require system heroes and bad-barrel regulators to accelerate the process. Time, heroes, and regulators can compress chronicity and halt the patently wrong acts by those who would manipulate social biases in order to get their way. Heroes and regulators must heed the "call to action and to service when others fail to act"[59] (Zimbardo, 2007, p. 461). In the case of the anthrax vaccine, the government must strive to enlist the confidence of the public in the medicines it stockpiles and always remember, "The public will not take the pill if it does not trust the doctor" (Glass & Schoch-Spana, 2002, p. 218).

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[59] Dr. Phillip Zimbardo offers a four-dimensional model of heroism, called the motivational and decisional framework. The model grids the "engagement style" vs. "risk type/sacrifice." The questioning of the anthrax vaccine occurs on the entire right side of the framework—both active (gallant) and passive (fortitude) across the full spectrum of the social sacrifice quadrants. Government leaders who go back and analyze the anthrax vaccine's potential role in Gulf War illness, the "failing" status that resulted in the recommended cancellation of the program in the summer of 2001, and the vaccine's suspected role as motive (per the FBI) in the anthrax letter attacks, will undoubtedly fill the void of civil-service heroes.

A third dimension on the grid includes "quest," i.e., whether or not a heroic quest serves to preserve life or preserve an ideal. The quest to challenge the anthrax vaccine program could be viewed as one of the preservation of life if one believes the vaccine to be unsafe or one of the preservation of an ideal if one focuses on the unethical or illegal aspects of the program. Clearly, it could also be a combination of the two as the illegalities could represent both unethical breaches, such as improper safety testing, which could lead to loss of life if left unchallenged. Dr. Zimbardo adds a fourth dimension to the model, that of "chronicity." By adopting this dimension, he acknowledges, "heroism can accrue over time." He adds that bravery in battle across time might be termed "valor," but adds, "There are not yet comparable terms to denote duration in civil heroism."

The long-term struggle to challenge the problems with anthrax vaccine could qualify. Dr. Zimbardo adds the term "collective heroism," which may likely serve as the best venue for success. Congressional leaders, judicial review across multiple jurisdictions, or members of a new executive branch team might represent "collective heroism" when applied to the anthrax vaccine example (Zimbardo, 2007, p. 480–82).

Over time, the DHS should choose the right course, steering clear of adopting potential sociopathic pathologies and biases in order to accomplish institutional objectives as appears to be the case with the DoD anthrax vaccine experience. Simply put, the DHS and the DHHS should do their own homework and avoid adopting the potentially flawed dogma of DoD policy. Internal systemic benefits will occur merely due to the independent inquiry of checks and balances. Clearly, a system that fails to do so defines unhealthy pathologies. Dr. Milgram cautioned, "The disappearance of a sense of responsibility is the most far-reaching consequence of submission to authority" (Milgram, 1974, p. 8). Awareness of social psychology factors, and their intrinsic biases, will help preclude such an eventuality and aid in checking the negative pathologies associated with anthrax vaccine over the long run.

2. Anthrax Vaccine as a Model "Blue Ocean" Strategy

The focus of the present thesis requests reflection on the DoD experience with anthrax vaccine to aid in a retrospective analysis by the DHS. We therefore borrow from the business concepts articulated in *Blue Ocean Strategy* (Kim & Mauborgne, 2005) in order to provide perspective and an explanation for the gaps existent with the anthrax vaccine's market-value innovation. In essence, the outlier case represented by the anthrax vaccine also characterizes the attractive marketplace gaps, or the uncultivated business opportunities provided due to the vaccine's cozy status of governmental support.

As a result, the anthrax vaccine enterprise hails as a "benchmark" in strategic "Blue Ocean" business ventures. As revealed through the event-cause relationships described in the Chapter III's case study, the DoD effectively served as an "intimate" business partner to the anthrax vaccine manufacturer based on "continuous involvement" in the manufacturing and procurement activities related to the vaccine. The business association with the DoD for procurement contracts of a biodefense countermeasure offered an uncontested market space when it came to anthrax vaccine. The competition was irrelevant based on "sole-source anthrax vaccine procurement" (HR, Committee on Government Reform (HR 106-36), 1999c).

The diagrams and narrative below retrospectively analyze and apply the "Blue Ocean" strategy as it relates to anthrax vaccine, both from the perspective of the first value-added proposition of sole source contracts with the DoD, but also in the second expanded value innovation market as a countermeasure component of the SNS for the DHS and the DHHS. In diagramming the market space, we compare classic "Red Ocean" strategies (i.e., bloody red, shark infested, waters) to that of traditional biopharma firms, such as Merck, Searle, and Pfizer. Prior to the 2001 bioterrorism crimes using anthrax letters, the absence of these traditional companies in the anthrax vaccine marketplace may be explained by their pursuit of classical medicine contracts and countermeasures for standard public-health threats, versus the more risky bioterrorism business. In comparison, the "Blue Ocean" strategy (i.e., no sharks or blood in the water), and value innovation for the anthrax vaccine manufacturer, with DoD as a de facto co-manufacturer, presented an entirely new and uncontested market-value curve.

The common denominator in the strategy entailed U.S. government or DoD subsidizing of myriad aspects of the anthrax vaccine business venture. Aspects included the patent, clinical trials, licensing, approved and unapproved manufacturing changes, renovations, price increases, extraordinary financial relief, supply of a captive market (soldiers within the DoD, or citizens with respect to the SNS), and indemnification or product liability protection. The FDA also facilitated the "Blue Ocean" before the letter attacks by ignoring compliance policy guidance to disapprove anthrax vaccine contracts due to the manufacturer's quality control deviations (FDA, 1981), and again after the anthrax letter attacks by approving previously unreported and unapproved manufacturing changes (GAO, 2001b; FDA, 1996). Not imagined at the time, because federal investigators confirmed a DoD scientist committed crimes to realize the threat, the business relationship also benefited from the dramatic creation of market demand. Finally, lobbying, effectively funded by the contract financing, assured the current and future contracts.

a. Eliminate, Reduce, Raise, Create Grid

The "Blue Ocean" strategy concept asks for entrepreneurs to grid and act on a "four actions framework" (Kim & Mauborgne, 2005, pp. 29–37) in order to generate a new value curve as depicted in the subsequent strategy canvas. This aspect of the gap analysis offers in Table 3 an Eliminate-Reduce-Raise-Create grid that illustrates the factors intended to advance market value.

Eliminated: - Informed Consent - rPA next-gen vaccine competitor product contracts - Liability / FDA enforcement	**Raised:** - Awareness of the threat - Impression that the vaccine will protect from the threat - Inertia to maintain sole-source contracts
Reduced: - Controversy via PR - Legal barriers via legislation - Oversight via lobbying - Questions about prior issues via education campaigns	**Created:** - "*a scenario, where people all of a sudden realize the need to have this vaccine*" (FBI, 2008, pp. 12-16)

Table 3. Eliminate-Reduce-Raise-Create Grid for Anthrax Vaccine

As Table 3 depicts, in the case of the anthrax vaccine, the DoD eliminated and reduced problems while effectively raising threat levels, or in the case of the anthrax letter perpetrator, creating scenarios to emphasize the threat and the need for the vaccine. As a result, the problems associated with the program, such as informed consent, were eliminated by the mandatory nature of the DoD program. Elimination of more modern products resulted from those products suffering from a lack of FDA approval; whereas the government helped the old anthrax vaccine manufacturer create the impression that its product was "fully FDA-approved" (DoD, 1998). DoD indemnification solved liability

problems. Elimination, or resolution, of prior FDA oversight and invalidation of the manufacturing process coincided with the expedited approval of the manufacturing process following the anthrax letter attacks. Heavily funded DoD public relations "education campaigns" allowed for a reduction of the controversial nature of the mandatory inoculations with respect to Gulf War illness. Similarly, joint lobbying initiatives by the DoD and the manufacturer on Capitol Hill reduced the inquiries of legislators, whereas legal initiatives such as the Emergency Use Authorization allowed continuation of the vaccine mandate following federal court injunctions. As far as raising market potential, an emphasis on the "threat," and the shift in scientific opinion about the vaccine's efficacy against the disease, assisted to ensure the sole source contracts. Ultimately, the FBI's revelations of the anthrax letter attack "scenario, where people all of a sudden realize the need to have this vaccine," created the most important aspect of the grid to ensure restoration and expansion of demand.

b. "Benchmark" Blue Ocean Strategy Canvas

As a complement to Table 3's grid for anthrax vaccine, Figure 5 represents a "Blue Ocean" strategy canvas. The canvas illustration provides a graphical depiction of the product's potential value in a market space against various factors of competition. Following Figure 5's strategy canvas, we detail each of the factors listed on the horizontal axis of the illustration to aid in explaining the market-value synergies in detail. The "continuous involvement" of the DoD again emerges as a common theme in the value innovation factors due to the DoD's institutional promotion of the product, extraordinary financial relief for the manufacturer, and significant assistance in renovating and modifying the manufacturing facilities and production processes. In the case of the DoD anthrax vaccine, success did not appear to be predicated on the superior nature of the product, but instead was based upon other innovative factors related to the relationships of the sole source manufacturer with the customer, as well as the customer's shared status as a de facto manufacturer.

In this case, the anthrax vaccine's biopharma-defense countermeasure "Blue Ocean" is compared to classic public-health industry "Red Ocean" investment factors as depicted in Figure 5 (Kim & Mauborgne, 2005, pp. 25–28).

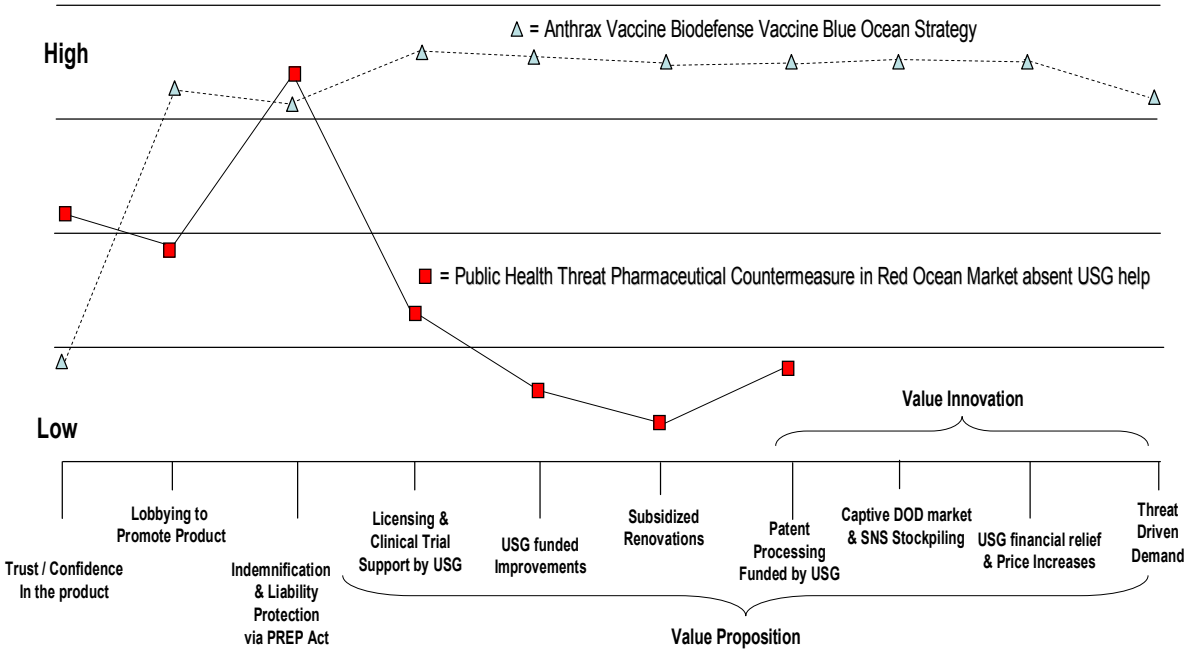

Figure 5. "Benchmark" Blue Ocean Strategy Canvas for Anthrax Vaccine

The notional graphic depictions reflect a significant market space between the classic "Red Ocean" and the "Blue Ocean" represented by the anthrax vaccine "value proposition and innovation" as compared to classic pharmaceutical products. The "value proposition" of government assistance makes the Blue Ocean attractive to the entrepreneur, with additional synergies provided based on minimal competition "value innovations" inherent in government-backed biodefense products. While not applauding the various iterations of anthrax vaccine manufacturers (MDPH, MBPI, BioPort, and presently Emergent BioSolutions), the methodological approaches advocated by this thesis do not seek accountability from the manufacturer, but instead the government for promoting such an environment. After all, who could blame a corporation for taking advantage of a lucrative business atmosphere?

The "continuous involvement" of the government began with the anthrax vaccine patent, sponsored and paid for according to the government patent by the "United

States of America as represented by the Secretary of the Army." The patent also detailed that the product of "invention described herein may be manufactured and used by or for the Government of the United States of America for government purposes" (Wright & Milton, 1965). Clinical trials were also coordinated and paid for by the government, as evidenced by the fact that the "investigation was supported by a contract with the U.S. Army Biological Center, Fort Detrick, Frederick, Md" (Brachman et al., 1966, p. 656). The FDA also confirmed that the "DoD has been significantly involved in developing the formulation and manufacturing process of all three versions of the anthrax vaccine." The FDA explained:

> DoD's continuous involvement with, and intimate knowledge of, the formulation and manufacturing processes of all of these versions of the anthrax vaccine provide a foundation for a determination that BioPort's anthrax vaccine is comparable to the original DoD vaccine. … DoD was involved in developing the three versions of the anthrax vaccine and had knowledge of the manufacturing processes of each version, DoD is thus similar to a manufacturer that made manufacturing changes to its product as contemplated by FDA's Comparability Guidance. (FDA, 2002b, p. 8)

As stated in the FDA quote above, the DoD effectively served as an anthrax vaccine producer, playing a key role in manufacturing changes, as well as the research and development of the product it invented and patented. As discussed in Chapter III's case study event-cause analysis, the DoD and the manufacturer "did not notify FDA of several changes to the manufacturing process in the early 1990s, and no specific studies were done to confirm that vaccine quality was not affected. FDA inspections found several deficiencies, many of which were not corrected in a timely manner" (GAO, 2001b, pp. 2, 4, fn. 9).

Ultimately, oversight of and accountability for the discrepancies appears lacking in the regulatory record, adding increased attractiveness to the "Blue Ocean" strategy potential to anthrax vaccine or similar market relationships. During the time frame of FDA oversight and nonvalidation of the anthrax vaccine manufacturing process, renovations paid for by the DoD, according to the GAO, enhanced the business value curve further. The GAO stated, "DoD has made a significant investment in renovating BioPort's biologic facility to meet the military's requirements for anthrax vaccine"

(GAO-NSIAD, 1999b, p. 3). The investment also entailed "significant" price increases according to the GAO, despite the fact that "the contractual price per dose was expected to decrease as production quantities increased" (GAO-NSIAD, 1999b, p. 4). Instead, the government supplied "extraordinary contractual relief to help the company with its cash flow problems and ensure continued production of the anthrax vaccine" and benefited from an "interest-free advance payment of $18.7 million" (GAO-NSIAD, 2000a, p. 3). The manufacturer enjoyed further price increases through present day equating to a 1,235% price increase for the vaccine from $2.26 to the current cost of $29.91 per dose (FBO, 2004; FBO, 2005; FBO, 2007; FBO, 2008).

Guaranteed or captive market scenarios also existed. Researchers documented that "military service members fear reprisal if they refuse to participate in the AVIP [anthrax vaccine immunization program]" Further, "research demonstrated that a substantial number of service members disagreed with issues regarding the ethics, safety, and efficacy of the AVIP." Finally, with regard to the "ethics dimension," research "clearly suggests that the mandatory nature of the AVIP is not endorsed by most military service members" (Pica-Branco & Hudak, 2008, 429–33). The DoD, versus the manufacturer, paid for the "education campaign" to attempt to overcome these problems (GAO-NSIAD, 2000b, p. 2), adding to the value innovation of the anthrax vaccine marketplace.

Regarding the safety dimensions of concern to the customers, historic and recent indemnification provided "targeted liability protections for anthrax countermeasures based on a credible risk that the threat of exposure to *Bacillus anthracis* and the resulting disease constitutes a public health emergency" (see Appendix 7) (Caldera, 1998; DHHS, 2005; DHHS, 2008b). The "threat of exposure" and declared public health emergencies unexpectedly served the motive of the silent partner, the perpetrator of the anthrax letter attacks. The FBI found, "with respect to the motive" and the "troubled nature of Dr. Ivins" that "his concern about the end of the vaccination program" created "a situation, a scenario, where people all of a sudden realize the need to have this vaccine," thus assuring continuation of the "Blue Ocean" strategy (see Appendix 11) (FBI, 2008, p. 12–15).

An additional important aspect of the business strategy lying behind the anthrax vaccine included lobbying efforts. According to a *Los Angeles Times* investigation, in 2005 the anthrax vaccine manufacturer's "yearly spending for lobbying nearly quadrupled, to $1.41 million." In 2006, "it reached $2.1 million, federal records show. All told, from 2004 through June 2007, the company used 52 lobbyists at a cost of $5.29 million, the records show" (Willman, 2007). According to another article, the company also used its contract proceeds to purchase "recombinant anthrax vaccine technology for the bargain-basement price of $2 million." In 2006, the previous recipient of contracts for the modern recombinant anthrax vaccine, Vaxgen, lost an $878 million contract with the DHHS. During this time frame, the old anthrax vaccine manufacturer's "politically connected" principals spent up to $220,000 for lobbying and campaign contributions. Reports that Emergent BioSolutions attempted to "paint Vaxgen as unreliable" highlight apparently effective attempts to eliminate and reduce the competition (Allen, 2008). The lobbying business strategy success in garnering contracts and influence with FDA as its regulator allowed additional "Blue Ocean" strategies to find new market value within existing contracts. When the FDA "granted a shelf life extension from 3 to 4 years," the company received additional funds totaling "$30 million for doses previously delivered" to the SNS (Business Wire, 2007; EBS, 2009; Marr, 2008). After the FBI revealed that the U.S. Army scientist committed the anthrax letter attacks, a reasonable expectation of contract review apparently did not occur, and instead the government vetted an additional $404-million contract for anthrax vaccine and published a simultaneous anthrax emergency declaration through the year 2015. During that time frame the old anthrax vaccine manufacturer, Emergent BioSolutions, "spent $575,000 lobbying the federal government," including paying for visits to the DoD, the DHHS and the DHS according to financial disclosures (Associated Press, 2008).

The value innovation surrounding the anthrax vaccine represents an enviable niche market where the government's "funding renovation efforts," plus "advance payments" and over 1,000% for "increasing contract prices" marked the epitome of a "Blue Ocean" enterprise (GAO-NSIAD, 1999b, pp. 1, 2). Of course, while the market methods and profit motivations remain irrelevant, the business factors

identified in this "Blue Ocean" strategy analysis may warrant review by government officials and awareness by the American people. In the end, the process irregularities, intimidate relationships, and the lax governmental oversight facilitated the steep value curve for anthrax vaccine. In retrospect, the market realities provide food for thought for officials interested in the "ethical dimensions" of future contracts for the SNS, particularly those requiring DHS endorsement.

3. Power, Policy and Politicization

The DHS strategic leadership challenge requires involvement of the stakeholders—the American people. This is contrasted with the DoD's ability to dictate policy and frame its use of the vaccine as a "Commander's program," implemented in the name of good order and with discipline. Clearly, this approach will not be effective with the U.S. citizenry. Analysis of the DoD experience, anticipating the interests of the U.S. public, may accordingly dictate alternative planning strategies or modification of the prior strategy canvas allowed to date on more captive markets. Strategic planning in the realm of biodefense offers both challenges and opportunities.

Using Kim and Mauborgne's *Blue Ocean Strategy* (Kim & Mauborgne, 2005), specifically Appendix B, as a template, we discover a guideline to compare classic versus progressive outlooks on strategic planning. Carrying the analysis further, the following examination attempts to compare the advantages of ideas put forth in John Bryson's *Strategic Planning for Public and Nonprofit Organizations: A Guide to Strengthening and Sustaining Organizational Achievement* (Bryson, 1995) to those of Brafman and Beckstrom's *The Starfish and the Spider*. This section of the thesis's gap analysis couples the most valuable and positive aspects of each into a value innovation planning strategy to derive effective and affordable national biodefense policy and procurement, with the current U.S. anthrax vaccine as the focal point.

The second appendix of *Blue Ocean Strategy* offers a tutorial on two schools of thought about how business architectures and actors approach their marketplaces. The "structuralist" view symbolizes the more classical perspective where "market structure" directly relates to "conduct," and in turn the "performance" of a business. Looking at an

alternative approach, one possibly more progressive in nature, we find the "reconstructionist" view. This approach empowers "endogenous" growth from within a business or marketplace in order to create new prospective markets (Kim & Mauborgne, 2005, p. 209). The present thesis promptly adopts the structuralist viewpoint in terms of policy-planning strategy, while acknowledging the propensity for a marketplace actor's attraction to a reconstructionist approach. That approach specifically looks for ways to stimulate demand in order to "expand existing markets and create new ones" (Kim & Mauborgne, 2005, p. 211). The anthrax letter attacks serve as a quintessential example within the U.S. military-industrial-biodefense-pharma apparatus where a reconstructionist individual unleashed anthrax spores on the U.S. public. The FBI offered the theory "that by launching these attacks, [the perpetrator] creates a situation, a scenario, where people all of a sudden realize the need to have this vaccine (FBI, 2008, pp. 12–15). Saving the "failing" anthrax vaccine program through the attacks represents an archetypal reconstructionist strategy, one that created a demand through fear. Unfortunately, this strategy served to promote a product through a crime and murders, versus the perpetuation of sound biodefense products and policy. This is precisely why the structuralist methodology must be emphasized in policy formulation as a counterweight to reconstructionist tactics. Dramatic increases in bioterrorism hoaxes, such as nearly 500 fake anthrax threats across two decades (Monterey, 2009), also represent the reconstructionist approach, though certainly not all were directly linked to the anthrax vaccine market creation as the primary motive. However, the hype and fear of these events served the same objective—to create new markets and demand. As a case in point, government appropriations increased in the range of over $50 billion for biodefense since the anthrax letter attacks and therefore document the new markets made possible through hoaxes and the domestic terrorism murders (Bryson, 1995; Mueller, 2006; Willman, 2007; Allen, 2008; Clark, 2009).

In contrast to the reconstructionist approach represented by the anthrax attacks, the structuralist approach, being more conventional in nature, fits well within the principles outline by Bryson, instrumentally serving the eventual recommendations formulated in the present thesis. The strategic management nature of Bryson's "Strategy

Change Cycle" emphasizes a process continuum beyond mere planning, and including implementation (Bryson, 1995, p. 31). This thesis encourages that continuum by the DHS. The cyclical aspect of Bryson's model lends well to the strategic oversight requirements necessary within the U.S. biodefense apparatus based on both the historic experience of the anthrax letter attacks, but also through commonsense due to the dangerous nature of potential unauthorized proliferations by nonstate actors. In addition, the book's planning process sponsorship principles emphasize the need for "creative thinking, constructive debate, and multiple sources of input and insight," as well as the willingness to "exercise power and authority to keep the process on track" (Bryson, 1995, pp. 301, 302). Such concepts are crucial, particularly in the realm of military bioresearch and defense culture. If not fostered, at times such attributes find themselves suppressed unless they promote institutional objectives. Most importantly, the Bryson ideas relate to the "enforcing of norms" (Bryson, 1995, pp. 314, 315), or rules and laws, an essential attribute for accountability in the realm of biodefense to ensure the security of the pathogens under research (Hernandez, 2009a; Hernandez, 2009b; Associated Press, 2009b).

Bryson's "interconnected leadership tasks" concepts hold direct relevance to the DHS anthrax vaccine and its strategy canvas outlined earlier (Bryson, 1995, p. 298). In evaluating the broader market for the DHS, as opposed to the more limited DoD market, chapter 11 of the Bryson text provides important reminders about "understanding the context" of any given strategy and the requirement that "leaders should be especially attentive to the possibilities for rather dramatic strategic change" (Bryson, 1995, p. 299). Anthrax vaccine use by the DHS presents an opportunity for "understanding the people involved," and remembering that "feedback from others is often highly useful" (Bryson, 1995, p. 300). With any future DHS effort in "sponsoring the process," leaders should "encourage and reward creative thinking, constructive debate, and multiple sources of input and insight" (Bryson, 1995, p. 301). Similarly, by "facilitating the process" the DHS should "press groups toward action and the assignment of responsibility for specific actions" (Bryson, 1995, pp. 305, 306). By doing so, DHS subordinate leadership will inevitably analyze the problematic DoD experience with the anthrax vaccine and realize

that these approaches were less active. The DoD experience reveals a seemingly Machiavellian "Commander's program" (Chu, 2005; Hersack, 2001; Shelton, 2001, p. 3, slide 2), one where the "team" approach was emphasized to quell dissent and questions about the vaccination program (Cragin, 1999). The 'get on board, or get out' strategy, though ultimately successful within the unique culture of the DoD, may not prove effective given DHS's target audience of first responders and the citizenry writ large. In this larger context, "enforcing norms, settling disputes, and managing residual conflicts" (Bryson, 1995, p. 314) must occur with thoroughness and transparency. Analyzing the legal problems identified in the DoD experience remains essential for the DHS as it evaluates the strategy canvas previously employed by the anthrax vaccine manufacturer and the DoD as an FDA-acknowledged co-manufacturer and client. By avoiding the legal pitfalls encountered by the DoD, the DHS will "foster organizational integrity and the education of others about ethics, constitutions, laws, and norms" pertaining to use of the vaccine on a larger market. A thorough review of the entire issue will facilitate the public servants responsible for the strategic planning in their efforts to "apply, adapt, and resolve" issues pertaining to both "laws and norms" (Bryson, 1995, p. 315).

a. Power

Another resource within Bryson's *Strategic Planning for Public and Nonprofit Organizations* offers a starting point in the process to review the DoD experience and evaluate how it translates to the larger DHS market through "stakeholder identification and analysis techniques." By applying the Power Versus Interest Grid, we help "planners identify the players or the people whose interests and power bases must be taken into account in order to address the problem or issue at hand" (Bryson, 1995, p. 338).

By reflecting on the DoD experience, soldiers as the "subjects" possessed a high interest but low power. The troop's position contrasted with DoD leadership's high level of interest and power, i.e., as "the players." First responders and DHS leadership accordingly represent the subjects and players respectively for anthrax vaccine use in a new market via the SNS. At the bottom of the grid, the citizenry at large represents the

"crowd," yet they might also share the upper-left quadrant if subjected to the vaccine. Finally, congressional and legislative lawmakers rest in the lower right of the grid as "context setters," with a potentially lessened direct interest, though a high level of power to impact the strategy, as they did within the DoD's experience. The DHS application of this same model would find citizens at the top of the chart as their interest in the subject increases due to potential exposure in a bioterrorism scenario with the product's distribution from the SNS. Table 4 depicts the Power versus Interest grid as it applies to anthrax vaccine use by the DHS.

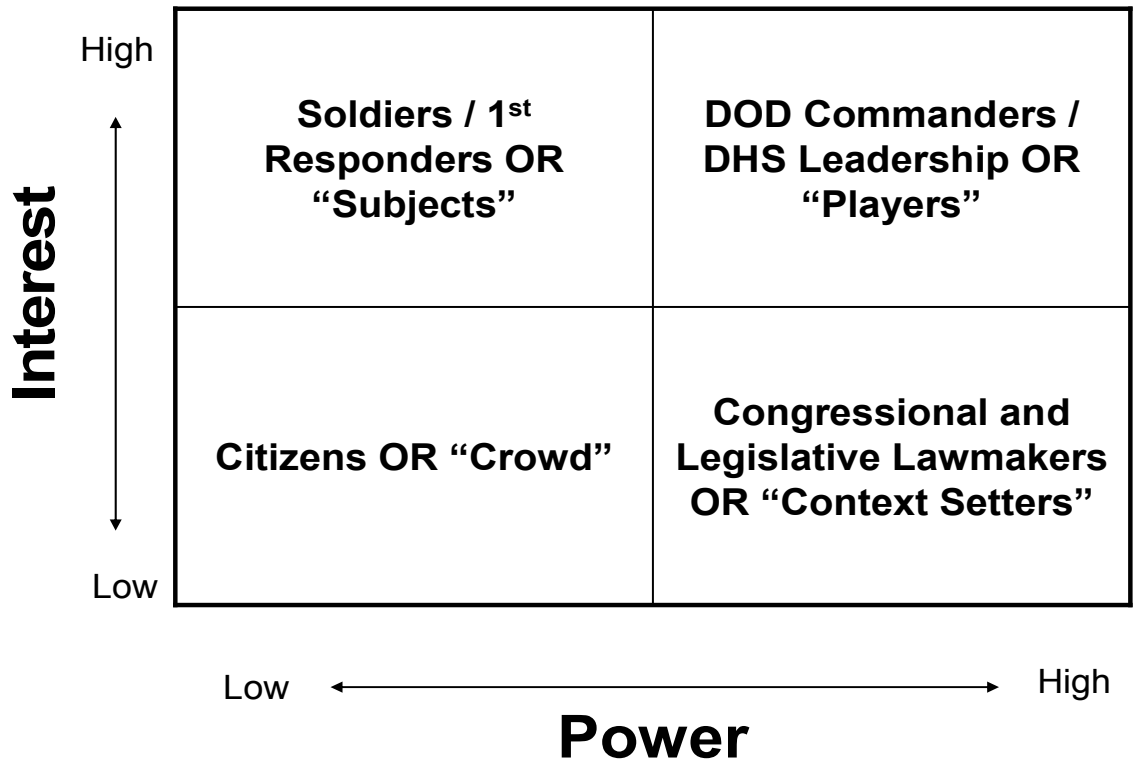

Table 4. Power versus Interest Grid

Additional tools from the Bryson text might also prove useful in the accountability efforts for a more complete analysis. These tools include the Problem-Frame Stakeholder Map, the Ethical Analysis Grid, the Policy Attractiveness Versus Stakeholder Capability Grid, and the Policy Implementation Strategy Development Grid (Bryson, 1995, pp. 347, 349, 352, 353).

b. Policy

Extrapolating on the accountability theme, using one of those tools from the Bryson resource offers a grid to model the attractiveness of anthrax vaccine policy procurement and use versus stakeholder capabilities to affect those policy processes (Bryson, 1995, p. 352). Table 5 depicts a Policy Attractiveness versus Stakeholder Capabilities grid.

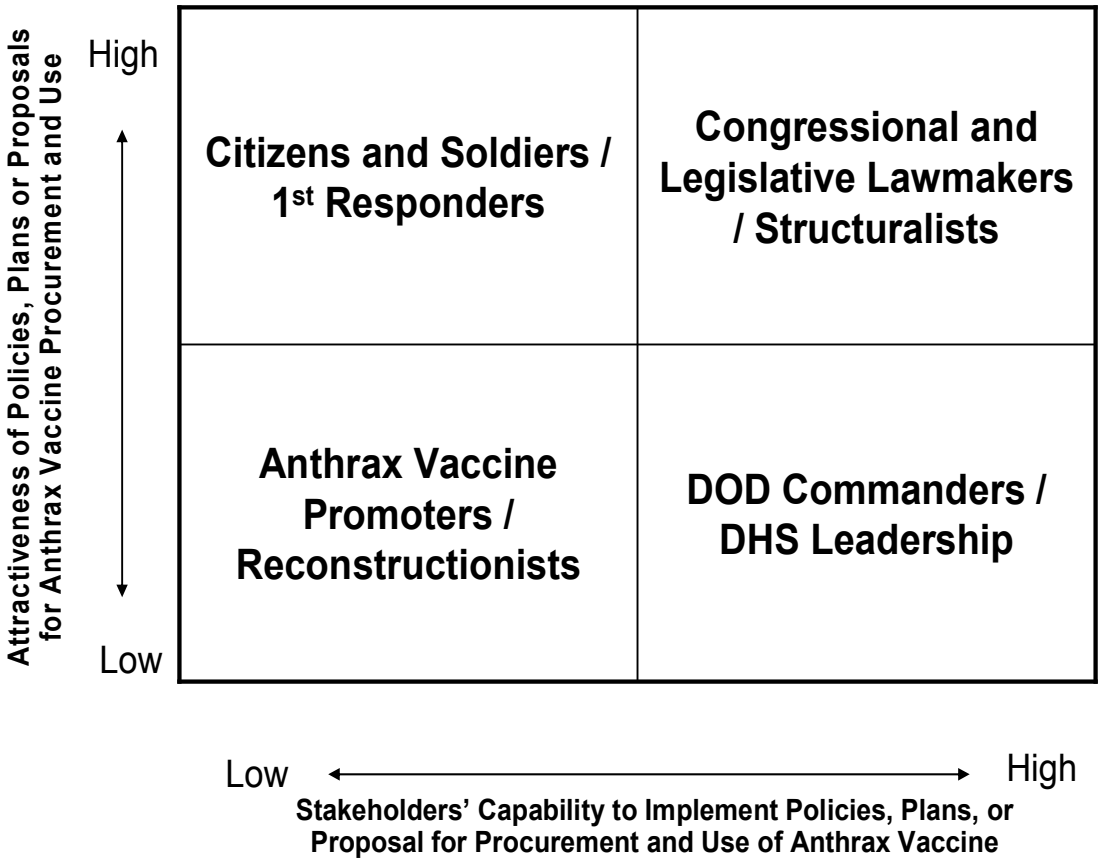

Table 5. Policy Attractiveness versus Stakeholder Capabilities

As opposed to the "power versus interest grid" depicted in Table 4, the citizen-soldiers and first responders swapped positions with the vaccine promoters on the vertical scale. Similarly, lawmakers and DoD or DHS leaders also exchanged positions.

The point is that the promoters of a product within a controversial market more reluctantly accept program guidance and policy planning. Likewise, DoD and DHS leadership may be less interested in the process than the lawmakers tasked with ensuring that such programs comply with the laws they legislate for oversight purposes. The lawmakers equate to the structuralists in this example, and the promoters of the vaccine fall into the reconstructionist category. For instance, the Army scientist who committed the anthrax crimes clearly fits the profile of someone who stimulated demand and created a new market, falling on the low and left quadrant of both the vertical and horizontal axis of the grid. Because of this disadvantaged position, the alleged perpetrator resorted to extraordinary measures to accomplish his goals as a stakeholder. Certainly, the potential reconstructionist tactics for market development, i.e., the demand-creating shortcut through crimes, hoaxes and unprecedented lobbying efforts (Allen, 2008; Associated Press, 2008; Willman, 2007) require the checks and balances of the structuralist school where proper planning appropriately reigns in the upper right-hand corner of the grid.

As a final and important metaphor for this section of the thesis, *The Starfish and the Spider: The Unstoppable Power of Leaderless Organizations* presents another facet for the proposed blended planning strategy, adding to the powerful synergy beyond that of "structuralism" versus "reconstructionism." In this case, the themes of "centralization" versus "decentralization" provide valuable potential for the planning process (Brafman & Beckstrom, 2008, pp. 21–45). The centralization themes blend well the structuralist concepts, driving the requisite processes through thorough planning and proper oversight. In contrast, the decentralization themes fit particularly well with the goal to acquire diversified biodefense products for different threats. Perhaps more importantly, the decentralization theme aligns with the logical goal of creating products that meet the demand of defending against multiple threats. As opposed to the anthrax vaccine and other biodefense initiatives, which focus on vaccinology to target singular threats, antibiotics serve to counter myriad potential known and unknown threats, and therefore present a decentralized approach to address diverse needs within the biodefense marketplace. Antiviral and antibiotic treatments also enjoy governmental recommendations for their use and further development (CDC-ACIP, 2008; CDC, n.d.;

Graham & Talent, 2008), whereas anthrax vaccine appears to extract significant governmental appropriations (FBO, 2004; FBO, 2005; FBO, 2007; FBO, 2008).

c. Politicization

Business strategy and discussions of power, interests, policy, and stakeholders aside, conceivably much of the anthrax vaccine issue perhaps boils down to politicization of the threat and the vaccine. As introduced in Chapter IV's program evaluation's qualitative analysis of intelligence, Dr. Mark Lowenthal, a former assistant director of the CIA captured the need for "intelligence products that are reliable, unbiased, and honest (i.e., free from politicization) (Lowenthal, 2006, p. 7). Lowenthal goes on to state, "These are all laudable goals, yet they are still different from truth." He calls our attention to the CIA HQ inscription that reads, "And ye shall know the truth, and the truth shall make you free." Following the quote he editorializes, "It is a nice sentiment, but it overstates and misrepresents what is going on in that building or any other intelligence agency." A literal read of these thoughts means that the former assistant director of the CIA, and former vice chair of the National Intelligence Council, argues that the byproducts of the intelligence community (IC) are not necessarily about the truth. Dr. Lowenthal's caveat that "the government and the underlying policy processes are essentially political in nature" supports this theme. Dr. Lowenthal also provides the insight that "politicization by intelligence officers may also be a question of perception" (Lowenthal, 2006, p. 138). Lowenthal touches on the FBI director's ten-year tenure as an example (Lowenthal, 2006, p. 39). He recounts how "politicization was always possible but did not become a reality until 1977" (the date when President Carter apparently ousted George Bush as the director of the CIA). Lowenthal touches on the hope that "proper training and internal reviews could avoid politicization of intelligence" (Lowenthal, 2006, 2006, p. 28). One way the IC might achieve this goal is to ensure that their information, intelligence, and final intelligence originates from solidly vetted truths.

Alternatively, Lowenthal specifically cautions that analysis written based upon "supposition" may fail to be convincing and may be more vulnerable to politicization (Lowenthal, 2006, p. 128). As Lowenthal alludes, the balance sought must

find an analytical truth somewhere between "evidence" and "supposition." Lowenthal also raises the reality of "winners and losers" and the risk that "intelligence officers may intentionally alter intelligence" due to "career interests, or outright pandering" (Lowenthal, 2006, p. 137). Lowenthal recalls how policymakers can apply professional pressures using the example of Vice President Cheney's repeated requests for briefings, sometimes from outside the IC during the controversies pertaining to WMD's in Iraq (Lowenthal, 2006, p. 186). Although Dr. Lowenthal's book explains that the Senate Select Committee on Intelligence ultimately "found there was no politicization of Intel" (Lowenthal, 2006, p. 194), a thorough read of the various bipartisan analyses of the issue after the Democratic party took control of the committee reveals differing conclusions (United States Senate, Intelligence Committee, 2008). [60] A disciplined, balanced, shoulder-to-shoulder front by the IC, sensitive to the perceptions of politicization, may be able to overcome such political pressure, but requires strong IC leaders. Those leaders must guard their intellectual objectivity vigilantly or risk reversion to scapegoat status. In an interview, President George W. Bush asserted accountability rested with the IC when responding to questions about failed intelligence assessments regarding WMD in Iraq. The president stated, "The biggest regret of all the presidency has to have been the intelligence failure in Iraq. Many people put their reputations on the line. ... I wish the intelligence had been different, I guess" (ABC News, 2008).

Reasonably, in the case of the anthrax vaccine, politicization of the process occurred. Early on military saw the "need to make the case that anthrax is currently the principal biological warfare (BW) threat" (see Appendix 3) (DoD-JPOBD,

[60] Competitive Analysis of the subject of intelligence politicization within the Senate Select Committee on Intelligence found conclusions refuting the appearance of politicization during the 108th Congress (2003–2005), when the Republicans held the majority. Alternatively, the 110th Congress (2007–2009) found the Democratic majority publishing Senate Report 110-76, "Prewar Intelligence Assessments About Postwar Iraq," Senate Report 110-345, "Report on Whether Public Statements Regarding Iraq by U.S. Government Officials Were Substantiated by Intelligence Information," and Senate Report 110-346, "Report on Intelligence Activities Relating to Iraq Conducted by the Policy Counterterrorism Evaluation Group and the Office of Special Plans Within the Office of the Under Secretary of Defense for Policy." The Senate Select Committee on Intelligence found, according to the DoD Inspector General, "inappropriate intelligence activities" where the IC misrepresented the intelligence and the threat, and of "significant claims that were not supported by the intelligence." Chairman Rockefeller asserted that the, "Bush Administration led the nation into war under false pretenses," and "relied on flawed intelligence ... deliberately," which were "not fully accurate" (United States Senate Intelligence Committee, 2008).

1995, p. 5). Other military generals recognized the DoD's vaccine "was NOT the one tested," as well as problems with asserting that "desert storm illnesses were not cause[d] by the anthrax vaccine," when there is "no record of who received the shots." Politicization and self-interests attempted to protect the program, the "DoD & the Administration" from the inevitable "big time trouble" (see Appendix 8) (HR, Committee on Government Reform (HR 106-26), 1999b; DoD-JPOBD, 1999; Miller, Engelberg, & Broad, 2002a, p. 266).

Analyzing the anthrax vaccine case study against the realities of power, policy, and politics applies valuable business strategies. The association allows us to "fold" or merge both *Blue Ocean Strategy* structuralism and reconstructionism with the classic concepts and tools presented in *Strategic Planning for Public and Nonprofit Organizations*, as well as the innovative adaptation concepts of centralization versus decentralization presented in *The Starfish and the Spider*. A possible approved recipe for strategic planning in biodefense emerges based on the case study of the anthrax vaccine experience. The recipe logically suggests that structuralism emphasized at the governmental oversight levels serves to counteract potentially destructive reconstructionism efforts, and preclude politicization and its aftermaths. Simultaneously, the centralization themes in the same light serve to ensure that the regulatory governance arena guides the policy, planning, and procurement process on a vector toward decentralized product development of treatments which prevent multiple or decentralized threats.

In conclusion, the DHS must attempt what the DoD potentially failed to do by ensuring that "effective strategic planning is a collective phenomenon, typically involving sponsors, champions, facilitators, teams, task forces, and others in various ways at various times" (Bryson, 1995, p. 316). The effective strategic planning process also requires transparency whenever possible. Ultimately, if any of these methodical strategy processes fail, national leaders may become the scapegoats when poorly conceived policy decisions go awry.

4. Multidisciplinary Approaches to Anthrax Vaccine

In addition to the social psychological, economic, and political explanations for the "gap," the following gap analysis section reviews historic multidisciplinary interactions related to the U.S. government's procurement of the anthrax vaccine. Illustrations from contrasting vignettes display diverse multidisciplinary views about the propriety of the vaccine. The split in opinion, across multiple professional and organizational lines, serves as supportive background for the thesis's course-of-action recommendation to perform a comprehensive review of anthrax vaccine procurement for the SNS. The contrasting examples of multidisciplinary inputs and oversight relate to the division of opinion over the propriety of the vaccine. Selected vignettes reveal some government officials attempting to act as "circuit breakers," highlighting the vaccine's regulatory and legality problems. In contrast, other government officials perpetuated the policy and obscured the legal barriers, effectively "politicizing" the process.

Since the 2001 anthrax letter attacks indeed successfully revitalized and expanded use of the vaccine, an intellectually honest review of past professional multidisciplinary interactions remains vital in terms of reevaluating how our nation formulates future biodefense policy and establishes appropriate procurement processes. The following multidisciplined oversight breakdowns included varied professions—doctors, lawyers, and scientists. Casting light on these vignettes offers an opportunity to correct past failures or, at a minimum, preclude repetition through the thesis's recommended courses of action. Aspects of those actions appear to comport with the agenda of the new FDA Commissioner, Dr. Margaret Hamburg. Therefore, Dr. Hamburg provides the analysis's first positive vignette by evaluating her professional assessments of the anthrax vaccine. Under Dr. Hamburg's leadership, we should expect a multidisciplinary review of both the vaccine and the highly complex organizational structure of the biodefense apparatus (Bonin, 2007, pp. 228–68).

a. Vignettes Critical of Anthrax Vaccine

The newly confirmed FDA commissioner, Dr. Margaret Hamburg, asserted in confirmation hearings that scientific and accountability-based operations

might renew public confidence (Alonso-Zaldivar, 2009). Dr. Hamburg's previous experiences demonstrate a reputation for a "science-driven" modus operandi, and "a proven track record of successfully managing large, complex organizations" (Richwine, 2009). Of note, Dr. Hamburg is not a stranger to this topic and has previously articulated the need for "new vaccines, especially against anthrax." She also expressed objectives to "shape policies against the nefarious use of biological agents, while safeguarding legitimate research" (Hamburg, 1999). Such on-the-record statements bode well for the present thesis's courses of action to review past and future biodefense strategies.

Clearly, the 2001 anthrax letter attacks appeared to outflank efforts by administration officials to "minimize" (Chu & Aldridge, 2001) continued use of the vaccine. Those efforts support the documentary record divulged in Chapter II's literature review and Chapter III's case study that demonstrated that the vast majority of scientists questioned the anthrax vaccine publicly prior to the DoD's initiation of force-wide mandatory inoculations in 1998. DoD scientists recognized the vaccine as an "experimental limited use vaccine" (Takafuji & Russell, 1990, p. 156) prior to the launch of DoD's mandatory program. Ultimately, such conclusions held weight with the courts and led to illegality rulings against the DoD mandate (*Doe v. Rumsfeld*, 2003; *Doe v. Rumsfeld*, 2004; *Doe v. Rumsfeld*, 2007). With respect to expanded use of the vaccine for the SNS, DoD scientists recommended prudence early on, stating that the "characteristics of the vaccine and the constraints on the present method of manufacturing argue strongly against procuring large amounts for civilian use" (Russell, 1999). Notably, literally every scientist or physician writing peer-reviewed articles questioned the vaccine's safety or efficacy prior to the mandatory DoD program and the 2001 anthrax letter attacks. One scientist who continued to confront the anthrax vaccine post-1998 included Dr. Walter Schumm, a retired U.S. Army Reserve Colonel working for Kansas State University. Dr. Schumm found significant associations between anthrax vaccine and the maladies associated with Gulf War illness (Schumm et al., 2007, p. 1414).[61] Additionally, Dr. Margaret Ryan, U.S. Navy, discovered a low incidence of birth defect associations (Ryan

[61] See also Schumm et al., 2007, p.457; Schumm & Nass, 2006, pp. 747–52; Schumm, Jurich, Bollman, Webb, & Castelo, 2005, pp. 342–48; Schumm & Webb, 2005, p. 331; Schumm, 2004, p. 977–78; Schumm et al., 2002).

et al., 2008, p. 434). Dr. Suzanne Timmer and a team of U.S. Navy doctors discovered pneumonitis links (Timmer et al., 2002, p. 741). Other non-DoD scientists discovered conclusions contrary to those of government scientists supporting the policy. They reported gastrointestinal adverse reactions (Geier & Geier, 2004, p. 762), "severe adverse events" (Geier & Geier, 2006, slide 33), and significant "joint related adverse reactions" (Geier & Geier, 2002, p. 217). The Journal of Emergency Medicine also reported on "Lymphocytic vasculitis associated with the anthrax vaccine" (Muniz, 2003, p. 271).

Moreover, one military physician refused to administer or receive the anthrax vaccine based on his concerns about the legality of the vaccine mandate and the manufacturer's known production line problems (see Appendix 6) (FDA, 1997). The doctor, Captain John Buck, believed he held "a responsibility to … protect the rights of the troops" (Katz, 2001) and his military oath's requirement to follow only legal orders (DoD, 1962; HR, Committee on Government Reform (HR 106-130), 1999, p. 186). The doctor's defense attorney argued that the military order was "patently illegal," but the military court prohibited any evidence at trial that questioned the presumption of legality of the order (Eberhart, 2001b). This nuance of military law, previously explained with the *Kisala* case described in Chapter IV's program evaluation's formative analysis subsection on judicial review, meant that a soldier could not challenge the legality or "inference of lawfulness" of the military mandate. Military law also explicitly maintains that the "inference does not apply to a patently illegal order, such as one that directs the commission of a crime" (DoD, 2008, p. 14.c.(2)(b)IV-19). Arguably, the mandatory vaccine program constituted a crime since the court subsequently declared it illegal (*Doe v. Rumsfeld*, 2003; *Doe v. Rumsfeld*, 2004; *Doe v. Rumsfeld*, 2007). At the time, the military tribunal found Dr. Buck guilty of disobeying a lawful order and precluded the defense from presenting evidence about the same illegalities later confirmed by the federal courts. Military attorneys commented on the circularity of the legal conundrum as an "uphill battle in getting evidence of the safety, efficacy and necessity" (Lynch, 2003, p. 60) heard in court. In essence, military legal authorities benefited from a procedural

environment where the "defense is left defenseless" (Katz, 2001, p. 1852, fn. 257)[62]. Ultimately, the military court sanctioned the doctor with restriction, fines, and a reprimand (Mientka, 2001b).

A retired FDA regulator, and former Air Force officer, Sammie R. Young, echoed Dr. Buck's concerns about production issues. Mr. Young submitted testimony to the FDA during the court-ordered licensing comment process in 2005 to ensure compliance with the federal regulations (Young, 2005, p. 1). An additional civilian practitioner, Dr. Meryl Nass, a long-time critic of the anthrax vaccine, based on her professional evaluations of soldiers suspected to suffer from adverse reactions, published several articles on the subject. According to Dr. Nass, vaccinees "report symptoms resembling Gulf War illnesses." She critically evaluated the FDA approval "retrospectively" based on "significant changes made to the vaccine's composition since 1990." She correctly asserted prior to the 2005 licensure including inhalation anthrax as an approved indication that the "mandatory use for inhalation anthrax [was] 'off-label,' " or not in accordance with the approved labeling of the product. Dr. Nass warned, "New trends could weaken prelicensure efficacy and safety review of medical products intended for biodefense and avoid manufacturer liability for their use" (Nass, 2002).

The above vignettes involving the atypical examples of medical professionals questioning the vaccine ultimately lost out to alternative multidisciplined efforts focused on sustaining and expanding the vaccine program after the anthrax letter attacks.

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[62] According to a legal analysis of the issue, when "the lawfulness of the order is in fact challenged, it is normally an issue of law to be resolved by the military judge as an interlocutory matter" (Lynch, 2003, pp. 54–55). In referencing a *Duke Law Journal* analysis (Katz, 2001), the author explains that a "military panel, as finder of fact, does not get the opportunity to consider defense evidence pertaining to safety, necessity and efficacy of the vaccine" (Lynch, 2003, p. 55). The legal evaluation suggests that the vaccine issue must be "viewed as a mixed question of law and fact that is properly resolved by a military panel as the ultimate finder of fact, not by the military judge" in order to "permit a military accused to offer evidence regarding the safety and efficacy" of the vaccine (Lynch, 2003, p. 71). "This approach … would at least allow a military accused the opportunity to present his or her argument to a finder of fact" (Lynch, 2003, p. 74).

b. Vignettes Supporting Anthrax Vaccine

Despite diverging threat assessments, past regulatory problems, and court rulings affirming past illegalities, additional vignettes illustrate numerous government professionals successfully defending anthrax vaccinations. Examples included affirmations of the threat after the anthrax letter attacks designed to reinstitute the policy (Keys & Taylor, 2005). [63] As early as 1995, the DoD emphasized the threat. Comments by Brigadier General Walter Busbee, Joint Program Manager for Biological Defense, documented in meeting minutes obtained by congressional investigators, stressed the "need to make the case that anthrax is currently the principal biological warfare (BW) threat" (see Appendix 3) (DoD-JPOBD, 1995, p. 5). Soldiers unconvinced by this case faced *ad hominem* disparagement by military generals who described the concerned troops as "refuseniks" and claimed they "don't want to be in the military (HR, Committee on Armed Services, 1999, pp. 22, 33, 56). Other military officers compared their soldiers' concerns to conspiracy theories and challenged their competence (Strawder, 1999). [64] In retrospect, court rulings vindicating the licensing problems place these tacit or outright attacks in perspective. Government reports commented on the dispute and found, "There

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[63] Hearing excerpts, Department of Defense Anthrax Vaccine Immunization Program: "You will die if you don't get a vaccine. That is the reason why this Department, when we got incontrovertible evidence in 1997 that we were facing weapons on the battlefield that were going to put anthrax on our troops, that we said we are going to have to inoculate" … "in 1997 we received unequivocal evidence, absolutely unequivocal evidence, that Iraq weaponized anthrax, and we have never, through the inspection regime, been able to confirm the destruction of those devices. We, therefore, have to conclude that anyone in General Zinni's theater of operations, if we were to get into combat again, could face an immediate anthrax attack. An anthrax attack is fatal if you are not inoculated, and therefore, we have to take these steps. It is unequivocal. ... As I said, it was in 1997 when we got absolute, uncontrovertible [sic] evidence that we have this threat, and that is when the Secretary said we are going to protect the troops," and "We have very few refuseniks, but to make a celebrity cause out of people who say they don't want to be, we have people who don't want to be in the military all the time" (HR, Committee on Armed Services, 1999, pp. 22, 33, 56).

[64] Excerpt from the Anthrax Vaccine Agency newsletter, June 1, 1999: "'Right to the Point'…Much of the hand-wringing and bizarre allegations about the vaccine is coming from a vocal minority of people who think the "field" is where a farmer works and "Gortex" is one of the Power Rangers. Most of these folks have never spent a single moment in harm's way and have no appreciation of what that sacrifice means—and they openly resent the limited budget currently used to finance our nation's defense. … Unfortunately, those of us who actually have to fight our nation's wars cannot afford such childlike optimism about the world we live in. Other groups believe that we are spreading a virus through vaccinations that will weaken our military and allow the uprisal [sic] of the New World Order. I don't make this stuff up ladies and gents … it's too rich even for Hollywood. … See you on the high ground, By Major Guy Strawder, United States Army, Director, AVIP Agency—For those who have had to fight for it, freedom has a special flavor the protected will never know…" (HR 106-556, 2000, p. 15).

was a general and pervasive degree of dissatisfaction among guard and reserve pilots and aircrew members about the completeness and accuracy of most of the information DoD provided on the anthrax vaccine" (GAO, 2002a, p. 23). The reports, and these examples, documented a clash of disciplines.[65] Some operationally oriented military members, accustomed to broken equipment being "grounded," uniformly rejected the anthrax vaccine program as a flawed policy based on the contradictory official assessments of the anthrax vaccine. In contrast, the vaccine proponents appeared to obscure the vaccine's problems with diversionary disparagement of their operationally trained colleagues, effectively impeding an otherwise healthy multidisciplinary dialogue.

Another example involved Lieutenant General Ronald R. Blanck, U.S. Army Surgeon General during the 1999 time frame. On one hand, General Blanck previously testified to Congress explaining, "Records of anthrax vaccinations are not suitable to evaluate safety." He added, "The vaccine's effectiveness against inhaled anthrax is unknown," concluding that the "vaccine should therefore be considered investigational when used as a protection against biological warfare." General Blanck admitted the vaccine was a potential cause of Gulf War illness (United States Senate, 1994, pp. 15, 35). Despite these admissions, the general later testified differently to the Senate about the vaccine's investigational license application for inhalation anthrax stating, "It is really for the facility, not for the vaccine per se." The inquiring senator responded, "Oh, I see, okay. All right. That clears that up." In fact, the anthrax vaccine license application specifically requested the FDA to approve anthrax vaccine for "inhalation anthrax" (see Appendix 5) (DoD, 1999b), a restriction that General Blanck had previously identified to the Senate in 1994. General Blanck also wrote opinion editorials to quell questions. General Blanck's essay for the *Army Times*, titled "Ignore the Paranoiacs; the Vaccine is Safe," incorrectly asserted that the vaccine had been

[65] The "clash of cultures" explained above owes its origins to the very training that the military gives its operationally oriented members. A part of the long-term multidiscipline analysis requires government officials to recognize when military members in particular become undutiful. Indeed, "within our school of military thought, higher authority does not consider itself infallible. Either in combat or out, any time a situation arises where a majority of military-trained Americans become undutiful, that is a very good reason for higher authority to resurvey its own judgments, disciplines and line of action" (DoD, 1975, p 51, item 13).

licensed by the Food and Drug Administration since 1970 (Blanck, 1999). In reality, the license remained unfinalized by the FDA until 2005, rendering the vaccine mandate illegal. Federal court injunctions in 2003 and 2004 contravened Blanck's assertions, along with the belated 2005 licensure (FDA, 2005b). General Blanck also insisted that manufacturing quality control problems related only to "record-keeping." FDA license revocation warnings explicitly contradicted this contention (see Appendix 6) (FDA, 1997). The General testified that the "threat is real," while his fellow U.S. Air Force Surgeon General, Lieutenant General Charles Roadman, framed concerns over the vaccine as "fear of immunization" (HR, Committee on Government Reform 1999, pp. 15–17). Both arguments ostensibly diverted from legitimate legal, regulatory, and medical issues. To some degree, the general was involved with the first Persian Gulf War unapproved manufacturing changes to the vaccine. General Blanck chaired an "Implementation Working Group," according to DoD documents and provided "weekly production reports" during the effort to "increase production" anthrax prior to the war (DoD, 1996, item 56). The manufacturing changes related to the attempt to increase quantities of the product but were unapproved at the time. The unapproved alterations and the vaccine's experimental use for inhalation anthrax both meant that soldiers deserved their legal right of informed consent. General Blanck clarified in subsequent congressional testimony that he understood those legal requirements. When asked by a legislator if he would "implement this same program if FDA did not approve the vaccine," the general responded, "Yes." He provided the caveat that DoD "would implement it differently because then the vaccine would be in an investigational new drug status, an IND status." While assuring "the same confidence in the vaccine," he explained the DoD "would then have to use informed consent and take other measures as part of our implementation program" (HR, Committee on Armed Services, 1999, p. 48).

Other disciplinarians shared Blanck's knowledge of challenges posed by the anthrax vaccine. An Army Chemical Corps officer, Brigadier General Eddie Cain, e-mailed colleagues concerning GAO testimony delivered during a 1999 hearing on anthrax vaccine. Cain confessed areas where DoD "came up flat," including concerns that DoD's vaccine "was NOT the one tested." General Cain discussed the slippery slope of

DoD reporting "desert storm illnesses were not cause[d] (sic) by the anthrax vaccine," when there is "no record of who received the shots." General Cain's e-mail expressed worry that the "DoD & the Administration" would be in "big time trouble" if they could not address these questions (see Appendix 8) (HR, Committee on Government Reform, 1999; DoD-JPOBD, 1999; Miller, Engelberg, & Broad, 2002a, p. 266). Whether General Cain eventually informed the Congress of these internal DoD concerns deserves further review. These unresolved issues go to the core of testing irregularities, licensing problems, early-1990 unapproved manufacturing changes, the known need for a new vaccine (see Appendix 2) (DoD, 1985, p. 3), and illnesses coincident to Gulf War service. The appearance of less-than-candid testimony left the program intact, shielding these matters from inquiry.

Another officer, Brigadier General Paul Weaver, director of the Air National Guard, received admonishment from the DoD inspector general for testimony that "lacked the necessary element of 'straightforwardness.' " The testimony in question related to personnel attrition caused by the vaccine program. Investigators found the general's testimony "inconsistent with guidelines for honesty as set forth by the Joint Ethics Regulations." The inspector general determined that the general had framed his testimony "in such a way as to lead recipients to confusion, misinterpretation, or inaccurate conclusions" (Eberhart, 2001). In addition, Marine Major General Randall West, the DoD Special Assistant on anthrax, received a verbal admonishment from Congress. West testified that he was unaware of, and could not comment on, a GAO report's conclusions. Congressional members took issue with West's contention that he was unaware of the GAO report findings, forcing the general to admit that he was in fact "briefed on what [GAO] intended to say and what they were going to present as testimony." Congressional members accused the general of providing "disingenuous" testimony (HR, Committee on Government Reform, 2000, p. 447). General West's experience adds to the impression that DoD leaders defended the policy potentially at the expense of institutional integrity.

Beyond testimonials, other military scientists acknowledged the "unsatisfactory"[66] nature of the vaccine (Brachman & Friedlander, 1994; Brachman & Friedlander, 1998, p.737) but later altered their opinions in support of the policy. Dr. (Colonel, U.S. Army) Arthur Friedlander wrote seemingly critical articles about the vaccine prior to the DoD mandate. His later articles contradicted previous critiques, inaccurately describing the vaccine as "FDA licensed" (Friedlander et al., 1999, pp. 2104–06). Significantly, Friedlander participated in the vaccine's "Investigational New Drug" (IND) (see Appendix 5) (DoD, 1999b) application process,[67] one which rendered the vaccine mandate unlawful (*Doe v. Rumsfeld*, 2004). Although Friedlander was aware that "no data on … efficacy in humans" existed for anthrax vaccine (Ivins, 1992), he later testified at a Canadian court martial that he was "not aware" of U.S. government licensing applications to obtain approval for the vaccine's investigational use against inhalation anthrax (Prober, 2000). Since Friedlander participated in these proceedings as a DoD officer and scientist, his subsequent denials about the investigational new drug process represented a multidisciplinary breakdown. Indeed, legal disciplinarians required the officer's candid scientific expertise to adjudicate a military legal issue during the court martial proceedings. Ultimately, the Canadian military dropped all charges, instead determining that the anthrax vaccine violated the Canadian Charter of Rights and Freedoms (DND, 2002). The current Canadian military position states, "At this point in time, we are not requiring our people to have anthrax vaccinations nor are we considering it" (Moore, 2007). Conceivably, the precedent of the negative impact of the anthrax vaccine experience in the 2002 time frame continues to

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[66] "The current vaccine against anthrax is unsatisfactory for several reasons." The "degree of purity is unknown." The "undefined nature of the vaccine and the presence of constituents that may be undesirable may account for the level of reactogenicity observed." … "There is also evidence in experimental animals that the vaccine may be less effective against some strains of anthrax" (Brachman & Friedlander, 1994).

[67] Dr. Friedlander was involved extensively with the investigational new drug license application, prepared by the U.S. Army in 1995, filed by the manufacturer in 1996, and updated in 1999. As a U.S. Army officer Friedlander attended joint FDA-DoD meetings related to the application and its updates. The meeting attendee list for the Investigational New Drug (IND), #BB-IND 6847, update meeting included "Col Art Friedlander, USAMRIID," and was held in Room 1A09, Building 29B, at 1300 hours on December 15, 1998. The FDA Form 1571 includes in block 7, "indications" for the Investigational New Drug Application as "Inhalation Anthrax" (DoD, 1999; DoD-JPOBD, 1995, p. 3).

trouble Canadian military authorities as that nation contemplates H1N1 inoculations for forces currently deployed to the Middle East (Brewster, 2009).

Officials for the new administration similarly comprise diverse disciplines and inevitably must chart their own courses of action on this complex issue. As a final vignette, we examine a new administration official with a professional background requiring threat emphasis. Dr. Tara O'Toole, appointed to serve as the DHS Undersecretary for Science and Technology, formerly directed the Center for Biosecurity at the University of Pittsburgh Medical Center (UPMC). Previously, she served as a co-founder of the Johns Hopkins Center for Civilian Biodefense Strategies (UPMC, 2009a; UPMC, 2009b).[68] Early on, her associates affiliated with John Hopkins defended the anthrax vaccine program. The announcement of Dr. O'Toole's nomination also noted her involvement with exercises such as "Dark Winter" and "Atlantic Storm." Dr. O'Toole's exercises emphasized the threat of biological attack (DHS, 2009a), providing her with skills potentially well suited for a DHS directorate known for an "emphasis on high-consequence biological threats" (Bonin, 2007, p. 239). Yet some expressing concerns about Dr. O'Toole relay their impressions of her unrealistically dire assessments, as documented by 2005 predictions of up to 40 million plus casualties potentially caused by the bird flu (Milbank, 2005). These causalities did not occur, although Dr. O'Toole was not alone with her forecasts. Dr. Gregory A. Poland[69] described the threat as the "most horrific disaster in modern history," adding "the clock is ticking. We've been warned." Other colleagues questioned that Dr. O'Toole's predictions "don't seem to be based on any reality," and publicly encouraged the administration to seek nominees who support "rational fact-based policies"[70] (Clark, 2009). Other UPMC Biosecurity Center

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[68] The $1 million seed money for the original center (Greenberg 1999) pales in comparison today to the almost $57 billion (Clark 2009) spent on biodefense since 2001 as a consequence of the result of the domestic anthrax letter attacks, and the over $1.2 billion spent on anthrax vaccine procurement (FBO, 2004; FBO, 2005; FBO, 2007; FBO, 2008).

[69] Dr. Poland also serves on the Defense Health Board and Armed Forces Epidemiological Board (DoD, 2007) with a history of advocating DoD's anthrax vaccine use prior to the program's being found to be illegal (*Doe v. Rumsfeld*, 2004; IOM, 2002, p. 7).

[70] Milton Leitenberg, a senior research scholar at the University of Maryland, wrote a study on biological weapons threats for the U.S. Army War College titled, "Assessing the Biological Weapons and Bioterrorism Threat" (Leitenberg, 2005).

colleagues vehemently defended Dr. O'Toole, such as retired U.S. Air Force Colonel Randall Larsen. Colonel Larsen dismisses O'Toole's critics by citing classified information to make his case.[71] Dr. O'Toole's confirmation process also advanced important ethical issues that oblige reflection, including her role as the strategic director for the Alliance for BioSecurity. The Alliance served as a collaborative corporate effort to promote biotechnologies, such as anthrax vaccines, and biodefense research. Reports allege that the Alliance has spent over $500,000 since 2005 in lobbying endeavors with the federal government, and apparently Dr. O'Toole failed to report her affiliations prior to her confirmation process. In her defense, DHS officials contend that reporting was not required due to the nonincorporated status of the Alliance. Critics suggest that such entities carry out "stealth lobbying" through avoidance of incorporation and violate the goal of transparency of government. Critics contend that the practice "runs counter to the intent of the law" (McElhatton, 2009). In fairness, several other anthrax countermeasure companies, including Emergent BioSolutions, manufacturer of the current anthrax vaccine, as well as Human Genome Sciences, Inc., and PharmAthene, makers of additional anthrax countermeasures, hold membership in the Alliance (UPMC, 2009a). Time will tell how appointees such as Dr. O'Toole perform and whether or not their future policy recommendations and threat assessments earn a reputation as sound and scientifically based.

[71] Col. Larsen is a decorated combat pilot and author of *Our Own Worst Enemy* (Grand Central Publications, 2007).

The aforementioned nonexclusive[72] multidisciplinary examples warrant a comprehensive review in any effort by the DHS to scrutinize relationships and past policy decisions regarding anthrax vaccine. Such a review may subsequently warrant elimination of the current anthrax vaccine from SNS, a rescission of the DHHS anthrax emergency declared in the fall of 2008, increased security measures for biological pathogens, and biodefense procurement policy using sound risk assessment for viable threats. At a minimum, such a review might instructively serve our new officials, such as Secretary Napolitano, Dr. Hamburg, and Dr. O'Toole, as they make their mark on this important debate.

Current or future officials must address past problems if they influence present policy, while discouraging exaggerations of the threat and disparagement of employees as tactics to override legitimate concerns. Most importantly, this recommended approach encourages new officials to forthrightly address the historical process issues related to the anthrax vaccine as they chart future policy in the best interests of civilian control of the military[73] by the executive departments they lead.

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[72] Another perceivably negative multidisciplinary example includes Dr. (Colonel, U.S. Army) Theodore Cieslak. On a positive note, the doctor and officer acknowledged that a multidisciplinary approach to biodefense "concerns the intelligence, law enforcement, medical, and public health communities" (Cieslak & Eitzen, 1999; Cieslak & Eitzen, 2000; Cieslak et al., 2000). He also recognized antibiotics as the "choice for treating victims of terrorism or warfare," while also emphasizing the need for "good intelligence" and a "heightened awareness of the threat" as a "cornerstone of bioterrorism defense," (Cieslak & Eitzen, 1999, pp. 554–55). Further analysis demonstrates Dr. Cieslak's attempts to allay other professionals' concerns regarding recommendations for the anthrax vaccine's future use by first responders. Specifically, in a recent meeting of the DHHS and Centers for Disease Control (CDC) Advisory Committee on Immunization Practices (ACIP), a 2008 summary report deemed "occupational groups engaged in response activities are not routinely recommended to receive anthrax vaccine due to lack of a calculable risk assessment." Meeting minutes captured Dr. Cieslak's participation, as well as his questioning of the recommendation. While acknowledging that the board did "not have enough information about risk," he advocated deferring to the earlier DHS recommendation based on the intelligence and "information to which Secretary Chertoff is privy." The meeting minutes accordingly clarified the correct interpretation of the DHS Secretary's memo, which actually confirmed, "There is not currently a domestic emergency involving anthrax." That memo also confirmed, "Additionally there is not currently heightened risk of an anthrax attack," and "we have no credible information indicating an imminent threat of anthrax involving *bacillus anthracis*" (CDC-ACIP, 2008, pp. 97, 101, 103–4).

[73] Samuel Huntington's *The Soldier and the State* outlined key qualities for any profession, including expertise, responsibility, and corporateness. These characteristics apply to the required multidisciplinary review of the anthrax vaccine issue. Huntington asked, "What does the military officer do when he is ordered by a statesman to take a measure which is militarily absurd when judged by professional standards?" Huntington answered, "The existence of professional standards justifies military disobedience" (Huntington, 1957, p. 8).

B. CLOSING THE GAP WITH TRUST

Trust—this core concept of the interaction of convictions and beliefs holds seemingly vast proportions, yet in fact is very simple. Some define trust simply as "confidence." Trust possesses grammatical qualities as verb and noun, a shared confidence in abilities and a mutual understanding of "integrity" (Covey & Merrill, 2006, pp. 5, 223). In other words, we trust due to trust. Whether the verb or noun comes first remains unimportant. What is important is the transitive nature of trust as verb and noun, versus which empowers the other. To have trust and to trust becomes a process, and that process completes a cycle of trust. The cycle of trust emerges as more important than the order of the words. While perhaps pedantic to some, the discussion of trust and the trust gap related to the anthrax vaccine requires inspection due to the myriad examples of scientific inconsistencies, regulatory deviations, and violations of the law that represent holes in the anthrax vaccine program's integrity.

Whereas integrity is a desired quality in any person or within a program, trust reflects integrity between two or more people, between those people and their organizations or perhaps between the people and the government's programs. The present thesis contends that a fundamental requirement for programmatic integrity and governmental trust exists just as the institutional requirements for the core value of integrity remains a *uniform* standard (United States Air Force [USAF], 1995) for the personnel subjected to the programs. Many examples outlined in the prior chapters of this thesis reveal that at times with the anthrax vaccine that cycle of trust appeared elusive.

Indeed, the United States, as well as English and Canadian allies, experienced a "decrease in levels of trust," both with respect to anthrax vaccines and with respect to the military institution. In response to suspicions, the governments rolled out education efforts to "increase confidence," yet these may have led to a "decrease in levels of trust" on both sides of the ocean (Murphy, Marteau, Hotopf, Rona, & Wessely, 2008). Within the United States, from all branches of the armed forces, the impression persists that "serious questions about the safety and efficacy of the vaccine remain unanswered" (Allison, 2002; Murphy et al., 2008). An Army attorney's academic effort in addressing the anthrax vaccine controversy suggested six years ago that "the Department of Defense

must act now to regain service members' trust if the program is to be as successful." His professional military and legal judgment concluded that the questions about the vaccine policy represented a "legitimate controversy" (Lynch, 2003, p. 78–80). Nonexclusive legitimate controversial factors included the documented safety questions resident in the earlier work of military researchers as described in the literature review in Chapter II, the prior awareness by the DoD about the vaccine's investigational status as detailed in the case study in Chapter III, and the debate over efficacy as explained in the program evaluation in Chapter IV. Concerning the controversy over efficaciousness, a respected attorney and legislator, Representative Christopher Shays, penned the congressional report concerning the vaccine's "unproven" status. He wrote:

> The AVIP should be suspended because it lacks an essential element in a medical program: trust. However well intentioned, the anthrax vaccine effort is viewed by many with suspicion. It is seen as another chapter in a long, unhappy history of military medical malfeasance in which the healing arts are corrupted to serve a lethal purpose (HR 106-556, 2000, p. 45).

Retired military leaders who reflected on that "unhappy history" acknowledged that the "level of trust began to deteriorate with the Defense Department's failure to come to grips with reports of the toxic effects of Agent Orange, the defoliant employed to destroy the jungles in Vietnam." The retired general added:

> The department was slow to respond to initial reports of illness from soldiers who had handled the defoliant during the war, and to the stories of cancers that appeared later. That failure was compounded in the 1990s by the department's perceived reluctance to resolve the complex questions raised by Gulf War syndrome—and by its apparent inability to refute the assertion that at least some of the reported medical problems were caused by hastily conceived combinations of medicines administered to soldiers to protect them from the potential effects of Saddam Hussein's biological and chemical weapons (Scott, 2000).

Ultimately, the relevance of the trust dilemma within the DoD anthrax vaccine experience between soldiers and the institution translates directly to the trust that the American people must have in their government regarding anthrax vaccine, or any other countermeasure, in the nation's SNS. Just as soldiers and citizens should be able to trust (v.) their government, public officials must similarly strive to earn their trust (n.). While

the courts confirmed the basis of the trust dilemma in findings, the Congress eloquently captured the essential missing element of trust in hearings[74] and reports[75] when describing the DoD anthrax vaccine experience (HR, Committee on Government Reform, 1999; HR 106-556, 2000). The factual record regarding anthrax vaccine, along with other defense-related medical controversies, gives credence to the DoD's understanding that "within our school of military thought, higher authority does not consider itself infallible," and that at times there is "very good reason for higher authority to resurvey its own judgments" (DoD, 1975, p. 41). The government and the DHS in particular can therefore learn from the negative externalities of the DoD anthrax vaccine experience, and also from the DoD's positive example with respect to the department's recognition of the organizational trust dynamics involved. The root causes of the DoD trust issues directly relate to the cycle of trust established by DHS as the department endorses countermeasures for the SNS for the nation's citizenry. Ultimately, Americans must trust (v.) DHS and must have trust (n.) in the products that the DHS uses its authorities to approve for the SNS (POTUS, 2004; POTUS, 2007a; POTUS, 2007b; POTUS, 2003c). The DHS has the wisdom of time and the opportunity to reflect on the DoD's cycle of trust, to help maintain its own stewardship of trust with the American people on this issue.

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[74] Trust quotes from HR 106-17 include, "The missing element of the mandatory anthrax vaccine program is trust" and "It comes down to trust. These are issues of trust. We are not in a combat situation, but when we are in a combat situation that is a vital element of our ability to perform" (HR 106-17, 1999a, p.1, 105).

[75] Trust quotes from HR 106-556 include, "Many members of the armed forces do not share that faith. They do not believe merely suggestive evidence of vaccine efficacy outweighs their concerns over the lack of evidence of long term vaccine safety. Nor do they trust DoD has learned the lessons of past military medical mistakes: atomic testing, Agent Orange, Persian Gulf war drugs, and vaccines. Heavy handed, one-sided informational materials only fuel suspicions the program understates adverse reaction risks in order to magnify the relative, admittedly marginal, benefits of the vaccine" and "the AVIP should be suspended because it lacks an essential element in a medical program: trust. However well-intentioned, the anthrax vaccine effort is viewed by many with suspicion. It is seen as another chapter in a long, unhappy history of military medical malfeasance in which the healing arts are corrupted to serve a lethal purpose" and "if there is one thing that the subcommittee learned from its review of DoD's anthrax vaccination program it is that the trust of many service members has been severely shaken. Acceptance of the recommendations in the subcommittee's report and reversal of prior disciplinary actions will go a long way toward rebuilding the trust of service members in the DoD and would be in the best interest of our Nation's armed forces" (HR 106-556, 2000, pp. 2, 45, 67, supplemental words of Representative Bernard Sanders).

Over time, the DHS must impartially evaluate the effectiveness of the DoD model. The mantra of obedience, with the firm message that "DoD must stay the course and never concede that force health protection should be a discretionary choice of each individual service member" (Curry, 2004), harmed the cycle of trust between soldiers and their command. A "bad" order effectively became a prejudice to good order and discipline. The DoD methods clearly seem incompatible in a DHS endeavor to protect the public health from the threat of anthrax due to bioterrorism.

As a former Assistant to the President for National Security Affairs, Stephen J. Hadley said, "Maintaining the trust and confidence of our men and women in uniform is critical to the future of our armed forces" (Public Broadcasting System [PBS], 2000). Similarly, the DHS must balance historic experiences and objective evaluations about the pallet of countermeasures available against maintaining the trust and confidence of the American people. The examples from all chapters of the above analysis demonstrate a tarnishing of the cycle of trust within the DoD anthrax vaccine experience. This thesis advocates that the DHS and the DHHS learn from this record and avoid creating an additional chapter for subsequent analyses.

C. SUMMARY ON THE OPENING & CLOSING OF THE GAP

As discussed in the program evaluation's summative analysis subsection on biosecurity, in Chapter IV, a recent GAO report speculated about the government's inability to "conclusively determine what motivated" the anthrax letter bioterrorism culprit. This indifferent view on motive perhaps misses the mark, particularly in light of the extensive work that the GAO has previously published on the problematic procedures relating to the anthrax vaccine (GAO, 2009, pp. 40–41). In effect, the motive of the anthrax attack perpetrator holds added importance in a retrospective effort to analyze the gaps and myriad broken processes underlying the countermeasure's history. Federal investigations to date fail to transparently evaluate these flawed processes in the post-2001 time frame, yet this process reigns as essential in the pursuit of determining the propriety of the old anthrax vaccine's inclusion in the SNS.

The DHS and governmental challenge in closing the gap and evaluating the failures or successes of the DoD anthrax vaccine history embodies the essential need to determine if that experience presents a "suitable foundation for contemporary national medical or public health policy" (Schumm et al., 2009, p. 597). In doing so public officials should avoid spackling over the documented problems. A solution path provided in the recommendations of the next chapter offers one template for how executive-level officials can exert the authority granted by the American people to restore trust and close the gap.

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VI. RECOMMENDATIONS

A. FUTURE COURSES OF ACTION

1. Phase III, Corrective Actions

Continuing from the phase I and II root-cause analysis processes (DOE, 1992) outlined, and partially exercised, within the case study in Chapter III, the thesis's multimethodology approach recommendations chapter presents the opportunity to suggest phase III corrective actions. The thesis recommends executive branch intervention through presidential establishment of a governmental entity to investigate and direct corrective actions following a formal, thorough root-cause assessment phase.

Renewed review of the anthrax vaccine begins with a collaborative effort between the DoD, the DHS, the DHHS, the DOJ and the FBI to recommence a comprehensive phase I data collection. Referring back to Chapter IV's program evaluation's summative analysis subsection on comparative policy, this thesis recommends a presidential study directive (PSD), followed by a presidential policy directive (PPD) (POTUS, 2009), to initiate this fresh start. The new presidential administration formalized the PPD and PSD process for related Homeland Security initiatives.[76]

The PSD allows the United States to conduct a thorough policy review, whereas the PPD enables promulgation of policy decisions. Resultant PPDs allow the United States to direct policy actions related to the anthrax vaccine. The PSD-PPD process reaffirms the nation's commitment to guard against illicit release of pathogens and adhere to the BTWC. Together, these actions will lead to less escalatory and controversial biological defense prophylaxis policies. Such an approach aligns with allied strategies, avoids BW escalation, and precludes facades of protection against multifarious threats.

[76] The Federation of American Scientists provide web site access to the single PSD and PPD published to date by the Obama administration; they are related to Homeland Security Council absorption into the National Security Council (POTUS, 2009).

a. Presidential Study Directive (PSD)

This thesis recommends initiation of a presidential study directive (PSD). The PSD process assures the current anthrax vaccine's inclusion as a component of the SNS represents a policy option worthy of transfer to, and adoption by, the new administration. The PSD must compel a systematic examination of the root causes behind the unauthorized 2001 release of anthrax by a nonstate actor from the U.S. biodefense program, as confirmed by the FBI. The new administration's selection for FDA commissioner, Dr. Margret Hamburg, previously advocated safeguarding biological technologies from proliferation and recommended the development of "new vaccines, especially against anthrax" (Hamburg, 1999; Richwine, 2009). Considering the commissioner's present position, the new administration's PSD process should therefore analyze the assumptions behind her 1999 recommendations, which parallel those presented in this thesis, and how they may apply to modifications of contemporary U.S. biodefense policy.

Despite the pre-2005 illegal use of the vaccine, based on the vaccine's unfinalized license and experimental status, current utilization of the product is ostensibly legal (*Rempfer v. Sharfstein,* 2009). The PSD team should address whether or not the current technical legal propriety of the vaccine equates to policy worthy of the American people given the historic safety and efficacy questions. In essence, simply because the FDA and DoD surmounted the legal challenges to the vaccine, and because courts choose to "defer to the FDA's judgment" (*Rempfer v. Sharfstein,* 2009, p. 13–14), the PSD panel must evaluate whether the countermeasure translates into an effective and necessary component of the SNS for the American population as a whole.

Examining these questions requires the PSD team to analyze the depth of past HSPD fulfillment, particularly given the requirement for the DHS to review the composition of countermeasures in the SNS. An exacting focus on the possibility that the department endorsed the anthrax vaccine unquestioningly, based on DoD or DHHS advisement, requires attention. A comprehensive review of the multidisciplinary and organizational relationships should proceed without ignoring the complete legal and regulatory schematic as potentially occurred with previous executive level reviews. The

PSD process requires a thoughtful attempt to restrategize the nation's biodefense doctrine, to monitor biodefense business relationships carefully, and to monitor any "intimate" or potentially unhealthy departmental-manufacturer associations closely.

If the PSD panel determines documented problems with the old vaccine continue to hold merit, planned use of the current anthrax vaccine on the civilian population via the SNS warrants review. If the PSD concludes that the "characteristics of the vaccine and the constraints on the present method of manufacturing argue strongly against procuring large amounts for civilian use" (Russell, 1999), a subsequent PPD allows the government to correct current policy and procurement directions.

b. Presidential Policy Directives (PPD)

Following the PSD review, the administration should consider a presidential policy directive (PPD) in order to modify procurement plans for the old anthrax vaccine and ensure increased security of the U.S. biological defense program. The PPD may find prudence in formally reaffirming U.S. commitments to guaranteeing nonproliferation and adherence to the BTWC. In addition to evaluating the anthrax vaccine's suitability as a component of the SNS, the PSD and resulting PPD should also reassess the propriety of the 2008 DHHS "anthrax emergency" declaration. A rescission of the declaration should necessitate conversion of unallocated or future BioShield resources to procurement of a new vaccine and FDA approved antibiotics based on CDC advice that BioThrax® remains "not recommended for routine pre-event anthrax vaccination" (CDC, n.d.; CIDRAP, 2008).

If the PSD process determines that the tenets of the HSPDs to review countermeasures in the SNS require reaccomplishment, the PPD serves as a mechanism to direct this action. As a byproduct, the PSD-PPD process assures proven countermeasures for viable threats when applied to future biodefense and procurement policy in order to avoid blindly adopting earlier attempts at corrective policy that may neglect the core problems involved.

c. Biodefense Czar Appointment

The PSD-PPD process should consider appointment of a biodefense czar, or equivalent position, based on the high-risk activities and perceptibly poor record of the U.S. biodefense community. The czar provides oversight for the departments assigned to comply with HSPDs.

The czar also offers a solution to the significant gap in biodefense accountability. A recent GAO report affirmed the need for governmental partnerships to create viable solutions to oversee current or planned high-containment laboratories[77] (GAO, 2009, pp. 10, 22). The GAO reiterated the FBI allegations about the U.S. Army scientist "sole culprit" status as the perpetrator of the 2001 anthrax attacks, that he "helped develop an anthrax vaccine for U.S. troops," and received the highest DoD awards for "helping solve technical problems in the manufacturing of licensed anthrax vaccine" (GAO, 2009, p. 37). While inconclusively addressing "motive," the GAO restated the fact that:

> At the time of the attacks, Ivins was under pressure at work to assist a private company that had lost its FDA approval to produce an anthrax vaccine the Army needed for U.S. troops, and which Ivins believed was essential for the anthrax program at USAMRIID (GAO, 2009, p. 39).

In the "Recommendations for Executive Action" of the report, the GAO specifically recommended executive branch–level collaboration, including the DHS, and advised the government to "identify a single entity charged with periodic government wide strategic evaluation of high-containment laboratories." The report recommended risk assessment and increased security reliability for both pathogen and personnel (GAO, 2009, pp. 68–69). The report's analysis and essential measures stopped short of addressing the root motivations of the 2001 anthrax letter attacks, intimate governmental-business relationships, organization dynamics, institutional inertia, and the human

[77] DHS BSL-4 facilities include the National Biodefense Analysis and Countermeasure Center, Fort Detrick, Maryland, and the National Bio- and Agro-Defense Facility (NBAF), Manhattan, Kansas (GAO, 2009, p. 22).

behavioral forces at the core of the emergency occurrence. Due diligence by the biodefense czar in the future must analyze those forces and their potential negative momentums.

As attempted in Chapters III through V of this thesis, by addressing the facts and motivations surrounding potential contributory causes and the subsequent problematic events, this thesis advocates the correction of past behavioral deviations and the strengthening of current or future oversight mechanisms. In doing so, the biodefense czar, or a similarly empowered entity, should possess the authority to make recommendations that might mitigate the institutional and behavioral forces at the root of the motives and circumstances behind the anthrax letter attacks. To stop shy of this level of thorough and retrospective analysis risks a repeat of the emergency occurrence, or at a minimum a perpetuation of unhealthy dynamics and relationships.

d. Biodefense Commission (BDC)

This thesis recommends decisive action through the PSD-PPD process for the additional formulation of a Biodefense Commission (BDC), potentially directed by the biodefense czar. The BDC will serve as a formal body to assist the biodefense czar in overseeing HSPD, regulatory, and legal compliance. BDC oversight authority should follow the historical model of the 1946 formulation of the Atomic Energy Commission, and its 1974 reorganization as the Nuclear Regulatory Commission.[78] The BDC may determine that a requirement exists for further accountability in order to reduce the probability for future problematic events, perhaps in coordination with the DOJ. BDC formulation serves to preclude future mismanagement, from a policy and appropriations perspective, by halting wasteful spending on known inadequate biological defenses.

The BDC's oversight power should consider reversal of current contracts for the current anthrax vaccine jointly endorsed by the DHS, the DHHS, and the DoD[79]

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[78] For U.S. Department of Energy historic information on the NRC and AEC, see NRC, n.d. The idea for emulation of AEC/NRC model was first espoused by Colonel John Richardson, USAFR, retired.

[79] GAO Report #08-88, "PROJECT BIOSHIELD: Actions Needed to Avoid Repeating Past Problems with Procuring New Anthrax Vaccine and Managing the Stockpile of Licensed Vaccine" (GAO, 2007d).

for the SNS[80] based on DOJ and FBI revelations of potency problems by the manufacturer preceding the vaccine's licensure. Considering the CDC excludes anthrax vaccine as a recommended "first line" treatment for inhalation anthrax infection, the present thesis encourages the BDC to reaffirm national biodefense policy centered on the resiliency of antibiotic procurement, such as penicillin, ciprofloxacin, and doxycycline for pre- and post-exposure of multiple threats (CDC, 2001). Prophylaxis procurement, such as multipurpose, proven, and recommended antibiotics, repairs the "doctrinal departures" represented by the past twenty years of anthrax vaccine prophylaxis.

The PSD-PPD process, biodefense czar appointment, and BDC establishment moves the United States in the right direction, in alignment with the "resilience" themes espoused by the DHS. The new "resilient" (DHS, 2009c; Napolitano, 2009) national state of mind desired for Homeland Security requires a complementary "resilience" (Ripley, 2009, pp. 85–107) of trust in the government and confidence in the resiliency of countermeasures stockpiled in the SNS. The BDC may determine that antibiotics provide the best recipe for resiliency as opposed to questionably effective vaccines focused against singular threats (HR 106-556, 2000, p. 17). Resiliency themes encouraged in this thesis also comport with the latest direction espoused by the President of the U.S. and the National Security Council with publication of the National Strategy for Countering Biological Threat*s*. The report expresses the goal to "improve international preparedness and global resilience against potentially catastrophic outbreaks of infectious disease," while "optimizing security of known virulent high-risk pathogens and toxins." The report encourages the "empowering an informed, involved, and observant citizenry," and "complying with our obligations" under the Biological and Toxin Weapons Convention (National Security Council, 2009, p. 6, 13, 15, 21).

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[80] Strategic National Stockpile regulatory history excerpt from CDC web site: "The Homeland Security Act of 2002 tasked the Department of Homeland Security DHS with defining the goals and performance requirements of the SNS Program, as well as managing the actual deployment of assets. Effective on 1 March 2003, the NPS became the Strategic National Stockpile (SNS) Program managed jointly by DHS and HHS. With the signing of the BioShield legislation, the SNS Program was returned to HHS for oversight and guidance. The SNS Program works with governmental and non-governmental partners to upgrade the nation's public health capacity to respond to a national emergency. Critical to the success of this initiative is ensuring capacity is developed at federal, state, and local levels to receive, stage, and dispense SNS assets" (CDC, n.d.).

The BDC provides a logical enforcement mechanism to the PSD-PPD process, as well as a leadership venue for the biodefense czar to oversee the belated development of a new anthrax vaccine called for 25 years ago. The BDC should expedite development of the new anthrax vaccine based on Institute of Medicine (IOM) findings that BioThrax® is "far from optimal" and a "new vaccine, developed according to more modern principles of vaccinology, is urgently needed" (IOM, 2002, p. 208). Adoption of the PSD-PPD-BDC proposal represents healthy change, whereas the current path risks a continuation of past problems and a lack of governmental accountability when viewed from a historical perspective.

e. Surveillance

The PSD-PPD process, and resultant BDC, should ensure surveillance of past BioThrax® vaccinees. The FDA's 2002 labeling for the vaccine included new revelations about adverse safety information, including birth defect possibilities and adverse reaction rates up to 175 times greater than previously acknowledged.[81] Post-anthrax vaccine program surveillance of previously inoculated citizens and soldiers remains a priority based on the unprecedented adverse reaction report rates submitted due to the vaccine.[82]

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[81] The FDA-approved anthrax vaccine label for the product now called Biothrax® included the following warnings, "Preliminary results of a recent unpublished retrospective study of infants born to women in the U.S. military service worldwide in 1998 and 1999 suggest that the vaccine may be linked with an increase in the number of birth defects." VAERS (Vaccine Adverse Event Reporting System) notes included: "Through October 2001, VAERS received approximately 1850 spontaneous reports of adverse events ... Approximately 6% of the reported events were listed as serious. Serious adverse events include those that result in death, hospitalization, permanent disability or are life-threatening." Also, "across these studies, systemic reactions were reported in 5–35% of vaccine recipients," which compares to .2%, from the previous label—an increase of 25 to 175 fold. Finally, "reports of fatalities included sudden cardiac arrest (2), myocardial infarction with polyarteritis nodosa (1), aplastic anemia (1), suicide (1) and central nervous system (CNS) lymphoma (1)" (FDA, 2002a).

[82] FDA-released Vaccine Adverse Event Reporting System (VAERS) data rose from 42 reports on March 24, 1999 for 634,000 inoculations, to 1,578 as of June 20, 1999 for 2,071,876 inoculations. Most recently, as of July 22, 2008, 5931 reports resulted from 7.5 million doses (FDA, 2008a). This approximately 1,000% or ten-fold increase in reporting for doses given may coincidentally correspond to the GAO's report of a 100-fold increase in vaccine potency. VAERS reporting also documented 19 deaths.

2. Phase IV, Inform

In line with the commendable transparency inherent in the FBI's revelations regarding the origins of the anthrax attacks, the PSD-PPD process should ensure that the BDC informs the U.S. Congress and the American people about releasable lessons learned and corrective actions following a methodical investigation. Additional recommended courses of action by BDC officials include the reaffirmation of biosurety regulations and the establishment of strict accountability measures for any future program discovered operating outside of the nation's regulatory and legal frameworks.

The first three recommendations of the most recent 2009 progress report on the 2008 Commission on the Prevention of WMD Proliferation and Terrorism study affirm the themes emphasized in this thesis. The need for transparency in reinforcing domestic biosecurity remains paramount, as does reassuring the international community about a U.S. commitment to guarantee biosecurity and nonproliferation (Graham & Talent, 2009, p. 25; Graham, 2008). The Commission's additional recommendation for high-level executive-branch restructuring and designation of a "White House principal advisor for WMD proliferation and terrorism" corresponds to this thesis's and PSD-PPD courses of action for appointment of a biodefense czar and a BDC (Graham & Talent, 2009, p. 26).

The final recommendation by the congressionally sponsored commission encourages the government to "work to openly and honestly engage the American citizen, encouraging a participatory approach to meeting the challenges of the new century" (Graham & Talent, 2009, p. 27). This suggested coherent direction firmly addresses the fundamental goal articulated in this thesis for transparency by the government and candidly informing the American people. These recommended courses of action serve to arrest a 50-year culture of extralegal activities and regulatory noncompliance permeating the history of the old anthrax vaccine.

3. Phase V, Follow-up

The follow-up phase ensures that corrective actions resolve the problems. In addition to providing oversight of DoD biosecurity and involvement in biologics in the future, the BDC must monitor DoD compliance with the 1972 Convention on the

Prohibition of the Development, Production and Stockpiling of Biological Weapons prohibiting the development of offensive biologic capabilities, as well as compliance with President Nixon's 1969 decree to discard offensive materials.[83] Considering the unauthorized anthrax attacks by a lone actor arguably represented an offensive release of aerosolized spores, albeit unauthorized, the status of the United States' reputation with international allies and cosigners warrants consideration based on the nation's pledge to comply with the convention. BDC follow-up reporting to Congress and the president regarding chartered responsibilities should occur annually, while the president concurrently reaffirms compliance intentions to international partners.

The BDC should capitalize on current collaborative checks-and-balances mechanisms for increased oversight, such as supporting a thorough 911 Commission–style inquiry as recommended by some members of Congress (Holt, 2009a; Holt, 2009b). Such a process facilitates an objective review regarding the causal chain of events preceding the anthrax attack emergency occurrence, as well as scrutinizes the government's reactive regulatory actions following the event. Application of the template presented in this thesis allows the DHS to simultaneously commence its own event-cause case study analysis and synthesize the historic scientific and regulatory processes in order to evaluate the suitability of the old anthrax vaccine's inclusion as a component of the SNS (United States Department of Education, 1985).

The follow-up phase seems prudent since inevitably future generations of Americans will do so in response to a documented void of reflective analysis following the anthrax letter attacks. This recommended follow-up process engenders trust, minimizes political and institutional biases, and increases the government's credibility.

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[83] The U.S. Department of State information on the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction includes the following background as an excerpt, "Shortly after President Nixon took office, he ordered a review of U.S. policy and programs regarding biological and chemical warfare. On November 25, 1969, the President declared that the United States unilaterally renounced first use of lethal or incapacitating chemical agents and weapons and unconditionally renounced all methods of biological warfare. Henceforth the U.S. biological program would be confined to research on strictly defined measures of defense, such as immunization. The Department of Defense was ordered to draw up a plan for the disposal of existing stocks of biological agents and weapons. On February 14, 1970, the White House announced extension of the ban to cover toxins (substances falling between biologicals and chemicals in that they act like chemicals but are ordinarily produced by biological or microbic processes)" (BTWC, 1975).

B. SUMMARY RECOMMENDED RESTORATION OF TRUST

Retired Lieutenant General James Terry Scott, who formerly served as the director of the National Security Program at the John F. Kennedy School of Government, Harvard University, wrote an article titled, "Sticking Point; In Defending Its Troops Against Anthrax, The Pentagon Has Injected Distrust Instead" (Scott, 2000). In this article about the anthrax vaccine controversy, General Scott discussed the Vietnam era genesis of the demise of trust within the military when dealing with medical issues. Former Assistant Secretary of Defense Lawrence Korb also addressed the fragile element of trust and the damage done if the government lacks the necessary vigilance. Mr. Korb commented about the anthrax vaccine's "terrible impact on morale." He added, "The Anthrax Immunization program was a disaster from its inception. It should have been voluntary, not mandatory, and should not have been started until there was much more evidence that it was needed and safe" (PBS, 2000).

The nation should not accept, nor can it afford, a similar "disaster" of uncertainty about the safety and efficacy of SNS anthrax countermeasures. The same language chosen by the federal courts when adjudicating these issues for the armed forces applies with heightened importance when reflecting on the government's responsibilities for America's citizens:

> The men and women of our armed forces deserve the assurance that the vaccines our government compels them to take into their bodies have been tested by the greatest scrutiny of all—public scrutiny. This is the process the FDA in its expert judgment has outlined, and this is the course this Court shall compel FDA to follow. … Accordingly, the involuntary anthrax vaccination program, as applied to all persons, is rendered illegal (*Doe v. Rumsfeld*, 2004, pp. 42–43).

The American people will know if the government acts in the "spirit of transparency," the "first key to restoring public trust" (Covey & Merrill, 2006, p. 154). Consideration of the PSD-PPD-BDC process to address these vital issues offers a logical, and perhaps overdue, first step to restore the public trust in the biodefense realm.

VII. CONCLUSION

The preceding thesis recommends that the DHS leadership ask the tough questions and modify SNS procurement strategy if necessary. The methodological quadrangulation sought to increase perspective and "box" in unresolved problems in order to help preclude future harm to national credibility in the realm of biodefense. The preceding case study timeline, and inclusive multiprism analysis, raise numerous non sequiturs. Follow-on logical questions include, why did the military mandate the old anthrax vaccine, despite knowledge of its unsatisfactory status and known legal hurdles? Further, why did the DHS endorse anthrax vaccine for the SNS in light of the problematic DoD experience? Finally, why did the government accelerate procurement after the FBI plausibly associated the 2001 anthrax attack motive to the vaccine's "failing" status?

In answering these questions, an analysis deficit appears to exist by the DHS and the DHHS in adopting the anthrax vaccine from the DoD. The answers may lie in the various cognitive "gaps" of failed examination outlined in this thesis. A failure of application of legal frameworks, doctrinal precedents, and advisory warnings precipitated the potentially dangerous shift. Willfully blind disregard of the recorded problems laid the foundation for the ensuing analysis deficit. The subsequent reluctance to evaluate the implications of FBI disclosures further widened the deficit. At some point in the process, reliance on the old vaccine delayed or halted the synthesis of alternative countermeasures. Consequential bureaucratic biases ultimately hampered the nation's current scientific, military, and governmental leaders' ability to rectify the past errors.

Taken as a whole, the collective application failures, analysis deficits, evaluation biases, and synthesis cessation require correction. Failing to cast light on the errors may constitute a cognitive condition worse than the preceding failures. Therefore, this thesis concludes that the anthrax vaccine experience represents an outlier case, with anomalies that deviate from the American people's expectations for good government and public health policy. The DHS must now resolve whether its message to the American people will be the "old boilerplate" script about "an extremely successful program," or whether the departments and leaders responsible choose a different path and strategic vision.

A. REVIEW OF CLAIMS, WARRANTS, AND EVIDENCE

The central research claim for the thesis argued that the existing anthrax vaccine should not be included in the SNS in light of the controversial scientific, regulatory, legislative, judicial, and ethical processes studied. Moreover, the claim asserts that the procurement of anthrax vaccine is indeed wasteful because alternatives with fewer liabilities exist. The examples outlined in the quadrangular methodology buttress the claim based on the documented application failures, analysis deficits, cessation of synthesis, and evaluation biases.

The warrants, or reasons, involve the complex regulatory, scientific, legal, and legislative landscapes "boxed" in by the quadrangular methodology. The documented government awareness of the safety, efficacy, and legality problems with the old, currently stockpiled, anthrax vaccine resulted from unhealthy centralized decision-making processes and extralegal regulatory mistakes bracketing the pivotal 2001 anthrax letter attacks. Evidence supporting the argument primarily originates from historic critical congressional reports, scientific assessments, and, most significantly, the documented awareness by the Defense Department about the need for a new vaccine as early as 1985.

FBI evidence bolsters thesis conclusions and recommendations based on the Bureau's findings about the scientific frustrations over vaccine potency problems. Those problems, and the vaccine's "failing" status, likely contributed to the anthrax attack motive. The evidence also demonstrates that the CDC recommends antibiotics to protect against the most deadly inhaled form of the disease in lieu of anthrax vaccine. Such evidence begs the question why the government did not reevaluate the suitability of the anthrax vaccine after the FBI's disclosures. Instead, the government accelerated purchases for an expanded market.

The warrants, claims, and evidence presented in this thesis effectively attempt to reinvigorate the proper legal, regulatory and procurement processes abandoned by the DoD, DHHS and DHS. Digesting the implications of the evidence, and acting on the conclusions, protects the nation's leaders from the deleterious impact of allowing bioterrorism crimes to dictate reactive bioterrorism procurement policy for the SNS.

B. LIMITATIONS OF THE RESEARCH

In this thesis the author leveraged a nonmedical background and operational skill set in order to proffer a fresh approach in scrutinizing the old anthrax vaccine issue. As a result, the author potentially avoids the biases and cognitive limitations discussed in Chapter V's gap explanations. Any concern as to the author's lack of objectivity should be alleviated by the fact that the official DoD position pre-1998 essentially mirrored those presented and advocated by the author. The 1999 opinions expressed by the new FDA commissioner similarly parallel the findings and recommendations of this thesis. Any concerns about the subjective limitations of the materials presented encourage the government to recommence additional levels of inquiry by the DHS as the lead agency for incident management and SNS stockpile composition under the auspices of HSPD 5, 8, 10, 18, and 21. The first order of business requires reconsideration of current policy in light of the fact that prior official positions of the DoD, and opinions of the new FDA commissioner one decade ago, closely resemble this author's current recommendations.

The thesis incorporated myriad threads of inductive reasoning through the four methodologies to derive a logical conclusion that anthrax vaccine inclusion in the SNS requires review based on the various tentacles of past problems. The quadrangular methodological approach supports the suggested courses of action articulated in the recommendations. Such a review does not guarantee successful accomplishment of the recommendations. A review also provides the possibility that additional information, unavailable to the author, will overcome the conclusions of the quadrangular analysis.

Additionally, alternative information may overcome the inductive reasoning approach of this thesis. On the other hand, the DoD's more deductive approach appears to rely on two premises: "Anthrax kills, vaccination protects" (Cragin, 1999). Regrettably, DoD records effectively contradict this sound bite. Therefore, the DHS must weigh the inductive reasoning presented in this thesis against the deductive conclusions of the DoD. The DHS may determine that DoD reasoning falls short based upon the lack of validation of both premises. As well, the DHS, as a relatively new actor in the executive landscape and with anthrax vaccine, may determine the fresh approach presented in this thesis of thorough retrospective review overrides any limitations within the research methods.

C. SIGNIFICANCE OF THE RESEARCH

In line with IOM determinations about the "paucity of published peer-reviewed literature on the safety of the anthrax vaccine" (IOM, 2000, p. 259), a similar scarcity of anthrax vaccine strategic review apparently exists. This thesis represents the author's attempt to fill the void of strategic review. Mushrooming procurement of the product for civilian applications dictates such a review as proposed by this thesis. A significant potential byproduct of the thesis exists if the policy and the product undergo a thorough and candid reevaluation. The consumers benefiting from the cost savings resulting from adoption of thesis recommendations include American taxpayers not yet directly subjected to the potential ill effects or inefficacy of the controversial old anthrax vaccine.

In addition, senior policymakers and Homeland Security practitioners benefit from a comprehensive review of the issues, one literally nonexistent in the post-2001 anthrax letter attack environment. Historic issues which should also be addressed as a consequence of this thesis include a study of the arguably adulterating manufacturing changes made to the anthrax vaccine before and after the first Persian Gulf War and their possible associations to Gulf War illnesses (21 U.S.C. §351, 1997). This thesis significantly recommends particular attention to the filtration changes reported by Dr. Ivins (Ivins et al., 1994, p. 873), as affirmed by the GAO (GAO, 2001b, pp. 4–5, nn. 8–10, 12). While ignored by the FDA and IOM, DoD coordinated manufacturing changes, and resulting plausible increases in vaccine potency, appear to be linked to the vaccine's "failing" status and the motives behind the 2001 bioterrorism attacks according to the FBI (FBI, 2008, pp. 12-15) (see Appendix 11). The crimes, purportedly by design, then led to the DoD anthrax vaccine program's revival, a belated 2002 approval of the vaccine manufacturing process, the vaccine's 2005 court ordered licensure, and ultimately the vaccine's expansion as a component of the SNS as biodefense countermeasure.

The preceding thesis served as an objective means to encourage similar reflection by the president and the DHS on the significance of these events. The resulting reassertion of civilian control may protect leaders from the inherited liabilities associated with continued use of the current anthrax vaccine. A thorough and transparent review will engender trust, while also strengthening future programmatic and procurement processes.

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STATUTES AND LEGISLATION

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APPENDIXES

APPENDIX 1: EARLY LICENSURE MEMORANDUMS

The National Institute of Health (NIH) noted the manufacturer failed to submit the required "scientific evidence for efficacy of the vaccine." The NIH granted the anthrax vaccine license pending efficacy data submission (Pittman, 1969a, p. 1; Pittman, 1969b, p.2). The Centers for Disease Control challenged the licensing application due to "no controlled evaluation studies" (Kokko, 1969, p. 2).

Memorandum from Dr. Margaret Pittman, NIH, Public Health Service, to Dr. Sam Gibson, Assistant Director, Licenses and Inspections, NIH, re anthrax vaccine, 1969, February 10 (Pittman, 1969a):

UNITED STATES GOVERNMENT

DEPARTMENT OF HEALTH, EDUCATION, AND WELF
PUBLIC HEALTH SERVICE

Memorandum

Concur 2-10-69

TO : Dr. Sam T. Gibson, Assistant Director, L & I

DATE: February 10, 1969

Ref 2067-7

FROM : Chief, LBP and
Chairman, Ad Hoc Committee

SUBJECT: Michigan Department of Health: Application for license for Anthrax Vaccine

On June 21, 1968 the Ad Hoc Committee recommended that license be granted following publication of Additional Standards: Anthrax Vaccine. It was noted also that clinical data establishing efficacy of the product had not been submitted and that data be requested from NCDC.

No comments were received on the Proposed Notice of Rule Making published December 14, 1968, and it is understood that these standards have been forwarded with request for publication in the Federal Register.

C

ened.

Safety data appear to be satisfactory.

Michigan has filed with the Division all required information and material for license except the results of an adequately controlled clinical investigation that establishes efficacy. No cases of anthrax have occurred among vaccinees. Laboratory data have been submitted that show that the product does have specific ability to protect guinea pigs. Therefore, it is recommended that license be granted and that NCDC (IND-180) be requested to obtain data with a view to determine human efficacy of the product.

Margaret Pittman

Margaret Pittman, Ph. D.

Memorandum from Dr. Margaret Pittman, NIH, Public Health Service, to Dr. Sam Gibson, Assistant Director, Licenses and Inspections, NIH, re anthrax vaccine, 1969, September 30 (Pittman, 1969b):

UNITED STATES GOVERNM. T

DEPARTMENT OF HL TH, EDUCATION, AND WEL:
PUBLIC HEALTH SERVICE

Memorandum

10-1-69

TO : Dr. Sam T. Gibson, Assistant Director, L & I

DATE: September 30, 1969

Ref. No. 67-70

FROM : Margaret Pittman, Ph. D., Chief, LBP/M.P.
Chairman, Ad Hoc Committee

SUBJECT: Michigan Department of Public Health, visit by Dr. George R. Anderson and Dr. J. R. Mitchell

Anthrax Vaccine
(DBS personnel: Drs. J. C. Feeley and M. Pittman)

The recent information submitted by NCDC and Ft. Detrick for DBS-IND-180 was discussed. It was emphasized that the epidemiological study did not provide control data, whereby the effectiveness of the vaccine could be evaluated. The fact that the vaccine has been used in a number of textile mills and that there has been no case of Anthrax was substantive but not conclusive evidence of efficacy.

It was also noted that Michigan Lot 3 was more reactive than one lot prepared by Ft. Detrick and one lot prepared by Merck, Sharp & Dohme. With gel diffusion tests it was demonstrated that the first two lots induced antibodies that were lower in titer and of shorter duration than did the MSD product. However, the first two lots were fractionated antigen and a true comparison could not be made.

Michigan Lot 2 now in current use was less reactive than Lot 3. Lot 7 will be put into use by the end of this year.

Dr. Anderson was informed that all requirements for filing the application for Anthrax Vaccine had been fulfilled but that license could not be issued until the Additional Standards: Anthrax Vaccine had been published. A nontechnical block was delaying their publication. Dr. Anderson was appreciative of the information.

The local sensitivity reactions to the vaccine as reported in the last annual report to you were: In the initial and booster series the moderate and severe reactions were < 1.0%.

I hope this information and the information that will probably be furnished by Dr. Wright, will be of some help to you.

Sincerely yours,

Morris T. Suggs

Morris T. Suggs, Dr.P.H.
Chief, Biological Reagents Section

Enclosures (5)

cc: Dr. George Wright
Dr. Phil Brachman

Memorandum from Penti Kokko, Director, Laboratory Division, CDC, Public Health Service, Department for Health Education and Welfare to Dr. Roderick Murray, Division of Biologics Standards, NIH, 1969, January 22 (Kokko, 1969):

NATIONAL
COMMUNICABLE DISEASE CENTER
ATLANTA, GEORGIA 30333
TELEPHONE: (404) 633-3311

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

January 22, 1969

Dr. Roderick Murray, Director
Division of Biologics Standards
National Institutes of Health
Bethesda, Maryland 20014

Dear Dr. Murray:

Following your review of the 1968 progress report for Anthrax Protective Antigen, Aluminum Hydroxide Adsorbed (DBS-IND 180), you asked for clarification of several points in your letter dated January 14, 1969.

Only those clinical reactions from the use of Lot 3 were included in the Progress Report #2. Lot 2 was introduced in July 1968, and the next progress report will include the surveillance of both Lots 2 and 3.

The Lot 2 label does not include the manufacturer. To comply with your request, the following information will be placed on each bottle:

Prepared by Bureau of Laboratories
MICHIGAN DEPARTMENT OF PUBLIC HEALTH
Lansing, Michigan 48914
U. S. License No. 99

The antibody assays employing the agar-gel precipitin inhibition technique were forwarded to this office on October 24, 1968. The enclosed figures and descriptions of the agar-gel test results were removed from the appropriate sections of the Second Annual Report to the Army Investigational Drug Review Board (AIDRB) submitted by Paul J. Kadull, M.D., Chief, Medical Investigational Division, Fort Detrick, Maryland.

There have been no controlled evaluation studies with the Michigan anthrax product as was done by Dr. Philip Brachman using the Merck, Sharp and Dohme product. Indirect evidence of the protection afforded by the Michigan product can be inferred from our experience with immunized populations in several goat hair processing plants. The textile mill in Talladega, Alabama employs approximately 600 people, and the goat hair is known to be contaminated by laboratory examinations. From past experience, Dr. Brachman stated that in an unimmunized population of 600, up to 10 cases of anthrax a year could be expected. There have been no reported cases of anthrax from the Talladega processing plant during the period in which the Michigan Anthrax Protective Antigen has been used.

If additional information is needed, please let me know.

Sincerely yours,

U. Pentti Kokko, M.D.
Director, Laboratory Division

Enclosures

APPENDIX 2: DOD REQUEST FOR PROPOSAL

The DoD Request for Proposal (RFP) for a new anthrax vaccine. The RFP stated, "There is an operational requirement to develop a safe and effective product which will protect US troops against exposure from virulent strains of Bacillus anthracis … There is no vaccine in current use which will safely and effectively protect military personnel against exposure to this hazardous bacterial agent" The RFP clarified that the current vaccine is, "highly reactogenic [reactive], requires multiple boosters to maintain immunity and may not be protective against all strains of the anthrax bacillus" (DoD, 1985, p. 4):

DEPARTMENT OF THE ARMY
U.S. ARMY MEDICAL RESEARCH ACQUISITION ACTIVITY
FORT DETRICK, FREDERICK, MD 21701-5014

REPLY TO ATTENTION OF

May 16, 1985

SGRD-RMA-RC

SUBJECT: Request for Proposals (RFP) No. DAMD17-85-R-0078
Date Issued: May 16, 1985
Date Due: July 15, 1985

Gentlemen:

You are invited to submit a proposal in accordance with the requirements of the enclosed RFP No. DAMD17-85-R-0078 for Production of Live Bacillus anthracis Spore Vaccine for Human Use."

Document No. DAMD17-85-R-0078
Page No. 4

SECTION C DESCRIPTION/SPECIFICATIONS/WORK STATEMENT

C.1. Background

C.1.1. There is an operational requirement to develop a safe and effective product which will protect US troops against exposure from virulent strains of Bacillus anthracis. There is no vaccine in current use which will safely and effectively protect military personnel against exposure to this hazardous bacterial agent.

C.1.2. Bacillus anthracis is a Gram positive spore-forming bacterium which in order to be considered fully virulent must not only produce a polyglutamic acid capsule but also produce a tripartite exotoxin. The toxin consists of three distinct proteins; protective antigen, lethal factor and edema factor. None of the protein components alone is biologically active however, protective antigen in combination with edema factor or lethal factor produces localized edema or death respectively in experimental animals.

C.1.3. A licensed vaccine against anthrax, which appears to afford some protection from the disease, is currently available for human use. This vaccine consists of alum-precipitated supernatant material obtained from fermenter cultures of an avirulent strain of Bacillus anthracis. The vaccine is composed primarily of the protective antigen component but does contain trace amounts of the lethal factor and edema factor components. The vaccine is, however, highly reactogenic, requires multiple boosters to maintain immunity and may not be protective against all strains of the anthrax bacillus.

APPENDIX 3: DOD LICENSING AMENDMENT

DoD's Joint Project Office for Biological Defense (JPOBD) recognized anthrax vaccine as "not licensed for a biological defense indication" based on the fact efficacy remained unproven (DoD-JPOBD, 1997, p. 5.5):

Industrial Capabilities Assessment Summary Report for the Production of the Anthrax Vaccine

Preliminary Report

Prepared for the

Joint Program Office for Biological Defense
Falls Church, Virginia

1997

5.4 Regulatory Issues

Several regulatory issues are of particular interest with respect to DoD biological defense vaccine requirements. Most current DoD vaccines are in Phase 2 or Phase 3 clinical studies. Anthrax and smallpox are the only licensed vaccines that are useful for the biological defense program, but they are not licensed for a biological defense indication. A PLA is in the preparation process for a tularemia vaccine. Under the constraints of the IND regulations, extensive record-keeping and informed consent procedures are normally required. These requirements may introduce many impediments to the goal of timely and efficient immunization of the military force. It is therefore highly desirable to proceed as expeditiously as possible toward licensure of all DoD vaccines. Since facility acceptability is an integral part of product licensure (both the facility and the product must be licensed), it is imperative that facility issues be properly addressed during product development. Another issue of concern to the DoD is the frequent requirement that vaccine inventory be distributed among multiple sites. FDA licensure requirements indicate that up to the point of dating and releasing the product a manufacturer must, at all times, be in

5.5 Responsiveness to DoD Biological Defense Needs

The DoD biological defense vaccine requirement presents a significant production challenge. It may be compared with the U.S. immunization program for public health, which provides protection for 22 diseases. The licensed public health vaccines are approximately equivalent to the diversity of products required for the biological defense program. Again, anthrax and smallpox, considered very effective vaccines, are the only licensed products in the biological defense program, but they are not licensed for a biological defense indication. Although small and fragile, the national vaccine manufacturing infrastructure for U.S. preventive medicine needs is well established. Merck and Company, Inc., has been in the biological manufacturing business for over 100 years.

Meeting minutes and slides related to the October 20, 1995 DoD "Meeting on Changing the Food and Drug Administration License for the Michigan Department of Public Health (MDPH) Anthrax Vaccine to Meet Military Requirements." The minutes detailed "the process for modifying the MDPH anthrax vaccine license to … expand the indication to include protection against aerosol challenge of spores." In discussing the previous clinical trials, the working group acknowledged, "there was insufficient data to demonstrate protection against inhalation disease" (DoD-JPOBD, 1995):

DEPARTMENT OF THE ARMY
JOINT PROGRAM OFFICE
FOR BIOLOGICAL DEFENSE
5201 Leesburg Pike
Skyline #3, Suite 1200
Falls Church, VA 22041-3203

JOINT PROGRAM OFFICE

REPLY TO ATTENTION OF
SFAE-BD (70-1z)

13 November 1995

MEMORANDUM FOR SEE DISTRIBUTION

SUBJECT: Minutes of the Meeting on Changing the Food and Drug Administration License for the Michigan Department of Public Health (MDPH) Anthrax Vaccine to Meet Military Requirements

A meeting was held on 20 October 1995 to discuss the process for modifying the MDPH anthrax vaccine license to indicate a reduced numbers of injections and to expand the indication to include protection against an aerosol challenge of spores. Attendees (see enclosure 1) met in the conference room of the Joint Program Office for Biological Defense (JPO-BD), located in Suite 1200, Skyline #3, 5201 Leesburg Pike, Falls Church, Virginia 22041.

The meeting was hosted by BG Walter L. Busbee, Joint Program Manager for Biological Defense, and LTC(P) David Danley, Deputy Joint Program Manager for Medical Systems, JPO-BD. BG Busbee opened the meeting with comments about recent events involving the Office of the Secretary of Defense (OSD) and the Joint Staff which could have significant impacts on both the medical and non-medical biological defense programs. He highlighted a key issue concerning the DoD vaccination policy, stating that a tour in some theaters is 13 months, whereas the dosage schedule for anthrax vaccine requires 18 months. This has raised questions among senior military leaders, such as: "How do you protect the force? What sector of the force do you protect? Do you inoculate all 1.5M service members because you don't know exactly who will be deployed?" He charged the audience to objectively, scientifically, and carefully articulate the pros and cons for the different options involving the anthrax vaccination schedule.

COL Arthur Friedlander, Chief, Bacteriology Division, U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID), presented a briefing covering three topics: (1) evidence for a reduction in the number of doses of anthrax vaccine, (2) evidence for vaccine efficacy against an aerosol challenge, and (3) progress toward an in vitro correlate of immunity. He opened the briefing by stating it is impossible to conduct human studies involving inhalation of anthrax spores; therefore, animal models must be developed, and the data related to humans.

With respect to reducing the number of doses in the immunization schedule, COL Friedlander said that the original series of 6 doses was established in the 1950's for an anthrax vaccine similar to but not identical with the MDPH vaccine. Studies of vaccine (not MDPH product) effectiveness in humans working in tanneries showed protection against cutaneous disease, but there was insufficient data to demonstrate protection against inhalational disease. The package insert for MDPH anthrax vaccine does not discriminate between different forms of anthrax, but does describe occupations that may involve anthrax exposure.

USAMRIID

PROBLEMS WITH CURRENT MDPH VACCINE

Prolonged immunization schedule

Reactogenicity:

Systemic reactions: 0.7-1.3%

Significant local reactions: 2.4-3.9% (5.7%)

Vaccine components completely undefined in terms of characterization and quantitation of the PA, and other bacterial products and constituents present

Significant lot-to-lot variation in the PA immunogen content

Human trials with similar but not identical vaccine showed protection against cutaneous anthrax but insuffcent data to show efficacy against inhalation anthrax

Made from spore-forming strain requiring dedicated production facility

Anthrax Vaccine License Amendment Project Plan

GPO-S 19 951020 0072

Anthrax Vaccine License Amendment Project Plan

Information Briefing

for

Joint Program Manager

DoD Biological Defense

October 20, 1995

10-19-95 page 1

SAIC An Employee-Owned Company

SAIC Project Description

- Provide the Director, Medical Biological Defense Research Program with a project plan to obtain an amendment to the Anthrax Vaccine product license
  - Reduce number of inoculations required
  - Obtain indication for protection against aerosol exposure
- Completed plan due in 30 days (15 Sep 95)

SAIC An Employee-Owned Company

Basis for Current Schedule (Anecdotal -- CDC)

- Based on old (weaker) anthrax vaccine (circa 1950s)
  - Three anthrax cases after first 3 doses (2 at Detrick and 1 at wool mill)
  - Arbitrarily added 3 more doses at 6-month intervals
- MDPH vaccine
  - Higher PA concentration
  - Much more immunogenic
- No schedule change recommended

SAIC An Employee-Owned Company

APPENDIX 4: "INHALATION ANTHRAX" APPLICATION

Investigational New Drug application—Form FDA 1571—Michigan Biologic Product Institute (MBPI)—for "inhalation anthrax, change in route of administration, and change in schedule" (block 7) (Myers, 1996):

MICHIGAN BIOLOGIC PRODUCTS INSTITUTE

ROBERT C. MYERS, D.V.M., DIRECTOR
3500 N. MARTIN LUTHER KING, JR., BLVD.
P.O. BOX 30033
LANSING, MICHIGAN 48909
TELEPHONE: (517) 335-8120
FAX: (517) 335-9486

JOHN ENGLER, GOVERNOR

MICHIGAN BIOLOGIC PRODUCTS COMMISSION
DENNIS L. SCHORNACK, CHAIR
JAMES K. HARTMAN, JR.
MARY A. LANNOTTI

September 20, 1996

Dr. Kathryn C. Zoon, Director
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Suite 200N
Rockville, MD 20852-1448
ATTN: HFM-99

Dear Dr. Zoon:

Enclosed, in triplicate, is an initial Investigational New Drug (IND) application for Anthrax Vaccine Adsorbed (AVA). This product is currently a Food and Drug Administration licensed vaccine. The purpose for filing this IND is to conduct clinical investigations designed to investigate changes in the approved labeling for the licensed product. The potential labeling changes would affect the specific clinical indication, route and vaccination schedule for AVA.

This IND makes reference to two regulatory filings sponsored by the Department of the Army, BB-MF 6052 and BB-IND 3723. A copy of the letter permitting the Agency to cross-reference BB-MF 6052 when reviewing the current IND follows this cover letter. Permission to cross reference BB-IND 3723 has been requested. A copy of the letter authorizing the Agency to cross-reference BB-IND 3723 will be forwarded as an amendment to this IND at a later date.

The clinical protocol, contained in Section 6.2 of this initial IND filing, is scheduled to begin on October 15, 1996. It is highly desirable to adhere to this starting date to avoid having to schedule volunteers for vaccinations during the Christmas Holiday period. I, therefore, respectfully request, as allowed for in 21 CFR 312.40(b)(2), to be notified as soon as the Agency has determined that there is no objection to proceeding with the proposed clinical protocol, rather than wait for the 30 day review period to elapse.

Should you have any questions, please contact me at (517) 335-9956.

Sincerely,

Robert C. Myers, DVM
Executive Director

Encl.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
INVESTIGATIONAL NEW DRUG APPLICATION (IND)
(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) Part 312)

Form Approved: OMB No. 0910-0014, Expiration Date: November 30, 1995. See OMB Statement on Reverse.

NOTE: No drug may be shipped or clinical investigation begun until an IND for that investigation is in effect (21 CFR 312.40)

1. NAME OF SPONSOR: Michigan Biologic Products Institute (Formerly Michigan Department of Public Health)

2. DATE OF SUBMISSION: September 20, 1996

3. ADDRESS (Number, Street, City, State and Zip Code): 3500 N. Martin Luther King Jr. Blvd. Lansing, MI 48906

4. TELEPHONE NUMBER (Include Area Code): (517) 335-9956

5. NAME(S) OF DRUG (Include all available names: Trade, Generic, Chemical, Code): Anthrax Vaccine Adsorbed

6. IND NUMBER (If previously assigned):

7. INDICATION(S) (Covered by this submission)
1. Inhalation Anthrax 2. Change in Route of Administraiton
3. Change in vaccination schedule

8. PHASE (S) OF CLINICAL INVESTIGATION TO BE CONDUCTED: ☐ PHASE 1 ☒ PHASE 2 ☐ PHASE 3 ☐ OTHER _____ (Specify)

9. LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS (21 CFR Part 312), NEW DRUG OR ANTIBIOTIC APPLICATIONS (21 CFR Part 314), DRUG MASTER FILES (21 CFR 314.420), AND PRODUCT LICENSE APPLICATIONS (21 CFR Part 601) REFERRED TO IN THIS APPLICATION.
Establishment License #99
DBS-IND 180
BB-MF 6052
BB-IND 3723

10. *IND submissions should be consecutively numbered. The initial IND should be numbered "Serial Number: 000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 001." Subsequent submissions should be numbered consecutively in the order in which they are submitted.*

SERIAL NUMBER: 000

11. THIS SUBMISSION CONTAINS THE FOLLOWING: (Check all that apply)

☒ INITIAL INVESTIGATIONAL NEW DRUG APPLICATION (IND) ☐ RESPONSE TO CLINICAL HOLD

PROTOCOL AMENDMENT(S):
☐ NEW PROTOCOL
☐ CHANGE IN PROTOCOL
☐ NEW INVESTIGATOR

INFORMATION AMENDMENT(S):
☐ CHEMISTRY/MICROBIOLOGY
☐ PHARMACOLOGY/TOXICOLOGY
☐ CLINICAL

IND SAFETY REPORT(S):
☐ INITIAL WRITTEN REPORT
☐ FOLLOW-UP TO A WRITTEN REPORT

☐ RESPONSE TO FDA REQUEST FOR INFORMATION ☐ ANNUAL REPORT ☐ GENERAL CORRESPONDENCE

☐ REQUEST FOR REINSTATEMENT OF IND THAT IS WITHDRAWN, INACTIVATED, TERMINATED OR DISCONTINUED ☐ OTHER _____ (Specify)

CHECK ONLY IF APPLICABLE

JUSTIFICATION STATEMENT MUST BE SUBMITTED WITH APPLICATION FOR ANY CHECKED BELOW. REFER TO THE CITED CFR SECTION FOR FURTHER INFORMATION.

☐ TREATMENT IND 21 CFR 312.35(b) ☐ TREATMENT PROTOCOL 21 CFR 312.35(b) ☐ CHANGE REQUIRING NOTIFICATION 21 CFR 312.70(b)

FOR FDA USE ONLY

CDR/DBIND/OGD RECEIPT STAMP	DDR RECEIPT STAMP	IND NUMBER ASSIGNED:
		DIVISION ASSIGNMENT:

FORM FDA 1571 (12/92) PREVIOUS EDITION IS OBSOLETE. PAGE 1 OF 2

APPENDIX 5: APPLICATION UPDATE TO FDA

Investigational New Drug Application—Form FDA 1571—submitted for the express purpose of updating the earlier application to obtain an indication for "inhalation anthrax" (see block 7) (DoD, 1999b):

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

INVESTIGATIONAL NEW DRUG APPLICATION (IND)
(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)

Form Approved: OMB No. 0910-0014.
Expiration Date: December 31, 1999
See OMB Statement on Reverse.

NOTE: No drug may be shipped or clinical investigation begun until an IND for that investigation is in effect (21 CFR 312.40).

1. NAME OF SPONSOR
BioPort Corporation

2. DATE OF SUBMISSION

3. ADDRESS *(Number, Street, City, State and Zip Code)*
3500 N. Martin Luther King, Jr. Boulevard
Lansing,MI 48906

4. TELEPHONE NUMBER *(Include Area Code)*
(517) 335-8540

5. NAME(S) OF DRUG *(Include all available names: Trade, Generic, Chemical, Code)*
Anthrax Vaccine Adsorbed

6. IND NUMBER *(If previously assigned)*
BB-IND 6847

7. INDICATION(S) *(Covered by this submission)*
Inhalation Anthrax

8. PHASE(S) OF CLINICAL INVESTIGATION TO BE CONDUCTED:
☐ PHASE 1 ☐ PHASE 2 ☑ PHASE 3 ☐ OTHER _____ *(Specify)*

9. LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS (21 CFR Part 312), NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, DRUG MASTER FILES *(21 CFR Part 314.420)*, AND PRODUCT LICENSE APPLICATIONS (21 CFR Part 601) REFERRED TO IN THIS APPLICATION.
Establishment License #99 BB-IND 3723
DBS-IND 180
BB-MF 6052

ARCHIVAL

10. *IND submission should be consecutively numbered. The initial IND should be numbered "Serial number: 000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 001." Subsequent submissions should be numbered consecutively in the order in which they are submitted.*

SERIAL NUMBER
009

11. THIS SUBMISSION CONTAINS THE FOLLOWING: *(Check all that apply)*
☐ INITIAL INVESTIGATIONAL NEW DRUG APPLICATION (IND) ☐ RESPONSE TO CLINICAL HOLD

PROTOCOL AMENDMENT(S):
☐ NEW PROTOCOL
☐ CHANGE IN PROTOCOL
☐ NEW INVESTIGATOR

INFORMATION AMENDMENT(S):
☐ CHEMISTRY/MICROBIOLOGY
☐ PHARMACOLOGY/TOXICOLOGY
☐ CLINICAL

IND SAFETY REPORT(S):
☐ INITIAL WRITTEN REPORT
☐ FOLLOW-UP TO A WRITTEN REPORT

☐ RESPONSE TO FDA REQUEST FOR INFORMATION ☐ ANNUAL REPORT ☐ GENERAL CORRESPONDENCE
☐ REQUEST FOR REINSTATEMENT OF IND THAT IS WITHDRAWN, INACTIVATED, TERMINATED OR DISCONTINUED ☑ OTHER Meeting Minutes, 15 December 1998 *(Specify)*

CHECK ONLY IF APPLICABLE

JUSTIFICATION STATEMENT MUST BE SUBMITTED WITH APPLICATION FOR ANY CHECKED BELOW. REFER TO THE CITED CFR SECTION FOR FURTHER INFORMATION.

☐ **TREATMENT IND 21 CFR 312.35(b)** ☐ **TREATMENT PROTOCOL 21 CFR 312.35(a)** ☐ **CHARGE REQUEST/NOTIFICATION 21 CFR312.7(d)**

FOR FDA USE ONLY

CDR/CBER/DGD RECEIPT STAMP
RECEIVED
CBER/DCC

CDR RECEIPT STAMP

DIVISION ASSIGNMENT:

IND NUMBER ASSIGNED:

FORM FDA 1571 (1/97) PREVIOUS EDITION IS OBSOLETE. PAGE 1 OF 2

APPENDIX 6: FDA REVOKE NOTICE & INSPECTIONS

The FDA filed a Notice of Intent to Revoke (NOIR) the manufacturer's license on March 11, 1997 (FDA, 1997) for deviations from cGMPs.

CBER

Blood | Therapeutics | Vaccines | Cellular & Gene Therapy | Allergenics | Tissue | Devices

Products | Manufacturers | Health Professionals | Reading Room | Meetings & Workshops | Research | About Us

FDA Warns Michigan Biologic Products Institute of Intention to Revoke Licenses

FDA issued a letter to the Michigan Biologic Products Institute (MBPI), Lansing, Michigan, on March 11, 1997, warning that the agency will initiate steps to revoke MBPI's establishment and product licenses unless immediate action is taken to correct deficiencies at the firm. MBPI is currently licensed to manufacture Diphtheria Toxoid Adsorbed, Tetanus Toxoid Adsorbed, Rabies Vaccine Adsorbed, Antihemophilic Factor (Human), Immune Globulin (Human), Albumin (Human), Anthrax Vaccine Adsorbed, Pertussis Vaccine Adsorbed, Diphtheria & Tetanus Toxoids Adsorbed, and Diphtheria & Tetanus Toxoids & Pertussis Vaccine Adsorbed. MBPI can remain open while it attempts to address the deficiencies cited by FDA.

An FDA inspection of MBPI conducted between November 18 and 27, 1996, documented numerous violations in the following areas: organization and personnel, buildings and facilities, equipment, control of components, drug product containers and closures, production and process controls, laboratory controls, and records and reports. Some examples include:

- failure of the quality control unit to approve or reject all components, drug product containers, closures, in-process materials, packaging material, labeling, and drug products;
- failure to have separate defined areas or other control systems for manufacturing and processing operations;
- failure to assure that equipment used in the manufacture, processing, packing or holding of a drug product is of appropriate design and of adequate size for its intended use and for its cleaning and maintenance;
- failure to properly store and handle components and drug product containers and closures;
- failure to calibrate instruments, apparatus, gauges and recording devices at suitable intervals; and
- failure to record the performance of each step in the manufacture and distribution of products.

Although similar deficiencies have been identified during past inspections, MBPI has failed to make satisfactory corrections. FDA has determined that continuing problems represent a failure to comply with the regulations that safeguard the drug and pharmaceutical industry. However, the agency is not aware of any injuries to recipients of these products as a result of the noted deviations.

In its letter, FDA requires MBPI to submit a written commitment for achieving full compliance within 10 days. MBPI must also submit a comprehensive plan for correcting all deficiencies within 30 days. The action plan must include corrective actions to ensure that the firm's quality assurance unit functions in an adequate, effective and timely manner, including addressing all quality assurance oversight deficiencies, and to conduct a thorough review of all standard operating procedures to achieve compliance with good manufacturing practices as specified in Subchapter C, Parts 210 and 211, Title 21, *Code of Federal Regulations*.

If MBPI fails to correct these deficiencies, FDA may begin the process for revoking the facility's licenses. Under FDA's procedures, MBPI can request a public hearing before an administrative law judge on the proposed revocation of its licenses. The revocation of the licenses would prohibit MBPI from distributing any of its products in interstate commerce.

file:///C|/Documents%20and%20Settings/localadmin/My%...date%20of%20Intention%20to%20Revoke%20License.htm (1 of 2)11/15/2009 6:10:17 AM

The FDA "Inspectional Observations" noted on line 1 that "the manufacturing process for anthrax vaccine is not validated" (FDA, 1998).

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER U.S. Food & Drug Adm. 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191	
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED To: Robert C. Myers, DVM	PERIOD OF INSPECTION 2/4-20/98	C.F. NUMBER 1873576
TITLE OF INDIVIDUAL Director	TYPE ESTABLISHMENT INSPECTED Blood Products Manufacturing	
FIRM NAME Michigan Biologic Products Inst	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same	
STREET ADDRESS 3500 N. Martin Luther King Jr. Blvd.	STREET ADDRESS OF PREMISES INSPECTED Same	
CITY AND STATE (Zip Code) Lansing, MI 48906	CITY AND STATE (Zip Code) Same	

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

ANTHRAX VACCINE

1. The manufacturing process for Anthrax Vaccine is not validated. For example,

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER CBER, Office of Compliance and Biologics Quality, HFM-605 1401 Rockville Pike Rockville, MD 20852 (301) 827-6191	
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED To: Fouad EL-Hibri	PERIOD OF INSPECTION 11/15-23/99	C.F. NUMBER -
TITLE OF INDIVIDUAL CEO	TYPE ESTABLISHMENT INSPECTED Biologics Manufacturer	
FIRM NAME BioPort Corporation	NAME OF FIRM, BRANCH OR UNIT INSPECTED Same	
STREET ADDRESS 3500 N. Martin Luther King, Jr. Blvd.	STREET ADDRESS OF PREMISES INSPECTED Same	
CITY AND STATE (Zip Code) Lansing, MI 48906	CITY AND STATE (Zip Code) Same	

DURING AN INSPECTION OF YOUR FIRM(S) (WE) OBSERVED:

1. The manufacturing process for the production of Anthrax Vaccine Adsorbed is not validated

APPENDIX 7: DOD INDEMNIFICATION DOCUMENTS

DoD indemnification documents revealed language omitted from public communications: "The obligation assumed by MBPI under this contract involves unusually hazardous risks associated with the potential for adverse reactions in some recipients and the possibility that the desired immunological effect will not be obtained by all recipients" (Caldera, 1998):

SECRETARY OF THE ARMY
WASHINGTON

September 3, 1998

MEMORANDUM OF DECISION

SUBJECT: Authority Under Public Law 85-804 to Include an Indemnification Clause in Contract DAMD17-91-C-1139 with Michigan Biologic Products Institute

Michigan Biologic Products Institute (MBPI), a temporary agency of the State of Michigan, has requested that the Department of the Army include an indemnification clause under Public Law 85-804 (50 U.S.C. 1431-1435) for Anthrax Vaccine Adsorbed (AVA) produced under Contract DAMD17-91-C-1139 with the U.S. Army Medical Research Acquisition Activity (USAMRAA).

The contract is a firm-fixed price effort for AVA production with insurance and facility renovations being provided on a cost reimbursement basis. At present, MBPI is storing over six million doses of AVA at their Lansing, Michigan facility. This vaccine has been accepted by the Government with storage costs identified as a part of the firm-fixed price. MBPI is also responsible under separate contract for the security, testing, labeling and shipping of the Government Material, as required.

The obligation assumed by MBPI under this contract involves unusually hazardous risks associated with the potential for adverse reactions in some recipients and the possibility that the desired immunological effect will not be obtained by all recipients. Although AVA has been extensively tested under the auspices of the Food and Drug Administration, the size of the proposed vaccination program may reveal unforewarned idiosyncratic adverse reactions. Moreover, there is no way to be certain that the pathogen used in tests measuring vaccine efficacy will be sufficiently similar to the pathogen that U.S. forces might encounter to confer immunity. These concerns, coupled with the uncertain and evolving state of product liability law with regard to vaccines, lead me to the conclusion that the performance of this contract will subject MBPI to certain unusually hazardous risks.

The definition of the unusually hazardous risks to which the contract indemnification clause will apply is as follows:

"The risk of adverse reactions, or the failure to confer immunity against anthrax, from the administration to any person of the vaccine

manufactured or delivered under this contract. For the purpose of this clause, the phrase "adverse reactions" includes anaphylaxis and any other foreseeable reactions, as well as any unforeseen reactions."

I have considered the availability, cost, and terms of private insurance to cover these risks, as well as the viability of self-insurance, and have concluded that adequate insurance to cover these unusually hazardous risks is not available to the contractor at a reasonable cost. While limited "claims-made" insurance is available to the contractor, the terms and conditions of the insurance are not deemed to be practicable. On the basis of this review, I find that the use of an indemnification clause in this contract will facilitate the national defense.

In view of the foregoing and pursuant to the authority vested in me by Public Law 85-804 (50 U.S.C. 1431-1435) and Executive Order 10789, as amended, I hereby authorize USAMRAA to include the indemnification clause set forth at FAR Subpart 52.250-1, together with Alternate I, in Contract No. DAMD17-91-C-1139, provided the contract defines unusually hazardous risks precisely as set forth above.

Should it prove necessary in implementing this Memorandum of Decision to incorporate language into the contract to clarify terms found in the indemnification clause, the contracting officer shall not include any such clarifying language without the prior review and approval of the Office of the Assistant Secretary of the Army (Research, Development and Acquisition).

It is not possible to determine the actual or estimated cost to the Government as the result of the use of this indemnification clause, inasmuch as the liability of the Government, if any, will depend upon the occurrence of an incident in the definition of unusually hazardous risks.

The contractual documents executed pursuant to this authorization shall comply with the requirements of FAR Subparts 28.3 and 50.4 as implemented by the Department of Defense and the Department of the Army. This Memorandum of Decision shall be incorporated in its entirety into Contract No. DAMD17-91-C-1139, and shall specifically cross reference FAR 52.250-1. The contracting officer shall not require, and the Army shall not reimburse the contractor for the cost of insurance coverage applicable to the unusually hazardous risks and in excess of the minimum required by FAR Subpart 28.3.

Louis Caldera

APPENDIX 8: TESTING AND POTENCY PROBLEMS

May 5, 1998 memo from Fort Detrick U.S. Army Contracting Officer, Joseph Little, confirming early problems with supplemental testing and potency of the anthrax vaccine. Excerpt: "suspend any further potency testing under the supplemental testing program because the results continue to be all over the board and then must be reported to the FDA" (Little, 1998):

Forward Header

Subject: Suspension of Supplemental Testing
Author: <joe_little_at_usamrsl__ftdetrck@ftdetrck-ccmail.army.mil > at InternetMail
Date: 5/5/98 7:43 AM

Mike:

Had a voice mail this morning from Tim Wibert with a message that Tony Luttrell wants to suspend any furhter potency testing under the supplemental testing program because the results continue to be all over the board and than must be reported to the FDA. He would like to do some experiments first to resolve the control lot problem and then proceed to complete the testing.

There currently is 826,790 doses ready for shipment at MSPI. I have no idea at this point how long this experimentation would take and how it would affect the schedule for completing the supplemental testing. I will get that from Tim as soon as possible.

Do you want to pursue this strategy or are there some questions you would like to ask of MSPI?

Joe L.

Brigadier General Eddie Cain e-mails concerning GAO testimony delivered during a 1999 hearing on anthrax vaccine included the general's statement that DoD "came up flat," and that DoD's vaccine "was NOT the one tested." General Cain discussed the DoD's reporting that "desert storm illnesses were not cause[d] (sic) by the anthrax vaccine," when there is "no record of who received the shots." Cain's e-mail expressed worry that the "DoD & the Administration" would be in "big time trouble" if they could not address these questions (DoD-JPOBD, 1999):

From: Cain, BG Eddie
Sent: Monday, May 03, 1999 6:34 PM
To: Borowski, LTC Bob
Subject: FW: Anthrax Vaccine

FYI

-----Original Message-----
From: Cain, BG Eddie
Sent: Monday, May 03, 1999 6:06 PM
To: Wade, COL John
Subject: RE: Anthrax Vaccine

Relax John, we should have all anticipated the media picking-up GAO's as oppose to DoD's "soundbites. I still believe we held our own & my people did a superb job getting me ready in such a short period of time. What's done is done; I think the key is to move forward. We keep talking about putting forth an aggressive showing, two key areas we came up flat were the GAO's assertion that #1, the anthrax vaccine licensed was NOT the one tested and # 2, how can DoD say that reported desert storm illnesses were not cause by the anthrax vaccine when we have no record of who received shots. If we can not answer these questions we (DoD & the Administration)are in big time trouble. I will work the BioPort oversight plan, but believe we are digging ourselve a hole that will be too difficult to crawl out off - if we provide anything oversight, BioPort could technically be called a GOCOM organization. And if you think Congressman Shays was critical of the current relationship between FDA & DoD, wait until he finds out that DoD is calling all the shots onsight.

-----Original Message-----
From: John V. Wade [mailto:WADEJV@acq.osd.mil]
Sent: Monday, May 03, 1999 2:54 PM
To: Cain, BG Eddie; fanellw@jpobd.osd.mil; gilbreathm@jpobd.osd.mil
Cc: Stanley H Lillie
Subject: Anthrax Vaccine

General Cain,
Just come from meeting with Mr. Oliver, Sue Daily, Pam Berkowsky, Fred Gerber, and reps from LA, OGC, USD(P&R) regarding the Shay's Hearing and follow-on actions. HA worked late into Friday evening, this was the follow-on. The feeling was that while FDA started strong and ended strong, GAO carried the day during the questioning. As a result of this there will likely be a 'single OSD point of contact for Anthrax" assigned. SECDEF will be calling either FDA or HHS with the message "we (DoD/FDA) didn't do to well on this one" requesting that they write to Shays, as will DoD (HA lead). Lots of questions regarding how we were "unprepared to answer/counter GAO's testimony." There will also, most likely be a letter to GAO discussing our displeasure with the "expertise" put on this project.

APPENDIX 9: KARL ROVE MEMO TO DOD

Presidential Senior Advisor, Karl Rove tasked DoD Undersecretaries of Defense (USD) Dr. David Chu and Edward Aldridge to review the "political problems" associated with the anthrax vaccine and Gulf War Illness (Rove, 2001):

THE WHITE HOUSE

WASHINGTON

2001 APR 27 PM 3:54

OSD
WHITE HOUSE SECTION

April 25, 2001

MEMORANDUM FOR PAUL WOLFOWITZ

FROM: KARL ROVE

SUBJECT: GULF WAR SYNDROME AND ANTHRAX

Here is material which has been sent to me by Ross Perot regarding the Gulf War Syndrome, as well as some material on the Anthrax vaccine problem.

He also offered me a packet of materials from the Lydon LaRouche crowd about Richard Armitage, but I turned him down.

I do think we need to examine the issues of both Gulf War Syndrome and the Anthrax vaccine and how they can be dealt with. They are political problems for us.

W00554 01

APPENDIX 10: DOD UNDERSECRETARY MEMO

DoD Undersecretaries Dr. David Chu and Edward Aldridge reviewed the "political problems" associated with the anthrax vaccine and Gulf War illness. The undersecretaries presented recommendations to Defense Secretary Donald Rumsfeld. Highlights included continuing the program only "at a minimum level"; implementing "an acquisition strategy to purchase additional bio-detectors and stockpiles of antibiotics to augment force protection in the absence of an anthrax vaccine"; developing a "coherent institutional process to assess and prioritize biological threats and approve the use of associated countermeasures"; and the development of a "national long-range vaccine that will address the full range of requirements of the DoD, DHHS, and other stakeholders in this plan" (Chu & Aldridge, 2001):

SECDEF HAS SEEN

AUG 10 2001

ACTION MEMO

August 10, 2001 8:00 AM

SECRETARY OF DEFENSE

Deputy Action

Mr. Edward C. Aldridge, Jr., USD (Acquisition, Technology & Logistics)
Dr. David S. C. Chu, USD (Personnel & Readiness)

SUBJECT: Strategy Development for Force Health Protection Against Biological Threats

I recommend the following course of action to carry out your plan for anthrax and other vaccines required for Force Health Protection:

- USD(AT&L) will review and assess performance of BioPort Corporation and make a determination of future funding to support the strategy outlined below. Report completed by Sept 01.
  The current Anthrax Vaccine Immunization Program will continue at a minimum level (critical personnel and projects only). USD(AT&L) will implement an acquisition strategy to purchase additional bio-detectors and stockpiles of antibiotics to augment force protection in the absence of an anthrax vaccine.
- USD(P&R) will request PA&E to provide the scenario analyses needed for future decisions related to the threat of biological agents. Report to USD(P&R) Dec 01.
- USD(P&R) will request DIA through C3I to provide a comprehensive review of the doctrinal positions of any State or group to use biological weapons as a part of their offensive/defensive strategies. Report to USD(P&R) by Dec 01.
- USD(P&R) will coordinate with appropriate DoD officials to develop a coherent institutional process to assess and prioritize biological threats and approve the use of associated countermeasures. Prepare DoD Directive for coordination by Dec 01.
- USD(AT&L) and USD(P&R) will continue their inter-agency efforts to develop a national long-range vaccine that will address the full range of requirements of the DOD, DHHS, and other stake-holders in this plan. This plan will include an evaluation of the need for a dedicated vaccine facility to serve the national interest. Provide an interim report to SecDef by Dec 01.

RECOMMENDATION: Secretary of Defense approves strategy development by initialing this page.

COORDINATION: None

Prepared By: Dr. David Chu, USD (Personnel & Readiness), 695-5254

SPECIAL ASSISTANT
SPECIAL ASSISTANT
SPECIAL ASSISTANT
EXECUTIVE SECRETARY

APPENDIX 11: FEDERAL BUREAU OF INVESTIGATION

Excerpts from a press release and transcript demonstrate the Federal Bureau of Investigation associated frustrations by a U.S. Army scientist over testing irregularities with the anthrax vaccine as a possible motive for the 2001 anthrax letter attacks. The FBI alleged a U.S. Army scientist's motive surrounded the fact the "anthrax vaccine he was working on was failing" due to potency problems (FBI, 2008, excerpts from press release/transcript and emails from affidavit).

Remarks Prepared for Delivery by U.S. Attorney Jeffrey Taylor at Amerithrax Investigation Press Conference

WASHINGTON, D.C.
Wednesday, August 06, 2008

Excerpt:

Fifth, as reflected in the court documents, Dr. Ivins had a history of mental health problems and was facing a difficult time professionally in the summer and fall of 2001 because an anthrax vaccine he was working on was failing. The affidavits describe one e-mail to a co-worker in which Dr. Ivins stated that he had "incredible paranoid, delusional thoughts at times," and feared that he might not be able to control his behavior.

Department of Justice

FOR IMMEDIATE RELEASE
Wednesday, August 6, 2008

Excerpt:

MR. TAYLOR: The other question you have, Dr. Ivins is a troubled individual, particularly so at that time. He's very concerned, according to the evidence, that this vaccination program he's been working on may come to an end. He's also very concerned that some have been criticizing and blaming that vaccination program in connection with illnesses suffered by soldiers from, I think, the first Gulf War. So that was going on, according to the evidence, in his mind at that particular time.

With respect to motive, I'll point again to -- with respect to the motive, the troubled nature of Dr. Ivins. And a possible motive is his concern about the end of the vaccination program. And the concerns had been raised, and one theory is that by launching these attacks, he creates a situation, a scenario, where people all of a sudden realize the need to have this vaccine.

FBI Affidavit Analysis Excerpts, p. 15:

AO106(Rev.5/85) Affidavit for Search Warrant

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

FILED

OCT 31 2007

NANCY MAYER WHITTINGTON, CLERK
U.S. DISTRICT COURT

In the Matter of the Search of

Residence at [redacted]
Frederick, Maryland,
owned by Bruce Edwards Ivins,
DOB [redacted] SSN [redacted]

APPLICATION AND AFFIDAVIT
FOR SEARCH WARRANT

CASE NUMBER: 07-524-M-01

Controversy concerning the anthrax vaccine

Beginning shortly after the first Gulf War and through 2001, USAMRIID and Dr. Ivins was the focus of public criticism concerning their introduction of a squalene adjuvant (or additive) to the AVA anthrax vaccine, which was blamed for the Gulf War Syndrome. In 2000 and 2001, as evident by the e-mails above, that same anthrax vaccine was having problems in the production phase at Bioport, a private company in Michigan responsible for manufacturing the vaccine. The Food and Drug Administration (FDA) had suspended further production at Bioport, and the U.S. government, specifically the Department of Defense, was running out of approved lots of the vaccine. The situation placed pressure on select staff members at USAMRIID, including Dr. Ivins, who were part of the Anthrax Potency Integrated Product Team (IPT). The purpose of the IPT was to assist in the resolution of technical issues that was plaguing Bioport's production of approved lots of the vaccines.

In the weeks immediately prior to the attacks, Dr. Ivins became aware that an investigative journalist who worked for NBC News had submitted a Freedom of Information Act (FOIA) requests on USAMRIID seeking detailed information from Dr. Ivins's laboratory notebooks as they related to the AVA vaccine and the use of adjuvants. On August 28, 2001, Dr. Ivins appeared angry about the request providing the following response in an e-mail: "Tell Matsumoto to kiss my ass. We've got better things to do than shine his shoes and pee on command. He's gotten everything from me he will get."

In early 2002, shortly after the anthrax letter attacks, the FDA re-approved the AVA vaccine for human use, production at Bioport resumed, and anthrax research at USAMRIID continued without interruption. As mentioned previously, one of the anthrax letters post marked on September 18, 2001, was addressed to Tom Brokaw, NBC News in New York. Dr. Ivins thereafter received "the highest honor given to Defense Department civilians at a Pentagon ceremony on March 14, 2003" for his work in "getting the anthrax vaccine back into production."

Excerpts from emails, p. 12-14:

June 28, 2000, "Apparently Gore (and maybe even Bush) is considering making the anthrax vaccine for the military voluntary, or even stopping the program. Unfortunately, since the BioPort people aren't scientists, the task of solving their problem has fallen on us. . . . . Believe me, with all the stress of home and work, your email letters to me are valuable beyond what you would ever imagine – and they help me keep my sanity…."

June 29, 2000, "BioPort just tested its final lot of AVA [anthrax vaccine] in a potency test. If it doesn't pass, then there are no more lots to test, and the program will come to a halt. That's bad for everyone concerned, including us. I'm sure that blame will be spread around."

July 6, 2000, "[redacted] I think the **** is about to hit the fan…bigtime. The final lot of AVA, lot 22, isn't passing the potency test, and now there's nothing to back it up. Plus, the control vaccine isn't working. It's just a fine mess. [redacted] are spending probably 95% of our time on this."

August 29, 2000, "[redacted] are 10% of the Bacteriology Division. If we quit, the anthrax program and BioPort would go down the drain. I'm not boasting, [redacted], but the three of us have a combined total of 52 years of research experience with anthrax. You just can't go out and find someone like [redacted] with their knowledge, skill and abilities. Ain't gonna happen."

September 7, 2001, "I was taken off the Special Immunization Program because of what happened last spring, and I've just gotten back on it, getting my anthrax and Yellow fever shots. We are currently finishing up the last of the AVA, and when that is gone, there's nothing to replace it with. I don't know what will happen to the research programs and hot suite work until we get a new lot. There are no approved lots currently available at BioPort. . . . [redacted] has been having us have biweekly meetings on the rPA vaccine progress, and on August 29 I went to the Pentagon – first time there – to go to a meeting in his place on the vaccine. There is a real bag of worms with a new lot of rPA produced by the BDP (a private company) for NCI, who is under contract to USAMRIID. BDP signed a sub-contract with to produce the rPA for a human use vaccine Phase I trial. They were paid and they produced it. Now they are refusing to release it unless the Army pays some incredible sum of money for lawsuit indemnification (about $200,000 per year for the next 50 years). The Army refuses to do that of course, and everything is in Limbo."

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