Enhanced Engagement: The Evolving Relationship between FDA and DoD Regulatory Authorities

JEREMIAH J. KELLY[1]

ABSTRACT

The U.S. Department of Defense (DoD) and U.S. Food and Drug Administration (FDA) relationship has, by necessity, evolved throughout the modern era as new national security and public health threats have shaped the authority, organization, and execution of each agency's unique mission. This continual evolution requires balancing FDA's interest in protecting the public health from unsafe and ineffective medical products with DoD's role in fighting and winning the nation's wars. There will always be a natural tension between the risk–benefit calculus of FDA decision-making for public health purposes and the risk–benefit calculus of DoD's warfighting mission in austere environments. The unique DoD–FDA relationship was enhanced by Congress' enactment of Public Law 115-92. But the DoD–FDA "enhanced engagement" relationship created by this statute must develop further. This Article will explore: 1) the history of DoD–FDA relations; 2) the dependency of DoD medical product authorities on FDA's legal framework; 3) the impact of P.L. 115-92 and the progress of the two organizations under this landmark statute; 4) opportunities for additional, mutually beneficial regulatory coordination; and 5) recommended solutions to systemic challenges to spur development of FDA-approved, licensed, or cleared medical products for the unique medical needs of the warfighter.

I. INTRODUCTION

The U.S. Department of Defense's (DoD's) role in medical care for soldiers traces its origin to the Revolutionary War, more than a century before even the earliest origins of the U.S. Food and Drug Administration (FDA).[2] Since the 1962 Kefauver–Harris

---

[1] Jeremiah J. Kelly is a Partner in the law firm of Venable, LLP in Washington, DC. At the time of the *Food and Drug Law Journal* Symposium panel, Mr. Kelly was the Chief of the FDA Regulatory Law Division, Office of the Staff Judge Advocate, U.S. Army Medical Research and Development Command (USAMDC) at Fort Detrick, Maryland. Mr. Kelly previously served in the U.S. Food and Drug Administration's Office of the Chief Counsel and Office of Legislation. The symposium included helpful comments from Elizabeth Sadove, FDA Office of Counterterrorism and Emerging Threats (OCET) and our Moderator, Professor Maxwell J. Mehlman of Case Western Reserve University School of Law. The author is grateful for the feedback on this paper from Dr. Laura Brosch of the Uniformed Services University, John Casciotti of the Defense Health Agency, Justin Coen of Venable, LLP, and Aimee Kelly. This author acknowledges the helpful assistance of his paralegals, Neidel Hamilton and Misa Morreall, without whom this paper would not be possible. The views expressed in this Article are those of the author alone and do not represent the views of any organization or client.

[2] Arthur O. Anderson, Jeffery E. Stephenson & Bret K. Purcell, *Ethical Issues in the Development of Drugs and Vaccines for Biodefense*, *in* MEDICAL ASPECTS OF BIOLOGICAL WARFARE 915, 918 (Joel

Amendments to the Federal Food, Drug, and Cosmetic Act (FDCA),[3] the relationship between FDA and DoD has evolved with respect to DoD's autonomy in decision-making over investigational or emergency use of medical products to treat the unique medical needs of the U.S. warfighter. Given the medical products needed to ensure the success of DoD's national security mission, DoD is dependent on FDA's role as an independent evaluator of the safety and efficacy of proposed medical solutions.

The DoD–FDA relationship has, by necessity, evolved throughout the modern era as new national security and public health threats have shaped the authority, organization, and execution of each agency's unique mission. This continual evolution requires balancing FDA's interest in protecting the public health from unsafe and ineffective medical products with DoD's role in fighting and winning the nation's wars. There will always be a natural tension between the risk–benefit calculus of FDA decision-making for public health purposes and the risk–benefit calculus of DoD's warfighting mission in austere environments. The unique DoD–FDA relationship was enhanced by Congress' enactment of Public Law 115-92,[4] which expanded the Emergency Use Authorization (EUA) authority for DoD, created a DoD-specific expedited approval mechanism, and established regular requirements for FDA–DoD meetings to facilitate collaboration related to DoD's highest medical product priorities.

In addition to Public Law 115-92, FDA's statutory authorities under the FDCA and the Public Health Service Act (PHSA) significantly impact and shape DoD's own internal Force Health Protection (FHP)[5] programs as well as its research and development (R&D) authorities. The relationship between DoD and FDA is critical given DoD's role in regulating and delivering the medical care of its soldier population, the creation of the new Defense Health Agency (DHA), and the ongoing need for medical countermeasure (MCM) development.

Very little in the academic literature has dealt with the DoD–FDA relationship as, typically, these subjects are bifurcated into separate categories of national defense and public health, which is reflected in the structure of the U.S. Code[6] and congressional committee jurisdiction.[7] This Article will explore: 1) the history of DoD–FDA relations; 2) the dependency of DoD medical product authorities on FDA's legal

---

Bozue, Christopher K. Cote & Pamela J. Glass eds., 2018), https://medcoe.army.mil/borden-tb-medical-aspects-bio-war (last visited June 19, 2023).

3 The Kefauver–Harris Amendments to the FDCA created the efficacy requirement for the approval of new drugs. *See* § 505(a) of the FDCA as amended by § 104 of Pub. L. No. 87-781, 76 Stat. 784 (codified as amended at 21 U.S.C. § 355, (1962 Supp.)); s*ee also* Part III, infra.

4 Act of Dec. 12, 2017, Pub. L. No. 115-92, 131 Stat. 2023–25.

5 Force Health Protection (FHP) is "simply the prevention of disease and injury in order to protect the strength and capabilities of the military population." Mary T. Brueggemeyer, *Force Health Protection*, *in* FUNDAMENTALS OF MILITARY MEDICINE 233, 234 (Francis G. O'Connor, Eric B. Schoomaker & Dale C. Smith eds., 2019), https://medcoeckapwstorprd01.blob.core.usgovcloudapi.net/pfw-images/dbimages/Fund%20ch%2016.pdf (last visited June 19, 2023).

6 *See* Federal Food and Drugs Act of 1906, 21 U.S.C. §§ 1, et seq. ; *see also* 10 U.S.C. §§ 101, et seq.

7 *See* U.S. HOUSE COMMITTEE ON ENERGY & COMMERCE, https://energycommerce.house.gov/ (last visited June 19, 2023); *see also* U.S. HOUSE ARMED SERVICES COMMITTEE, https://armedservices.house.gov/ (last visited June 19, 2023); U.S. SENATE COMMITTEE ON HEALTH, EDUCATION, LABOR & PENSIONS (HELP), https://www.help.senate.gov/ (last visited June 19, 2023); U.S. SENATE COMMITTEE ON ARMED SERVICES, https://www.armed-services.senate.gov/ (last visited June 19, 2023).

framework; 3) the impact of Public Law 115-92 and the progress of the two organizations under this landmark statute; 4) opportunities for additional, mutually beneficial regulatory coordination; and 5) recommended solutions to systemic challenges to spur development of FDA-approved, licensed, or cleared medical products for the unique medical needs of the warfighter. As has always been the case, the DoD–FDA relationship will require continued analysis, evolution, and collaboration to deal with future national security threats where DoD still finds its need to win in warfare ill-fitted at times with the modern FDA regulatory paradigm.

A. Historical Context: DoD's Surgeon General-Led Model of FHP and Medical R&D

DoD sends its men and women in uniform across the globe to fight the nation's wars in harsh and life-threatening environments. U.S. warfighters often encounter significant battlefield injury and trauma, are exposed to rare infectious diseases endemic to a foreign region of the world, and experience clinical and rehabilitative needs due to brain, extremity, or tissue damage. Accordingly, DoD is tasked with the R&D of drugs, biologics, and devices to treat the unique needs of the warfighter to accomplish its diverse national security mission. DoD's nearly 1.4 million force strength[8] requires medical care in traditional settings, but also FHP measures to ensure soldiers are protected from all possible threats on the battlefield. FHP is a continuous, ongoing obligation to provide the medical solutions to the warfighter where and when it is needed. This FHP paradigm includes three phases: pre-deployment, deployment, and post-deployment.[9] Accordingly, DoD requires continuous investments in medical R&D—basic, applied, and advanced R&D—to continually provide the U.S. warfighter with an edge. The following sums up this FHP prerogative:

> Contagion and catastrophic illnesses have affected the outcome of wars throughout history. Military officers have duties to protect their soldiers from becoming disease casualties, conserve their fighting strength, and ensure the success of the mission. Discharging those duties requires more than site sanitation and encouraging personal cleanliness. Armies need to have, and should have, at their disposal the best available vaccines and medicines directed against specific disease hazards. The ability to provide procedures, remedies, antidotes, and medical countermeasures has been almost as important as good military training and advanced weaponry in the success of military operations.[10]

The origins of DoD's medical care, the FHP paradigm, and its research apparatus predate even the earliest origins of FDA. FDA traces its roots back to the Agricultural Division in the Patent Office of 1848, but its official creation occurred with the passage

---

[8] *DoD Personnel, Workforce Reports & Publications, "Armed Forces Strength Summary" for August 31, 2022*, DEF. MANPOWER DATA CTR., https://dwp.dmdc.osd.mil/dwp/app/dod-data-reports/workforce-reports (last visited June 19, 2023).

[9] Brueggemeyer, *supra* note 5, at 242–44. It is helpful to compare Figure 16-2 (*id.* at 242), "Health Risk Assessment" and Figure 16-4 (*id.* at 244), "Preventative Countermeasures," to get an understanding of the wide scope of the FHP need.

[10] James R. Swearengen & Arthur O. Anderson, *Scientific and Ethical Importance of Animal models in Biodefense Research*, *in* BIODEFENSE RESEARCH METHODOLOGY AND ANIMAL MODELS 25, 27 (Swearengen ed., 2d ed., 2012).

of the 1906 Pure Food and Drugs Act.[11] But DoD has an even longer history in the medical field. Since General George Washington immunized[12] the Continental troops in 1777 during the Revolutionary War[13] to the present, DoD and its predecessor organizations[14] have been entrusted with the medical care and medical readiness of its forces. The U.S. Army's contributions to the creation of a regular medical program dedicated to the prevention of illness and the treatment of disease and injury are staggering. In both Dr. Benjamin Rush's 1778 *Directions for Preserving the Health of Soldiers Recommended to the Officers of the United States Army*,[15] and Inspector General of the Army Major General Baron von Steuben's *Regulations for the Order and Discipline of the Troops of the United States*,[16] the responsibility is placed on the "line officer" and the "regimental commander" for the medical care of their troops: "[t]he preservation of the soldier's health should be his first and greatest care . . . ."[17] These Revolutionary War documents formed the basis for the military medical officer's role. However, it was not until 1818 that Congress created a permanent Army Medical Department (AMEDD). This followed the initial creation of the Army Medical Corps in 1813 with the installation of Joseph Lovell, MD, as the first Surgeon General of the U.S. Army during the War of 1812.[18] Dr. Lovell would go on to improve the caliber of practitioners in the service by instituting examinations for all those desiring to join the AMEDD, and later, in 1847, Congress passed legislation giving medical officers in the Army true commissions and "real as opposed to assimilated rank, in part trying to improve the effectiveness of the medical operations in the field."[19] Subsequently, the exploits of Florence Nightingale helping British hospitals during the 1853–1856 war in Crimea due to the failure of preparation and lack of preventative medicine by the British army, and the observation of suffering on the battlefield by a traveling Swiss businessman, Henri Dunant in 1859, led to the creation of the Red Cross (1863) and the Geneva Convention (1864), respectively. The mid-19th Century showed increasing public concern with the healthcare of those who serve our nation in modern warfare.

---

[11] *See When and Why was FDA Formed?*, U.S. FOOD & DRUG ADMIN., "https://www.fda.gov/about-fda/fda-basics/when-and-why-was-fda-formed#:~:text=Though%20FDA%20can%20trace%20its,Pure%20Food%20and%20Drugs%20Act. (last visited June 19, 2023).

[12] General Washington used an earlier method of immunizing solders against smallpox called variolation whereby the patient is infected with the pustules of patients with a mild form of the disease. *See* Anderson, Stephenson & Purcell, *supra* note 2, at 918.

[13] *Id.* at 918.

[14] The U.S. Army was America's first national institution, created June 14, 1775. *See, e.g.*, U.S. ARMY, https://www.army.mil/1775/ (last visited June 19, 2023).

[15] BENJAMIN RUSH, DIRECTIONS FOR PRESERVING THE HEALTH OF SOLDIERS (Fry & Kammerer 1808).

[16] FRIEDRICH WILHELM VON STEUBEN, REGULATIONS FOR THE ORDER AND DISCIPLINE OF THE TROOPS OF THE UNITED STATES (Styner & Cist 1779).

[17] Dale C. Smith, *The History of the Military Medical Officer*, *in* FUNDAMENTALS OF MILITARY MEDICINE 7 (Francis G. O'Connor, Eric B. Schoomaker & Dale C. Smith eds., 2019), https://medcoeckapwstorprd01.blob.core.usgovcloudapi.net/pfw-images/dbimages/Fund%20ch%201.pdf.

[18] *Id.* at 9; *see also* Stephen J. Craig, *Joseph Lovell, MD (1788-1836): First US Army Surgeon General*, 24 J. MED. BIOGRAPHY 309 (2016).

[19] Smith, *supra* note 17, at 12.

The Surgeon General-led model of preventative and therapeutic medical care within the armed forces continued into the Civil War period with Major Jonathan Letterman as medical director of the Amy of the Potomac, the principal element of the Union Army. During the early stages of the Civil War, disease rates exceeded battle casualties, medical support was disorganized, and the medical officer's ability to command troops on the battlefield was only developing. In 1862, Letterman would prevail upon Major General Ambrose Burnside to approve several proposals, including medical command of all field hospitals, medical officer coordination of all evacuations from the battlefield to a more organized system of hospitals, and centrally controlled medical supplies. Thus, a "medically commanded field medical system came into existence for the first time."[20] "This resulting Letterman system was complete: from prevention to echeloned care, the military medical officer had a set of new roles and responsibilities in the deployed force, roles that could be met only by those with military authority."[21] This progress would ebb and flow throughout the discovery of microbiology and camp diseases in the 1890s, typhoid fever in the Spanish–American War (1898), and the increased specialization and mobilization of the medical corps leading up to the U.S. involvement in World War I, also referred to as the Great War, in 1916.[22] World War I led to the use of forward medics trained by the medical officers, assuring the training of combat medics and assuring their role in "coordinated field care environment because a critical function of medical officers."[23] Both World War I and World War II had proven the "absolutely essential nature of specialists as part of the regular AMEDD" and, after the war, all DoD service components would create graduate medical education programs that specialized in combat medical care.[24]

In addition to its achievements in developing its Surgeon General-led model of FHP, DoD has often blazed the trail in how it conducts medical research that yields battlefield MCMs. For example, General George M. Sternberg, Army Surgeon General, appointed Major Walter Reed to command the Yellow Fever Commission in 1900 to study Yellow Fever in Cuba, which resulted in not only the finding that Yellow Fever was transmitted by mosquitos and could thus be prevented, but also the concept of voluntary advanced informed consent in research.[25] In the 1950s, military researchers at the Armed Forces Institute of Pathology (AFIP) identified seven types of adenovirus and created vaccines against them, a "classic example of quick, successful medical countermeasure development."[26] After the ten principles of the Nuremburg Code for the ethical standards for research involving human subjects were developed in 1946 by Dr. Andrew Ivy and Dr. Leo Alexander, Secretary of Defense Charles Wilson issued a groundbreaking memorandum for all military branches on February 26, 1953 (the "Wilson Memo") adopting all ten principles of the Nuremburg

---

[20] *Id.* at 14.

[21] *Id.*

[22] *Id.* at 17–18.

[23] *Id.* at 18.

[24] *Id.* at 18.

[25] Swearengen & Anderson, *supra* note 10, at 29 .

[26] Anderson, Stephenson & Purcell, *supra* note 2, at 921.

Code as official DoD guidance related to ethical research involving human subjects.[27] From 1954 to 1973, "Operation Whitecoat" included experiments with non-combatant, conscientious objectors at Camp Detrick (later, Fort Detrick), Maryland, for the purpose of determining the extent to which humans are susceptible for infection from biological warfare agents.[28] The Surgeon General of the U.S. Army carefully managed the research:

> Approximately 153 studies related to the diagnosis, prevention, and treatment of various diseases were completed during Operation Whitecoat, including research on Q fever and tularemia infections and staphylococcal enterotoxins. Vaccines to be used against Venezuelan equine encephalitis, plague, tularemia, Rocky Mountain Spotted Fever, and Rift Valley Fever were tested for evidence of safety in humans.[29]

The AMEDD would remain at the forefront in the development of DoD medicine, winning the Lasker Award for the administration of medical research during World War II, which included mass production of penicillin for troops at the battlefront, the search for better antimalarials and insecticides, and "hundreds of other important research projects."[30] This work included major breakthroughs in cancer chemotherapy and the 1981 Nobel Prize in Physiology or Medicine for the discoveries concerning information processing in the visual system by Dr. David Hubel and Dr. Torsten Wisel. The U.S. Army Medical Research and Development Command (USAMRDC)[31] was created on August 20, 1958, at the direction of Army Surgeon General Silas B. Hayes under the Office of the Surgeon General (OTSG). USAMRDC included ten original laboratories, including several overseas laboratories.[32] Currently, USAMRDC includes thirteen subordinate laboratories, including the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) and the Walter Reed Army Institute of Research (WRAIR); the U.S. Army Institute of Surgical Research (USAISR); the U.S. Army Medical Research Institute of Chemical Defense (USAMRICD); the U.S. Army

---

[27] Wilson Memorandum from the Secretary of Defense to the Secretaries of the Army, Navy, and Air Force (Feb. 23, 1953), https://nsarchive2.gwu.edu//radiation/dir/mstreet/commeet/meet3/brief3.gfr/tab_h/br3h2b.txt (last visited Mar. 30, 2023); *see also* John McManus, Sumeru G. Mehta, Annette R. McClinton, Robert A. De Lorenzo & Toney W. Baskin, *Informed Consent and Ethical Issues in Military Medical Research*, 12 ACAD. EMERGENCY MED. 1120, 1121 (2005); *see also* NAT'L RSCH. COUNCIL (US) COMM. ON THE USE OF THIRD PARTY TOXICITY RSCH. WITH HUM. RSCH. PARTICIPANTS, INTENTIONAL HUMAN DOSING STUDIES FOR EPA REGULATORY PURPOSES: SCIENTIFIC AND ETHICAL ISSUES 47 (National Academies Press 2004). In addition, the Wilson Memo is regularly cited by DoD research organizations as its principal framework for human subject protections. *See, e.g.*, *Questions & Answers Regarding Human Subject Research at Fort Detrick*, DEF. HEALTH AGENCY, https://www.health.mil/Reference-Center/Frequently-Asked-Questions/Human-Subject-Research-at-Fort-Detrick (last visited June 20, 2023).

[28] Anderson, Stephenson & Purcell, *supra* note 2, at 923.

[29] *Id.* at 924.

[30] U.S. ARMY MED. RSCH. & DEV. COMMAND, USAMRC: 50 YEARS OF DEDICATION TO THE WARFIGHTER (1958–2008) 14 (2008), https://mrdc.health.mil/assets/docs/about/USAMRMC_history.pdf (last visited June 20, 2023).

[31] USAMRDC would later be called the U.S. Army Medical Research and Material Command (USAMRMC) until a recent reorganization led the Army to revert its original name, USAMRDC. *Command History*, U.S. ARMY MED. RSCH. & DEV. COMMAND, https://mrdc.health.mil/index.cfm/about/history (last visited June 20, 2023).

[32] USAMRC: 50 YEARS OF DEDICATION TO THE WARFIGHTER, *supra* note 30, at 14–23.

Research Institute of Environmental Medicine (USARIEM); and laboratories in Nairobi, Kenya; Bangkok, Thailand; and Tbilisi, Georgia.[33]

Currently, DoD, through the USAMRDC, the Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense (JPEO–CBRND) and other DoD Components, has fielded revolutionary medical products that have impacted not only the warfighter, but also global health as those innovations become adopted by the general public.[34] If you have heard of medical breakthroughs in infectious disease, trauma care, diagnostics, or countermeasures against chemical, biological, radiological, or nuclear (CBRN) threats, there is a high likelihood that you can trace this innovation back to DoD R&D. USAMRDC—now a component of the Defense Health Agency (DHA)[35]—executes research in five basic areas: 1) military infectious diseases, 2) combat casualty care, 3) military operational medicine, 4) chemical and biological defense, and 5) clinical and rehabilitative medicine. USAMRDC currently operates the Military Infectious Disease Research Program (MIDRP), the Combat Casualty Care Research Program (CCCRP), the Military Operational Medicine Research Program (MOMRP), and the Medical Chemical and Biological Defense Research Program and directs nearly $2 billion a year in congressionally directed medical research.[36] In a separate but related mission, the JPEO–CBRND "manages our nation's investments in chemical, biological, radiological, and nuclear (CBRN) defense equipment and medical countermeasures."[37] As part of DoD's Chemical and Biological Defense Program (CBDP), which operates under the authority of the Deputy Assistant Secretary of Defense for Chemical and Biological Defense, JPEO–CBRND undertakes medical countermeasure development R&D of therapeutics, vaccines, diagnostics, and other equipment to protect soldiers from a CBRN bio-warfare threat.[38]

---

[33] *See Subordinate Commands*, U.S. ARMY MED. RSCH. & DEV. COMMAND, https://mrdc.health.mil/index.cfm/about/subordinate_commands (last visited June 20, 2023).

[34] While the primary medical product developers within DoD are USAMRMC (now part of DHA) and JPEO-CBRND, there are other DoD Components that also fund earlier stage research regulated by FDA, including the Joint Science and Technology Office of the Defense Threat Reduction Agency (DTRA) and the Defense Advanced Research Projects Agency (DARPA). The USAMRDC serves as regulatory sponsor, when one is required for DoD, under the U.S. Army Surgeon's delegated authority.

[35] *See* 10 U.S.C. § 1073c(e)(1)(B) (requiring the Secretary of Defense to move the U.S. Army Medical Research and Materiel Command (USAMRMC, now the U.S. Army Medical Research & Development Command or "USAMRDC") to the Defense Health Agency along with "such other medical research organizations and activities of the armed forces as the Secretary considers appropriate"). It is unclear at this point whether SECDEF will utilize this opportunity to further consolidate its medical R&D assets under a single, centralized organization or continue with the distributed, service-led model that has been the historical norm. As of June 2023, USAMRDC is listed in public documents as a sub-agency of DHA, but it is clear that much work remains to implement this transition. *See, e.g.*, *Strategic Planning and Campaign Plan Development and Implementation*, SAM.GOV, https://sam.gov/opp/379037b80703476c8ef3f7d0bb68a3b4/view. Further, it may be worthwhile to consider which other organizations should be included under the DHA medical R&D umbrella.

[36] *See Medical Research and Development*, U.S. ARMY MED. RESEARCH & DEV. COMMAND, https://mrdc.health.mil/index.cfm/program_areas/medical_research_and_development (last visited June 20, 2023).

[37] *We Are JPEO,* JOINT PROGRAM EXEC. OFF. FOR CHEM., BIOLOGICAL, RADIOLOGICAL & NUCLEAR DEFENSE, https://www.jpeocbrnd.osd.mil/ (last visited June 20, 2023).

[38] For a description of the distinction between naturally occurring infectious disease and weaponized biological warfare agents, see Matthew S. Halpin, *Biological Warfare: The Weaponizing of Naturally-Occurring Biological Diseases*, 16 HOUSTON J. HEALTH L. & POL'Y 259, 266 (2016).

DoD has had to adjust over time to the evolving public health expectations associated with FDA's legal authority and jurisdiction and its impact on DoD FHP, medical treatment, and research elements. To this day, we are seeing DoD itself evolve from service-led, service-specific medical care under Surgeons General of each component (e.g., Army, Navy, Air Force, Marines, etc.) to a centralized model within the DHA, which was created as the key element of a military health system governance reform effort.[39] Under the new model, DHA will act as "a joint, integrated Combat Support Agency that enables Army, Navy, and Air Force medical services to provide a medically ready force and ready medical force to Combatant Commands in both peacetime and wartime."[40]

II. CONSTANT EVOLUTION: THE HISTORY OF DOD–FDA INTERACTIONS

The 1962 Kefauver–Harris Amendments to the FDCA created a fundamental shift in DoD–FDA relations. These amendments were driven by the increasing concern that newly introduced drug products were ineffective or had serious undiscovered side effects.[41] These concerns were highlighted in the heroic decision of an FDA reviewer, Francis Oldham Kelsey, who refused FDA approval of thalidomide based on a lack of reliable safety evidence and concerns over birth abnormalities associated with the product's use overseas.[42] Thalidomide was used widely in the 1950s and early 1960s for the treatment of nausea in pregnant women; however, it became apparent later in the 1960s that thalidomide treatment caused severe birth defects in thousands of children.[43] Kelsey's action led to a series of U.S. Senate hearings and, ultimately, the Kefauver–Harris Amendments.[44] Not only was efficacy now required for new drug approvals, the introduction of Section 355(i) to the FDCA established requirements for the Investigational New Drug (IND) application for all research using an investigational drug product. At the time, DoD's medical approach included the use of medications that would, under the higher efficacy standard, be illegal. Furthermore, the extensive DoD medical R&D enterprise would now be required to comply with new regulatory filings for this purpose. This change in FDA's legal authority required an evolution from DoD's Surgeon General-led model of medical care and research to the new expectation that DoD would fully comply with FDA's regulatory paradigm, with FDA serving as an independent evaluator of DoD medical product decision-making in the areas of medical R&D and FHP.

---

[39] *See Elements of the Military Health* System, DEF. HEALTH AGENCY, https://www.health.mil/About-MHS/MHS-Elements (last visited on June 20, 2023).

[40] *See Our Organization*, DEF. HEALTH AGENCY, https://www.health.mil/About-MHS/OASDHA (last visited June 20, 2023).

[41] Swearengen & Anderson, *supra* note 10, at 33.

[42] *See Francis Oldham Kelsey: Medical Reviewer Famous for Averting a Public Health Tragedy*, U.S. FOOD & DRUG ADMIN. (Feb. 1, 2018), https://www.fda.gov/about-fda/fda-history-exhibits/frances-oldham-kelsey-medical-reviewer-famous-averting-public-health-tragedy (last visited June 20, 2023); *see also* Swearengen & Anderson, *supra* note 10, at 33.

[43] James H. Kim & Anthony R. Scialli, *Thalidomide: The Tragedy of Birth Defects and the Effective Treatment of Disease*, 122 TOXICOLOGICAL SCIS. 1, 1–6 (2011).

[44] Swearengen & Anderson, *supra* note 10, at 33.

A. The 1964 Memorandum of Understanding

The Kefauver–Harris Amendments led DoD and FDA to enter into a Memorandum of Understanding (MOU) to:

> state the procedures that will be followed by the Department of Defense and Health, Education, and Welfare to insure that the requirements of the FDCA and the investigational drug regulations issued under the FDCA are fully met without jeopardizing or impeding the requirements of national security or the requirements of Federal laws and regulations related to such use of drugs.[45]

This MOU cites the Kefauver–Harris Amendments, Public Law 87-781 (1962)[46] specifically as the driver of this change[47] and points to the initial IND regulations published at 28 Federal Register 179 (1963), which would become 21 C.F.R. § 130 "New Drugs."[48] This section was later renumbered to 21 C.F.R. § 312 and pertains to IND requirements, whereas 21 C.F.R. § 314 pertains to new drugs.

The 1964 MOU acknowledges that each military department's Surgeon General has established a "Review Board" (predecessor to the Institutional Review Board (IRB)) "staffed with professional people capable of performing competent review of such research proposals to insure adequate protection of human subjects."[49] The agreement also states that DoD "assumes full responsibility for the protection of humans involved in research under its sponsorship whether this involved investigational drugs or other hazards."[50] The MOU included three central elements. The first states:

> Clinical investigations that are "classified for reasons of national security will not require the filing of a formal "Claim for Exemption" . . . . [A]pproval of the test by the appropriate Review Board and Surgeon General will automatically exempt the drug being deployed from the application of the new drug section of the [FDCA] during the investigational study. The [DoD] will report to FDA findings associated with such studies which FDA should be aware of in order to make a sound evaluation of non-classified studies proposed on the same or similar drugs. Additionally, the [DoD] will discuss its classified investigations of drugs periodically with FDA personnel who have proper security clearance."[51]

The second central element of the MOU states:

> In the case of non-classified security research programs sponsored by the [DoD] and conducted within its research facilities or for the Department

---

[45] Memorandum of Understanding between the Department of Health, Education, and Welfare and the Department of Defense Concerning the Investigational Use of Drugs by the Department of Defense para. 3 (May 12, 1964) [hereinafter 1964 MOU].

[46] *Id.* at para. 1 (citing new Section 505(a) of the FDCA "as amended by Section 104 of P.L. 87-781, 76 Stat. 784, 21 U.S.C. Sec. 355, (1962 Supp.)").

[47] *Id.* at para 1; *see also infra* note 67.

[48] 1964 MOU, *supra* note 45, at para. 1.

[49] *Id.* at para. 4.

[50] *Id.*

[51] *Id.* at para. 7.

> upon contract, copies of the request for approval submitted to the appropriate DoD Review Board, the Review Board's evaluation and approval, and notice of approval by the appropriate Surgeon General will be filed with FDA as the claim for exemption for the investigational drug.[52]

Third, the MOU outlines that where DoD is performing clinical tests "upon new drugs being sponsored by the pharmaceutical industry, the ordinary claim for exemption (Form 1571 of the Investigational Drug Regulations) will be filed with the [FDA]."[53]

The important developments of the 1964 MOU were the parties' recognition that there was a need for a balance of regulatory compliance "*without jeopardizing or impeding the requirements of national security or the requirements of Federal laws and regulations related to such use of drugs*."[54] This also reflected deference to DoD's Surgeons General for classified medical product decisions and, where unclassified, significant reliance on the determinations of DoD's Surgeons General. There was a DoD concern driving this MOU, namely, that the "clinical efficacy requirement would perilously put humans in harm's way" by delaying products that, in DoD's mind, were already proven safe and effective.[55] Further, as it relates to the research needed, DoD had "no intention to conduct hazardous challenge studies in humans to provide clinical efficacy."[56] This MOU reportedly:

> allowed DoD to continue to approve its own use of these products without having to comply with FDA requirements for providing investigational products to soldiers under a clinical trial format when this could confuse the intent to benefit in emergency operations with an unintended objective, that of conducting an experiment for marketing approval.[57]

Noticeably absent here, however, is any resolution that would fit DoD's ongoing use of fielded products—marketed without having yet complied with the Kefauver–Harris Amendments' efficacy requirement—into the new IND research paradigm for "clinical investigations." DoD medical treatment and medical research was not distinguished in this MOU.

B. The 1974 Memorandum of Understanding

The DoD–FDA relationship evolved further by a 1974 MOU signed by Commissioner of Food and Drugs, Alexander M. Schmidt, MD (Commissioner from July 1973 to November 1976) and the Acting Assistant Secretary of Defense for Health and Environment, Lester Martinez-Lopez, MD. This MOU explicitly replaced the 1964 MOU[58] and referenced the updated IND regulations at 21 C.F.R. § 312 (formerly "130.3") and was intended to "establish the procedures to be followed by

---

[52] *Id.* at para. 8.

[53] *Id.* at para. 9.

[54] *Id.* at para. 3 (emphasis added).

[55] Swearengen & Anderson, *supra* note 10, at 31.

[56] *Id.*

[57] *Id.*

[58] Memorandum of Understanding between the Food and Drug Administration and the Department of Defense concerning investigational use of Drugs by the Department of Defense para. 2 (Oct. 24, 1974).

the Department of Defense and the Food and Drug Administration regarding the investigational use of drugs by the Department of Defense."[59] The 1974 MOU included most of the basic terms of the 1964 MOU, but added:

> [e]xperience in operation under this Memorandum of Understanding from 1964 to 1974 indicates that the DOD adheres to the standards of the FDA; that human subjects have been adequately protected in the DOD-sponsored studies; that DOD has been able to effectively carry out its responsibilities for national security without compromise of the intent of the above-cited statutes and regulations and *that certain exemptions provided DOD from meeting the ordinary requirements of the [IND] regulations are no longer necessary*.[60]

The 1974 MOU again allowed for classified clinical investigations to avoid a formal IND filing, deferring to the appropriate Surgeon General for approval of these studies, and requiring DoD to discuss its findings from these studies with FDA.[61] Nothing in the first or third elements of the 1964 MOU were changed in any fundamental way.

The second element, however, was modified substantially to deal with the need for medical use of investigational products:

> When the unique requirements of the military dictate the extensive use in military personnel of drugs which, though not yet approved, have been tested under the Investigational New Drug Regulations, sufficiently to establish with reasonable certainty their safety and efficacy, special ad hoc review and approval for such use will be effected expeditiously through joint action by representatives of the [DOD] and the [FDA] to ensure timely response to the military need. DOD will report to FDA findings associated with such use which FDA should be aware of in order to make a sound evaluation of other studies proposed on the same or similar drug.[62]

This agreement was to cover "an indefinite period of time."[63] The 1974 MOU reflected DoD's fidelity to the rigorous human subject protection standards required by FDA regulations, but also, for the first time, acknowledged the "gap" in clinical research for new drug approvals under the IND regulations, as well as the need for recognition of how the "*unique requirements* of the military dictate the extensive use in military personnel" of unapproved drugs that have been studied to the point of "reasonable certainty of their safety and efficacy."[64] The MOU also reflected "ad hoc" review and the need for "expeditious review" through "joint action" to ensure "timely response."[65]

The 1974 MOU is the first to recognize the need for rapid DoD–FDA collaboration on FHP (as opposed to research) measures to support the unique needs of the U.S.

---

[59] *Id.* at para. 2.

[60] *Id.* at para. 7 (emphasis added).

[61] *Id.* at para. 8.

[62] *Id.* at para. 7, § I.2 (emphasis added).

[63] *Id.* at para. 16, § IV.

[64] *Id.* at para. 10, § I.2 (emphasis added).

[65] *Id.* (emphasis added).

military. This gives credibility to the notion that DoD's risk–benefit calculus is different than typical medical care in public health. In fact, this MOU also acknowledges the inadequacy of a rigid regulatory paradigm that may not be flexible enough to deal with DoD's unique medical needs. Some commentators have stated that this 1974 MOU "restricted DoD authority to use investigational products for health protection of armed forces."[66] But actually, this MOU *systematizes* the FHP practice for the benefit of both the national security and public health mission. This MOU recognizes that, for the purpose of the medical R&D element of its mission, DoD can comply in the normal course of medical R&D, yet, where FHP is concerned, the relationship needed to evolve further.

C. The 1987 Memorandum of Understanding

The next phase of the DoD–FDA relationship was instituted, again, by signature of an MOU, by Acting Assistant Secretary of Defense for Health Affairs, William Mayer, MD, and Frank Young, PhD, Commissioner of Food and Drugs, on 21 May 1987. The scope of this MOU was expanded from the 1964 and 1974 MOUs to establish "the procedures to be followed regarding the investigational use of drugs, including antibiotics and biologics, and medical devices by DoD."[67] This agreement explicitly replaced the 1974 MOU[68] and included not only references to IND procedures, but also to the investigational device exemption (IDE) for medical devices and an explicit citation to Section 351 of the Public Health Service Act for biological products.[69]

The most significant addition to the 1987 MOU was the explanation of DoD's implementation of its own human subject protection regulations at 32 C.F.R. § 219 and DoD Directive 3216.2, which "generally adopt the system of Institutional Review Boards (IRBs) established under 21 CFR §56."[70] This MOU described key differences in the DoD system:

> [F]unctions of research protocol review and approval are separate in the Department of Defense. The function of protocol review remains with the IRB which recommends approval. The function of approval is held by the commander to whom the review committee reports. In addition, the Surgeon General of each Service may require that the final review and approval for use of investigational drugs, biologics, or medical devices, remain within his or her office.[71]

In addition, the MOU cited the history of the DoD–FDA collaboration and concluded as follows:

> Experience in operating under these MOUs from 1964 to 1987 indicates that the DOD and FDA have a record of cooperation; that human subject

---

[66] Swearengen & Anderson, *supra* note 10, at 35.

[67] Memorandum of Understanding between the Food and Drug Administration and the Department of Defense Concerning the Investigational Use of Drugs, Antibiotics, Biologics and Medical Devices by the Department of Defense para. 1 (May 21, 1987), https://www.fda.gov/about-fda/domestic-mous/mou-224-75-3003 (last visited June 20, 2023).

[68] *Id.* at para. 1.

[69] *Id.* at para. 2.

[70] *Id.* at para. 4.

[71] *Id.* at Section II, p.2, at para. 2.

> concerns have been adequately addressed in DOD-sponsored studies; and that the DOD has been able to carry out effectively its responsibilities for national security without compromising the intent of the above-cited statutes and regulations.[72]

The MOU goes on to state that exemptions from the IND and IDE requirements are "no longer necessary."[73] Like the 1964 and 1974 MOUs, there are three elements to the substance of the agreement. First, clinical testing of investigational drugs sponsored or conducted by DoD will comply with IND regulations at 21 C.F.R. § 312, the IDE regulations at 21 C.F.R. § 812, and—a new addition—"FDA's informed consent and Institutional Review Board regulations (21 CFR 50 and 21 CFR 56)."[74] Second, the parties "will continue to cooperate in meeting the requirements of the [FDCA] and its implementing regulations without jeopardizing the mission of the DoD."[75] To accomplish this goal, they agree that an expeditious review of special DoD requirements to meet national defense considerations will be carried out by FDA. This review would consist of an FDA review of available data on a drug, biologic, or device under IND or IDE to determine if stockpiling for future use, or use in an expanded military population, is appropriate. When necessary, special reporting requirements would also be established by FDA.[76] Lastly, while DoD does not generally classify medical research and development, the MOU created "special provisions" for DoD's submission of a "classified IND or IDE" to be reviewed by FDA personnel who hold "required security clearances."[77]

The 1987 MOU reinforced the need for continued cooperation "without jeopardizing the mission of the DoD."[78] This MOU created an "expeditious review of special DOD requirements" and the ability for FDA to establish "special reporting requirements."[79] Here again, we see the flexibility required for satisfaction of DoD national security mission by a willing FDA. In addition to these expedited procedures, DoD acknowledged its expectation to comply with all good clinical practice guidelines (GCPs) articulated by FDA regulations at 21 C.F.R. §§ 50–56. Some commentators have stated that this MOU required "complete compliance" with FDA regulations and that "DoD could no longer exclude from FDA requirements products they wished to use in contingency situations or for health protection of armed forces."[80]

Operation under this MOU as the Persian Gulf War (August 1990 to February 1991) approached presented a "moral dichotomy" to DoD because "some of the medical countermeasures that might be used to protect or treat solders for chemical or biological hazards were still not approved by the FDA."[81] It was once possible for DoD to use intent as a means of determination of how a product would be used and

---

[72] *Id.* at para. 5.

[73] *Id.* at Section II, p.2, para. 3.

[74] *Id.* at Section III. A. at p. 3.

[75] *Id.* at para. 7.

[76] *Id.* at Section III. B. at p. 3.

[77] *Id.* at. Section III. C. at pp. 3–4.

[78] *Id.* at para. 7.

[79] *Id.*

[80] Swearengen & Anderson, *supra* note 10, at 34.

[81] *Id.*

under what kinds of restrictions. Was the intended use of investigational products *research* or *treatment*?[82] Further, "the new MOU [1987] made the ability to use products labeled IND to benefit war fighters and laboratory personnel less clear."[83] For DoD, it presented a difficult question: "what if investigational status prevented life-saving use of the only available product to protect against anticipated mass casualties produced by biological weapons?"[84] For DoD at this time, "[c]reating the pretense of experiment to get around the moratorium on use of unlicensed products seem[ed] disingenuous when the basis of the intent [to treat] is really based on the knowledge of human safety and animal efficacy of the product."[85] Also, the need to move expeditiously to provide this treatment for a large force may require "drastic emergency actions not anticipated by clinical trial protocols . . . . The alternative choice of not providing soldiers prophylaxis or treatment because a product is not FDA approved was also an unsatisfactory solution."[86]

D. The Inadequacy of the IND Framework in the Persian Gulf War, the Interim Rule on Waivers of Informed Consent, and the Presidential Advisory Committee on Gulf War Veteran's Illness

Throughout the course of the 1964, 1974, and 1987 MOUs,[87] we observe increasing flexibility offered to DoD for use of investigational products in its national security mission, whereas DoD commits to full application of the GCP and IND/IDE frameworks in the normal course of medical R&D. This distinction between R&D and special processes to deal with mission-specific threats—some classified—continued into the future. Additionally, we observe the ever-expanding scope of FDA's jurisdiction over drugs, biologics and devices, and clinical investigations of investigational products as well as DoD's attempt, through these MOUs and its own DoD regulations, to meet the high standards of ethics in medical R&D. The MOUs governing the DoD–FDA relationship, however, lacked a framework for dealing with urgent CBRN threats, failed to augment the research-driven IND regulatory structure, and did not detail the specific challenges of national security interests and solutions to deal with them. These limitations would be exposed in the lead up to and aftermath of the Gulf War in the early 1990s where the chemical or biological warfare ("ChemBio") threat led to the Interim Final Rule for Waivers of Informed Consent for use of investigational products under IND.

Through the 1987 MOU, the DoD–FDA relationship had been largely defined in terms of DoD clinical testing of investigational new drugs, biologics, and devices under routine, peacetime circumstances. The MOU described above did not provide a policy framework for dealing with the use of investigational or unapproved drugs in

---

[82] *Id.*

[83] *Id.*

[84] *Id.*

[85] *Id.* (clarification added).

[86] *Id.*

[87] This paper analyzes these three MOUs as they are DoD-level MOUs with FDA. There are other element-specific MOUs that deal with mission-specific elements that this paper. See, e.g., MOU 225-15-016 (July 2015), an agreement between the Defense Logistics Agency and FDA to allow FDA to provide quality assurance support for DLA's centrally managed contracts for drugs, biologics, and medical devices.

the context of a real ChemBio threat.[88] The ChemBio threat present at the time of Iraq's invasion of Kuwait in August 1990 was markedly different from anything contemplated under the 1964, 1974, and 1987 MOUs. While all of those documents discuss the balance needed for national security, specific solutions for deploying medical countermeasures against an Iraqi military capability that "included both chemical warfare and biological warfare (CW/BW) agents" were not discussed.[89] This unique risk–benefit context would present significant challenges to DoD and FDA and, despite pre-coordination and intense efforts to identify solutions, the "fog of war" and the fact that "military combat is different" would lead to intense scrutiny of DoD and important regulatory developments for DoD and FDA.

In Operation Desert Shield and Operation Desert Storm (collectively, "ODS"),[90] the ChemBio threat posed by the Iraqi military was well publicized and later confirmed in detail by a United Nations Special Commission.[91] The threat was believed to include chemical nerve, vesicant, and blood agents[92] with the primary threat to be organophosphate nerve agents. The threat also included the potential biowarfare threat of anthrax, caused by a highly toxic microorganism *Bacillus anthracis*, and botulism (botulinum toxin), which is produced by the bacterium *Clostridium botulinum*.[93] DoD's preparation for the two Operations included significant personal protective equipment, but also a series of medical countermeasures (MCMs). Medical management of nerve agent exposure involves a three-drug regimen: pretreatment with pyridostigmine bromide (PB) before exposure and administration of two antidotes, atropine sulfate (Atropine) and pralidoxime chloride (2-PAM), intramuscularly by auto-injectors after actual exposure. "In short, PB pre-treatment is indicated because it offers sufficient protection against rapid-acting nerve agent (sic) to permit therapy to be administered."[94] Of the three MCMs used in Operation Desert Storm—PB,

---

[88] RICHARD A. RETTIG, *The History of the Interim Rule*, *in* MILITARY USE OF DRUGS NOT YET APPROVED BY THE FDA FOR CW/BW DEFENSE Chapter 2, at 2 (RAND National Defense Research Institute, MR-1018/9-OSD, Apr. 5, 1999), https://www.rand.org/pubs/monograph_reports/MR1018z9.html (last visited Dec. 14, 2022).

[89] *Id.* at Chapter 1, at 2. It is important to note that this study was one of several commissioned by the Special Assistant to the Deputy Secretary of Defense for Gulf War Illnesses. It deals with the Interim Rule, adopted in December 1990, which established the authority of the Commissioner of Food and Drugs to waive informed consent for using investigational drugs in certain military contingencies. The contingency for which it was adopted and in which it was used was the 1991 Gulf War, when U.S. and coalition forces confronted the possibility of chemical and biological weapons being used by the Iraqi military. The investigational drugs in question were pyridostigmine bromide and botulinum toxoid vaccine. *See id.* at *Preface*.

[90] The Gulf War (August 2, 1990–February 28, 1991) was a war waged by coalition forces from thirty-five nations led by the United States against Iraq in response to Iraq's invasion and annexation of Kuwait. The war consisted of two phases. The first was codenamed Operation Desert Shield (August 2, 1990–January 17, 1991) for operations leading to the buildup of troops and defense of Saudi Arabia. And the second was Operation Desert Storm (January 17, 1991–February 28, 1991) was the combat phase. *See The Gulf War 1990-1991*, NAVAL HIST. & HERITAGE COMMAND, https://www.history.navy.mil/our-collections/art/exhibits/conflicts-and-operations/the-gulf-war-1990-1991--operation-desert-shield--desert-storm-.html; *see also* Shannon Collins, *Desert Storm: A Look Back*, U.S. Department of Defense (Jan. 11, 2019), https://www.defense.gov/News/Feature-Stories/story/Article/1728715/desert-storm-a-look-back/.

[91] RETTIG, *supra* note 88, Chapter 1.

[92] *Id.*

[93] *Id.*

[94] *Id.*

Anthrax Vaccine (AX), and Botulinum Toxin (BT) vaccine—only the AX was FDA-licensed for its proposed indication of use in the operation. PB was licensed for two indications distinct from pretreatment for nerve agency exposure,[95] and the BT vaccine was investigational[96] at the time of the Gulf War.

With the status of these products in mind, the FDCA would render PB and BT vaccine investigational and, as such, use by DoD would require an investigational new drug application (IND) under 21 C.F.R. § 312. DoD approached FDA seeking use of these products and others[97] under its IND framework, but indicated that obtaining informed consent as required by the IND would not be feasible in ODS. On October 30, 1990, DoD requested FDA to establish by rulemaking a waiver of informed consent for use of investigational drugs for use in military emergencies.[98] FDA issued an interim rule, "Informed Consent for Human Drugs and Biologics; Determination that Informed Consent is Not Feasible," to this effect on December 21, 1990.[99] The interim rule, which would be codified at 21 C.F.R. § 50.23(d), allowed FDA to make a determination, in response to a specific DoD request, that obtaining informed consent from military personnel for the use of an investigational drug or biologic was not feasible in certain battlefield or combat scenarios.[100] DoD requested FDA issue waivers for PB and the BT vaccine under this interim rule, and FDA granted the waivers on January 8, 1991. The interim rule was challenged but ultimately upheld by the U.S. Circuit Court for the District of Columbia in July 1991.[101]

The interim rule presented several questions that continue to challenge the DoD–FDA relationship to this day. First, to what degree can we expect the ethical concerns associated with an IND, which is designed for clinical investigations in a research setting, to apply and meet DoD's need for treatment use of investigational products in the Gulf War? Second, to what degree must the Commander-in-Chief of the U.S. military and its commissioned officers comply with directives of the FDCA, which

---

[95] PB is FDA-approved for the treatment of myasthenia gravis (NDA No. 9829, April 7, 1955) at "average daily dosages as much as six times greater than those used in the Gulf War for nerve agent pretreatment." The product is also FDA-approved as Regenol for reversing some of the effects of anesthetics. *See* RETTIG, *supra* note 88, Chapter 1.

[96] It is important to note that the FDCA renders a product *investigational* for both 1) a drug unapproved for any indication, and 2) as a reference to use outside the indication on the FDA-approved labeling where the product is approved. Accordingly, the term "investigational" is often used synonymously with "experimental," but that is inaccurate. Importantly, drugs approved for any indication do not require advanced informed consent prior to use off-label (though, in medical practice, this often occurs), but investigational products lacking any FDA approval would require informed consent under an IND or, in certain circumstances, an EUA (which, at this point in the early 1990s, did not exist).

[97] *See* RETTIG, *supra* note 88, Chapter 1, Table 1, "Medical Products Under IND Regulation Required or Under Consideration for Use in or Support of ODS, August–September 1990."

[98] *Id.* at Chapter 1.

[99] Informed Consent for Human Drugs and Biologics; Determination that Informed Consent is Not Feasible, 55 Fed. Reg. 52814 (proposed Dec. 21, 1990) (to be codified at 21 C.F.R. § 50.23(d)).

[100] *See* Human Drugs and Biologics; Determination That Informed Consent is NOT Feasible or Is Contrary to the Best Interest of Recipients; Revocation of 1990 Interim Final Rule; Establishment of New Interim Final Rule, 64 Fed. Reg. 54180 (Oct. 5, 1999) (to be codified at 21 C.F.R. pts. 50, 312).

[101] Doe v. Sullivan, 291 U.S. App. D.C. 111, 938 F.2d 1370 (1991) (court held that promulgation of the Interim Rule was within FDA's rulemaking authority under the act because obtaining the servicemen's consent to administer the drugs was not feasible or practical in combat); *see also* John A. Casciotti, *The Food, Drug, and Cosmetic Act's Emergency Use Authorization: A Pandemic Vaccine Godsend with Devils in the Details*, 77 FOOD & DRUG L.J. 67 (Aug. 2022).

were not designed specifically for the "special needs of military drug development and use?"[102] Third, "how should the complex relationship between military drug development and use and the FDA be organized?"[103] These three questions would continue to persist related to how DoD communicated information about the risks and benefits of the use of investigational products, the administration of the IND, record keeping, etc. These questions persist also as DoD dealt with the notion that its decision-making regarding use of investigational products is no longer within the *exclusive* realm of DoD decision-making (which had been its nature and history as described above). Instead, DoD relies on FDA participation and concurrence with the way forward. In discerning the ultimate merits of the interim rule and DoD's implementation, the RAND study report published by DoD's Special Assistant for Gulf War Illness points out that "DoD implementation of the waivers of informed consent for PB and BT [vaccine] was not well-executed in the Gulf War and, consequently, has reflected badly on the policy itself."[104]

What is also striking about the historical record leading up to the Gulf War and the interim rule is that DoD and FDA had "deliberated carefully before initiating rulemaking, for DoD to require troops to take PB and BT vaccines as pretreatments for possible [chemical and biological warfare (CBW)] agents without FDA approval of the products for that purpose."[105] The RAND report states that DoD and FDA had undertaken "an urgent and orderly course of action under the circumstances to devise a means to address the real threat of chemical and biological warfare in the Gulf War."[106] During these deliberations, and given that "no clear congressional statute or judicial guidance existed for such a contingency," DoD considered that it should issue its own regulations appropriate for the military operation without reference to the FDCA or PHSA at all.[107]

However, the decision to subordinate its own Command decision-making to FDA—potentially driven by the desire to have a civilian agency ratify its approach—would have the "effect of framing the discussion in terms of FDA regulations, the adequacy of those regulations for dealing with the Iraqi threat, and DoD's perceived need for an exemption on the issue of informed consent."[108] DoD was clear that the requirements for informed consent at 21 C.F.R. § 50, at the time, "could not be met in armed conflict and in circumstances of potential armed conflict for deployed and deployable units."[109] FDA responded to DoD's request by offering two options: 1) the use of export licensing approach that acknowledged that the IND products would be used overseas would not require labeling or informed consent, which was deemed "the quickest and most feasible approach"; and 2) to use the IND model with an amendment to the

---

[102] RETTIG, *supra*, note 88, Chapter 1.

[103] *Id.*

[104] *Id.*

[105] PRESIDENTIAL ADVISORY COMMITTEE ON GULF WAR VETERANS' ILLNESSES: FINAL REPORT 18 (Washington, DC: U.S. Government Printing Office, Dec. 31, 1996) [hereinafter PAC FINAL REPORT].

[106] RETTIG, *supra* note 88, Chapter 2 at 2.

[107] *Id.*

[108] *Id.*

[109] *Id.* (internal quotations omitted). It should be noted that the use of advanced informed consent on a large, pre-deployment force has been done in DoD successfully since this time.

informed consent regulations at 21 C.F.R. § 50.[110] Ultimately, the second approach was selected, but it raised the issues of DoD complying with the onerous requirements of clinical research INDs in the context of warfare, and it also raised the question of what DoD options exist if FDA does not grant the waiver under the proposed rule.[111] DoD expressed concern about the labeling, supply control, IRB, investigator record-keeping requirements, and other constraints on the IND.[112] Several issues arose in the DoD–FDA deliberations that centered on whether or not this use constituted research or therapeutic use.[113] Importantly, it was also the case that there were no alternative therapeutics available for the threats outlined by DoD.

FDA had previously, in a meeting on September 14, 1990, objected to DoD's preferred use of a treatment IND and expressed a preference to the regulation IND approach under 21 C.F.R. § 312 with a proposal to issue the interim rule and proceed with case-by-case waivers of informed consent where that requirement of an IND was not feasible in certain military use cases.[114] This acquiescence to the FDA clinical research paradigm also framed the post-war criticism directed at DoD, where DoD did not satisfy the requirements of INDs despite acknowledging its limitations for military operations throughout the pre-war deliberations. In agreeing with FDA's proposed approach at the publication of the interim rule, DoD requested waivers of advanced informed consent for use of PB and BT vaccine in a memo dated October 11, 1990, from Dr. Enrique Mendez, Jr., Assistant Secretary of Defense for Health Affairs to the Assistant Secretary of Health (the "Mendez Letter").[115]

The Mendez Letter requesting waivers under the interim rule articulated DoD's position:

> Our planning for Desert Shield contingencies has convinced us that another circumstance should be recognized in the FDA regulation in

---

[110] *Id.* at 3. Rettig raises the issue of the extent of FDA's jurisdiction over medical products intended for use overseas. It is important to note that FDA's authority overseas is more limited than its authority within the United States. However, FDA still has some authority overseas (especially, but not solely, with respect to imports). *See, e.g.*, 21 U.S.C. § 337a ("There is extraterritorial jurisdiction over any violation of this chapter relating to any article regulated under this chapter if such article was intended for import into the United States or if any act in furtherance of the violation was committed in the United States.").

[111] RETTIG, *supra* note 88, Chapter 2 at 3.

[112] *Id.* Chapter 2 at 4–5.

[113] DoD Office of the General Counsel opinioned in 1990, via a memo by Assistant General Counsel of DoD Gilliat ("the Gilliat Memo") that the key legal issues were whether or not the potential uses constituted "research involving human being as an experimental subject" within the meaning of 10 U.S.C. § 980, a provision added to a DoD appropriations statute in 1972 to require advanced informed consent under these circumstances. The Gilliat Memo determined that this use was not "research," but rather "it is clear that the proposed uses are not in any usual sense of the word for 'research' purposes, but rather to assure the best possible preventative and therapeutic treatment possible for all contingencies presented." The Gilliat Memo concluded that "the proposed uses of the drugs in question are, in fact, primarily treatment uses, not uses primarily for the investigational or research purposes." *See* RETTIG, *supra* note 82, Chapter 2 at 7 (citing the Gilliat Memo). This distinction had already been established in a 1983 DoD Directive on "Protection of Human Subjects in DoD-Supported Research," where DoD established the view that some drugs and devices FDA deemed "investigational" were not considered as "research" under 10 U.S.C. § 980. *See id.*, Chapter 3 at 8.

[114] RETTIG, *supra* note 88, Chapter 2 at 9.

[115] Informed Consent for Human Drugs and Biologics; Determination that Informed Consent is Not Feasible, 55 Fed. Reg. 52814, 52814–17 (proposed Dec. 21, 1990) (to be codified at 21 C.F.R. § 50.23(d)) (Dec. 21, 1990).

> which it would be consistent with the statute and ethically appropriate for medical professionals to "deem it not feasible" to obtain informed consent of the patient, that circumstance being the existence of military combat exigencies, coupled with a determination that the use of the product is in the best interests of the individual. By "military combat exigencies," we mean military combat (actual or threatened) circumstances in which the health of the individual, the safety of other personnel and the accomplishment of the military mission require that a particular treatment be provided to a specified group of military personnel, *without regard to what might be any individual's personal preference for no treatment or for some alternative treatment*.[116]

The Mendez Letter concedes that DoD is committed to informed consent and its ethical foundations in all peacetime applications; however, it sets forth "the doctrine of military authority"[117] by reasoning:

> In all peacetime applications, we believe strongly in informed consent and its ethical foundations. In peacetime applications, we readily agree to tell military personnel, as provided in FDA regulations, that research is involved, that there may be risks or discomforts, that participation is voluntary and that refusal to participate will involve no penalty. *But military combat is different.* If a soldier's life will be endangered by nerve gas, for example, it is not acceptable from a military standpoint to defer to whatever might be the soldiers' personal preference concerning a preventive or therapeutic treatment that might save his life, avoid endangerment of the other personnel in his unit, and accomplish the combat mission. Based on *unalterable requirements of the military field commander*, it is not an option to excuse a non-consenting soldier from the military mission, nor would it be defensible—militarily or ethically—to send the soldier unprotected into danger.
>
> To those familiar with military command requirements, this is, of course, elementary. It is also very solidly established in law through a number of Supreme Court cases establishing that special military exigencies sometimes must supersede normal rights and procedures that apply in the civilian community. Consistent with this, long-standing military regulations state that military members may be required to submit to medical care determined necessary to preserve life, alleviate suffering or protect the health of others.
>
> Such special military authority carries with it special responsibility for the well-being of the military personnel involved. Thus, we propose specific procedural limitations on the "not feasible" waiver of informed consent based on military combat exigencies.[118]

The Mendez Letter articulated five (5) limitations to the waiver: 1) that drug-by-drug requests for the waiver be accompanied by a written justification based on the

---

[116] *Id.* (emphasis added).

[117] RETTIG, *supra* note 88, Chapter 2 at 9.

[118] Informed Consent for Human Drugs and Biologics, 55 Fed. Reg. at 52815.

intended use and military circumstances involved, 2) that no satisfactory alternative treatment is available, 3) that available safety and efficacy data support the proposed use of the drug or biologic product, 4) that each such request be approved by the applicable DoD Institutional Review Board, and 5) that the waivers be time-limited.[119] FDA's proposed rule stated its agreement with the DoD position:

> FDA has determined that, in the special circumstances that may be created by the use of troops in combat and consistent with its obligations under Sections 505(i) and 507(d), FDA may narrowly expand the circumstances in which the Commissioner may determine that obtaining informed consent is not feasible. FDA agrees with DOD's judgement that in certain combat-related situations, it may be appropriate to conclude that obtaining informed consent from military personnel for the use of investigational drugs is not feasible and withholding treatment could be contrary to the best interests of military personnel involved. DOD has the right and responsibility to make command decisions that expose troops to the possibility of combat and has the concomitant responsibility to protect the welfare of those troops both individually and as a group.[120]

On January 8, 1991, FDA Commissioner David Kessler signed the waivers of informed consent for the use of PB for nerve agent pretreatment and for BT vaccine, effective for one year.[121] In March of 1991, Dr. Mendez informed FDA that hostilities had ended and the waivers were no longer needed.[122]

The actual war experience with PB and BT vaccine does not reflect well on DoD. Hostilities in the Gulf War broke out within days of the approval of the PB and BT vaccine waivers, and "the administration of these investigational drugs differed appreciably from expectations based on the DoD policy and the DoD–FDA discussions that led to the Interim Rule."[123] Some soldiers received PB and some soldiers received BT vaccine, but "record-keeping was quite poor."[124] The record shows that: 1) information provided to service members and healthcare providers about these products was inadequate, and 2) record-keeping was poor and without uniformity regarding which soldiers received which product (e.g., PB was self-administered and the BT vaccine was not recorded on the soldiers' vaccination cards).[125] The contrast between expectations and experience related to the short

---

[119] *Id.*

[120] *Id.* FDA makes an important distinction in the proposed rule, explaining that informed consent may be infeasible, but it's that fact coupled with the fact that withholding treatment is contrary to the best interest of the soldier: "it is not sufficient as an ethical matter to waive informed consent in the military context where obtaining informed consent is 'not feasible,' unless it is also the case that withholding the treatment would be contrary to the best interests of the individuals involved." *Id.* In addition, FDA acknowledges that this waiver may be needed in "combat situations where obtaining informed consent is not feasible and where withholding treatment may be contrary to the best interests of military personnel *even outside battlefield conditions*." *Id.* (emphasis added).

[121] RETTIG, *supra* note 88, Chapter 2 at 15.

[122] *Id.*

[123] *Id.* at 18. A guidance document from U.S. Army Forces Command (FORSCOM) regarding the use of PD as a pretreatment for nerve agent exposure is cited at page 18 with the references "FM 8-285, 7 August 1990."

[124] *Id.*

[125] *Id.* at 20.

timeframes for implementation of the waivers (only a week between waiver grant and war) rendered "[p]reparation for orderly process [sic] next to impossible."[126] In addition, communication flows were complicated given the role of the Assistant Secretary of Defense for Health Affairs (ASD(HA)) to communicate with FDA and then communicate FDA's response to the Joint Staff and Central Command (CENTCOM) and the CENTCOM Surgeon. "The faithful transmission of compliance information is difficult under normal circumstances. In preparation for active conflict, it is likely to be very, very difficult."[127] The final complications stemmed from the lack of available product and "order of battle" considerations requiring implementation at the "unit level." This perspective is not an override of FDA expectations for uniform administration of PB, but rather "the exercise of time-honored, and legally protected, exercise of battlefield discretion within the chain of command."[128] Given that PB was identified as a "possible risk factor in Gulf War veterans' illnesses, especially when used in combination with diethyl-m-toluamide (DEET), a pesticide used in the Gulf War by deployed troops," DoD's failure to maintain control and documentation related to the use of these products resulted in the criticism of the Interim Rule's waiver approach entirely. This also led to substantial overhauls of congressional constraints placed on DoD's use of investigational products.

After the Gulf War ended in the spring of 1991, DoD asked FDA to complete the rule-making process, but this was ultimately delayed and "the Gulf War receded in public consciousness, the urgency associated with rule-making also receded, and differences of view emerged within FDA about the appropriate course of action."[129] The Presidential Advisory Committee on Gulf War Illnesses (PAC)[130] published its Final Report in December 1996, recommending that FDA complete the rule-making process.[131]

The Presidential Advisory Committee Final Report recommended that FDA "devise better long-term methods for governing military use of drugs and vaccines for CBW defense.[132] It also noted that DoD's lack of response to recommendations on routinely informing troops about the possible use of investigational products "contributes to the perception of many that U.S. troops were inappropriately subjected to investigational drugs or vaccines during the Gulf War."[133]

---

[126] *Id.* at 20.

[127] *Id.* at 20.

[128] *Id.* at 21.

[129] RETTIG, *supra* note 88, Chapter 1.

[130] The Presidential Advisory Committee on Gulf War Veterans' Illnesses was established by Executive Order 12961 on May 26, 1995. Exec. Order No. 12,961, 60 Fed. Reg. 28507 (May 31, 1995). The purpose of the Advisory Committee was the oversight of the ongoing investigation being conducted by the Department of Defense and other executive departments and agencies into possible chemical or biological warfare agent exposures during the Gulf War. The Presidential Advisory Committee was terminated upon the issuance of its special report of October 31, 1997. *See Presidential Advisory Committee on Gulf War Veterans' Illnesses*, FED. REG., https://www.federalregister.gov/agencies/presidential-advisory-committee-on-gulf-war-veterans-illnesses (last visited Dec. 15, 2022).

[131] *See* PAC FINAL REPORT, *supra* note 105, at 52.

[132] *Id.*

[133] *Id.* at 27–28.

E. The 1997 Friedman Letter Criticizes DoD's Use of IND Products in Bosnia

On July 22, 1997, Dr. Michael A. Friedman, Lead Deputy Commissioner, FDA, sent a letter to Dr. Edward D. Martin, Acting Assistant Secretary of Defense for Health Affairs (the "Friedman Letter"), addressing several concerns over DoD's use of investigational products used under the 1990 waivers, but also DoD's responses to the Presidential Advisory Committee on Gulf War Veterans' Illnesses, the General Accountability Office, and various congressional committees.[134] This was the beginning of several instances of FDA criticism of DoD for its failures in complying with FDA's regulatory paradigm. Specifically, the letter addresses DoD's "use of a tick-borne encephalitis (TBE) vaccine in Bosnia under an investigational new drug application" that resulted from the above-referenced inquiries but also an FDA inspection related to the TBE vaccine conducted at Fort Detrick, Maryland.[135] The letter identifies "significant deviations from federal regulations published in Title 21, Code of Federal Regulations, Parts 50 and 312 (21 CFR §50 and §312)." The "deviations in Bosnia show that DoD has not corrected its procedures to prevent the recurrence of problems in the use of investigational products that arose during the Persian Gulf War."[136]

The Friedman Letter pointed out that the IND study governing the use of the TBE vaccine: 1) was not being conducted in accordance with the protocol as required by 21 C.F.R. § 312.50; 2) there was illegal promotion of the investigational TBE vaccine via a DoD briefing claim the product was "very safe and extremely effective in preventing TBE" in violation of 21 C.F.R. § 312.7(a); 3) there was no IRB approval of informed consent documents as required by 21 C.F.R. § 312.53(c)(1)(vi)(d); and 4) cited a May 1997 GAO report highlighting the U.S. Army's failure to document all immunizations during military deployments.[137]

Furthermore, the Friedman Letter raised additional concerns about DoD's use of PB and BT vaccine in the Persian Gulf War. The letter states that "the deviations identified in DoD's use of investigational products during the Persian Gulf War were similar to those identified in Bosnia" and included failure to meet the conditions set by FDA for granting the waiver for advanced informed consent requirements under the Interim Rule for PB.[138] FDA concluded that "the information sheet on pyridostigmine was not provided and disseminated to all military personnel in the Gulf as had clearly been anticipated as one of the conditions of the Commissioner granting the waiver under the interim rule."[139] FDA also found a failure to "collect, review, and make reports of adverse experiences attributed to the use of" PB in a timely manner as required by 21 C.F.R. § 312.32 (which had waived the three and ten day time limits

---

[134] For a contemporaneous legal perspective these issues, see Robyn Pforr Ryan, *Should Combat Troops be Given the Optional of Refusing Investigational Drug Treatment?*, 52 FOOD & DRUG L.J. 377 (1997).

[135] *See* Letter from Dr. Michael A. Friedman, Lead Deputy Commissioner, FDA, to Dr. Edward D. Martin, Acting Assistant Secretary of Defense for Health Affairs (July 22, 1997), https://gulflink.health.mil/library/senate/appx_ee.pdf.

[136] *See id.*

[137] *See id.* at 3–4.

[138] *See id.* at 4.

[139] *See id.* at 6.

for reporting adverse events).[140] "Although DoD was expected to adequately collect serious and unexpected adverse events associated with the use of pyridostigmine bromide, this was not done."[141] Finally, FDA found that DoD failed to place "For military use and evaluation" on the PB product as required by the waiver issued under the Interim Rule: "it is not clear from the information provided whether the pyridostigmine bromide that was distributed to military personnel in the Persian Gulf was labeled as required by the conditions of the waiver."[142]

The Friedman Letter also criticized DoD for its failure to ensure that the BT vaccine was used consistent with the investigational plan as required by 21 C.F.R. § 312.50, and for a failure to maintain adequate records showing the receipt, shipment, and disposition of the investigational BT vaccine. FDA questioned whether informed consent was documented and retained where the product was used *outside* the narrow limitations of the waiver granted under the Interim Rule (e.g., the waiver was granted on the grounds that the need demanded it be used *involuntary*) as the product was administered on a *voluntary* basis to military personnel.[143] The letter states that "[w]ithout signed consent forms to document that informed consent was obtained and based on testimony from Persian Gulf War veterans that information on the vaccine was not uniformly given to military personnel . . . , we are unable to verify that informed consent was obtained from military personnel who received the botulinum toxoid vaccine."[144]

The Friedman letter includes the following summary that highlights the "discontinuity" in DoD structure for the administration of IND products:

> These regulatory deviations, taken as a whole, point to an underlying inability for DOD to carry out its obligations under INDs for drugs and biologics intended to provide potential protection to deployed military personnel. . . . We suggest that DOD's difficulties may result, in part, from a discontinuity between the military command that plans the IND study and provides assurances to this agency and the command that ultimately must carry out the study. This discontinuity in command appears to occur within the Army itself (e.g., personnel from the Office of the Surgeon General, Department of the Army submit the IND, but the administration of the IND is carried out by other combat command structures in the Army) and may occur DOD-wide (the Department of the Army's INDs provide for the administration of the investigational products to personnel in other military services). We believe that unless the command(s) that provides the assurance to this agency about the conduct of the IND have control of, or at least substantial influence over the actual conduct of the IND, there will be continued difficulties of the types cited above.[145]

---

[140] *See id.*

[141] *See id.* at 7.

[142] *See id.* at 8.

[143] *See id.* at 7.

[144] *See id.* at 10.

[145] *See id.* at 10.

This FDA response would precede, by four months, one of the largest changes in DoD–FDA relationship. In November of 1997, Congress enacted an overhaul of DoD's use of investigational products at 10 U.S.C. § 1107,[146] and FDA would revoke the 1990 Interim Rule and propose what would become the current model for DoD's use of investigational products under an IND where informed consent is not feasible under 21 C.F.R. § 50.23(d).

F. Final Regulations at 21 C.F.R. § 50.23(d) Creates a Presidential Waiver of Advanced Informed Consent for Use of Investigational Products (1999)

On October 5, 1999, FDA would revoke the 1990 Interim Final Rule and, due to the enactment of the Strom Thurmond National Defense Authorization Act for Fiscal Year 1999 (the Defense Authorization Act), which established that "the President is authorized to waive the FDCA's informed consent requirements in military operations if the President finds that obtaining consent is infeasible or contrary to the best interest of recipients and on an additional ground that obtaining consent is contrary to national security interests."[147] FDA's issuance of a new interim rule with an immediate effective date was issued because FDA believed "it is critical to have in place adequate criteria and standards for the President to apply in making an informed consent waiver determination."[148] The issuance of the new Interim Final Rule included a review of the comments submitted in response to the 1990 Interim Rule and detailed the inadequacy of DoD's management of the use of investigational use of PB and BT vaccine during the Persian Gulf War, citing the Friedman Letter expressing concerns over the Bosnian experience. The new Interim Rule concluded:

> [e]xperience with the use of the waiver provision of the 1990 Interim Rule suggest two conclusions: (1) To the extent possible, military personnel should receive treatments whose safety and effectiveness have been fully evaluated; (2) where it is necessary to utilize investigational agents and to waive informed consent, new standards and criteria for doing so should be developed that will better ensure protection of the troops receiving the investigational product.[149]

As the Defense Authorization Act "answered the controversial question of whether waiver of informed consent in military operations is ever appropriate,"[150] FDA addressed the comments to the 1990 Interim Final Rule, which pointed out areas to strengthen the rule:

---

[146] *See* National Defense Authorization Act for Fiscal Year 1998, 10 U.S.C. § 1107, Pub. L. No. 105–85, div. A, title VII, § 766(a), 111 Stat. 1827 (Nov. 18, 1997).

[147] *See* Human Drugs and Biologics; Determination That Informed Consent is NOT Feasible or Is Contrary to the Best Interest of Recipients; Revocation of 1990 Interim Final Rule; Establishment of New Interim Final Rule, 64 Fed. Reg. 54180 (Oct. 5, 1999) (to be codified at 21 C.F.R. pts. 50, 312).

[148] *See id.* Relatedly, FDA used this notice to request to ask "what evidence of efficacy, other than that from human trials, would be appropriate to demonstrate the safety and efficacy of products that may provide protection against toxic chemical and biological substances." *Id.* at 54180. This line of inquiry would ultimately become 21 C.F.R. § 314(I), the "Animal Efficacy Rule," after the Anthrax attacks of 2001 and the Bioterrorism Act of 2002.

[149] *See* 64 Fed. Reg. at 54184.

[150] *See id.* at 54181.

> provision of adequate information about an investigational product before its use; adequate follow up to assess whether there are adverse health consequences that result from the use of the investigational product; adequate oversight, accountability, and recordkeeping when investigational agents are used; and involvement of non-DOD personnel in decisions to use investigational products without informed consent.[151]

FDA attempted to address all these concerns in the new Interim Rule, which became 21 C.F.R. § 50.23(d).[152]

In its rationale for the new rule, FDA concludes:

> that there are important ways for the agency to contribute to DOD's mandate to protect military personnel that are consistent with FDA's mission and regulations. FDA's existing mechanisms for providing access to investigational products under an IND will continue to be available to any entity that complies with the agency's specified requirements. Both DOD and FDA recognize, however, that some of the IND requirements may not be feasible in certain combat situations. Based on the lessons from the use of investigational agents during the Gulf War, the agency believes that DOD's needs can best be met through DOD's support of drug development efforts leading to approval of products found to be safe and effective.[153]

The ultimate conclusions from this Interim Rule process are twofold: 1) DoD should advance the full approval of MCMs, and 2) participate in a working group with FDA "for the purpose of assisting DOD in its drug development efforts related to these products."[154] As past is prologue, these issues continue to strain the DoD–FDA relationship.

III. THE SHIFT TO DOD DEPENDANCE ON FDA'S REGULATORY FRAMEWORK

After the Gulf War era, Congress substantially changed DoD's authority over the use of investigational or off-label products. Driven by emerging concerns over causes of "Gulf War Syndrome," an illness with multi-various symptoms without a direct causal relationship clearly established, Congress placed significant restrictions on DoD in the realm of FHP and created a permanent statutory link between Title 10, "Armed Forces," and Title 21, "Food and Drugs," that did not exist prior. This development included the enactment of 10 U.S.C. § 1107, the Clinton Administration's issuance of Executive Order 13139, and several internal DoD issuances that remain largely in effect today, namely, Department of Defense Instruction 6200.02, "Force Health Protection," and Army Regulation 40-7, "Use of Investigational Drugs and Controlled Substances." Other authorities, like the

---

151 *See id.*

152 *See id.* For a critique of DoD and this rule in its proposed form, see Keri D. Brown, Comment, *An Ethical Obligation to Our Servicemembers: Meaningful Benefit for Informed Consent Violations*, 47 S. TEX. L. REV. 919 (2006).

153 *See* 64 Fed. Reg. at 54184–85.

154 *See id.* at 54185.

Emergency Use Authorization (EUA) under Section 564 of the FDCA and an adjacent provision at 10 U.S.C. § 1107a, would emerge from the September 11th Terrorist and Anthrax Letter attacks of 2001. This section will highlight the main features of each authority and demonstrate their dependance on FDA's regulatory framework.

A. Title 10 U.S.C. § 1107

Title 10 U.S.C. § 1107, subsection (a) states that "[w]henever the Secretary of Defense requests or requires a member of the armed forces to receive an investigational new drug or a drug unapproved for its applied use, the Secretary shall provide the member with notice containing the information specified in subsection (d) [Content of Notice]."[155] Section 1107(g) defines "investigational new drug" as "a drug covered by Section 505(i) of the [FDCA] (21 U.S.C. § 355(i))."[156] This section also defines "drug unapproved for its applied use" as a "drug administered for a use not described in the approved labeling of the drug under Section 505 of the [FDCA], 21 U.S.C. 355."[157] This is typically referred to as "off-label" use.

In addition, Section 1107(f) allows DoD to seek a Presidential waiver of the 1107(a) notice requirement:

> 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

---

[155] National Defense Authorization Act for Fiscal Year 1998, 10 U.S.C. § 1107, Pub. L. No. 105–85, div. A, title VII, § 766(a), 111 Stat. 1827 (Nov. 18, 1997) (clarification added).

[156] *Id.* 21 U.S.C. § 355(i) provides the exemption to the prohibition against introducing a new drug into interstate commerce absent approval under Sections 505(b) or 505(j). *See* 21 U.S.C. § 355(a). Title 21 U.S.C. § 355(i) is the statutory basis for the Investigational New Drug (IND) Application framework that we observe at 21 C.F.R. § 312. An IND is required for all "clinical investigations" of products subject to approval under § 505 of the FDCA or the licensing provisions of the Public Health Service Act. *See* 21 C.F.R. § 312.2(a). The IND requirement includes the following exceptions: 1) the investigation involves the study of a lawfully marketed drug; 2) the investigation is not intended to be submitted to FDA as an adequate and well-controlled trial; 3) the investigation is not intended to support advertising change; 4) the investigation does not include a change in route of administration or dosage level or other factor that significantly increases risks associated with use of the product; 5) the investigation complies with 21 C.F.R. § 50 (informed consent) and § 56 (institutional review); and 6) does not violate 21 C.F.R. § 312.7 (precluding promotion of an unapproved product). *Id.*

[157] 10 U.S.C. § 1107(g). In general, FDA approves a product where the risks outweigh the benefits for a specific intended use. "Intended use" refers to the "objective intent of the persons legally responsible for the labeling of the drugs. The intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article." 21 C.F.R. § 201.128. "Labeling" means "all labels and other written, printed or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article." 21 U.S.C. § 321(n). The Supreme Court interprets this statutory phrase "accompanying such article" broadly: "[o]ne thing or article is accompanied by another when it supplements or explains it, in the manner that a committee report of the Congress accompanies a bill. No physical attachment one to the other is necessary. It is the textual relationship that is significant." Kordel v. United States, 335 U.S. 345, 350 (1948) (Court held that instructions for use sent separately from the drug product itself were indeed labeling). Title 21 C.F.R. § 201.50–58 (Subpart B) provides labeling requirements for prescription drugs products, namely 21 C.F.R. § 201.56 ("Requirements on content and format of labeling for human prescription drug and biological products") and 21 C.F.R. § 201.57 ("Specific requirements on content and format . . . ."). 21 C.F.R. § 201.57(a)(6) requires the label include "indications and usage" whereby the label includes a "concise statement of each of the product's indications." Furthermore, 21 C.F.R. § 201.57(c)(2) requires that a prescription drug include "full prescribing information," whereby the label "must state that the drug is indicated for the treatment, prevention, mitigation, cure, or diagnosis of a recognized disease or condition, . . . or for the relief of symptoms associated with a recognized disease or condition."

> 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 [FDCA] may be waived only by the President. The President may grant such a waiver only if the President determines, in writing, that obtaining consent is not in the interests of national security.[158]

The statute gives the Secretary of Defense (SECDEF) a non-delegable right to request this Presidential waiver and, if granted, requires SECDEF to submit to the Chairman and Ranking Member of each Defense Committee its justification for use of such a drug.[159]

The plain text of the statute is clear that Congress intends for DoD to provide notice to the soldier before they are "requested or required" to take an investigational drug or a drug used "off-label." However, there are several interpretive challenges with this statute. First, what is the scope of what the "Secretary of Defense *requests* or *requires*"? Is this an official order only? What might "request" look like in the context of DoD medical care or force health protection programs? In addition, does this preclude off-label use of medical products in the routine practice of medicine by DoD healthcare providers? This view, of course, would unduly limit DoD medical care as compared with its private sector analog.

The legislative history of 10 U.S.C. § 1107 can provide insight into these questions. First, there was an emphasis on ensuring that soldiers "at least be notified" when they were receiving something other than an FDA-approved drug used for its labeled indication.[160] The requirement for "notice to all service personnel whenever new or experimental drugs are being administered" was coupled with the requirement that "all service members' medical records accurately document the administration of these drugs, so that possible involvement in future post-war illnesses can be better studied."[161] The Conference Report for the statute was clear: this new DoD notice requirement was not intended to apply to standard medical practice within DoD.[162]

---

[158] 10 U.S.C. § 1107(f)(1).

[159] 10 U.S.C. § 1107(f)(3).

[160] 143 CONG. REC. S7048, 7049 (July 9, 1997) (statement of Sen. Chris Dodd) ("Concerning the fact that troops in the Persian Gulf were given drugs that did not yet receive FDA approval for usage, this amendment would require that members of the Armed Forces *at least be notified when they receive an investigational new drug*. That way, if such drugs are required, at least our troops will not have any mistaken impressions about them.") (emphasis added); *see also* 143 CONG. REC. D655, 657 (June 23, 1997) (the Buyer amendment to H.R. 1119 "requires the Secretary of Defense to provide *a notice with specified information to each member of the armed forces whenever an investigational new drug is administered*") (emphasis added).

[161] *See* 143 CONG. REC. S7253, 7253–54 (July 11, 1997) (statement of Sen. Robert Byrd).

[162] *See* 144 CONG. REC. H8097, 8396 (Sept. 22, 1998) (Conference Report): "The Senate amendment contained a provision (sec. 713) that would require that an investigational new drug or a drug unapproved for its applied use not be administered to a member of the armed forces unless the member provides prior consent. The recommended provision would permit the Secretary of Defense to request the President waive the requirement for prior consent if the Secretary determines that obtaining consent is not feasible, is contrary to the best interests of the members involved, or is not in the best interests of national security. The House bill contained no similar provision. The House recedes with a clarifying amendment. *The conferees note that presidential approval, Congressional reports, and prior written notice to the member do not apply to [FDA] informed consent exceptions applicable to standard medical practice in the United States, as distinguished from informed consent exceptions that relate specifically to military functions and activities*.").

The courts would later analyze 10 U.S.C. § 1107 in the context of DoD's mandatory anthrax vaccine immunization program (AVIP) against the harmful effects of anthrax[163] exposure in 1998, when the U.S. District Court for the District of Columbia granted a preliminary injunction to service members instructed to submit to inoculation under the AVIP without their consent or after a Presidential waiver.[164] In reviewing the legislative history and text of Section 1107, the court stated:

> In 1998, in response to concerns about the use of investigational new drugs during the 1991 Gulf War that may have led to the unexplained illnesses among veterans, Congress signed into law 10 U.S.C. § 1107. This provision prohibits the *administration* of investigational new drugs, or drugs unapproved for their intended use, to service members without their informed consent. The consent requirement may be waived only by the President.[165]

In granting the preliminary injunction, the opinion stated: "the Court is not convinced that requiring DoD to obtain informed consent will interfere with the smooth functioning of the military. However, if obtaining informed consent were to significantly interfere with military function, defendants are free to seek a presidential waiver."[166] The court's decision hinged not on DoD's interpretation of 10 U.S.C. § 1107, but on FDA's view of whether the anthrax vaccine absorbed (AVA) was "investigational" for purposes of inhalation anthrax versus the approved indication of cutaneous anthrax exposure.[167]

It's important to note that *Doe v. Rumsfeld* is litigation involving a DoD *requirement* to submit to vaccination; it's a vaccine mandate. What is less clear is interpreting the scope of the word "request" in the 10 U.S.C. § 1107(a) notice requirement. "Request" is defined as "the act or an instance of asking for something,"[168] and it is unclear what a "request" from SECDEF looks like and whether this is inclusive of other DoD organizations outside of the Office of the Secretary of Defense (OSD), such as DoD's FHP program. Furthermore, there is nothing in 10 U.S.C. § 1107 that deals with medical devices, even though their use can cause adverse events just as serious as those caused by drug products.

---

[163] Anthrax is an acute bacterial disease caused by infection with spores of *Bacillus anthracis*, which can enter the body in three ways: by skin contact (cutaneous), by ingestion (gastrointestinal), and by breathing (inhalation). *See* Biological Products; Bacterial Vaccines and Toxoids; Implementation of Efficacy Review, 50 Fed. Reg. 51,002, 51,058 (Dec. 13, 1985).

[164] *See* Doe v. Rumsfeld, 297 F. Supp. 2d 119 (D.D.C. 2003); *see also* Doe v. Rumsfeld, 341 F. Supp. 2d 1 (D.D.C. 2004) (court remanded a Final Order published by FDA that expanded the licensed indication for AVA to include anthrax exposure, "independent of *route* of exposure," for an additional notice and comment period under the Administrative Procedures Act).

[165] *Doe*, 297 F. Supp. 2d at 125.

[166] *Id.* at 134; *see also Doe*, 341 F. Supp. at 10.

[167] *See Doe*, 297 F. Supp. 2d at 131–32 ("While defendants' arguments concerning deference are correct, the dispute in this case has not focused on the language of a particular *DoD* statute. Rather, it is the *FDA's* term 'investigational' that is at the heart of the dispute. Title 10 U.S.C. § 1107 and the attendant DoD regulation apply only if the *FDA* determines that AVA is an investigational drug or a drug unapproved for its present purpose."). It is important to note that both 10 U.S.C. § 1107 and the courts' application of this statute reflect the high degree of DoD dependence on FDA's determination regarding the investigational status of drugs and the scope and wording of FDA-approve labeling.

[168] MERRIAM-WEBSTER DICTIONARY (1997 ed.).

Finally, the 10 U.S.C. § 1107(a) notice requirement does not explicitly state that it is inapplicable to standard medical practice within DoD. This "practice of medicine" exception is based on the mechanics of the statute[169] and its legislative history. In cases where off-label use is clearly within the standard practice of medicine operating between a medical provider and a patient, these exceptions are clear and accepted. However, the farther away DoD gets from the individual doctor-patient relationship, the more careful it must be not to run afoul of the 10 U.S.C. § 1107 notice requirement for actions that may be construed as a "request" for a soldier to take an off-label product. For example, DoD regularly includes disclaimers in its clinical practice guidelines to ensure neither the doctor nor the patient can construe the practice of medicine as an activity covered under this statute. DoD aims to make clear that such issuances are not to interfere with the independent discretion of the physician operating within the practice of medicine.

B. Executive Order 13139 (1999)

After the enactment of 10 U.S.C. § 1107 in 1997, the Clinton Administration issued an Executive Order on September 30, 1999, entitled, "Improving Health Protection of Military Personnel Participating in Particular Military Operations." The policy articulated in this Executive Order, which implemented 10 U.S.C. § 1107, is as follows:

> Military personnel deployed in particular military operations could potentially be exposed to a range of chemical, biological, and radiological weapons as well as diseases endemic to an area of operations. It is the policy of the United States Government to provide our military personnel with safe and effective vaccines, antidotes, and treatments that will negate or minimize the effects of these health threats.[170]

Importantly, the order states the policy that:

> [i]t is the expectation that the United States Government will administer products approved for their intended use by the Food and Drug Administration (FDA). However, in the event that the Secretary considers a product to represent the most appropriate countermeasure for diseases endemic to the area of operations or to protect against possible chemical, biological, or radiological weapons, but the product has not yet been approved by FDA for its intended use, the product may, under certain circumstances and strict controls, be administered to provide potential

---

[169] The § 1107(f) Presidential waiver capability includes, at §1107(f)(1), the clear mechanics that the notice provision of § 1107(a) applies only to those products for which an IND is required. *See* 10 U.S.C. § 1107(f)(1) ("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."); *see also id.* at § 1107(f)(2) ("The waiver authority provided in paragraph (1) shall not be construed to apply to any case other than a case in which prior consent for administration of a particular drug is required by reason of a determination by the Secretary of Health and Human Services that such drug is subject to the investigational new drug requirements of section 505(i) [the requirement for an IND].").

[170] Exec. Order No.13139, 64 Fed. Reg. 54,175 (Sept. 30, 1999).

> protection for the health and well-being of deployed military personnel in order to ensure the success of the military operation.[171]

Furthermore, the Executive Order states that "[b]efore administering an investigational drug to members of the Armed Forces, the Department of Defense (DoD) must obtain informed consent from each individual unless the Secretary can justify to the President a need for a waiver of informed consent in accordance with 10 U.S.C. § 1107(f)."[172] This Executive Order explains that "[w]aivers of informed consent will be granted only when absolutely necessary."[173]

Furthermore, the Executive Order elaborates on the requirements for the § 1107(f) Presidential waiver and cites the obligation of the administration to follow FDA's implementing regulations at 21 C.F.R. § 50.23(d) regarding the criteria for issuance of the waiver and the required content of the SECDEF request. The Executive Order requires that SECDEF include the following elements in its request for the Presidential waiver: 1) "[a] full description of the threat, including the potential for exposure. If the threat is a chemical, biological, or radiological weapon, the waiver request shall contain an analysis of the probability the weapon will be used, the method or methods of delivery, and the likely magnitude of its effect on an exposed individuals";[174] 2) documentation that the Secretary has complied with 21 C.F.R. § 50.23(d), including either a certification that each criteria of 21 C.F.R. § 50.23(d) has been met[175] or "[i]f the Secretary finds it highly impracticable to certify that the criteria and standards set forth in 21 CFR §50.23(d) have been fully met because doing so would significantly impair the Secretary's ability to carry out the particular military mission, a written justification that documents which criteria and standards have or have not been met, explains the reasons for failing to meet any of the criteria and standards, and provides additional justification why a waiver should be granted solely in the interests of national security."[176] The Executive Order requires SECDEF to develop the waiver "in consultation" with FDA[177] and submit the request to the President and send a copy to the Commissioner of Food and Drugs.[178] The Executive Order requires the Commissioner of Food and Drugs to review the waiver request "expeditiously" and "certify" to the Assistant to the President for National Security Affairs (APNSA) and the Assistant to the President for Science and Technology (APST):

> whether the standards and criteria of the relevant FDA regulations have been adequately addressed and whether the investigational new drug protocol may proceed subject to a decision by the President on the informed consent waiver request. FDA shall base its decision on, and the certification shall include an analysis describing, the extent and strength of the evidence on the safety and effectiveness of the investigational new

---

171 *Id.* at § 2(b).

172 *Id.* at § 3(a).

173 *Id.*

174 *Id.* at § 3(d)(1).

175 *Id.* at § 3(d)(2)(A).

176 *Id.* at § 3(d)(2)(B).

177 *Id.* at § 3(e).

178 *Id.* at § 3(f).

> drug in relation to the medical risk that could be encountered during the military operation.[179]

After a joint advisory opinion from the listed staff, the President will approve or deny the request and inform the SECDEF and Commissioner of the decision.[180] The waivers expire after one year (or a specified time period less than one year).[181] Section 5 of the Executive Order requires significant training if a § 1107(f) waiver is granted: "the DoD shall provide training to all military personnel conducting the waiver protocol and health risk communication to all military personnel receiving the specific investigational drug to be administered prior to its use."[182]

C. Department of Defense Instruction (DODI) 6200.02 (2000)

After the issuance of Executive Order 13139 in 1999, the Department of Defense issued its own implementing regulation, DODI 6200.2 (dated August 1, 2000), entitled, "Application of Food and Drug Administration (FDA) Rules to Department of Defense Force Health Protection Programs."[183] Instruction derived from both 10 U.S.C. § 1107 and the Executive Order itself. The purpose of this DODI is to implement these authorities within DoD[184] and "[d]esignate[] the Secretary of the Army as the DoD Executive Agent for the use of investigational new drugs for force health protection."[185] Importantly, the DODI defines "Force Health Protection" as "an organized program of healthcare preventative or therapeutic treatment, or preparations for such treatment, designed to meet the actual, anticipated, or potential needs of a group of military personnel in relation to military missions."[186] It reiterates the Executive Order's policy that "[p]ersonnel carrying out military operations shall be provided the best possible medical countermeasures to chemical, biological, or radiological warfare or terrorism and other health threats. The DoD Components shall make preferential use of products approved by the FDA for general commercial marketing, when available, to provide the needed medical countermeasure."[187] The DODI deals, however, with the inevitable capability gap—"when no FDA-approved product is available to meet a foreseeable threat"—by requiring "appropriate research and development program activities directed toward obtaining general commercial marketing approval by FDA of safe and effective medical countermeasures."[188]

---

[179] *Id.* at § 3(g).

[180] *Id.* at §§ 3(h), 3(i).

[181] *Id.* at § 4(d).

[182] *Id.* at § 5(b).

[183] It is important to note that DODI 6200.2 (Aug. 1, 2000) was replaced by DODI 6200.02 (Feb. 27, 2008), https://www.esd.whs.mil/Portals/54/Documents/DD/issuances/dodi/620002p.pdf. Unless specified in the notes, this paper cites from the 2008 version.

[184] *See* DODI 6200.2 § 1.1. (Aug. 1, 2000).

[185] *Id.* at § 1.2.

[186] *See id.* at § 3.1. By way of background, FHP is defined as "all measures taken by Commanders . . . and the [Military Health System] to promote, protect, improve, conserve, and restore the mental and physical well-being of Service members across the range of military activities and operations." DODI 6200.04 at E2.1.2. (Oct. 9, 2004).

[187] DODI 6200.2 § 4.1.1. (citing 10 U.S.C. §§ 1107, 1107(a)).

[188] *Id.* at § 4.1.2.

The DODI also allows DoD Components to request the use of an IND product under 21 C.F.R. § 312 when "no safe and effective FDA-approved drug or biological product is available."[189] This request for SECDEF approval must be justified based on the "safety and efficacy of the drug and the nature and degree of the threat to personnel."[190] Importantly, this Instruction establishes the Army "as Lead Component for development of medical protocols and regulatory submissions to FDA under this Instruction," which includes any request for the use of an investigational medical product under an IND or EUA.[191] The Army, as Lead Component, must also prepare an annual plan "for using medical products under EUAs or IND protocols under [FHP] programs against health threats when there is no satisfactory approved medical product available. This plan shall establish responsibilities and action timelines to make the best possible medical products available."[192]

Even within DoD, it can be challenging to determine when a medical product should be included in the FHP program under DODI 6200.02. The DODI applies to address "force health protection programs [FHP] of the Department of Defense involving medical products required to be used under an Emergency Use Authorization (EUA) or an investigational new drug (IND) application."[193] DODI 6200.02 defines FHP program as: "an *organized program* of healthcare preventive or therapeutic treatment, or preparations for such treatment, designed to meet the actual, anticipated, or potential needs of *a group of military personnel* in relation to *military missions*."[194] The DODI emphasizes applicability to *military missions* (effectively the same as "operations"),[195] by stating under the Policy: "[p]ersonnel carrying out *military operations* shall be provided the best possible medical countermeasures to chemical, biological, or radiological warfare or terrorism and other health threats."[196] In short, the FHP program: 1) applies to medical products, 2) is intended to be used under EUA or IND, and 3) applies to the FHP program as indicated by either potential use by a "group of military personnel" and/or "in relation to military missions" and formal adoption into the "organized program."

---

[189] *Id.* at § 4.1.3. Furthermore, "[w]hen using INDs for force health protection, DoD Components shall comply with 10 U.S.C. § 1107, E.O. 13139, and applicable FDA regulations." *Id.* at § 4.1.4 The DODI requires a specific treatment protocol for use of the investigational new drug and, absent a Presidential waiver, must include advanced informed consent. *See id.* at § 4.2.2.

[190] *Id.* at § 4.1.3.

[191] DODI 6200.02 §§ 5.2.1.3., 5.2.2., & 5.3 (Feb. 27, 2008) (emphasis supplied.)

[192] *Id.* at § 5.3.4.

[193] *Id.* at § 1.2. DODI 6200.02 (Feb. 27, 2008) defines the term "Medical Product" as "A drug, including a biological product, or a medical device." *Id.* at E2.5. Given that 10 U.S.C. § 1107 does not apply to medical devices and this statute ostensibly led to DODI 6200.02, DoD organizations question the degree to which DODI 6200.02 applies to devices. This definition explicitly includes FDA-regulated medical devices insofar as those devices meet the remaining FHP criteria. Accordingly, if a DoD entity plans to submit an EUA for a medical device, that filing should be coordinated with the Army as the "Lead Component" for FHP and ASD(HA) as required by DODI 6200.02. Where there is an EUA filing from private industry (e.g., Biofire NGDS COVID-19 assay EUA), it is not automatically included in the FHP program. Whether the use of a privately filed EUA should be coordinated with ASD(HA) under DODI 6200.02 should depend on the FDCA risk classification (Class 1, 2, or 3) and the medical risk associated with its use.

[194] *Id.* at E2.2 (emphasis added).

[195] *Id.* at E2.6.

[196] *Id.* at § 4.1.

DODI 6200.02 does not apply to "[u]ses of medical products by DoD Components, including uses under IND applications that are *not* part of a force health protection program."[197] The mere fact that a product is used by DoD under an IND does not mean that such use is subject to DODI 6200.02. The IND or EUA product *must also be part of* a FHP program for it to be subject to DODI 6200.02. Non-medical products are not included in the ambit of DODI 6200.02.

The scope of DODI 6200.02 is limited to FHP, which is distinguishable from standard practice of medicine within DoD. The DODI explicitly carves out the practice of medicine: this DODI "[d]oes not apply to actions by DoD healthcare providers that are within the standard medical practice in the United States and are not subject or applicable to investigational medical products."[198] The DODI's definition of "Drug Unapproved for its Applied Use" makes this same distinction: "an FDA-approved drug or biological product administered for a use not described in the approved labeling of the drug or biological product . . . and for which requirements of use authorization and prior informed consent . . . are applicable" but *not including drug uses to which* "*investigational new drug requirements are inapplicable based on standard medical practice in the United States*."[199]

The DODI's description of a medical product being adopted into the "organized program" of FHP provides some discretion to the "Heads of DoD Components" regarding when to request formal inclusion of a medical product when it uses the words "[m]ay" and "request approval."[200] DODI 6200.02 does not begin with the premise that all uses under IND or EUA are automatically included in the FHP program.[201] There appears to be a "bottom up" request option, as opposed to a "top down" directive that all such uses will be funneled to FHP.

When outside of FHP under DODI 6200.02, other authorities exist that would allow the U.S. Army Medical Command (acting through USAMRDC) or other DoD organizations to file an investigator IND or a treatment IND for this purpose.[202] Furthermore, the legal capability of any medical organization to file a treatment IND exists under FDA regulations at 21 C.F.R. § 312.305 *et seq*. Failure to acknowledge the capability of medical components to make use of the expanded access IND regulations at 21 C.F.R. § 312.305, *et seq*. outside the FHP program would put military medicine at a medical disadvantage over other non-DoD treatment facilities.[203] Even where it is unclear if an action is an FHP or not, DoD organizations do well to

---

[197] *Id.* at § 2.2.2 (emphasis added).

[198] *Id.* at § 2.2.1. Section "(c)" of the DODI cites Title 21, Code of Federal Regulations, Parts 50, 56, 312, Subpart I of Part 314, and Subpart G of Part 601 (clarification added).

[199] *Id.* at E2.4 (emphasis added).

[200] *Id.* at § 5.2.1.

[201] Often, the presumption is the opposite. If this is the policy goal, the DODI needs to be revised.

[202] *See, e.g.*, DODI 6000.08, "Defense Health Program Research and Clinical Investigation Programs," Army Regulation 40-7 ("Use of U.S. Food and Drug Administration-Regulated Investigational Products in Humans Including Schedule I Controlled Substances"), the Surgeon General's authority as Chief Medical Advisor to the Secretary of the Army at 10 U.S.C. § 3036(f), and the service Secretaries' and Commanders' authorities to provide medical care during a public health emergency under DODI 6200.03.

[203] While a doctor could file a treatment IND under 21 C.F.R. § 312.320 and does not need to go through the formal FHP program, using this directive could expedite the process. Coordinating with the FHP program could improve the process administratively and provide a quicker response to an evolving national security threat.

coordinate with the U.S. Army as "Lead Component"[204] under DODI 6200.02 and the ASD(HA) to determine if inclusion in the FHP program, and DoD-wide coordination it provides, would be in the best interest of DoD. In many cases, it is advisable for DoD entities to coordinate with FHP leadership even when it is not required by the explicit terms of DODI 6200.02. DoD organizations must consider these factors where application of the DODI is unclear: 1) the risk–benefit calculus of the investigational medical product; 2) the risks of severe adverse reactions; 3) the degree of interagency coordination; 4) the breadth of DoD's medical need for the product (e.g., CONUS, OCONUS, specific geographical regions, etc.); 5) the regulatory expertise of the interested DoD entity; and 6) the political attention being given to the threat or the medical intervention.

D. Project BioShield of 2004, the Emergency Use Authorization, and 10 U.S.C. § 1107a (2003)

The notion of DoD–FDA collaboration on medical countermeasures was relatively quiet until the 9/11 terrorist attacks and anthrax letter attacks highlighted the nation's lack of preparedness for chemical and biological attacks. As a result, Congress enacted the Bioterrorism Act of 2002, which directed FDA to complete its rulemaking, started earlier, to create the Animal Rule (21 C.F.R. § 314 Subpart I)[205] and created the Strategic National Stockpile (SNS).[206] Furthermore, the Project BioShield Act of 2004 gave the Commissioner of Food and Drugs the ability to authorize the use of unapproved medical products during CBRN emergencies provided that the either the Secretary of HHS, DHA, or DoD determine that there is "a heightened risk of attack with a biological, chemical, radiological, or nuclear agent or agents."[207] FDA may grant an emergency use authorization (EUA) where the agent referenced in the Secretary-level determination "can cause a serious or life-threatening disease or condition," where "based on the totality of scientific evidence" available that the product may be effective in "diagnosing, treating or preventing" the disease referenced in the determination, the "known and potential benefits . . . outweigh the known and potential risks" and "there is no adequate, approved and available alternative to the product for diagnosing, preventing or threatening such disease or condition."[208] "In determining whether "the known and potential benefits of the product outweigh the

---

[204] DODI 6200.02 (Feb. 27, 2008) identifies the U.S. Army as "Lead Component" for the Force Health Protection Program. "The Secretary of the Army shall serve as Lead Component for development of medical protocols and regulatory submissions to the FDA under this Instruction." *Id.*

[205] *See* Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Pub. L. No. 107-188, § 123, 116 Stat. 594 ("[T]he Secretary of Health and Human Services shall complete the process of rulemaking that was commenced under authority of section 505 of the Federal Food, Drug, and Cosmetic Act and section 351 of the Public Health Service Act with the issuance of the proposed rule entitled 'New Drug and Biological Drug Products; Evidence Needed to Demonstrate Efficacy of New Drugs for Use Against Lethal or Permanently Disabling Toxic Substances When Efficacy Studies in Humans Ethically Cannot be Conducted' published in the Federal Register on October 5, 1999 (64 Fed. Reg. 53960), and shall promulgate a final rule.") (codified as amended at 42 U.S.C. § 201, *et seq.*).

[206] *Id.* § 121.

[207] *See* Project Bioshield Act of 2004, Pub. L. No. 108-276, 118 Stat. 835 (amending 21 U.S.C. § 360bbb-3(b)(1)).

[208] 21 U.S.C. § 360bbb-3(c) (2022); see also Casciotti, *supra* note 101, at 66–92 for an excellent discussion of the EUA authority, including its origins and use in the COVID-19 context and recommendations for future reform.

known and potential risks," FDA intends to look at the "totality of the scientific evidence to make an overall risk–benefit determination."[209]

It is important to note SECDEF's ability to determine that there "is a military emergency, or a significant potential for a military emergency, involving heightened risk to the United States military forces" was originally confined to an "attack" with "a biological, chemical, radiological or nuclear agent or agents."[210] Legal commentators hailed the EUA as the solution to the inadequacy of the IND model of clinical research to deal with the treatment needs of the warfighter:

> This really does not work. It's a square peg in a round hole to try to use those [IND] processes which are designed for the regulation of clinical research trials to try to carry out a critical public health emergency program. The military's success in trying this has been poor, and CDC's success in the context of the 2001 response to the anthrax postal attacks was not very effective either. The solution to this problem is the EUA.[211]

At its passage, the EUA did not include the ability for DoD to get an EUA for MCMs against non-CBRN agents of combat; there was no "all hazards" DoD EUA capability. This broad capability to authorize products for the specialized need of the warfighter was evident as early as the 1974 MOU.[212] Alongside the EUA's original enactment in the National Defense Authorization Act of 2004 was an adjacent provision enacted at 10 U.S.C. § 1107a that stated that any EUA must include a provision "designed to ensure that individuals are informed of an option to accept or refuse administration of a product, [which] may be waived only by the President only if the President determines, in writing, that complying with such requirement is not in the interests of national security."[213] This statute also included flexibility for the

---

[209] FDCA § 564 (codified at 21 U.S.C. §360bbb-3(c)); *see also* U.S. FOOD & DRUG ADMIN., EMERGENCY USE AUTHORIZATION OF MEDICAL PRODUCTS AND RELATED AUTHORITIES—GUIDANCE FOR INDUSTRY AND OTHER STAKEHOLDERS 8 (Jan. 2017), https://www.fda.gov/media/97321/download [hereinafter FDA, EUA MEDICAL PRODUCTS AND RELATED AUTHORITIES].

[210] 21 U.S.C. § 360bbb-3(b)(1). The scope of a Secretary of Defense determination was expanded by Pub. L. 115-92 as discussed in Section IV.B, *infra*.

[211] John Casciotti, Cynthia Ryan, Dean Gerald Sienko & Robert C. Williams, *Law at the Intersection of Civilian and Military Public Health Practice*, 35 J.L., MED & ETHICS 83, 85–56; *see also* Casciotti, *supra* note 101, at 70; *see also* Gail H. Javitt, *Old Legacies and New Paradigms: Confusing "Research" and "Treatment" and its Consequences in Responding to Emerging Health Threats: Symposium: Eliminating Legal, Regulatory and Economic Barriers to Biodefense Vaccine Development*, 8 J. HEALTH CARE L. & POL'Y 38 (2005).

[212] *See supra* Section II.B.

[213] 10 U.S.C. § 1107a(a), enacted as Pub. L. No. 108–136, 117 Stat. 1689, div. A, title XVI, § 1603(b)(1) (Nov. 24, 2003). It is important to point out that 10 U.S.C. § 1107a is a cognate provision to the "base" EUA statute at § 564 of the FDCA, which includes the requirement that a patient be "informed . . . of the option to accept or refuse administration of the product, of the consequences, if any, of refusing administration of the product, and of the alternatives to the product that are available and of their benefits and risk." 21 U.S.C. § 360bbb-3(e)(1)(A). Even before COVID-19, FDA's 2017 EUA Guidance was imprecise as it relates to the various situations where "the option to accept or refuse" may or may not be a condition of the EUA. *Compare, e.g.*, Casciotti, *supra* note 101, at 72 n.22 ("Indeed there may be circumstances, such as first responders or to deal with a highly communicable disease, in which it may be appropriate not to have an option to refuse for selected groups pf people, but instead have a mandatory program. I think it would be wise to keep all options on the table."), *with* FDA, EMERGENCY USE AUTHORIZATION OF MEDICAL PRODUCTS AND RELATED AUTHORITIES, *supra* note 209, at 24 ("informed to the extent practicable given the applicable circumstances"); *and*, in the COVID-19 vaccine mandate context, Whether Section 564 of the Food, Drug and Cosmetic Act Prohibits Entities from Requiring the Use of a

provision of EUA product information where there is a "determination that it is not feasible based on time limitations for the information . . . to be provided to a member of the armed forces prior to the administration of the product."[214] This statute also had a conforming section exempting the notice provision requirements of 10 U.S.C. § 1107(a) from applying in the case of an EUA.[215]

E. Army Regulation 40-7 (2009)

In addition to the Executive Order and DODI 6200.02, the Army, as both Lead Component under the FHP program and DoD's primary research and development organization through the USAMRDC and the JPEO-CBRND, institutes Army-specific regulations under the authority of The Surgeon General of the U.S. Army (TSG). Army Regulation (AR) 40-7, entitled, "Use of U.S. Food and Drug Administration-Regulated Investigational Products in Humans Including Schedule I Controlled Substances," is intended to "implement[] DODD 3216.1, DODD 3216.2, and DODI 6200.02" and

> reaffirms Army compliance with U.S. Food and Drug Administration rules and regulations on the use of investigational products; includes citations for the use of International Conference on Harmonisation Guidelines for Good Clinical Practice in the use of investigational products; adds procedures for the control of investigational drugs used to treat patients moving among U.S. Army Medical Centers and U.S. Army Medical Department Activities.[216]

AR 40-7 is both a research-enabling regulation and a force health protection regulation. Under the previous Army model, the Army Medical Command—led by OTSG—included both military treatment facilities (MTFs) and research and development activities. Under this MEDCOM model, this regulation was to allow the TSG to file INDs and IDEs with FDA for purpose of clinical investigations as well as expanded access INDs for medical care. This regulation controls who, within the

---

Vaccine Subject to Emergency Use Authorization, 45 Op. O.L.C. 7-9, at 16–18 (July 6, 2021) (Memorandum Opinion for the Deputy Counsel to the President, from Dawn Johnsen, Acting Assistant Attorney General), https://www.justice.gov/olc/file/1415446/download ("DOD informs us that it has understood section 1107a to mean that DOD may not require service members to take an EUA product that is subject to the condition regarding the option to refuse, unless the President exercises the waiver authority contained in Section 1107a. . . . DOD is required to provide service members with the specified notification [Fact Sheet containing the "it's your choice"] unless the President waives the condition pursuant to 10 U.S.C. § 1107a. . . . DOD should seek a presidential waiver before it imposes a vaccination requirement."). The analysis of the 10 U.S.C. § 1107a Presidential waiver of the "option to accept of refuse" is straightforward in the OLC opinion (pp. 16–18); however, rendering the inclusion of the "option" as *information only* outside the military context (pp. 7–9) raises a number of questions: should a product under an EUA ever become mandatory? If the "option" is informational only, does it mean that FDA lacks authority to issue a mandatory EUA for public health purposes? In the larger context of the FDCA with its requirements for informed consent under the IND or IDE regulations and acknowledging that EUA is *not* full approval, did the OLC opinion render this "option to refuse" meaningless in a way that a patient now finds it harder to distinguish between an EUA product, an investigational product under an IND or IDE, and a licensed product?

[214] 10 U.S.C. § 1107a(b).

[215] 10 U.S.C. § 1107a(c).

[216] DEP'T OF THE ARMY, AR 40-7, USE OF U.S. FOOD AND DRUG ADMINISTRATION-REGULATED INVESTIGATIONAL PRODUCTS IN HUMANS INCLUDING SCHEDULE I CONTROLLED SUBSTANCES (Oct. 19, 2009), https://armypubs.army.mil/epubs/DR_pubs/DR_a/pdf/web/r40_7.pdf (last visited June 22, 2023).

Army, may undertake the significant legal risk of these important regulatory filings. Importantly, the delegations in the regulation delegate the TSG's prerogative to sponsor INDs and IDEs on behalf of the U.S. Army to the U.S. Army Medical Research and Material Command (now, USAMRDC), with specific regulatory affairs responsibilities and human subject protection responsibilities flowing to staff elements of USAMRDC.[217] While this regulation remains in effect, the Army's MTFs have moved to the Defense Health Agency (DHA),[218] and the USAMRDC research and development organization itself is required by statute to move to DHA as well.[219] AR 40-7 applies equally to JPEO-CBRND, which has responsibility over the Army's CBRN MCM portfolio, via Title 50 U.S.C. § 1522, which designates the U.S. Army as the Executive Agent for DoD chemical and biological warfare defense program.[220]

F. Human Subject Protection Regulations in DoD

Up to this point, the predominant focus of this paper is the shift from a Surgeon General-led model of FHP decision-making to a model whereby DoD is dependent on the FDA regulatory paradigm. However, this dependency began initially in the realm of human subject protection regulations after the Nuremburg Code in 1947 and evolved through the Declaration of Helsinki of 1964 and the Belmont Report of

---

[217] AR 40-7 states that the TSG's Sponsor's Representative (SR) will (among other things) "[s]erve as the primary contact for formal and informal communications with FDA" and "[c]oordinate with other organizations that develop TSG-sponsored FDA-regulated products to ensure sponsor responsibilities are fulfilled." *Id.* at Ch. 2–3. The state of the TSG Sponsor's representative role was already in flux before the DHA transition, with multiple Army entities frustrated by the need to coordinate FDA engagement with the TSG-SR. Under this regulation, the TSG-SR must also "coordinate" with other organizations where TSG sponsorship is potentially in view under Chapter 2–3, § j. AR 40-7 does *not* specify the means by which the end goals of SR "primary" communication and "coordination" are achieved. A continuum is likely appropriate whereby there is minimum TSG-SR involvement and coordination in the earliest stages of FDA-regulated medical product development and greater TSG-SR involvement and coordination as the efforts progress to include formal sponsorship. While multiple sponsors' representatives are possible with an amended or re-issued regulation, this author counsels that DHA centralize this role as did MEDCOM.

[218] 10 U.S.C. § 1073c, Pub. L. No. 114–328, § 702(a)(1), 130 Stat. 2193, div. A, title VII (Dec. 23, 2016).

[219] *See* 10 U.S.C. § 1073c. Subsection (e) of this statute created a subcomponent of DHA called "Defense Health Agency Research and Development" that is to include, by September 30, 2022, "the Army Medical Research and Materiel Command and such other medical research organizations and activities of the armed forces as the Secretary considers appropriate." 10 U.S.C. § 1073c(e)(1)(B); *see also* HQDA EXORD 013-19 (Oct. 3, 2018) moving the U.S. Army Medical Research and Materiel Command (USAMRMC) from Army Medical Command to Army Materiel Command and then potentially to Army Futures Command. The EXORD emphasizes that "all USAMRMC policies and procedures will remain in place unless directed otherwise."

[220] "The Secretary of Defense shall designate the Army as executive agent for the Department of Defense to coordinate and integrate research, development, test, and evaluation, and acquisition, requirements of the military departments for chemical and biological warfare defense programs of the Department of Defense." 50 U.S.C. § 1522(c)(1). JPEO-CBRND ultimately reports to the Assistant Secretary of the Army for Acquisition, Logistics, and Technology (ASA(ALT)). *See* U.S. GOV'T ACCOUNTABILITY OFF., GAO-15-257, CHEMICAL AND BIOLOGICAL DEFENSE—DESIGNATED ENTITY NEEDED TO IDENTIFY, ALIGN, AND MANAGE DOD'S INFRASTRUCTURE 7 at Fig. 1 (June 2015), https://www.gao.gov/assets/680/671004.pdf. Furthermore, the Army Surgeon General is the "principal advisor to the Secretary of the Army . . . on all health and medical matters of the Army" and "serves as the chief medical advisor of the Army to the Director of the Defense Health Agency on matters pertaining to military health readiness requirements and safety of members of the Army." 10 U.S.C. § 3036; *see also* 10 U.S.C. § 3067.

1979[221] eras. [222] The Department of Defense adopted, along with fifteen other federal agencies, the HHS regulations regarding human subject protections at 45 C.F.R. § 46, also known as "The Common Rule." The Common Rule applies to all research by the federal government, regardless of whether this research is intramural or extramural. The Common Rule incorporates the principal elements of the Belmont Report, namely, informed consent of the subject or the subjects' legally authorized representative before participation in a study, the creation and use of an institutional review board (IRB), and other requirements.

Within DoD, as referenced above, 10 U.S.C. § 980, "Limitation on the use of humans as experimental subjects," applies to research funded by DoD only; the statute constrains DoD's ability to conduct or fund research that would otherwise be in compliance with the Common Rule. This statute requires advanced informed consent and, where not possible, requires the legal representative of the subject to provide this consent and requires an "intent to benefit" the subject. This presents several challenges in DoD-funded research. Furthermore, DoD Instruction 3216.02 creates additional DoD-unique obligations for research involving human subjects conducted or sponsored by DoD.[223]

In addition to these DoD-specific authorities, where the clinical research involves a test article that is likewise subject to FDA's IND requirements, then FDA's Good Clinical Practice Guidelines at 21 C.F.R. §§ 50–56 regarding advanced informed consent (Part 50), IRBs (Part 56), financial disclosures by clinical investigators (Part 54), and the requirements of INDs (Part 312) and IDEs (Part 812) apply.[224]

As evidenced above, through congressional action and DoD policy, FDA's regulatory paradigm is built into the function of DoD's medical R&D and FHP missions. The challenge is inescapable: keeping this set of DoD and Army policies up to date to reflect statutory changes to FDA's authorities or monumental DHA-related restructuring will require constant collaboration between DoD and FDA. The DHA transition itself presents significant concerns that the regulatory systems created within

---

[221] DEP'T OF HEALTH & HUM. SERVS., THE NAT'L COMM'N FOR THE PROTECTION OF HUM. SUBJECTS OF BIOMEDICAL & BEHAVIORAL RSCH., THE BELMONT REPORT—ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH (1979), https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html.

[222] Stephen Maleson, *Biomedical Research Involving Human Subjects*, U.S. ARMY MED. DEP'T J., Jan.–Mar. 2010, at 33.

[223] DEP'T OF DEF., DODI 3216.02, PROTECTION OF HUMAN SUBJECTS AND ADHERENCE TO ETHICAL STANDARDS IN DOD-CONDUCTED AND SUPPORTED RESEARCH (June 2022), https://www.esd.whs.mil/Portals/54/Documents/DD/issuances/dodi/321602p.pdf.

[224] A future study would be appropriate to examine overall informed consent requirements across the Common Rule, FDA regulations, and DoD issuances. For a recent attempt in the genomics research context, see Maxwell J. Mehlman & Tracy Yeheng Li, *Ethical, Legal, Social, and Policy Issues in the Use of Genomic Technology by the U.S. Military*, 47 CASE W. RSRV. J. INT'L L. 115 (2015). Such a future study should note that the notion of any waiver of advanced informed consent related to a solider—Presidential waiver under 21 C.F.R. § 50.23(d) and 10 U.S.C. § 1107a or not—remains a hotly debated topic in the legal literature. *See, e.g.*, Michael J. O'Conner, Note, *Bearing True Faith and Allegiance? Allowing Recovery for Soldiers under Fire in Military Experience that Violate the Nuremberg Code*, 25 SUFFOLK TRANSNATIONAL L. REV. 649 (2002); Ashley R. Melson, *Bioterrorism, Biodefense and Biotechnology in the Military: A Comparative Analysis of Legal and Ethical Issues in the Research, Development, and Use of Biotechnological Products on American and British Soldiers*, 14 ALB. L.J. SCI. & TECH. 497 (2004); Lars Noah, *Coerced Participation in Clinical Trials: Conscripting Human Research Subjects*, 62 ADMIN. L. REV. 329 (2010); Efthimios Parasidis, *The Military Biomedical Complex: Are Service Members a Vulnerable Population*, 16 HOUS. J. HEALTH L. & POL'Y 113 (2016).

DoD to ensure compliance with FDA's requirements will become fractured and ineffective absent the development of DHA regulations. This could present the risk of harm to patients and delays in delivering life-saving drugs, vaccines, blood products, and devices to the warfighter. These authorities will require revision through internal collaboration and insight from FDA as well.

IV. ENHANCED ENGAGEMENT: A NEW ERA OF COLLABORATION BETWEEN DOD AND FDA UNDER P.L. 115-92[225]

The legal framework governing collaboration between DoD and FDA underwent its most significant evolution on December 12, 2017, when Congress passed and the President signed Public Law (P.L.) 115-92 into law. P.L. 115-92 expanded the emergency use authority for DoD under § 564 of the FDCA and created a new era of collaboration between DoD and FDA related to the development of medical products to treat the unique needs of military personnel.[226]

A. The Catalyst for P.L. 115-92: French Freeze-Dried Plasma (FFDP)

In the fall of 2017, French freeze-dried plasma (FFDP) was licensed and available in other countries and used by DoD special operators under an expanded access IND (EAP IND) protocol under 21 C.F.R. § 312.315. DoD was concerned that FFDP may not be available for use in conventional forces should a "live fire" conflict with North Korea break out. An expanded access IND would be suboptimal given the significant constraints on the use of this research protocol, and DoD simply concluded that it would not be possible. After consultation with senior DoD leadership and considering this concern, Congress added § 716, "Additional Emergency Uses of Medical Products to Reduce Deaths and Severity of Injuries Caused by Agents of War," to H.R. 2810, the Fiscal Year 2018 National Defense Authorization Act (FY 18 NDAA). This provision provided SECDEF the authority to authorize emergency uses of investigational medical products where it was unrelated to a CBRN threat.[227] This "DoD EUA" approach was confined to the U.S. military force and use outside the United States, where FDA has more limited jurisdiction. This DoD approach would have shifted the ultimate responsibility of EUA decision-making from FDA to DoD.[228]

Section 716 of P.L. 115-91, entitled "Additional Emergency Uses for Medical Products to Reduce Deaths and Severity of Injuries caused by Agents of War," provided:

> In a case in which an emergency use of an unapproved product or an emergency unapproved use of an approved product cannot be authorized under section 564 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–3) because the emergency does not involve an actual or

---

[225] This section of the paper was originally published in a shorter form as Jeremiah J. Kelly, *Public Law 115-92: A New Era of Collaboration between DoD and FDA*, FDLI UPDATE MAG. (Aug. 2018), https://www.fdli.org/2018/08/update-public-law-115-92-a-new-era-of-collaboration-between-DOD-and-fda/ (last visited on June 22, 2023).

[226] Pub. L. No. 115-92, 131 Stat. 2023-2025 (Dec. 12, 2017).

[227] Pub. L. No. 115-91, § 716, 131 Stat. 1283 (Dec. 12, 2017).

[228] *Id.* at added section (d)(1).

> threatened attack with a biological, chemical, radiological, or nuclear agent or agents, the Secretary of Defense may authorize an emergency use outside the United States of the product to reduce the number of deaths or the severity of harm to members of the armed forces (or individuals associated with deployed members of the armed forces) caused by a risk or agent of war.[229]

P.L. 115-91 gave SECDEF decision-making authority that would "have the same effect with respect to the armed forces as an emergency use authorization under section 564 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–3)."[230] This new statute created a "Department of Defense Emergency Use Authorization Committee" that would operate to "advise the Assistant Secretary of Defense for Health Affairs on proposed authorizations."[231] This Committee would be comprised of "prominent health care professionals who are not employees of the Department of Defense (other than for purposes of serving as a member of the Committee)."[232] This law would allow a DoD-issued EUA only if:

> the Assistant Secretary of Defense for Health Affairs makes a written determination, after *consultation with the Commissioner of Food and Drugs*, that, based on the totality of scientific evidence available to the Assistant Secretary, criteria comparable to those specified in section 564(c) of the Federal Food, Drug, and Cosmetic Act have been met.[233]

In DoD's push for this legislative solution, a few things are evident: 1) there was a clear DoD dissatisfaction with the expanded access IND capability to provide the treatment solution needed by DoD in the event of "live fire" warfare; 2) even after the significant developments of the Project BioShield Act of 2004, DoD is still left without an "all hazards" EUA capability;[234] and 3) DoD's prerogative remained ensuring the safety of its soldiers. To some within DoD, the notion that this authority would only apply outside the United States where, arguably, FDA's jurisdiction is more limited, would make this DoD decision-making palatable to the U.S. public so long as this was done "*in consultation* with the Commissioner of Food and Drugs."[235]

---

[229] *See* Pub. L. No. 115-91, § 716, 131 Stat. 1283 (adding subsection "(d)" to existing 10 U.S.C. § 1107a.).

[230] *Id.* at § (d)(2).

[231] *Id.* at § (d)(5); *see also id.* § (d)(3)(B).

[232] *Id.* at § (d)(5)(B).

[233] *Id.* at § (d)(3)(B) (emphasis added).

[234] The EUA authority at this point in 2017 was confined to CBRN threats only; typical life-threatening risks of modern warfare, which include battlefield trauma, pain, ballistics injuries, and blood-loss incident to use of traditional military weaponry, were not eligible for an EUA.

[235] Pub. L. No. 115-91, § (d)(3)(B), 131 Stat. 1283 (emphasis added).

FDA and other interested parties objected to this approach,[236] leading to a brief legislative struggle between the two agencies.[237] On November 9, 2017, five former FDA Commissioners sent a letter to Senator John McCain, Chairman of the Senate Armed Services Committee (SASC), expressing concerns over the proposed legislation:

> For more than 100 years, the U.S. Congress has empowered FDA to ensure the safety and efficacy of medical products for U.S. consumers, including our military personnel. In contrast, the proposed review panel in the Department of Defense will never have the resources or the expertise that FDA brings to ensure the safety and efficacy of medical products, even in the limited cases of emergency use. These five external advisors are not likely to have the requisite knowledge about the chemistry, manufacturing, and controls that are part of every FDA review, nor will they have access to the raw data that are part of every new product application to FDA. They will have no authority to require post market studies, as FDA does, and it is unclear how they will be able to monitor post-market safety more generally.
>
> Access to better therapies to protect war fighters is a critical public priority. Because the development of and access to reliable and effective treatments for military personnel in harm's way also depends on the latest science and effective review mechanisms, medical innovation for these personnel is best served by utilizing the expertise and support that FDA brings to medical product development. Building on FDA's capabilities and tradition of adapting to address new public health problems, FDA Commissioner and bipartisan members of Congress are working to assure that the agency has the necessary authorities and initiatives in place to address urgent military needs for medical products. We support these efforts.
>
> This provision, on the other hand, undermines that longstanding statutory framework and likely increases the risks for our military personnel. It is often assumed that products that are relatively advanced in the development process are highly likely to be safe and effective.[238]

---

[236] *See* Letter to Senator John McCain et al. from Five Former FDA Commissioners (Nov. 9, 2017), https://www.cspinet.org/sites/default/files/attachment/former-commissioners-letter.pdf; *see also* Laurie McGinley, *Clash Over Drugs: Defense Bill Would Allow Combat Troops to Use Unapproved Pills, Devices*, WASH. POST (Nov. 10, 2017), https://www.pressreader.com/usa/the-washington-post/20171110/281526521335893.

[237] *See* Robert King, *FDA and Pentagon in Turf War Over Product Approvals*, WASH. EXAMINER (Nov. 7, 2017), https://www.washingtonexaminer.com/fda-and-pentagon-in-turf-war-over-product-approvals; Robert Book, *FDA-DoD Turf War Sheds Light on Larger Problem*, FORBES (Nov. 29, 2017), https://www.forbes.com/sites/theapothecary/2017/11/29/fda-dod-turf-war-sheds-light-on-larger-problem/?sh=48e91e88d4e9; Terry Turner, *Defense Bill Could Bypass FDA Drug, Device Approvals*, DRUG WATCH (Nov. 8, 2017, modified Apr. 17, 2018), https://www.drugwatch.com/news/2017/11/08/defense-bill-bypass-fda-drug-device-approvals/; Dan Diamond, *How to Reboot the FDA*, POLITICO: THE AGENDA (Dec. 13, 2017), https://www.politico.com/agenda/story/2017/12/13/fda-approval-alternatives-000593/.

[238] *See* Letter to Senator John McCain et al. from 5 Former FDA Commissioners (Nov. 9, 2017), https://www.cspinet.org/sites/default/files/attachment/former-commissioners-letter.pdf.

DoD and FDA held well-reasoned positions on how best to balance the needs to eliminate the gap in the current EUA authority, prioritize DoD medical products, and protect soldiers through the objective and rigorous risk–benefit calculus required of EUA decision-making. DoD held to its long-standing position that its responsibility to protect soldiers from imminent harm predominated, justifying its own autonomy in decision-making. The SECDEF statute did not allow DoD to make decisions in a vacuum; "consultation" with FDA was required and DoD's reliance on outside medical expertise (akin to an FDA Advisory Committee) would help ensure the right risk–benefit was struck in decision-making. DoD's perspective was summed up well in the following statement:

> [G]reat attention is given to the potential harm that could result from approval of the wrong drugs, but it seems that *much less attention* is given to the just as real harm that results from delaying approval of beneficial drugs. Furthermore, it seems that little attention is given to the relative harm that might result from the non-use of various products. . . . [A] wounded soldier *about to bleed to death if nothing is done is probably not all that concerned with, say, long-run cardiovascular damage that might results if something is wrong with the freeze dried plasma*. If the freeze-dried plasma isn't available, there isn't going to be a "long run" to worry about.[239]

This "turf war"[240] would require an alternative, compromise approach that would "head off an agency brawl over the authority for approving new drugs used by service members."[241] While Congress was in Conference over the National Defense Authorization Act of 2018, FDA and DoD leadership met on October 27, 2017,[242] to determine if a compromise approach could be reached. FDA objected to DoD's approach on the grounds that it impeded their statutory authority and questioned DoD's ability to make correct risk–benefit calculations. FDA's compromise proposal was "breakthrough designation" for DoD priority drugs and biologics. DoD rejected FDA's offer of an expedited approval mechanism because the proposal did not cover medical devices and did not include an expansion of the EUA to cover "all hazards."

After White House intervention, Congress adopted a DoD and FDA compromise in November 2017 to both expand the scope of the EUA and provide an expedited approval mechanism for DoD medical priorities *via a concurrent legislative vehicle*, H.R. 4374. Under this new compromise framework, DoD would get both the expansion of the EUA authority beyond CBRN threats for battlefield trauma care *and* an expedited approval mechanism for DoD medical priorities, but FDA would retain the exclusive authority to authorize an EUA. This compromise approach was signed into law as P.L. 115-92 on December 12, 2017, immediately repealing the momentary DoD EUA authority of § 716 of the 2018 Fiscal Year National Defense Authorization Act, which became law hours earlier.[243]

---

239 *See* Book, *supra* note 237.

240 *See id.*

241 *See* King, *supra* note 237.

242 The reader should know that the author was a participant in this meeting, in associated events, and negotiations as described in this section as it relates to Pub. L. 115-92.

243 "REPEAL – Effective as of the enactment of the National Defense Authorization Act for Fiscal Year 2018, subsection (d) of section 1107a of title 10, United States Code, as added by section 716 of the

Importantly, given the timeline of the negotiations over the compromise proposal, the DoD EUA proposal was enacted. The National Defense Authorization Act for Fiscal Year 2018 (H.R. 2810) included § 711 (formerly 732) with OSD's approach to EUA expansion and became Public Law No. 115-91 on December 12, 2017. For a few short hours, DoD had the authority and autonomy to award its own EUAs for military use of investigational products.

B. P.L. 115-92 Expands the Emergency Use Authority at § 564 of the FDCA

There are four major provisions of P.L. 115-92. The first—and arguably most urgent given the FFDP needs and the risk in 2017 of potential for hostilities with a brazen North Korea—was the expansion of the EUA statute at § 564 of the FDCA (21 U.S.C. § 360bbb-3) by broadening the scope of a potential SECDEF determination of a military emergency to read as follows:

> (B) a determination by the Secretary of Defense that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to United States military forces, including personnel operating under the authority of title 10 or title 50, United States Code, of attack with—(i) a biological, chemical, radiological, or nuclear agent or agents; or (ii) *an agent or agents that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to United States military forces.*[244]

The new subsection (b) of § 564 is now given two subsections. The first retains the pre-existing CBRN basis for a SECDEF determination, but the second adds a completely new basis, namely, the risk of attack by "an agent or agents that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to United States military forces."[245] This expansion of the EUA capability for DoD is significant because the pre-existing scope of a potential DoD determination was limited to CBRN threats only. DoD medical product developers were often unable to justify an EUA request for urgently needed investigational medical treatments for battlefield trauma scenarios where there is no clear link to a CBRN threat. This gap in the EUA capability left mass casualty and battlefield trauma care options limited to expanded access IND use.

Importantly, on July 10, 2018, FDA granted DoD emergency use authorization (EUA) under § 564 of the FDCA to enable the emergency use of Pathogen-Reduced Leukocyte-Depleted Freeze-Dried Plasma manufactured by the French military (referred to in the EUA as French FDP).[246] FDA's action is significant for the medical care of the nation's warfighters, but it was also the first EUA of its kind to rely on statutory change in P.L. 115-92 that expanded the ability for DoD to request an EUA

National Defense Authorization Act for Fiscal Year 2018, is repealed." Pub. L. No. 115-92, 131 Stat. 2025, § 1 (c) (Dec. 12, 2017).

[244] *Id.* at § 1(a) (emphasis added).

[245] *Id.*

[246] U.S. Food & Drug Admin., News Release, FDA Takes Action to Support American Military Personnel by Granting an Authorization for Freeze-Dried Plasma Product to Enable Broader Access while the Agency Works Toward Approval of the Product (July 10, 2018), https://www.fda.gov/news-events/press-announcements/fda-takes-action-support-american-military-personnel-granting-authorization-freeze-dried-plasma (last visited June 22, 2023).

against agents that pose an "imminently life-threatening and specific risk to U.S. military forces." The scope of "imminently life-threatening" and "specific risk" will be determined over time as new national security threats emerge. Questions of "how imminent?" and "how specific?" are fair questions. At minimum, there must be a time-related nexus between the "agent," the degree of harm (it must be "life threatening"), and a precise need ("specific risk"). These matters of statutory interpretation will need to be worked out by DoD and FDA legal counsel over time. However, DoD's capabilities are enhanced by this broad authority to request an EUA for typical threats of modern warfare unconnected to a CBRN threat.

C. P.L. 115-92 Provides an Expedited Approval Mechanism for DoD Medical Product Applications

Public Law 115-92 at section (b)(1) allows SECDEF to:

> [R]equest that the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, take actions *to expedite the development of a medical product*, review of investigational new drug applications under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) [INDs], review of investigational device exemptions under section 520(g) of such Act (21 U.S.C. 360j(g)) [IDEs], and review of applications for approval and clearance of medical products under sections 505 [NDAs], 510(k), and 515 of such Act (21 U.S.C. 355, 360(k), 360(e)) [PMAs] and section 351 of the Public Health Service Act (42 U.S.C. 262), including applications for licensing of vaccines or blood as biological products under such section 351 [BLAs], or applications for review of regenerative medicine advanced therapy products under section 506(g) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356(g)), if there is a military emergency, or significant potential for a military emergency, involving a specific and imminently life-threatening risk to United States military forces of attack with an agent or agents, and the medical product that is the subject of such application, submission, or notification would be reasonably likely to diagnose, prevent, treat, or mitigate such life-threatening risk.[247]

This section covers all investigational or premarket approval or notice applications of both the FDCA for drugs and devices, and the PHSA for biologics. This section requires DoD to substantiate its request for expedited review by citation of a potential for a military emergency involving a "specific and imminently life threatening risk"—or at least the "potential" for such a risk—to the warfighter and a direct relationship between that threat and the indication for use of the product. While this text does not require that DoD be the sponsor of the regulatory application at issue, the request must come from DoD and, accordingly, there must be a relationship between DoD and (if DoD is not the sponsor) the private entity or other federal agency sponsoring that medical product application. Furthermore, the statutory text is explicit that SECDEF's request is to "expedite" the application for the potentially effective medical response to the threat.

In response to a DoD request described above, the statute gives FDA authority to "*take action to expedite the development and review* of an applicable application or

[247] Pub. L. No. 115-92, § 1(b)(1), 131 Stat. 2025 (clarification added).

notification with respect to a medical product described in paragraph (1) . . . ."[248] Section 1(b)(2) of the statute goes on to list a series of non-exclusive means by which FDA can "expedite" DoD medical product application, including holding meetings with the sponsor and the review division, providing the sponsor with guidance on efficient clinical and non-clinical needs for approval or clearance, involving senior FDA leadership, using cross-disciplinary teams for review, providing advice on efficient trial designs, applying any expedited approval program to expedite the development and review of the medical product, and permitting expanded access to the medical product during the investigational phase.[249]

Section 1(b)(2) gives FDA the authority to bring to bear a wide range of tools to expedite development of DoD medical product priorities. In fact, FDA may use a tool not specifically enumerated in this section if appropriate to expedite development and review of DoD's stated medical product priority.[250] Here, Congress is authorizing FDA to use these expedited approval mechanisms in response to the need articulated by DoD's request pursuant to § 1(b)(1) of the statute *even absent absolute compliance* with the full terms of the underlying expedited review program contemplated. Section (b)(2)(F) lists that FDA "may, as appropriate" apply "any applicable Food and Drug Administration program intended to expedite the development and review of a medical product."[251] FDA's perspective is that this list confines FDA's expedited approval activity to existing expedited approval mechanisms—Fast Track, Breakthrough Therapy or Device, Accelerated Approval, Priority Review—all of which involve consideration of the serious condition the product is intended to treat, the lack of currently available therapies, and the unmet medical need of the patient.[252] Certainly, most if not all of DoD's medical product priorities will be "capability gaps," meaning, there is not a product available for that threat. However, in the event DoD's request does not fit squarely within a pre-defined expedited approval mechanism, the statute is clear that FDA has the authority to "take action to expedite the development and review of an application[.]"[253] For example, a marginal improvement in battlefield pain management may not be considered an "unmet medical need" or a "significant improvement in safety or effectiveness" under pre-existing expedited approval mechanisms like breakthrough therapy designation or priority review, but to DoD and the warfighter, this marginal improvement over existing therapies may be a significant advantage for DoD's specific context. Yes, breakthrough therapy and priority *could*—if one strains in looking at the fact pattern to say "close enough"—get the DoD product to the outcome desired, but the statute does not require this. The statute allows FDA to give appropriate weight to the DoD-articulated need. To read the statute to confine

---

[248] *Id.* at § 1(b)(2).

[249] *Id.* at § 1(b)(2).

[250] The statute at § (b)(2) provides an enumerated lists of tools at FDA's disposal, yet, that list is proceeded by the phrase "*may* include," which is generally permissive. *See* CONG. RSCH. SERV., CRS97-589, STATUTORY INTERPRETATION: GENERAL PRINCIPLES AND RECENT TRENDS 10 (Sept. 24, 2014), https://www.everycrsreport.com/files/20140924_97-589_3222be21f7f00c8569c461b506639be98c482e2c.pdf.

[251] P.L. 115-92 at § (b)(2)(F).

[252] U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: EXPEDITED PROGRAMS FOR SERIOUS CONDITIONS—DRUGS AND BIOLOGICS (2014), https://www.fda.gov/media/86377/download.

[253] See P.L. 115-92 § (b)(2), which is predicated on the "specific and immanently life-threatening risk" to the warfighter that was the basis of the SECDEF request in the first instance.

FDA's actions to existing expedited approval mechanisms is inconsistent with the statutory construction, which gives FDA broad authority with the words "shall expedite" and would limit and subordinate the overarching process of SECDEF requesting and FDA granting expedited approval to pre-existing mechanics only. Such a view of the text would subordinate the remainder of the non-exhaustive list of tools at § (b)(2) at FDA's disposal to support SECDEF's request to a framework referenced in a single subsection of this provision. Such a reading would be inconsistent with the text and its intent. If this is an area of statutory ambiguity in FDA's view, then the statute must be clarified by Congress.

D. P.L. 115-92 Directs Regular Meetings Between DoD and FDA at the Senior Leadership and Center Director Levels

In addition, there are two sections of P.L. 115-92 that direct DoD and FDA to engage in "enhanced collaboration and communication."[254] First, Section (b)(3)(A) requires a semi-annual meeting between DoD and FDA for "the purposes of conducting a full review of the relevant products in the Department of Defense portfolio."[255] Second, Section 1(b)(3)(B) requires quarterly DoD and CBER meetings "to discuss the development status of regenerative medicine advanced therapy, blood, and vaccine medical products and projects that are the highest priorities to the Department of Defense (which may include freeze dried plasma products and platelet alternatives)."[256] These meetings offer the hope of long-standing communication and collaboration between DoD and FDA. In addition, this statutorily directed communication and coordination forces both parties to improve their own end of the relationship. DoD must communicate with a "single voice" on its most urgent medical product priorities, and FDA, in turn, is now forced to give appropriate and sustained attention to DoD medical product development priorities.

E. The 2018 Memorandum of Understanding Implements P.L. 115-92

On November 2, 2018, DoD and FDA, led by DoD Principal Assistant Secretary of Defense for Health Affairs, Mr. Tom McCaffery, and Dr. Scott Gottlieb, Commissioner of Food and Drugs, met at the headquarters of the USAMRDC at Fort Detrick, Maryland, for the first semi-annual meeting between the agencies as required by P.L. 115-92. This semi-annual meeting included a complete overview of the DoD medical product priority list (the Priority List) and presentations to FDA senior leadership and Center directors. Importantly, the parties signed an MOU to implement "the framework for this Congressionally-directed collaboration between DoD and FDA[.]"[257]

The 2018 MOU included several goals, most of which are outlined in the P.L. 115-92 statute itself. However, the MOU sheds light on several areas of collaboration and clarification regarding the "enhanced engagement" relationship between the parties.

---

[254] *Id.* at § 1(b)(3).

[255] *Id.* at § 1(b)(3)(A).

[256] *Id.* at § 1(b)(3)(B).

[257] Memorandum of Understanding Concerning Coordination with the Food and Drug Administration Regarding Department of Defense Medical Product Development and Assessment, MOU 225-19-001 (May 2, 2020), https://www.fda.gov/about-fda/domestic-mous/mou-225-19-001 (last visited Apr. 15, 2023) [hereinafter MOU 225-19-001]. The author was an original drafter and negotiator of this MOU and was a participant and presenter at the November 2, 2018, meeting at Fort Detrick, Maryland.

First, the MOU clarifies that the goal is to focus on "facilitat[ing] access to medical products for use during military emergencies," to "[f]acilitate, through enhanced engagements, DoD's development of promising safe and effective medical products that are reasonably likely to address a life-threatening military emergency," and to "[f]acilitate communication of information related to the safety, efficacy and utilization of medical products in the DoD portfolio," which the MOU refers to as DoD's "medical product priorities" (MPPs).[258] The MOU outlines "*semi-annual*" meetings between senior DoD and FDA leadership to "facilitate enhanced collaboration and communication on DoD MPPs that are the highest priorities to DoD."[259] FDA may "clarify the DoD's actions necessary to support timely development of DoD MPPs" and "[c]larify FDA requirements applicable to MPPs that are being sponsored or otherwise supported or needed by DoD."[260] This includes product-specific engagement, but also FDA feedback on "enabling scientific tools, technologies, and regulatory science approaches" to facilitate DoD MPP availability.[261] And finally, the MOU includes important protections for industry partners' commercial confidential and trade secret information that is relevant to P.L. 115-92 interactions.[262] Primary to these protections is a robust letter of authorization (LOA) process, built largely on the model used for the 2013 Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) MOU, that allows sponsors to provide affirmative authorization for FDA or DoD to discuss open applications currently with FDA for DoD MPPs where those applications are not sponsored by DoD.[263]

Among the most significant contributions of this MOU is the forcing function requiring the development and annual presentation of the DoD Medical Product Priority List ("the Priority List" or "DoD Priority List").[264] As observed throughout this paper, there is often a "discontinuity" of effort across the vast DoD enterprise; however, this MOU organizes USAMRDC, JPEO-CBRND, the Joint Science and Technology Office (JSTO), the Defense Threat Reduction Agency (DTRA) and Defense Advanced Research Projects Agency (DARPA),[265] and many other DoD organizations that would be organized under the DoD charter creating the Medical Product Acceleration Committee (MPAC). The MPAC's purpose is:

---

[258] *Id.* at §§ I.a., I.b., I.e. MPPs are defined in the Preamble.

[259] *Id.* at § I.c.

[260] *Id.* at §§ I.h., I.i.

[261] *Id.* at § I.g.

[262] *Id.* at § I.j.

[263] Memorandum of Understanding Concerning Information-Sharing Exchanges Involving FDA Among Agencies Participating in the Public Health Emergency Medical Countermeasure Enterprise (PHEMCE) Offices and Agencies of the Department of Health and Human Services, MOU 225-13-0029 (Apr. 9, 2019), https://www.fda.gov/about-fda/domestic-mous/mou-225-13-0028 (regarding the creation of the PHEMCE). DoD is a signatory to the PHEMCE. In addition, a model authorization for industry is included as Exhibit B to the 2019 MOU, and USAMRDC lists this on its website for potential industry partners as a best practice to ensure it can use P.L. 115-92 when needed for a specific medical product development effort. *See Public Law (PL) 115-92*, U.S. ARMY MED. RSCH. & DEV. COMMAND: STAFF JUDGE ADVOCATE, https://mrdc.health.mil/index.cfm/about/jag/pl_115-92.

[264] MOU 225-19-001, *supra* note 257, at § IV.b.1.

[265] *Id.* at § III.

> [T]o manage the creation and maintenance of the DoD Priority List of MPPs that will be communicated to FDA, via the Assistant Secretary of Defense for Health Affairs (ASD(HA)), at the Semi-Annual and CBER Quarterly meetings required by the [P.L. 115-92] statute. The MPAC is intended to serve as the DoD enterprise-wide forum for discussions on which products are identified as DoD MPPs for the Priority List. The MPAC aims to achieve a DoD "one voice" approach envisioned by the statute.[266]

The DoD MPAC "one voice" approach is central to the creation of the DoD Priority List under P.L. 115-92 given the robust medical product portfolios of the Army, Navy, and Air Force—many of which are now under the larger DHA umbrella—but also the unique needs and contributions of DoD assets like the DoD Special Operations Command (SOCOM) (often the first users of emerging medical technology), the DoD Joint Staff Surgeon (JSS) (among the chief medical advisors to the Joint Staff), the Uniformed Services University of the Health Sciences (USU) (which trains DoD medical staff), and many others.

The MOU forces DoD assets onto the same page to develop and maintain the Priority List.[267] The Priority List is "intended to reflect the DoD-wide view on the most important and urgent medical product needs of military personnel that require increased interaction with FDA or elevation to the appropriate FDA Center Director and/or FDA Commissioner, as needed, consistent with the intent of P.L. 115-92."[268] The Priority List is organized by the type of support needed from FDA such as planning for an EUA, seeking expedited approval, and posing cross-cutting regulatory sciences questions.[269] The Priority List includes MPPs "ranked by their priority," in a "1-n" format, with "adjectival ratings," and "organized by the FDA center of jurisdiction."[270] Exhibit A to the MOU includes an example of "Model DoD Priority List Data Elements for DoD Medical Product Priorities (MPPs)" that explains DoD's methods for ranking MPPs for presentation to FDA.[271] The elements required for evaluation for and listing on the DoD Priority List include the product name, "applicant/sponsor," "proposed indication/use," "regulatory status," FDA Review Office/Division, DoD lead, and "DoD Priority Rank."[272] Importantly, Exhibit A to the MOU also provides DoD's thinking on how it would rank its MPPs as follows:

> DoD will evaluate and rank MPPs based on <u>need</u> (i.e., risk-to-mission of an unmet medical need and/or capability gap) and <u>feasibility</u> (i.e., is the product mature enough in the development pathway and capable of deployment to offer a significant improvement over current medical treatments), as well as describe whether the MPP will require emergency

---

266 *Public Law (PL) 115-92*, *supra* note 263.

267 MOU 225-19-001, *supra* note 257, at § IV.b.1.

268 *Id.* at § IV.b.1.b.

269 *Id.* at § IV.b.c.i–iii.

270 *Id.* at § IV.d.

271 *Id.* at Ex. A.

272 *Id.*

> use, accelerated management, or whether there is a cross-cutting regulatory science issue or some combination thereof.[273]

The MPAC creation of the Priority List will require judgements about relative priority among an incredibly vast list of DoD capability gaps. This will require DoD leadership saying "no" to less important and immature product development efforts in favor of ensuring the list is populated with the highest MPPs as intended by the statute and MOU. DoD overinclusion will simply dilute the limited resources FDA can bring to bear on the DoD portfolio even further.

While the MOU places the burden on DoD to "independently rank its MPPs" in terms of "need" and "feasibility," the MOU acknowledges that "FDA's input on the Priority List is valuable" and the parties may alter the priority rankings and use adjectival ratings to ensure fidelity in the DoD Priority List for presentation.[274] The DoD list is presented at the semi-annual DoD–FDA meeting under P.L. 115-92. However, it is important to note that nothing in P.L. 115-92 and this implementing MOU limits regular, non-Priority List regulatory interactions between DoD product developers or DoD collaborators and FDA.[275] The goal of the MPAC, however, is to ensure enterprise-wide situational awareness so that MPPs can get on the DoD Priority List efficiently and regular DoD medical product development is efficient and successful as possible.[276] In fact, the MPAC may rapidly add new countermeasures to the Priority List for presentation to FDA in response to a national security threat as it did with COVID-19 countermeasures, such as COVID convalescent plasma (CPP), remdesivir (Veklury®), and other products.

Importantly, the DoD–FDA interactions under this MOU are governed by protections of industry sponsor's information, careful respect of any provision of classified information between the parties, protections against conflicts of interest, and ensuring the integrity of FDA regulatory decision-making.[277] The MOU also establishes the Office of Counterterrorism and Emerging Threats (OCET) within the Office of the Chief Scientist in the Office of the Commissioner, and the Deputy Assistant Secretary of Defense for Health Readiness Policy and Oversight (HRP&O) as the "liaison officers" to facilitate the relationship of the parties under the MOU.[278]

F. P.L. 115-92 Enhanced Engagement between DoD and FDA is Working

P.L. 115-92 and the 2018 MOU framework for "enhanced engagement" is yielding substantial gains for military medical preparedness. In addition to the 2018 EUA for FFDP mentioned above, the enhanced engagement between DoD and FDA has in some measure yielded FDA licensure, approval, or clearance of the following products from the DoD Priority List:

---

[273] *Id.* at Ex. A, h.i. (emphasis in original).

[274] *Id.* at Ex. A., h.i.3.

[275] *Id.* at § IV.b.2.d.

[276] The MPAC operated under a draft charter since its creation in 2018. The MPAC charter was finalized late in 2022, however, has not been posted in any public forum at this time of this publication.

[277] MOU 225-19-001, *supra* note 257, at §§ V–VII.

[278] *Id.* at § IX.

- Arakoda® (tafenoquine) was approved by FDA on July 18, 2018, after 60 Degrees Pharmaceutical's submission of a 505(b)(1) NDA after receipt of Orphan Drug and Breakthrough Therapy designation;[279]
- RAFA's atropine Auto-Injector was FDA approved on July 9, 2018,[280] after the company's submission of a 505(b)(2) NDA for the prevention of status epilepticus, a significant health consequence of organophosphate nerve agent exposure;
- RECELL® received pre-market approval (PMA) from CDRH on September 18, 2018,[281] after Avita Medical Americas, LLC's PMA submission for its autologous harvesting device indicated for the treatment of burn wounds via Regenerative Epidermal Suspension. This product will be used by DoD in the treatment of battlefield burn wounds;
- Dsuvia® (sufentanil) was approved by FDA on November 18, 2018,[282] after a 505(b)(2) NDA submission. Acel Rx Pharmaceutical's sufentanil sublingual tablet 30 mcg, delivered via a single-dose applicator (SDA), will provide another option for battlefield pain management among the injured solider population. This product includes a risk evaluation and mitigation strategy (REMS) for controlling diversion and is only to be used in a medical care setting under the supervision of medical personnel;
- Intravenous Artesunate (IVAS) was FDA approved on May 26, 2020,[283] after Amivas, LLC's submission of a 505(b)(2) NDA, alongside orphan drug exclusivity and a tropical disease priority review voucher;
- Abbott's 510(k) for its i-Stat Alinity® rapid traumatic brain injury (TBI) field deployable plasma test was cleared in 2021[284] for the diagnosis of concussions by identifying blood markers in blood

---

279 U.S. FOOD & DRUG ADMIN., *Letter from Edward M. Cox, MD, MPH., Dir. Office of Antimicrobial Products Regarding NDA 210795 for Tafenoquine* (July 20, 2018), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/210795Orig1s000Ltr.pdf.

280 CTR. FOR DRUG EVALUATION & RESEARCH, *Letter from Billy Dunn, MD, Dir. Division of Neurology Office of Drug Evaluation I Regarding NDA 212319 for RAFA Atropine Auto-Injector* (July 9, 2018), https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/212319Orig1s000Approv.pdf.

281 U.S. FOOD & DRUG ADMIN., *Letter from Wilson W. Bryan, MD, Director Office of Tissues and Advanced Therapies Regarding BP 170122 for RECELL® Autologous Cell Harvesting Device* (Sept. 20, 2018), https://www.fda.gov/media/116379/download.

282 U.S. FOOD & DRUG ADMIN., *Letter from Sharon Hertz, MD Dir. Division of Anesthesia, Analgesia, and Addiction Products Regarding NDA 209128 for DSUVIA (sufentanil sublingual tablet)* (Nov. 2, 2018), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/209128Orig1s000Ltr.pdf.

283 U.S. FOOD & DRUG ADMIN., *Letter from John J. Farley, MD, MPH, Acting Dir. Office of Infectious Diseases Regarding NDA 213036 for Artesunate for Injection* (May 26, 2020), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2020/213036Orig1s000ltr.pdf.

284 U.S. FOOD & DRUG ADMIN., *Letter from Lea Carrington, Dir. Division of Immunology and Hematology Devices Regarding K201778 for i-STAT TBI Plasma Cartridge with the i-STAT Alinity System* (Jan. 8, 2021), https://www.accessdata.fda.gov/cdrh_docs/pdf20/K201778.pdf.

plasma and serum correlated to brain injury. This will help DoD diagnose concussions in warfighters suffering from blast injuries from improvised explosive devices (IED);

- Pfizer's tick-borne encephalitis (TBE) vaccine received BLA licensure from CBER on August 13, 2021,[285] to prevent TBE in soldiers stationed in eastern Europe;
- Kaleo, Inc's 505(b)(2) NDA approval for its Rapid Opioid Countermeasure System on February 28, 2022;[286]
- Rafa Laboratories's 505(b)(2) NDA for its midazolam auto-injector on August 8, 2022; [287] and
- Abbott's Alinity i TBI blood test was 510(k) cleared by FDA on March 2, 2023, which will provide clinicians with an objective way to quickly assess individuals with mild TBIs, also known as concussions.[288]

FDA maintains a full list of P.L. 115-92 accomplishments entitled, "Enhanced Engagements for Products Relevant to the Department of Defense (DoD)," which includes these and other product approvals.[289]

This DoD–FDA progress would not be possible without P.L. 115-92 and the incredible dedication of DoD and FDA staff that are committed to this collaboration. This list is reflective of the challenge facing military medicine: there is a constant need for battlefield pain solutions, wound-care, solutions for battlefield hemorrhage and blast injury, and CBRND countermeasures against nerve agent exposure and both naturally occurring and weaponized infectious disease. While one can celebrate this progress, the need for continued progress remains.

V. HOW CAN DOD AND FDA BUILD FOR FUTURE SUCCESS?

There are longstanding tensions between DoD's national security mission and FDA's role in protecting the public health. As this paper analyzes the historical relationship between the two agencies, the following becomes apparent: Federal law has increasingly subordinated DoD Command decision-making for use of investigational products to FDA's regulatory paradigm. The relationship between

---

285 U.S. FOOD & DRUG ADMIN., *Letter from Marion Gruber, PhD, Dir. Office of Vaccines Research and Review Regarding BLA 125740/0 for Tick-Borne Encephalitis Vaccine* (Aug. 13, 2021), https://www.fda.gov/media/151516/download.

286 U.S. FOOD & DRUG ADMIN., *Letter from Rigoberto Roca, MD, Dir. Division of Anesthesiology, Addiction Medicine and Pain Medicine Regarding NDA 215457/Original 1 for Naloxone Hydrochloride Injection* (Feb. 28, 2022), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/215457Orig1s000ltr.pdf.

287 U.S. FOOD & DRUG ADMIN., *Letter from Nick Kozauer, MD, Dir. Division of Neurology 2; Office of Neuroscience Regarding NDA 216359 for Midazolam Injection, 10 mg/0.7 mL, Autoinjector* (Aug. 8, 2022), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/216359Orig1s000ltr.pdf.

288 U.S. FOOD & DRUG ADMIN., *510(k) Premarket Notification to Abbott Laboratories* (Mar. 2, 2023), https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K223602.

289 U.S. FOOD & DRUG ADMIN., *Enhanced Engagements for Products Relevant to the Department of Defense* (Mar. 29, 2023), https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/fdadod-collaborations (last visited Apr. 27, 2023).

FDA's IND requirements at § 505(i) of the FDCA, its IND regulations at 21 C.F.R. § 312, and its informed consent regulations at 21 C.F.R. § 50.23(d) alongside DoD's requirements to comply with 10 U.S.C. § 1107 and § 1107(a) are "baked in"; the inter-dependence is here to stay. While P.L. 115-92 answered several of the long-standing areas of tension between DoD and FDA—namely, expedited approval, the expansion of the EUA, and a mandatory framework for enhanced engagement—remaining are several significant "red flags" in DoD–FDA relationship that should be resolved in peacetime to prepare for the real threat of future warfare. Even with the progress of DoD medical product priority approvals under P.L. 115-92, there remains significant headway needed for operational readiness.

A. Reinforce DoD's Development of FDA Approved, Licensed, or Cleared Medical Countermeasures with Operation Warp Speed-Infrastructure, Funding, and Focus

First, what was true in FDA's publication of the second Interim Rule for waivers of advanced informed consent in military emergencies in 1999 remains true today: the best option for both DoD and FDA is to expedite the approval, clearance, or authorization of needed DoD medical countermeasures to treat, prevent, or diagnose CBRN and non-CBRN threats and fill other critical medical capability gaps in DoD's medical portfolio. This is, of course, a long-standing challenge that is largely *outside* the control of FDA. The most important variable for DoD-medical product development is sustained, appropriated funding from Congress. Medical product development is a high-failure-rate endeavor; it can cost over $2.5 billion to develop a new small molecule drug product and over $3 billion for a new biologic.[290] It regularly takes eight failures to achieve a single medical product approval. Neither the USAMRDC nor the JPEO-CBRND receive the needed funding to propel their portfolios forward. Combined with the low appropriated dollars, the impact of DoD medical product development is diluted by the myriad DoD organizations that are spending funds in an uncoordinated, untargeted way. This results in elongated development timelines, mistakes in medical R&D, and other issues that impact cost, schedule, and performance.

DoD has a suite of medical R&D acquisition tools like research and prototype project other transaction agreements (OTAs) under 10 U.S.C. § 4026 (rOTAs) and § 4022 (pOTAs), respectively, experimental supply agreements under 10 U.S.C. § 4023, and a robust technology transfer (T2) program that can speed medical R&D. However, mature pharmaceutical and biotechnology companies are often reluctant to partner with DoD because the programs are a "black box," the points of entry are unclear, the unique DoD authorities are under-utilized, and the programs are under-funded. In addition, the hassle—real or perceived—of dealing with the Federal Acquisition Regulation (FAR) system is not worth the effort. There are significant opportunities to reinforce the DoD's capability and resolve some of these barriers to finding "win-win" R&D collaborations with emerging and accomplished pharmaceutical and biotechnology companies.

---

[290] *See* Joseph A. DiMasi, Henry G. Grabowski & Ronald W. Hansen, *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. HEALTH ECON. 20 (May 2016). For background on the calculations and methodology, see *Tufts CSDD's 2016 Cost Study*, TUFTS CTR. FOR THE STUDY OF DRUG DEV., https://csdd.tufts.edu/cost-study (last visited Dec. 17, 2022).

DoD's significant role in the federal COVID-19 response illustrates the potential that can be unlocked where there is dedicated resources and a focused, well-led infrastructure. Operation Warp Speed (OWS) was created in May 2020 with the mandate to "develop[], manufactur[e] and distribut[e] a COVID-19 vaccine for Americans by 2021."[291] OWS's success in rapidly developing, manufacturing, and distributing multiple FDA-authorized—and eventually licensed—vaccines was due in large measure to DoD leadership and MCM expertise, single-minded purpose, and flexible public-private partnership arrangements. The "ambitious timelines" required by the COVID-19 pandemic "required incisive leadership and firm funding commitments . . . [and] calculated risk-taking to shorten the time between development and manufacture[.]"[292] OWS investments focused on a range of vaccine platforms,[293] "underwriting in advance the production of promising candidates as clinical trials were being conducted to evaluate the efficacy and safety or each vaccines. These efforts ensure that missions of doses of promising vaccine candidates were ready upon" FDA authorization.[294] One of the most significant contributions of the OWS model was "the remarkable degree of institutional flexibility, allowing all agencies to work together pragmatically in a new institutional structure. This collaborative approach and lack of rigidity provides a powerful set of lessons on which to model . . . U.S. Government efforts."[295]

The DoD cannot sustain this level of "surge" engagement as displayed during its execution of over $83 billion in COVID-19 medical R&D and acquisition response.[296] Furthermore, DoD medical product development efforts must learn from the flexible but coordinated leadership model deployed during OWS and the rest of DoD's response to COVID-19. Distributed and de-centralized medical product development that is uncoordinated and without clear measurements for investment and evaluation will continue to impact DoD product development success. It is also obvious that funding for DoD FHP and MCM needs is paramount. A recent report on DoD's contribution to the COVID-19 pandemic underscores this point: "[a]dvances in malaria, Ebola and other hemorrhagic fevers, research establishing the mRNA platform; early success toward an HIV vaccine; protection against vector-borne diseases; and advanced in biosafety and biosecurity against especially dangerous pathogens have all resulted from the work of relatively unknown DoD laboratories and

---

[291] U.S. DEP'T OF HEALTH & HUM. SERVS., FACT SHEET: EXPLAINING OPERATION WARP SPEED (2020), https://www.nihb.org/covid-19/wp-content/uploads/2020/08/Fact-sheet-operation-warp-speed.pdf.

[292] THOMAS R. CULLISON & J. STEPHEN MORRISON, THE DEPARTMENT OF DEFENSE CONTRIBUTIONS TO PANDEMIC RESPONSE, A REPORT OF THE CSIS COMMISSION ON STRENGTHENING AMERICA'S HEALTH SECURITY 8 (May 2022), https://csis-website-prod.s3.amazonaws.com/s3fs-public/publication/220506_Cullison_DOD_Contributions_Pandemic.pdf?VersionId=6ZQ8sjVZi_u9X61SHfJghstd7iLI.nmo.

[293] U.S. GOV'T ACCOUNTABILITY OFF., GAO-21-319, OPERATION WARP SPEED: ACCELERATED COVID-19 VACCINE DEVELOPMENT STATUS AND EFFORTS TO ADDRESS MANUFACTURING CHALLENGES 10 (Feb. 2021), https://www.gao.gov/assets/gao-21-319.pdf [hereinafter GAO, OPERATION WARP SPEED].

[294] *Id.*

[295] *Id.*

[296] JPEO-CBRND supported the U.S. government's COVID-19 response by executing every OWS vaccine contract, all monoclonal antibody therapeutic contracts, acquisitions for diagnostics, enablers, personal protective equipment. DoD executed acquisitions for international vaccine donations and industrial base expansion, not to mention substantial research and development efforts. *See The JPEO's COVID-19 Support*, JOINT PROGRAM EXEC. OFF. FOR CHEM., BIOLOGICAL, RADIOLOGICAL & NUCLEAR DEF., https://www.jpeocbrnd.osd.mil/Coronavirus/ (last visited Apr. 16, 2023).

scientists," and "[n]ow is the moment to acknowledge these [DoD's] capabilities as vital national assets to be reinforced, funded, protected and deployed as needed for advancing a U.S. global health security strategy."[297]

Building on the success of OWS, DoD could create a centralized and organized medical product development agency that brings in the flexibilities displayed during OWS and the rest of DoD's significant contributions to the COVID-19 pandemic and avoid "business as usual" models. In addition, DoD must implement its own integrated technology readiness levels (TRLs) that are understood across the enterprise with FDA input on mapping these TRLs to the FDA regulatory process with specific focus on the unique risk–benefit calculus of the U.S. warfighter need.[298] As noted above, Congress should prioritize and protect innovative DoD medical R&D acquisition authorities that allow DoD to partner with non-traditional defense contractors,[299] and increase and sustain appropriated funding for DoD product development. Doing so would decrease disjointed and segmented product development and allow for freedom to negotiate "win-win" collaborations.

While the limitations on the current DoD medical product development model are evident, the fact remains that any use of an investigational medical product under an IND or an EUA in a wartime scenario will make it very difficult for DoD to comply fully with the important, but detailed terms of those regulatory requirements. The only way to avoid future post-Persian Gulf War-like scrutiny entirely is to develop and deploy FDA-approved, -licensed, or -cleared medical products. This is the best option for DoD, FDA, and the military personnel who deserve the very best FHP measures possible. It is incumbent upon Congress to reinforce the DoD medical product development enterprise and for DoD and FDA to utilize the expedited approval mechanism of P.L. 115-92 to deliver medical breakthroughs for the warfighter to reduce, to the maximum degree possible, the need for DoD to rely on the IND or EUA mechanism.

B. Medical Countermeasure Reciprocity and Military Use Only Designations Where Foreign-Approved Products are the only Available Countermeasures

In circumstances where there is no FDA-approved medical countermeasure for a CBRND threat or a threat specific to the military forces, DoD may continue to use expanded access INDs under 21 C.F.R. § 314 and pursue an EUA under § 564 of the FDCA for the use of investigational products. However, DoD regularly works with other North Atlantic Treaty Organization (NATO) allies on the development of medical countermeasures, and, in some cases, there are foreign approved products that are licensed by mature regulatory agencies that would fill the capability gap for U.S. military personnel. In many cases, the companies holding the foreign approvals have

---

[297] CULLISON & MORRISON, *supra* note 292, at 27.

[298] GAO, OPERATION WARP SPEED, *supra* note 293, at 16. *See also* U.S. GOV'T ACCOUNTABILITY OFF., GAO-22-105357, OTHER TRANSACTION AGREEMENTS: DOD CAN IMPROVE PLANNING FOR CONSORTIA AWARDS (Sept. 2022), https://www.gao.gov/assets/gao-22-105357.pdf.

[299] *See* U.S. GOV'T ACCOUNTABILITY OFF., GAO-22-104453, COVID-19: HHS AND DOD TRANSITIONED VACCINE RESPONSIBILITIES TO HHS BUT NEED TO ADDRESS OUTSTANDING ISSUES App'x II (Jan. 2022), https://www.gao.gov/assets/gao-22-104453.pdf (detailing the use of the broad agency announcement, other transaction agreements, commercial solutions openings, technology investment agreements, the Defense Production Act).

no incentive or interest to file an NDA or BLA with FDA because: 1) there is no market for the product in the United States, and 2) any filing with FDA could potentially disrupt their licensure in the foreign jurisdiction. In some cases, reciprocity among foreign regulatory jurisdictions and FDA for MCM approvals where the regulatory agencies are sophisticated would help to answer the challenge facing the U.S. warfighter. DoD already has international agreements with foreign countries on MCM funding priorities.[300] It should be possible for FDA to engage foreign regulatory bodies with a reciprocity plan for foreign-approved MCMs where there is no such product licensed or approved for that threat in the U.S. market.

If reciprocity cannot be achieved by FDA, Congress could allow a "military use only" designation[301]—analogous to an EUA—that is specific to foreign-approved products licensed by other nations' regulatory bodies where that organization is a member and compliant with International Council on Harmonization practices for drug development and manufacturing. This authorization would be for a limited time and only available where: 1) there is no alternative available in the United States, 2) there is a foreign approved drug or biologic that has been found safe and effective by an ICH member regulatory body, 3) that product is available to NATO allies, and 4) the product is intended for use primarily outside the United States.

C. Create a "Biowarfare Shield" Reserve Fund for DoD Medical Countermeasures

Throughout the DoD–FDA relationship, the lack of FDA-approved MCMs is the force that applies pressure to FDA's system to respond to DoD's unique needs. Solving MCM funding long-term would reduce the number of times the FDA regulatory paradigm is "pressure tested" for the use of investigational products for DoD's need. Some federal medical programs—particularly public health medical countermeasure programs—have a history of being funded on a multi-year basis, frequently with bipartisan, bicameral support. The Pandemic and All-Hazards Preparedness Act[302] and the Project BioShield Act[303] (BioShield) are two recent examples. Project BioShield targets material threats to the U.S. public health designated under § 319 of the Public Health Service Act (PHSA).[304] Although there are similarities in the mission, there is no analogous long-term funding mechanism and solution set targeting medical countermeasure development against DoD-validated CBRN threats facing national security threats. DoD pursues approval for different, and often more stringent, pre- and

---

[300] *See, e.g.*, U.S. DEP'T OF STATE, *Memorandum of Understanding between the United States Department of Defense, the Department of National Defense of Canada, the Secretary of State for Defense of the United Kingdom of Great Britain and Northern Ireland, of America, and the Department of Defense of Australia regarding Research, Development and Acquisition of Chemical, Biological and Radiological Defense Material* (June 1, 2000, as amended on Sept. 8, 2006), https://www.state.gov/wp-content/uploads/2019/02/00-601-Multilateral-Defense-R-and-D-Agmt-and-Amend.pdf.

[301] The terminology here is intentional. Military use "labeling" is always available and such approach depends on FDA's review of the safety and efficacy data supplied to its center of jurisdiction. In this case, the idea is not FDA conducting a duplicative review, but rather creating a narrow, specifically tailored solution where there are foreign MCMs approved by trustworthy regulatory bodies where FDA can designate a product for this use without a full application and review.

[302] Pandemic and All-Hazards Preparedness Act of Dec. 19, 2006, Pub. L. No. 109-417, 120 Stat. 2831.

[303] Act of July 21, 2004, Pub. L. No. 108-276, 116 Stat. 2212.

[304] 42 U.S.C. § 247d.

post-exposure indications to protect warfighters than are required for general public health response, which typically focus on post-exposure therapeutic treatment.

DoD medical R&D for CBRND threats is currently funded on an annual basis with two-year, defense-wide research, development, test, and evaluation (RDT&E) funding. This model and the repeated use of continuing resolutions puts DoD at a disadvantage because future funding often remains tenuous. This uncertainty makes strategic planning difficult for DoD and its collaborators because many of its projects develop over an extended period, sometimes spanning ten to fifteen years to achieve FDA licensure. Some contractors have cited this uncertainty as a reason why they have not pursued DoD research and development projects, as they are not able to justify the substantial investment of time and capital to shareholders absent a more secure source of funding. An innovative funding source for CBRN MCM development in the biowarfare space is a critical gap given a longer and more varied threat list than the material threat MCM list at § 319 of the PHSA, and the national security interest demands the harmonization of tools and strategies across the MCM enterprise.

Congress should create a multi-year BioWarfare Shield fund—analogous to the BioShield reserve fund—for MCM development targeting advanced research and development of DoD-validated CBRN threats. Doing so would not only provide stability to DoD's MCM mission, but would help attract greater external collaboration and funding, thereby reducing the ultimate financial demand on the taxpayer while ensuring that the American warfighter is equipped with the prophylactic and therapeutic tools needed on the modern battlefield.

D. The Defense Health Agency (DHA) Transition Must Prioritize FDA Regulatory Capabilities and Compliance

As mentioned above, Congress has consolidated the medical care delivery platforms of the component services into a single, integrated Defense Health Agency (DHA).[305] The recent incorporation of the USAMRDC into the DHA is adding a significant R&D element to an organization that is, at this point in its development, centered on healthcare delivery. These are related, but distinct platforms for operation. Importantly, the concern over "discontinuity of effort" that emerged from the post-Persian Gulf War was related to the disorganization of the medical R&D and the Surgeon General apparatus communicating with FDA, while being disconnected from the Combatant Commands who must then implement the IND or EUA approaches deemed appropriate. In the DHA transition, DoD authorities and structures erected to respond to this "discontinuity of effort" via the Surgeon General-led model are being changed in the most significant overhaul of how DoD does FDA-regulated medical product development since the late 1990s. Accordingly, DoD should: 1) pay specific attention to ensuring a continuity of the medical R&D regulatory expertise resident within the USAMRDC and JPEO-CBRND; 2) create a specific, one-star (preferably higher) or senior executive service (SES) DHA official, with medical training as a key qualification, to assume the legal responsibilities and risks associated with DoD-sponsored INDs and EUA to ensure full compliance with those terms throughout the Combatant Commands; and 3) make sure that lines of communications to leaders and soldiers are beta tested during peacetime to ensure that, in the "fog of war," these

[305] *See generally* 10 U.S.C. § 1072.

processes for communicating FDA compliance information are "second nature" for DoD enterprise.

In addition, while the DHA statutory requirements moved USAMRDC into the DHA fold, the U.S. Army will retain the JPEO-CBRND and several other elements undertaking FDA-regulated medical product development. If this is to be a true consolidation, it will require difficult decisions to put these medical R&D elements under a single, DoD-level parent. Without this, DoD organization responsible for FHP—USAMRDC under DODI 6200.02—will be disconnected from the primary MCM product developer, the Army's JPEO-CBRND. While good professionals at these organizations will certainly continue to be the "glue" that holds the enterprise together, the organizational structure fundamentally impacts organizational outcomes. DHA should assume responsibility for all medical R&D elements with a specific goal to align them under MEDCOM-like structure led, perhaps not by the Surgeon General of the Army, but likely the Joint Staff Surgeon (JSS) in the DHA. Consolidation of R&D resources coupled with strong FDA compliance functionality will ensure the highest level of fidelity to FDA requirements for both medical R&D and FHP. Any discontinuity in DoD's FDA regulatory compliance will be a significant setback for DoD medicine.

E. Build Operational Testing into DoD's Medical Product Acceleration Committee (MPAC) Model to Ensure Readiness for IND and EUA Compliance During Combat Operations

As the Persian Gulf War experience shows, DoD could struggle with regulatory compliance in the areas of informed consent, provision of product fact sheets, adverse event reporting, product accountability and destruction, and medical record keeping. Even though Congress has expanded the tools for the use of investigational products via the expanded access IND program under 21 C.F.R. § 312 or an EUA under § 564 of the FDCA, those terms could nevertheless present a challenge in a live-fire conflict.

For example, while the EUA for FFDP has been sufficient for the Special Operations Command (SOCOM) mission, a full-scale operation would require compliance with the terms of the authorization, the following of which could prove difficult:

> (1) "[s]ignificant excursions from the labeled storage conditions should be documented to the extent practicable given the circumstances of an emergency,"[306]
>
> (2) "inventory control,"[307]
>
> (3) "DoD will make available to applicable DoD components through applicable DoD communication channels and procedures the authorized Fact Sheet for U.S. Military Medical Personnel, the authorized Fact Sheet for Recipients, and any other Fact Sheets that FDA may authorize, as well as any authorized amendments thereto. U.S. military forces administering the authorized French FDP will ensure that the authorized Fact Sheet for

---

[306] U.S. FOOD & DRUG ADMIN., *Letter from Robert E. Miller, PhD, Senior Regulatory Affairs Advisor, Office of Regulated Activities, Dep't of the Army* 6 (July 9, 2018), https://www.fda.gov/media/114282/download.

[307] *Id.* at 7.

> Recipients has been made available to U.S. military forces that receive French FDP through appropriate means, to the extent feasible given the emergency circumstances. Under exigent circumstances, other appropriate means for disseminating these Fact Sheets may be used,"[308] and
>
> (4) "DoD will inform applicable DoD components about the need to have a process in place for performing adverse event monitoring and compliance activities designed to ensure that adverse events and all medication errors associated with the use of the authorized French FDP are reported to FDA, to the extent practicable given emergency circumstances, as follows: complete the MedWatch FDA Form 3500."[309]

DoD's MPAC could develop an operational element that can run "tabletop" simulations with the COCOMs to ensure that DoD can execute the IND or EUA program at a high level under the stresses of military combat. DoD would invite FDA Center leadership to participate via detail in the MPAC operational testing process to provide insight and counsel on how to institute the requirements of the IND or EUA. Placing FDA staff on the MPAC for this purpose would also eliminate an "us vs. them" mentality in working to implement critical programs. While this may not translate to the battlefield in all circumstances, simulating the "playbook" would help to ensure FDA regulatory compliance should the need to use investigational products become necessary in a future fight.

F. Develop Additional Regulatory Incentives—Like Priority Review Vouchers—to Propel Countermeasure Development

DoD medical product development is challenging given that DoD's purchase power alone is not often sufficient to ensure a return-on-investment for a commercial partner. Accordingly, DoD will often prioritize "dual use" technology that can be used for both DoD and the commercial marketplace. Doing so ensures a broader market for the medical product and, thereby, a more sustainable long-term acquisition partner to supply that medical product to DoD. Given the DoD market is often small, there are "push and pull" incentives that are available to help in developing medical products for the unique medical needs of the warfighter. Several of these incentives have been functioning well. For example, priority review voucher (PRV) programs created a transferable asset for companies that achieve FDA approval or licensure of a novel drug or biologic where the approval satisfied certain statutory criteria. Congress created PRV programs to incentivize drug development in under-served patient populations (e.g., tropical diseases, rare pediatric diseases, and material threat medical countermeasures). PRVs function by incentivizing novel drug approvals for one of these three statutory purposes. At a qualifying approval, FDA then awards a PRV to the sponsor of the NDA or BLA. At this point, the company receiving the PRV may either 1) use it in the future to guarantee priority review of a subsequent drug application (shortening FDA PDUFA review timeline from ten months to six

---

[308] *Id.* § IV. There is a footnote here acknowledging the difficulty of an operational environment for full compliance with this term; however, a full approval would obviate the need for DoD to comply with a provision that both parties acknowledge will be incredibly difficult in a live-fire war. *Id.* at 7 n.13.

[309] *Id.* at 8; this element includes adverse event follow-up.

months[310]), or 2) sell to a third party for their future use on an application to the agency for the reduced review time. PRVs have sold for between $53 million and $350 million, providing the awardee an immediate return-on-investment for the substantial investment in R&D required for drug development.[311]

The tropical disease priority review voucher program was created by the Food and Drug Administration Amendments Act of 2007 by adding § 524(a) (21 U.S.C. § 360n) to the FDCA.[312] This program allows for a voucher to be awarded for approval of applications for drugs to treat or prevent certain statutorily enumerated tropical diseases (e.g., malaria, dengue, filovirus, zika virus) or "other infectious disease for which there is no significant market in developed nations and that disproportionately affects poor and marginalized populations, designated *by order* of the Secretary."[313] The tropical disease PRV program is a permanent statutory feature; it does not have a sunset date. As described above, it has contributed to the approval of several DoD-led countermeasures against malaria, such as intravenous artesunate and tafenoquine.

In addition, the 21st Century Cures Act[314] added a PRV program targeted towards the development of "material threat medical countermeasures." The statute defines a "material treatment medical countermeasure application" as a:

> human drug application intended for use: to prevent, or treat harm from a biological, chemical, radiological, or nuclear agent identified as a material threat under §319F–2(c)(2)(A)(ii) of the Public Health Service Act; or to mitigate, prevent, or treat harm from a condition that may result in adverse health consequences or death and may be caused by administering a drug or biological product against such agent.[315]

Under § 319F–2(c)(2)(A)(ii) of the PHSA, agents are identified as a "material threat" by the U.S. Department of Homeland Security (DHS) in consultation with the Secretary of HHS and the heads of other agencies as appropriate, on an ongoing basis

---

[310] *See* U.S. FOOD & DRUG ADMIN., PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2023 THROUGH 2027 at 9, https://www.fda.gov/media/151712/download (last visited June 22, 2023).

[311] The literature includes multiple perspectives associated with the merits of the PRV programs. *See, e.g.*, Oulu Wang, *Buying and Selling Prioritized Regulatory Review: The Market for Priority Review Vouchers as Quasi-Intellectual Property*, 73 FOOD & DRUG L.J. 383 (2018), https://www.fdli.org/wp-content/uploads/2018/09/FDLI-Journal-73-3-Wang.pdf (taking the position that another decade is needed to fully evaluate the merits of the programs). *See also* Kyle Wamstad, *Priority Review Vouchers—A Piece of the Incentive Puzzle*, 14 VA. J.L. & TECH. 127 (2009), https://www.vjolt.org/volume-14 ("The social value of having a treatment for a neglected disease is compounded by expedited access to a blockbuster drug in developed economies. Interestingly, the same disjunction between economic and social value that requires non-patent mechanisms to bridge the gap in incentives also allows for the possibility that a priority review voucher could work."); Aaron S. Kesselheim, *Drug Development for Neglected Diseases—The Trouble with FDA Review Vouchers*, 359 NEW ENG. J. MED. 1981, 1981 (2008), https://www.nejm.org/doi/full/10.1056/NEJMp0806684 ("represent an inefficient and potentially dangerous way of encouraging research").

[312] Act of Sept. 27, 2007, Pub. L. No. 110–85, title XI, § 1102, 121 Stat. 972.

[313] 21 U.S.C. § 360n(a)(3)(s).

[314] Act of Dec. 13, 2016, Pub. L. No. 114-255, 130 Stat. 1033.

[315] Section 3086 of the 21st Century Cures Act (Pub. L. 114-255) titled "Encouraging Treatments for Agents that Present a National Security Threat," added section 565A to the Federal Food, Drug, and Cosmetic Act. 21 U.S.C. § 360bbb-4a, June 25, 1938, ch. 675, § 565A, as added Pub. L. No. 114–255, div. A, title III, § 3086, Dec. 13, 2016, 130 Stat. 1144; Pub. L. No. 117–9, § 1(a)(5), Apr. 23, 2021, 135 Stat. 258.

by "assessing current and emerging threats of chemical, biological, radiological, and nuclear agents; and determining which of such agents present a material threat against the United States population sufficient to affect national security."[316]

The first material threat medical countermeasure (MTMCM) PRV was awarded to SIGA Technologies in 2018 for achieving the approval of the first treatment for smallpox, TPOXX®.[317] This statute also directly contributed to FDA approval of Gilead's Veklury® (remdesivir), which was being developed in collaboration with DoD for the treatment of filoviruses since 2016. Although there is a limited U.S. market for filovirus medications, filoviruses were a "voucherable" target under the tropical disease PRV program, which enhanced the business case for development of the product. Largely due to this development for a filovirus indication, the product was mature enough to be the first fully FDA-licensed countermeasure against SARS-CoV-2 in the COVID-19 pandemic. Gilead was awarded a MTMCM PRV for Veklury® in 2020.[318]

Importantly, the MTMCM PRV program is expired on October 1, 2023.The Senate HELP Committee recently included in its managers amendment to the Pandemic and All-Hazards Preparedness and Response Act (PAHPA) section 601, "Medical Countermeasure Priority Review Voucher," which would extend the program by five years.[319] Including the reauthorization of the MTMCM PRV program in the PAHPA reauthorization is important because both programs deal with preparedness for public health and national security emergencies. This effort builds on the substantial interest from Senate HELP and DoD. The Senate HELP Committee's recent discussion draft included for PAHPA reauthorization also included a proposal to extend the MTMCM PRV program by five years.[320] The Administration—with DoD and FDA support—had earlier proposed an amendment to section 565A of the FDCA (21 U.S.C. § 360bbb-4a) to extend the MTMCM PRV program through October 1, 2029. This proposal was submitted to Congress on May 6, 2022, as an official legislative proposal of the Biden Administration.[321]Another recent Senate

---

316 42 U.S.C. § 247d-6b(a)(2)(A).

317 *See SIGA Announces Priority Review Voucher Transaction Totaling $80 Million*, SIGA TECHNOLOGIES (Nov. 1, 2018), https://investor.siga.com/news-releases/news-release-details/siga-announces-priority-review-voucher-transaction-totaling-80 (last visited Dec. 18, 2022).

318 U.S. Food & Drug Admin., Press Release, FDA Approves First Treatment for COVID-19 (Oct. 22, 2020), https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-covid-19 (last visited Dec. 18, 2022). Note, the PRV was awarded for the COVID-19 indication, and not filovirus.

319 *See* David Lim, *Sanders, Cassidy Strike Deal on PAHPA*, POLITICOPRO (July 18, 2023), https://subscriber.politicopro.com/article/2023/07/sanders-cassidy-strike-deal-on-pahpa-00106819?source=email; The "Manager's Amendment" cited in this article is available at: https://subscriber.politicopro.com/f/?id=00000189-69b3-d579-a38b-7bf7874e0000&source=email.

320 *See* U.S. Senate Comm. on Health, Educ., Labor & Pensions, Press Release, NEWS: Senate HELP Committee Release Staff Bipartisan Discussion Draft Legislation to Reauthorize the Pandemic and All-Hazards Preparedness Act (July 3, 2023), https://www.help.senate.gov/chair/newsroom/press/news-senate-help-committee-release-staff-bipartisan-discussion-draft-legislation-to-reauthorize-the-pandemic-and-all-hazards-preparedness-act. The MTMCM PRV extension is referenced at Subtitle B, proposed Section 611, "Priority Review to Encourage Treatments for Agents that Present National Security Threats," at pages 77–80, available here: https://www.help.senate.gov/imo/media/doc/pahpa_discussion_draft.pdf.

321 *See* May 6, 2022 Letter to Speaker of the House Nancy Pelosi and May 6, 2022, Letter to President of the Senate, Senator Kamila Harris, from Acting Director of the Office of Management and Budget (OMB), Thomas J. Macinelli sharing the material threat medical countermeasure PRV extension proposal as part of the legislative package for the National Defense Authorization Act of 2023. The full set of

proposal outside of PAHPA reauthorization, S. 1122, entitled "Prioritizing Medical Countermeasures for National Security Act of 2023," was introduced by Senator Joni Ernst (R-IA) on March 30, 2023.[322] This proposal mirrors the larger DoD FY23 NDAA proposal to create a stronger role for DoD in the creation of the material threat list.

This momentum is promising. However, even the DoD proposal and S. 1122 reflect DoD's compromise position. A five- or six-year extension is insufficient for industry to rely on the PRV program being active at the time when many products currently in development will be licensed or approved. The current approach limits the power of the incentive to reach further "upstream" in a company's pipeline. To achieve the full potential of the PRV, the MTMCM PRV program should be a *permanent* incentive with a *publicly available* material threat list. These are both features of the successful tropical disease PRV program.[323] Furthermore, having DoD input is essential. DoD's need to protect soldiers against weaponized biowarfare threats go beyond the current material threat determinations made by DHS under § 319 of the PHSA. DoD does not have input into these determinations and, as such, its needs are not sufficiently met with the current framework

Incentives like the PRV programs are critical to spur DoD medical product development. The "push" and "pull" of these incentives bring collaborators into this product development space and incentivize them to stay engaged through FDA licensure. Other suggestions have been raised, such as wild card marketing exclusivity,[324] prize competitions for the first approval for a given threat, additional patent term restoration for MCMs, and tax incentives that would offset the high cost of MCM R&D for private product developers.[325] These ideas merit further analysis and consideration to solve this difficult challenge.

G. Clarify DoD Authorities Connected to FDA Regulatory Paradigm

There are several statutes that could be clarified in order to improve DoD and FDA's relationship. First, 10 U.S.C. § 1107 does not have definitions to "request" or "require" in its notice provision, which regularly challenges DoD in evaluating potential off-label uses of medical products. For example, publication of updates to clinical practice guidelines (CPGs) are regularly scrutinized under this statute, even though the statute was never intended to regulate the practice of medicine in DoD military treatment facilities. It would be an advantage to have these terms defined to explicitly carve out

---

proposals is available from the Office of Legislative Counsel at https://ogc.osd.mil/Portals/99/OLC%20FY%202023%20Proposals/6May2022Proposals.pdf?ver=3b5kPGnN3eKj8s7ro8Mt4g%3d%3d (last visited Dec. 18, 2022); *see also* DoD's FY24 NDAA proposal, DoD Proposal, "Extension of Medical Countermeasure Priority Review Voucher Program," submitted to Congress in fourth package of legislative proposals for inclusion in the NDAA for FY24 on April 14, 2023, pp. 123–26, available at: https://ogc.osd.mil/Portals/99/OLC%20FY%202024%20Proposals/14Apr2023Proposals%20(Corrected).pdf?ver=ld vHjetgWR0p7njYjYY1SA%3d%3d. The reader should know that the author was principally involved in drafting these proposals for DoD.

[322] Prioritizing Medical Countermeasures for National Security Act of 2023, S. 1122, 118th Cong. (2023), https://www.congress.gov/118/bills/s1122/BILLS-118s1122is.pdf (sponsored by Sen. Joni Ernst (R-IA)).

[323] *Tropical Disease Priority Review Voucher Program*, U.S. FOOD & DRUG ADMIN. (July 15, 2020), https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/tropical-disease-priority-review-voucher-program (last visited Apr. 3, 2023).

[324] Daniel A. Kracov, *Preparing for Disease X*, 76 FOOD & DRUG L.J. 177, 196 (2021).

[325] *Id.*

the practice of medicine as well as other regular administrative issuances that are not compelling, using SECDEF's authority, that a soldier take an unapproved or off-label use of a medical product.

Another area of statutory confusion between DoD and FDA involves the EUA "option to refuse" in the public health context under § 564 of the FDCA and how that language functions in the military context under 10 U.S.C. § 1107a.[326] Even before COVID-19, FDA's 2017 EUA Guidance was imprecise as it relates to the various situations where "the option to accept or refuse" may or may not be a condition of an EUA.[327] The analysis of the 10 U.S.C. § 1107a Presidential waiver of the "option to accept or refuse" is straightforward according to the recent Office of Legal Counsel (OLC) EUA opinion;[328] however, rendering the inclusion of the "option" as *information only* outside the military context[329] raises a number of questions: should a product under an EUA ever become mandatory? If the "option" is informational only, does it mean that FDA lacks authority to issue a mandatory EUA for public health purposes? In the larger context of the FDCA with its requirements for informed consent under the IND or IDE regulations and acknowledging that EUA is *not* full approval, did the OLC opinion render this "option to refuse" meaningless in a way that a patient now finds it harder to distinguish between an EUA product, an investigational product under an IND or IDE, and a licensed product? And how, exactly, does this impact future vaccine mandates under EUA or full licensure for DoD? With ongoing litigation on this topic and congressional interest high, this requires additional analysis and greater legislative clarity.[330]

---

[326] *See supra* Section III.D at n. 206.

[327] *Compare* Casciotti, *supra* note 101 ("[i]ndeed there may be circumstances, such as first responders or to deal with a highly communicable disease, in which it may be appropriate not to have an option to refuse for selected groups pf people, but instead have a mandatory program. I think it would be wise to keep all options on the table."), *with* FDA, EUA MEDICAL PRODUCTS AND RELATED AUTHORITIES, *supra* note 209, at 24 ("informed to the extent practicable given the applicable circumstances"); *and*, in the COVID-19 vaccine mandate context, *Whether Section 564 of the Food, Drug and Cosmetic Act Prohibits Entities from Requiring the Use of a Vaccine Subject to Emergency Use Authorization*, 45 Op. O.L.C. 7–9 (2021) (Memorandum Opinion for the Deputy Counsel to the President, from Dawn Johnsen, Acting Assistant Attorney General), https://www.justice.gov/olc/file/1415446/download ("DoD informs us that it has understood section 1107a to mean that DoD may not require service members to take an EUA product that is subject to the condition regarding the option to refuse, unless the President exercises the waiver authority constraint in Section 1107a . . . DoD is required to provide service members with the specified notification [Fact Sheet containing the "its your choice"] unless the President waives the condition pursuant to 10 U.S.C. § 1107a . . . DoD should seek a presidential waiver before it imposes a vaccination requirement.") [hereinafter OLC EUA Opinion].

[328] OLC EUA Opinion, *supra* note 327, at 16–18. *See also supra* Section III.D, at n. 206.

[329] OLC EUA Opinion, *supra* note 327, at 7–9.

[330] While not the subject of this paper, the issue of use and mandates of authorized or licensed vaccines continues to provoke legal challenges. *See* U.S. Navy Seals 1-26 et al. v. Biden, No. 22-10077 (5th Cir. Feb. 28, 2022) (Fifth Circuit denied defendants' motion for a partial stay of the district court's preliminary injunction enjoining the government from enforcing certain COVID-19 vaccination requirements against thirty-five Navy special warfare personnel and prohibiting any adverse actions based on their religious accommodation requests). *See also* James M. Inhofe National Defense Authorization Act for Fiscal Year 2023, Pub. L. No. 117-263, §§ 524–525 (Dec. 23, 2022) (rescinding the COVID vaccine mandate); Kevin McGill, *Military's COVID-19 Vaccine Mandate Lifted, but Litigation Lingers*, MIL. TIMES (Feb. 6, 2023), https://www.militarytimes.com/news/your-military/2023/02/06/militarys-covid-19-vaccine-mandate-lifted-but-litigation-lingers/.

Finally, to the degree that P.L. 115-92 is unclear on FDA having the authority to expedite the review and approval of DoD medical product applications, this should be clarified by statutory amendment to ensure clarity that FDA may so act. As discussed above, the offer of breakthrough therapy designation was a key element of the negotiations that led to P.L. 115-92, but DoD should not be limited to expedited approval mechanisms that pre-dated the enhanced engagement statute. In addition, while it has been the regular practice of both DoD and FDA to include CDER and CDRH in all required CBER quarterly meetings, it would strengthen the relationship to ensure that CDER and CDRH staff are also mandatory participants in P.L. 115-92 meetings. These minor technical amendments to P.L. 115-92 could strengthen the relationship between DoD and FDA.

VI. CONCLUSION

This paper illustrates the evolution of DoD's FHP and medical R&D model from a Surgeon General-led endeavor under military command and control to a process substantially dependent on FDA and its regulatory authorities. From the passing of the Kefauver–Harris efficacy amendments in 1962 to the passage of P.L. 115-92, we see tension between DoD's national security mission and FDA's public health mission. While there have been monumental successes in DoD's medical product development, DoD military operations have an uneven FDA compliance record, highlighted by the Gulf War experience. However, the record outlined above shows that DoD has aimed to place compliance with FDA's regulatory paradigm among its highest priorities during peacetime operations. Congress forced legislative constraints like 10 U.S.C. § 1107 and § 1107a on DoD. However, the "fog of war" and ultimate medical readiness of the U.S. forces will continue to necessitate unique regulatory solutions given the pressure and strain warfare can place on DoD's ability to fully comply with all elements of FDA's regulatory framework. The creation of the DHA and the movement of the USAMRDC—and hopefully other DoD medical R&D organizations—into this new organization gives DoD the opportunity to update its legal authorities to reflect the best approaches to managing its FDA regulatory compliance activities. DHA can build on the Operation Warp Speed model—centralized, flat leadership with prioritized investments with non-standard approaches—to facilitate FDA-regulated medical product development. Both in updating its authorities and prioritizing FDA compliance in its leadership structure, DHA has the ability—perhaps "tabletop" simulations via DoD's Medical Product Acceleration Committee—to shape future battlefield success and FDA compliance.

This paper reflects that P.L. 115-92 created a new era of collaboration between DoD and FDA. This statute resolved long-standing challenges of a limited EUA authority for DoD and created an expedited approval mechanism for DoD that was long overdue. If sustained, this collaboration and communication will yield improved battlefield medical care for our nation's warfighters. P.L. 115-92 is a "win-win" for both DoD and FDA as well as a "win-win" for military medicine and global health. The P.L. 115-92 statutorily directed communication and coordination forces both parties to improve their own end of this relationship. These provisions require DoD to communicate with a "single voice" on its most urgent medical product priorities. In turn, FDA is now forced to give appropriate and sustained attention to DoD medical product development priorities. Among the next steps in this relationship is the ability for DoD to identify capability gaps that could be filled by foreign-approved products

for which FDA may issue a military use designation or afford reciprocity to speed those products to the warfighter in limited circumstances. Creating new authorities to this end and clarifying any remaining interpretive issues with P.L. 115-92 will also improve the interagency collaboration and spur mission success.

Given the unique risk–benefit calculus applicable to battlefield situations and the urgent need for CBRN medical countermeasures, there will likely continue to be tension between how best to meet the medical needs of the warfighter and how DoD should comply with FDA regulatory requirements. Increased funding and dedicated programs like "BioWarfare Shield" and incentive programs like priority review vouchers, wild card exclusivity, and increased patent term restoration could lead to more products approved to meet DoD's capability gaps, reducing the pressure and strain that DoD's unique demands place on FDA's regulatory paradigm. As demonstrated above, the DoD–FDA relationship needs to continually evolve to meet the unique and novel national security challenges facing the nation. Armed with lessons from history and opportunities for continual improvement, the DoD–FDA relationship will continue to balance the need for success on the battlefield with the need to ensure safe and effective medical products are approved, licensed, cleared, or authorized for the unique medical needs of the warfighter. With a new statutory framework and interagency success in multiple key product development areas as a result, there is significant cause for optimism that DoD and FDA will continue partnering to achieve the best medical product outcomes of the soldiers who sacrifice so much to protect our nation.