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THESIS

THE MORAL OBLIGATION TO EXPLORE THE MILITARY USE OF PERFORMANCE-ENHANCING SUPPLEMENTS AND DRUGS

by

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Special Operations Forces (SOF) are closely involved with many of the military's developments to maintain a high readiness force. SOF emphasizes proper training and education, high physical and mental fitness, and proper moral awareness. In that respect, performance enhancing supplements or drugs (PES/D) can make a major contribution and be a next step in military development. But what is the impact of such a step? Accepting or even experimenting with PES/Ds will have far-reaching effects and raises medical, legal, and above all, ethical concerns.

In light of this, our research question is: "Could conditions be met such that it is morally justifiable to allow Special Operations Forces to use performance-enhancing supplements or drugs to improve individual capabilities, develop greater resiliency, and expand the overall performance of SOF units and, if so, what are the implications?"

To answer this question, this thesis reviews scholarly literature on ethics and history of military's use of drugs, drug and supplement factsheets, and survey of SOF members who would be the potential "test systems."

We contend that there *are* ethically permissible uses for PES/Ds within the military, and by SOF, in particular. Moreover, our examination of a sampling of SOF attitudes toward such use likewise supports our conclusion. Based on our findings, we assess that the broader SOF community should be open and willing to engage in the research and testing necessary to see whether such a conclusion deserves to stand. To that end, the type of PES/Ds, the extent of their use, and the conditions under which they would be utilized need to be explored through more rigorous testing—under safe but realistic conditions.

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ABSTRACT

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LIST OF ACRONYMS AND ABBREVIATIONS

AAS	Anabolic-Androgenic Steroids
ADHD	Attention Deficit And Hyperactivity Disorder
AMPA	α-amino-3hydroxy-5methyl-4isooxalopropionic Acid
CCMO	Central Committee On Research Involving Human Subjects (Dutch to English translation)
CFR	Code of Federal Regulation
CNS	Central Nervous System
DODD	Department of Defense Directive
EPO	Endogenous Erythropoietin
FDA	Federal Drug Administration
GMO	Genetically Modified Organisms
HBOC	Hemoglobin-Based Oxygen Carriers
IGF-1	Insulin Growth Factor-1
IHE	Intermittent Hypoxic Exposure
PES/D	Performance Enhancement Supplements or Drugs
POTFF	Preservation of The Force and Family
rHuEPO	Erythropoietin
SOF	Special Operations forces
Sr. NCO	Senior Non-Commissioned Officers
THOR3	Tactical Human Optimization Rapid Rehabilitation and Reconditioning
UCMJ	Uniformed Code Of Military Justice
USARIEM	U.S. Army Research Institute of Environmental Medicine
USSOCOM	U.S. Special Operations Command
VROM	Ministry of Housing, Spatial Planning, and The Environment (Dutch to English translation)

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EXECUTIVE SUMMARY

Optimizing military performance by improving the mental and physical capabilities of soldiers features prominently in military development. Performance enhancing supplements or drugs (PES/D) can play an important role in this process. PES/Ds have the potential to make soldiers stronger, healthier, more cognitively adaptable, more resilient, and less prone to injury. In fact, PES/Ds even have the ability to push the boundaries of standard human limitations. But such supplements and drugs bring a host of risks and possible pitfalls. Are the potential gains that PES/Ds offer worth the risks of their use? If we consider times when the benefits of enhanced performance enabled by PES/Ds outweigh the risks, then it is worth exploring conditions when the risks are justifiable.

Use of or experimentation with PES/Ds inevitably raises medical, legal, and above all, ethical concerns. When examining the usefulness and the corollary moral dilemma posed by PES/Ds it is necessary to understand what is acceptable, what is not, and why. We must understand the medical and legal implications, as well as the moral responsibilities, and we must take into account the soldier's view surrounding military use of PES/Ds.

As "the tip of the spear," Special Operations Forces (SOF) are closely involved with many of the military's developments to maintain a high readiness force. As such, SOF emphasizes proper training and education, and high physical and mental standards. In that respect, performance enhancing supplements or drugs can make a major contribution and be a next step in military development. Consequently, SOF provides an appropriate opportunity to explore the ethical considerations for the use of PES/Ds.

In light of this, our research question is: "Could conditions be met such that it is morally justifiable to allow Special Operations Forces to use performance-enhancing supplements or drugs to improve individual capabilities, develop greater resiliency, and expand the overall performance of SOF units and, if so, what are the implications?"

To answer this question, this thesis reviews scholarly literature on ethics and history of military's use of drugs, drug and supplement factsheets, and survey of SOF members who would be the potential "test systems."

We contend that there are certain conditions, either for the potential direct benefit to the soldier or to mission success, in which it is morally justifiable to use PES/Ds, and there is a moral obligation to explore PES/Ds to understand the potential harm such use could bring about. Moreover, our examination of a sampling of SOF attitudes toward such use likewise supports our conclusion. Based on our findings, we assess that the broader SOF community should be open and willing to engage in the research and testing necessary to see whether such a conclusion deserves to stand. To that end, the type of PES/Ds, the extent of their use, and the conditions under which they would be utilized need to be explored through more rigorous testing—under safe but realistic conditions.

I. INTRODUCTION

Trending global security risks such as violent extremism, failed and failing states, increased competition for resources, changes in political climates, and shifts in the global balance of power will dictate why, where, and how military forces engage in future conflicts. These rapid changes make it increasingly difficult to predict and prepare for the next conflict. Most militaries aim to maintain a high readiness force or fill capability gaps by focusing on technological improvements or adjustments in training and education. Many improvements involve advances in weaponry, developing sophisticated and integrated communications systems, improving protective equipment that is both stronger and lighter weight, and technologies that make it easier, safer, and less resource intensive to experiment with tactics and techniques. These endeavors all aim to improve military performance and, to some extent, compensate for the inherent mental and physical limitations of humans.

But, what about our most precious resource: human capital? How much research is conducted to enhance the human being operating the equipment and conducting the mission? As of now, the individual soldier is limited to his natural biological abilities, and it seems that in many scenarios the operator is often the weakest link. So why not improve the weakest link? Why not boost both the cognitive and the physical capabilities of the human soldier using performance-enhancing supplements or drugs (PES/D)? Such improvements could ultimately increase mission success while providing valuable risk mitigation relating to stress, fatigue, injury, illness, and psychological damage.

Human performance enhancement sounds appealing and maybe even seems the most logical move for the militaries of tomorrow. But what are the possible impacts of administering PES/Ds? Accepting or even experimenting with PES/Ds will have far-reaching effects that may not all be beneficial. History offers numerous examples when militaries fueled their warfighters with substances to improve performance in battle with both positive and negative outcomes. However, in general, militaries have little experience with officially administrated use of PES/Ds and are reluctant to conduct formal research in this area today. Although attention has been paid to the medical and legal aspects of using or experimenting with PES/Ds, the moral boundaries for setting up enhancement programs based on supplementation or drugs have not been fully examined and are still open for debate. For instance, what seems morally wrong in one situation could well prove permissible in another where the conditions or stakes have changed. So, before embracing PES/Ds as the next step in military evolution and as a possible game changer in future conflicts, we need to understand the consequences of adopting PES/Ds, not only from a medical or legal perspective, but also from an ethical viewpoint.

Special Operations Forces (SOF) are closely involved with many of the military's developments to maintain a high readiness force. These elite soldiers are selected and trained to operate autonomously in hostile environments while conducting highly sensitive operations, which can have significant impacts at the strategic level. As such, the expectations and demands for mission success are extremely high. SOF operators need to think critically and make decisions that produce the best possible outcome by balancing the interests of the organization with what will keep operators alive and healthy. It is no surprise, then, that SOF emphasizes proper training and education, high physical and mental fitness, and proper moral awareness. Indeed, the military provides conceptual frameworks of codes designed to help servicemen understand how they are expected to act. Consequently, SOF provides an appropriate opportunity to explore the ethical considerations for the use of PES/Ds.

The U.S. Special Operations Command (USSOCOM) is also well aware of the SOF operator's unique position within the armed forces. Just recently, USSOCOM began looking to private industries and academia for options to enhance soldiers' capabilities by using PES/Ds and "pushing operators to increase pain tolerance, injury prevention and recovery, and physical performance in austere environments."[1] According to Ben Chitty, a senior project manager involved in biomedical and human performance initiatives at USSOCOM, "for performance enhancing drugs, we'll have to look at the makeup and safety in consultation with our surgeon and the medical folks before making any decisions

[1] David B. Larter, "'Performance Enhancing Drugs' Considered for Special Operations Soldiers," *Defense News*, accessed May 19, 2017, http://www.defensenews.com/articles/special-operations-command-wants-to-develop-super-soldiers?

on it. […] We're not cutting any corners. […] We want to make sure it's safe first and then we want to look at the effectiveness of it."[2]

Although the issue of safety is central to this debate, the ethics of this topic go beyond medical insights and understanding. Also, safety itself has a broad meaning that involves the safety of the individual and the force, as well as the safety of the mission. The cost of a mild headache seems to be a reasonable price to pay if using PES/Ds mitigates the risks to personnel on a dangerous mission. Nonetheless, accepting possible *unknown side effects* is more problematic. And, a reasonable comparison about long-term side effects only seems possible if we take into account all aspects of the debate from the start.

A. RESEARCH QUESTION

Is it worth the health risk to allow our soldiers to use PES/Ds to be stronger, more cognitively adaptable, more resilient, and less prone to injury? Under what conditions or at what threshold is mission success worth the risks? Some PES/Ds could improve overall soldier wellbeing, while others are more beneficial for the success of a particular mission. It is imperative to note that utilizing PES/Ds to ensure mission success could ultimately save lives, but the use of the PES/Ds could also produce some long-term side effects upon those whose very lives it saves. In light of this, our research question is: *Could conditions be met such that it is morally justifiable to allow Special Operations Forces to use performance-enhancing supplements or drugs to improve individual capabilities, develop greater resiliency, and expand the overall performance of SOF units and, if so, what are the implications?*

B. RESEARCH METHODOLOGY

This thesis reviews facts about performance enhancement, supplements, and drugs; historical examples of military use of performance enhancing drugs; and current regulations and legislation surrounding PES/Ds. Our research included no medical experimentation on the effects of PES/Ds. Medical information included in this thesis was collected via a literature review and originates from prior studies.

[2] Larter, "'Performance Enhancing Drugs' Considered for Special Operations Soldiers."

To fully understand the ethical issues and potential limitations of developing a human optimization program incorporating PES/Ds, it is important to understand what actually *is* morally acceptable, as well as what the military community *believes* is morally acceptable. Since these beliefs can differ from society to society, and from military to military, we surveyed individuals in the SOF community from both the Netherlands and the United States. We assessed their attitudes toward the acceptability of PES/Ds, as well as their concerns regarding side effects.

As for now, use of PES/Ds is almost completely prohibited for a variety of reasons that we discuss in later chapters. In examining specific PES/Ds, their uses, and effects (both positive and negative) we focus on the regulations and policies guiding their use experimental or otherwise. This information, coupled with our survey data, allows us to examine what is currently morally acceptable according to the prevailing normative attitudes toward PES/Ds. We present several arguments and counter-arguments for the use and application of PES/Ds, and then we present the attitudes and beliefs of real warfighters in order to gauge the actual normative beliefs of members of the SOF community. In the end, we find a surprising and even encouraging convergence of views about when the use of PES/Ds can be considered morally justifiable.

II. FRAMING THE ISSUE

Combat is exhausting. Extreme weather conditions, sleep loss, heavy loads, fear, and anxiety can push a soldier's physical and mental abilities beyond his or her breaking point. Several historical examples illustrate how militaries have attempted to counter these limitations by administering or experimenting with PES/Ds. The primary reasons for doing so have almost always been based on short-term effects and strategic national interests rather than concern for the individual warfighter. This conflict of interest should raise healthy skepticism about the permissible use of PES/Ds. To lay the groundwork for better understanding the potential benefits, limitations, and side effects of PES/Ds, this chapter describes how militaries and SOF units currently deal with physical and mental challenges. We then review some historical examples of why militaries used or experimented with PES/Ds and the consequences these decisions had on battles and on individuals. We also examine claims made to justify or oppose the use of PES/Ds, which introduces contextual and ethical concerns.

A. DEALING WITH INCREASING DEMANDS

In SOF there are five core "SOF Truths." The first, "humans are more important than hardware," suggests that we need to place a higher priority on taking care of our personnel as the most important aspect of our force.[3] With an ever-growing demand for Special Operations, and forces spread thin, it is easy to see how it is progressively more challenging to maintain operational readiness while at the same time preventing the overloading of operators.

Notwithstanding the growing demand, another SOF truth suggests that SOF cannot be mass-produced.[4] Selection, training, and education are rigorous, extensive, and often come with high dropout rates. SOF personnel are trained for unique mission sets, which require months if not years of training and development. If an operator is no longer mission

[3] "USSOCOM SOF Truths," United States Special Operations Command, last modified May 5, 2017, http://www.socom.mil/about/sof-truths.

[4] United States Special Operations Command, "USSOCOM SOF Truths."

capable, the effects are detrimental for the entire team, if not the whole organization. An operator who is removed from a team does not just render that position vacant, but his absence changes the dynamic of the team and can even place missions at risk. Even in less dramatic circumstances, it can take months to find a replacement while additional time is then needed to prepare and re-set that team. When one takes all of this into consideration, it should be obvious that people—not equipment—make the critical difference.

The complexity of today's operating environment demands a substantial amount of problem solving and that our soldiers be responsive and mentally agile. Operating in austere environments under difficult conditions can leave warfighters overloaded with physical and mental stress and fatigue. This could cloud their judgment and hinder their performance and ability to meet operational requirements.

Another potential concern with rapid, repeated, and prolonged deployments is the physical stress associated with increasing physical demands. Take, for instance, the heavier loads warfighters are expected to carry. To lower the risk of injury and exhaustion, the medical community recommends that the total amount of weight that troops carry should not exceed 30 percent of their body weight.[5] Besides maximum capacity, it is also important to understand the decline in performance due to heavier loads. One study estimated the decline in performance to be equivalent to about 1% per kilogram of load.[6]

Despite awareness of this information, the amount of weight soldiers must carry is not decreasing. On the contrary, according to a study examining nine U.S. Army Light Infantry positions, expected weights carried by individuals can range from 116 to 167 pounds.[7] If the average body weight of a solider is 190 pounds, this suggests that soldiers are expected to carry almost their own weight in equipment. This is well over the recommended limit, and is difficult to sustain without increased occurrences of injury.

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[5] E. P. Cathcart, D. T. Richardson, and W. Campbell, "Army Hygiene Advisory Committee Report No 3: On the Maximum Load to be Carried by the Soldier," *Journal of the Royal Army Medical Corps* 41, no. 3 (1923): 161–178.

[6] M. Holewijn, and W. A. Lotens, "The Influence of Backpack Design on Physical Performance," *Ergonomics,* no. 35 (1992): 149–157.

[7] Joseph Knapikand and Katy Reynolds, *Load Carriage in Military Operations: A Review of Historical, Physiological, Biochemical, and Medical Aspects.* (Washington, DC: Borden Institute, n.d.).

To better prepare and deal with the evolving physical and mental demands associated with modern warfare, militaries focus more and more on functional fitness training, and increasingly recognize the importance of rest and rehabilitation, nutrition education, and comprehensive support programs. There are several extensive programs specifically created to preserve those who serve in SOF. The goal is to better prepare individuals and teams for frequent deployment, as well as to maintain operational readiness over longer periods of time.

The current program of record in the United States, the Preservation of the Force and Family (POTFF) adopted by U.S. Special Forces Command (USSOCOM), concentrates on optimizing human performance through integrating physical and psychological healthcare under one initiative. POTFF not only focuses on rehabilitation, but also on resiliency by taking a holistic approach to preventive healthcare. POTFF provides services to soldiers and families alike, addressing the emotional and psychological aspects of wellbeing associated with an individual's support system. POTFF encompasses physical training, physical therapy, diet and nutritional counseling, and behavioral health. The POTFF program includes mechanisms to administer and monitor performance-enhancing initiatives for the benefit of both the individual warfighter and the organization as a whole.

One current example of a tailored initiative is the utilization of the Tactical Human Optimization, Rapid Rehabilitation and Reconditioning (THOR3), an $84 million program to incorporate the latest advances in the fields of human performance and rehabilitation.[8] THOR3 trainers provide physical fitness programs to promote functional fitness in preparation of unique occupational tasks. Instead of focusing on basic physical health and fitness, this program is tailored to conditions operators may encounter on the battlefield.

Nevertheless, human optimization programs, whether tailored or holistic, can only improve physical performance and resiliency within a person's physical and mental reach. So far, research to advance a soldier's biological capabilities *beyond* his natural limits to better accommodate the increasing operational tempo have stalemated at nutrition

[8] Benjamin Knipscher, "THOR 3: Humans Are More Important than Hardware" (master's thesis, Naval Postgraduate School, 2010), http://hdl.handle.net/10945/5069.

counseling, behavioral health, and functional fitness training. Here is where it seems natural to begin to explore alternatives, such as PES/Ds—especially since PES/Ds are already available and in use in other venues.

For example, in competitive sports, performance enhancement was used at least as early as 668 BC, when athletes tried to improve their performance by experimenting with their diets.[9] There are, of course, some ways in which competitive sports differ from combat. First, athletes tend to work in predictable and controllable environments, whereas the military is exposed to continuously changing and less then predictable circumstances. Second, athletes formulate their training plans to excel in a specific discipline or sport. Militaries must operate both physically and mentally at "all around" events and are expected to excel in every situation. Third, militaries aim for the highest physical levels possible, but at the same time, need to be able to standardize physical fitness. Again, it is not enough for an operator to excel in one discipline; he needs to be able to overcome any physical challenge. Consequently, an operator who has to work harder to perform alongside the strongest team members is subject to more physical overload, and subsequently has a higher chance of getting injured. Fourth, using performance enhancers in competitive sports is widely considered unfair and a violation of "the spirit" of sport, while "competition" on the battlefield does not revolve around these same ideals.[10] Nevertheless, there is much to learn from sports with regard to how healthy individuals react to PES/Ds.

Still we should wonder: if the stigma of fairness does not exist and PES/Ds have the potential to transform performance *and* recovery, why are they not already in wide military use? This is a particularly interesting question to pose since there are several historical examples of militaries administering and experimenting with PES/Ds. Considering the interests at stake, if one could increase the likelihood of winning in battle by issuing PES/Ds, surely it seems reasonable to do so. How, then, did militaries who used PESD/s in the past decide what was reasonable and what was not?

[9] R. J. A. Wilson, M. I. Finley, and H. W. Pleket, "The Olympic Games: The First Thousand Years," (1976): 78–80. In Charles E. Yesalis and Michael S. Bahrke, "History of Doping in Sport," *International Sports Studies* 24, no. 1 (2002): 42–76.

[10] World Anti-Doping Agency, *World Anti-Doping Code* (Montreal. World Anti-Doping Agency, 2015), 14, accessed September 25, 2016, http://www.wada-ama.org/en.

B. THE HISTORICAL USE OF PES/DS IN A MILITARY SETTING

In 1879, an independent Zulu army stood in the way of Britain's push to colonize South Africa. On January 22, in the battle of Isandlwana, a Zulu army of 20,000–25,000 fanatical, dedicated, and angry warriors decisively defeated a British force of 1,700 men in hand-to-hand combat.[11] Armed and fortified by their shaman doctors with potent toxicants, the Zulus went into battle utterly without fear. They believed they were protected by their gods and were thereby impervious to British bullets.[12] The battle took the lives of 1,300 British soldiers and between 1,000 and 3,000 of the Zulus.[13] The defeat was a catastrophic debacle and perhaps one of the most humiliating defeats in British military history.[14]

During World War II, amphetamines were widely used by the United States, Great Britain, Japan, and Germany to reduce combat fatigue, increase alertness, and more importantly, increase confidence, aggression, and morale in battle.[15] Superior tactics, advanced weapon systems, and a methamphetamine-based performance enhancer called Pervitin were, in fact, engines that contributed to Germany's military successes at the beginning of the war. In *Shooting Up*, Lukasz Kamienski provides an interesting view of how German war efforts were closely tied in to the use of certain intoxicants. According to Kamienski, "pharmacology became a built-in feature of the blitzkrieg to such an extent that it should be seen equal to other recognized parts of the German revolution in land warfare, that is, tanks, planes, radio communication, and armored infantry."[16] At the peak of the German Blitzkrieg, the Nazis supplied their forces with at least 35,000,000 "energy pills."[17]

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[11] Elaine Unterhalter, "Confronting Imperialism: The People of Nquthu and the Invasion of Zululand," *The Anglo-Zulu War: New Perspectives* (1981): 103.

[12] Lukasz Kamienski, *Shooting Up: A Short History of Drugs and War* (New York: Oxford University Press, 2016), 86.

[13] Unterhalter, "Confronting Imperialism: The People of Nquthu and the Invasion of Zululand," 103.

[14] Kamienski, *Shooting Up: A Short History of Drugs and War*, 85.

[15] L. Grinspoon, "Drug Dependence: Non-Narcotic Agents," in *Comprehensive Textbook in Psychiatry,* ed. A. H. Freedman, H. Kaplan, B. Saddock (Baltimore: Williams and Wilkinson Co.), 1975, 1317–31; Nicolas Rasmussen, "Medical Science and the Military: The Allies' Use of Amphetamine during World War II," *Journal of Interdisciplinary History* 42, no. 2 (2011): 205–233.

[16] Kamienski, *Shooting Up: A Short History of Drugs and War*, 110.

[17] Nicolas Rasmussen, *On Speed: The Many Lives of Amphetamine* (New York: New York University Press, 2008), 54.

England also introduced amphetamines at the beginning of World War II. After studying the effects, risks, and operational utility of amphetamines, the British Royal Air Force approved the routine dose of two, five-milligram, Benzedrine tablets on long air missions.[18] It was concluded that pilots who used amphetamines performed better than those who did not and that their use generated the right combination of optimism and aggressiveness, enabling the pilots to achieve "peak efficiency" in combat.[19] Japan even went so far as to issue methamphetamines not only to its soldiers, but also to every civilian working in sectors critical to supporting its war efforts.[20]

Even though Pervitin helped contribute to the Nazis' initial successes in battle, early enthusiasm quickly turned to concern when academic studies confirmed what the military leadership had already observed on the battlefield. The stimulant was highly addictive and caused extreme aggression, depression, lassitude, anxiety, nervousness, irritability, restlessness, tremors, sleeplessness, hallucinations, panic states, and suicidal tendencies.[21] Pervitin was therefore considered unreliable and a dangerously addictive drug. Its untoward effects eventually made the Nazis more cautious in administering the substance, and drove them to investigate alternatives. One of these alternatives was dubbed "project D-IX."

In a desperate attempt to regain the upper hand in 1944, the Nazis began working on a stimulant that they hoped would turn the tide of the war. At a conference of pharmacologists and army commanders, Vice-Admiral Hellmuth Heye directed the pharmacists to manufacture a drug "that can keep soldiers ready for battle when they are asked to continue fighting beyond a period considered normal, while at the same time boosting their self-esteem."[22] Heye's request led to the creation of D-IX, a methamphetamine-based performance-enhancing pill that contained 5 milligrams of

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[18] Rasmussen, *On Speed: The Many Lives of Amphetamine*, 60–61.

[19] Ibid., 65.

[20] Kamienski, *Shooting Up: A Short History of Drugs and War*, 128.

[21] J. P. S. Cathcart, "The Emotions in Gastro-Intestinal Disturbances," *Canadian Medical Association Journal* 55, no. 5 (1946): 465; Rasmussen, "Medical Science and the Military: The Allies' Use of Amphetamine during World War II," 205–233.

[22] Andreas Ulrich, "The Nazi Death Machine: Hitler's Drugged Soldiers," *Spiegel Online*, May 6, 2005, accessed November 28, 2016, http://www.spiegel.de/international/the-nazi-death-machine-hitler-s-drugged-soldiers-a-354606.html.

Eukodal (a morphine-related painkiller), 5 milligrams of cocaine, and 3 milligrams of Pervitin.[23] Before putting this "wonder" drug into production, it was first tested on prisoners at the Sachenhausen concentration camp who were forced to march in circles with 20-kilogram backpacks for more than 24 hours.[24] Although the prisoners were in poor physical shape some of them were able to march up to 90 kilometers without resting.[25] Most of the inmates, however, fell dead to the ground or were barely alive at the end of the experiment.[26] D-IX effectively turned human beings into robots by pushing a person's mental will to a point where its only stopping point was physical limitations.

Although the war ended before the drug was put in production, the project not only reveals the potential that PES/Ds can have, along with their side effects. Furthermore, it illustrates the willingness of a desperate nation to disregard ethical and legal boundaries given a high stakes situation.

In this respect, the allied forces took similar measures. Intrigued and worried by the Nazis' early accomplishments, the Allied Forces officially authorized the use of amphetamines at almost the same time that the Germans tried to ban their use.[27] After discovering methamphetamine pills on downed German pilots, the British started studying the operational utility of methamphetamine and Benzedrine.[28] R.H. Windfield, a medical officer from the Royal Air Force's psychological laboratory, was asked to examine the effects of methamphetamine use during convoy patrol flights and later during bombing raids.[29] Windfield's initial findings led to the approval of methamphetamine use on long air missions.[30] After he completed his second test series, Windfield concluded that the drugs boosted the aircrew's determination and willingness to take risks, and the pilots showed

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[23] Lawrence Paterson, *Weapons of Desperation: German Frogmen and Midget Submarines of the Second World War* (Annapolis: Naval Institute Press, 2006), 16.

[24] Jeevan Vasagar, "Nazis Tested Cocaine on Camp Inmates," *Guardian*, November 19, 2002, accessed November 28, 2016, https://www.theguardian.com/world/2002/nov/19/research.germany.

[25] Vasagar, "Nazis Tested Cocaine on Camp Inmates."

[26] Ibid.

[27] Rasmussen, *On Speed: The Many Lives of Amphetamine*, 61.

[28] Kamienski, *Shooting Up: A Short History of Drugs and War*, 86.

[29] Rasmussen, *On Speed: The Many Lives of Amphetamine*, 60–65.

[30] Ibid.

more courage.[31] The hope that amphetamines would be the solution to many of Britain's problems, though, seemed merely to be father to the thought. Additional extensive testing by other scientists did not result in objective evidence to support the proclaimed performance-enhancing traits that Windfield described.[32] Yet, in desperate need of military success, both the Royal Army and Navy ignored the new findings and issued the pills anyway. The U.S. military, which showed interest in amphetamines at the same time as Britain, also investigated the usefulness of the drug in combat. Like Britain, the United States began supplying its forces with large amounts of Benzedrine pills before the completion of its drug tests.[33]

The United States and Great Britain faced similar ethical dilemmas in balancing national interests and an individual's wellbeing. When weighing the decision to use these substances, Kamienski makes the following observation:

> The stakes of total war loosened the brakes of ethics. The victory of democracy and freedom over the dark forces of totalitarianism and enslavement had to be given priority over the dilemmas concerning the harmful effects of psychoactive substances. Research that aimed at extending the boundaries of human performance could not be overly inhibited by ethical considerations.[34]

Ultimately, both the United Kingdom and the United States decided to issue the compounds through medical officers and in first-aid kits without truly understanding the impact and without creating appropriate control mechanisms to prevent abuse.[35] During the war, the allied forces supplied over 150 million Benzedrine Sulfate tablets to its servicemen.[36] The U.S. military even continued supplying its forces with amphetamines in the wars to come. In fact, to this day, Air Force and Navy pilots can still use "go-pills" (speed) to stay alert during stressful and extended flight missions or "no-pills" (sedatives) to induce sleep.

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31 Kamienski, *Shooting Up: A Short History of Drugs and War*, 118

32 Rasmussen, *On Speed: The Many Lives of Amphetamine*, 66–67.

33 Ibid., 75–76.

34 Kamienski, *Shooting Up: A Short History of Drugs and War*, 121.

35 Rasmussen, *On Speed: The Many Lives of Amphetamine*, 76–81.

36 W. R. Bett, "Benzedrine Sulphate in Clinical Medicine," *Postgraduate Medical Journal* 22, no. 250 (1946): 205.

C. DISCUSSION

Aside from the obvious dangerous medical side effects, there are other important implications associated with PES/Ds use. For example, the amphetamines used during World War II not only caused sleeplessness, nervousness, high blood pressure, and increased heart rate, but also made soldiers aggressive, addicted, and unpredictable. Such behavioral side effects raise a variety of questions about individual moral responsibility while using PES/Ds.

For instance, recently, two U.S. Air Force pilots under the influence of amphetamines were involved in a friendly fire incident.[37] They claimed that the use of amphetamines undermined their moral judgment and that the drugs contributed to their catastrophic mistake. According to Jessica Wolfendale, associate professor of philosophy at West Virginia University, one must consider whether a soldier is responsible for his actions when he uses performance-enhancing drugs that affect his moral judgment.[38] She argues that the use of performance-enhancement medication that can cloud judgment must be limited so that military personnel may retain their moral responsibility.[39] Because the issue of whether military personnel can be held properly accountable for their actions when they are medically manipulated raises a plausible argument against the use of PES/Ds.[40] The use of unnatural chemical substances to alter human performance has legal and not just policy implications. We return to this vexing question of legal liability in Chapter VI.

Neuroscientists Michael Russo, Michael Arnett, Maria Thomas, and John Caldwell contend there *are* situations and conditions under which the use of certain PES/Ds that affect cognition can be ethically utilized. Russo et al. introduce the term "cogniceuticals" to categorize pharmaceuticals that affect cognition. These authors present five principle guidelines for the justifiable use of cogniceuticals:

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[37] Rhonda Cornum, John Caldwell, and Kory Cornum, "Stimulant Use in Extended Flight Operations," *Airpower Journal* 11*,* no. 1 (1997): 53.

[38] Jessica Wolfendale, "Performance-Enhancing Technologies and Moral Responsibility in the Military," *American Journal of Bioethics* 2, no. 2 (2008): 28–38.

[39] Wolfendale, "Performance-Enhancing Technologies and Moral Responsibility in the Military," 28–38.

[40] . Ibid.

> 1) The use of the compound is truly informed and voluntary; 2) The medication itself is safe for the individual and can be safely used within the context of the environment; 3) The intended use of the cogniceutical is consistent with its dosage and pharmacological function; 4) The cogniceutical is used with appropriate medical supervision; and 5) The non-pharmacologic alternatives have been fully utilized.[41]

Russo et al.'s guidelines create a clear structure and can serve as a solid decision-making tool for examining the moral implications of PES/Ds. In Chapter VI we use their five principle guidelines to discuss various ethical arguments and counter-arguments.

Richard Ashcroft, a professor of biomedical ethics at Queen Mary University of London, strongly opposes militaries using PES/Ds. He argues that current international regulations fall short and need to be adjusted. Ashcroft proposes an international code of military ethics and honor, as well as modifications to international humanitarian law and bioethics norms, to prevent or exclude the military application of enhancement technologies.[42] We cite Ashcroft here because his position raises important questions regarding who should decide the norm. Then, if (or when) there is a consensus, what should be the control mechanisms to monitor compliance? There are already many different views about what should be permissible.

For instance, the U.S. military approves the use of caffeine, dexamphetamine, and Modafinil by Air Force members during extended flight operations. As stated in the U.S. *Navy Medical Pamphlet-6410*, dated January 1, 2010: "The Commanding Officer, following consultation with the Air Wing Commander (or his equivalent) and flight surgeon, may authorize the use of stimulants and/or sedatives for pilots, NFO's and aircrew men." In contrast, the Netherlands does not authorize this kind of drug use at all.[43] The

[41] Michael B. Russo et al., "Ethical use of Cogniceuticals in the Military of Democratic Nations," *American Journal of Bioethics* 8, no 2 (2008): 39–41; Michael B. Russo, "Recommendations for the Ethical Use of Pharmacologic Fatigue Countermeasures in the U.S. Military," *Aviation, Space, and Environmental Medicine* 78, suppl. 5 (2007): 119–127.

[42] Richard E. Ashcroft, "Regulating Biomedical Enhancements in the Military," *American Journal of Bioethics* 2, no 2 (2008): 47–49.

[43] Marten Meijer, "A Human Performance Perspective on the Ethical Use of Congiceuticals: Commentary on 'Recommendations for the Ethical Use of Pharmacologic Fatigue Countermeasures in the U.S. Military,'" *Aviation, Space, and Environmental Medicine* 78, no. 5, section II (2007): B131−B133.

reasons for disagreement are complicated and reflect broader differences regarding national interests, medical norms, cross-cultural differences, and even historical experiences.

Relevant to this debate, too, are discussions surrounding human subject experiments. Jonathan D. Moreno, an expert in medical ethics and health policy at the Perelman School of Medicine at the University of Pennsylvania, argues that the current regulations are unclear. He stresses the importance of transparency, especially when it comes to individual rights versus national security issues. Philosophers Patrick Lin and Fritz Allhoff advocate that the arguments in favor of human enhancement must be more compelling and philosophically rigorous then they currently are.[44] Sports philosopher, Leon Culbertson echoes this claim, and calls for reaching consensus on the terms involved in human subject experiments.[45] Essentially, all these scholars consider human enhancement an irreversible development and stress the importance of regulation and the need for clear and precise definitions of the terms involved.

Interestingly, one perspective that has not yet been taken into account in these discussions is that of the soldiers who will actually be taking the PES/Ds. Will a soldier be willing to use PES/Ds if they help him perform better? What types of pharmaceuticals will he be willing to use? How far will he be willing to go? And, what is morally permissible when it comes to *ordering* someone to take a particular PES/D, particularly if the individual does not want to take it? Where do the moral parameters lie? Surely, if we want to reach any kind of consensus on the topic, we must include the views of the persons who will be using or asked to use the substances; that is the impetus for this study, the first of its kind, which we detail in Chapter VII.

D. CONCLUSION

History suggests that physical and mental demands associated with modern warfare will impel militaries to investigate ways to both continue to optimize human performance and even push the bounds of human limitations. One option will be to adopt or increase the

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[44] Patrick Lin and Fritz Allhoff, "Nanoethics and Human Enhancement: A Critical Evaluation of Recent Arguments," *Nanotechnology Perceptions* 2, no. 1 (2006): 47.

[45] Leon Culbertson, "'Human-Ness,' 'Dehumanization' and Performance Enhancement," *Sport, Ethics and Philosophy* 1, no. 2 (2007): 195–217, doi:10.1080/17511320701439877.

use of PES/Ds. Until now, and as the discussion thus far should suggest, having the ability to push the boundaries of human limitations raises medical, legal, and, above all, ethical concerns. Conclusions about what militaries should do are far from clear. Current interpretations and concerns are therefore both contradictory and compelling. History reveals that PES/Ds can have a significant—in some cases even decisive—impact on the outcome of conflicts. Yet, it also makes clear that the aims of such use were almost always extremely shortsighted and ignored the rights of the individual.

Nevertheless, not every situation is the same and some situations may indeed justify the use of PES/Ds, while others do not. Advances underway in the health sciences could help shorten recovery periods, enhance overall wellbeing, improve performance, and mitigate the effects of physical and psychological overload. Therefore, at a minimum, it seems prudent to explore PES/Ds alongside these options. At the same time, however, when examining the usefulness of PES/Ds, it is vital to take into account what is acceptable, what is not, and why. The question of moral responsibility matters, as does eliciting and understanding soldiers' views. At a minimum, too, there must be a consensus about what performance enhancement actually means.

III. DEFINING HUMAN ENHANCEMENT

As mentioned in the previous chapter, it is important to have a clear and precise understanding of the terms involved. So, before categorizing PES/Ds or including the views of SOF operators, we must first decide how to define human enhancement. This task, though, is more challenging than it appears. The term itself is relative, ambiguous, open to different interpretations, and leads to a debate about the essence of even being human. The purposes for, and the situations in which, enhancements are used lead to different insights and objections. For example, the legitimacy of using anabolic steroids in sports to boost an athlete's performance versus using the same drug in a medical situation to help a patient regain strength will often spark starkly different reactions. Perhaps this is why it has proven so challenging to reach a consensus about how to define human enhancement. Because it goes beyond the scope of this thesis to compose a perfect definition that covers all viewpoints, we use a definition that best reflects the use of PES/Ds in a military specific environment. Our definition of enhancement draws on bioethicist Eric Juengst's definition of enhancement and includes *"any medical or biological intervention that aims to temporarily or permanently improve current performance, appearance, or capabilities besides what is necessary to achieve, sustain, or restore health."*[46] The intervention is artificial, internal, or non-therapeutic in nature.

This chapter briefly analyzes existing definitions of human enhancement by clustering them into four approaches and clarifying the essence of each concept and its limitations.

A. COMMONLY USED DEFINITIONS

The basic definition of enhance is to "intensify, increase, or further improve the quality, value, or extent of something."[47] As such, any improvement of a human's current

[46] Eric Juengst, "The Meaning of Enhancement," in *Enhancing Human Traits: Ethical and Social Implications,* ed. Erik Parens, (Washington, DC: Georgetown University Press, 2000), 29–47; Maxwell Mehlman, Patrick Lin, and Keith Abney, "Enhanced Warfighters: Risk, Ethics, and Policy," *Case Legal Studies Research Paper*, no. 2 (2013), accessed November 25, 2016, http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2202982. (emphasis ours).

[47] Angus Stevenson, *Oxford Dictionary of English* (London: Oxford University Press, 2010), 582.

physical or mental state can count as human enhancement. Going to the gym to gain physical strength or going to college to become more knowledgeable both fit this description. There is, of course, more to consider. The literature reveals several overlapping, but also contradictory definitions of human enhancement. Unfortunately, the different perspectives scientists use are inconsistent and can be confusing. Having analyzed the most common definitions, Vincent Menuz, an associate researcher of the OMICS-ETHICS group at the Bioethics Programs of the University of Montreal, clustered them into four approaches: the implicit approach; the therapy-enhancement distinction approach; the improvement of general abilities approach; and the increase of natural wellbeing approach.[48] We use his framework as we describe and discuss types of enhancements and comment on what might or might not be appropriate in military settings.

1. The Implicit Approach

The implicit approach treats the "result of some given technological interventions on human beings as a human enhancement, without offering further explanation to define it as such."[49] Consequently, a variety of interventions are now implicitly considered human enhancements because they meet certain criteria. Undergoing liposuction surgery to alter one's physical appearance or using steroids to gain physical strength are both examples of technological interventions that, for instance, the Irish Council for Bioethics views as human enhancement.[50]

At first glance, this implicit approach seems to create clarity. Thus, an overview of such interventions should suffice as a tool for establishing policies around enhancement programs. The danger with compiling a list, however, is that it narrows our view and oversimplifies the complexity of the debate. As noted by Menuz et al., "the defenders of such an approach seem to deny the existence of plural social and political values across societies

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[48] Vincent Menuz, Thierry Hurlimann, and Béatrice Godard, "Is Human Enhancement Also a Personal Matter?," *Science and Engineering Ethics* 19, no. 1 (2013): 161–177.

[49] Menuz, Hurlimann, and Godard, "Is Human Enhancement Also a Personal Matter?," 164.

[50] Ibid., 165.

and individuals by assuming that if a given intervention is a human enhancement from their perspective, it should be the case in everyone's perspective."[51]

James Canton, a social scientist who specializes in futurology, believes that "the future may hold different definitions of human enhancement that affect culture, intelligence, memory, physical performance, even longevity. Different cultures will define human performance based on their social and political values. It is for our nation to define these values and chart the future of human performance."[52] Canton's relativistic approach seems pragmatic, especially since different militaries and societies will likely have different views about what is and what is not an enhancement. But while cultural and political differences will account for some of these divergent views, developments in the field of nanotechnology, biotechnology, information technology, and cognitive science will complicate the debate even internal to countries since certain research and development programs will remain classified. Militaries can, of course, decide to pursue research based on national security needs. Yet full disclosure of such research would be prohibited, leaving ethicists and others with only partial information on which to make judgments This will make it all the more difficult to reach any kind of agreements internationally. As technology spreads, cultural, political, or national preferences will be further tested, and any debate about international law and regulations will only become more fraught.

2. Therapy-Enhancement Distinction Approach

The second category Menuz et al. identify is the therapy-enhancement distinction approach, according to which "all interventions aiming at healing or improving health enter into the 'treatment' category, while in contrast, all interventions that do not have such purposes would be human enhancements."[53] This means that interventions that do not aim to cure an illness or disability or improve a person's medical condition back to a normal healthy baseline are automatically enhancements. This position seems less subjective and rigid than

[51] Menuz, Hurlimann, and Godard, "Is Human Enhancement Also a Personal Matter?," 165.

[52] James Canton, "The Impact of Convergent Technologies and the Future of Business and the Economy," in *Converging Technologies For Improving Human Performance-Nanotechnology, Biotechnology, Information Technology and Cognitive Science,* ed. Mihail C. Roco and William. S. Bainbridge (Dordrecht: Springer Netherlands, 2003), 78.

[53] Menuz, Hurlimann, and Godard, "Is Human Enhancement Also a Personal Matter?," 166.

the implicit approach. The therapeutic use of steroids, for example, would no longer be an enhancement, but would now be considered a treatment. Yet, what if the treatment gives the patient strength beyond his normal functioning, or beyond that of humans in general? In other words, when does a treatment *become* an enhancement?

To answer this question, we need to know whether there is a baseline or threshold for normal human functioning. Bioethicist Norm Daniels proposes to define "normal" by determining the natural functional organization of members of a species.[54] He has designed a "species-typical functioning" model to serve as a reference, allowing societies to define the degree and type of treatment its members are entitled to receive. In his view, "a society has an obligation to provide services that, to the degree possible, raise the level of functioning of any citizen with deficits to the species-typical level. Yet that same society has no obligation to provide services that raise a citizen's function above the typical level for the species as a whole."[55]

Daniels understands that his tailored solution to distinguish treatment from enhancement is highly sensitive to context and not applicable for every trait. Patrick Lin et al. use the example of a drug that gives an average person the IQ of Albert Einstein. Since Einstein's IQ exceeds the species-typical range, the use of the drug would be an enhancement. Yet, if Einstein himself used the drug after suffering from a brain injury that reduced his IQ to restore his abilities, it would be a treatment.[56]

Philosopher and bioethicist Julian Savulescu comments on this dilemma by narrowing the definition of enhancement. He suggests "any change in the biology or psychology of a person, which increases species typical normal functioning above some statistically defined level, constitutes an enhancement."[57] In Einstein's case, Savulescu recommends using the definition of intellectual disability as a baseline to decide whether an intervention is a treatment or an enhancement. An IQ below 70 is a disability and should

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[54] Norman Daniels, "Normal Functioning and the Treatment-Enhancement Distinction," *Cambridge Quarterly of Healthcare Ethics* 9, no. 3 (2000): 309–322.

[55] Daniels, "Normal Functioning and the Treatment-Enhancement Distinction," 309–322.

[56] Mehlman, Lin, and Abney, "Enhanced Warfighters: Risk, Ethics, and Policy," 14.

[57] Julian Savulescu, "Justice, Fairness, and Enhancement," *Annals of the New York Academy of Sciences* 1093, no.1 (2006): 324.

therefore be treated as a disease. Raising someone's IQ from 60 to 70 is a treatment, while raising it from 70 to 80 is an enhancement.

These different positions about this one fairly measurable trait reflect the difficulties that inhere in this debate. It grows even more complex when the trait or the treatment is less obvious. As pointed out by sociologist and bioethicist Paul Wolpe, determining a "species-typical norm" for happiness, shyness, or cognition raises the question about how happy we humans are designed to be.[58] Of course, to arrive at any such norm would first mean discounting any potential (perceived) differences among groups, societies, or nationalities, which would be extremely difficult if not impossible.

Another angle from which to consider this treatment versus enhancement debate is that of vaccinations. Since vaccines do not aim to treat an illness or improve a medical condition to normal, but aim to boost a person's immune system; then by the therapy-enhancement distinction approach, they are enhancements. Although technically correct, perhaps, this conclusion seems awkward. Waiting for a person to become ill when one has the ability to prevent the illness seems illogical. Lin et al. rightly pose the question, "why should it matter if a therapeutic intervention—that is, designed to restore health back to normal—is administered before or after an illness?"[59] Indeed, it should not. Therefore, and for the purposes of the thesis, we consider a vaccine a preventive therapy and not an enhancement.

The therapy-enhancement distinction approach attempts to offer more flexibility and a logical division based on the notion of healing. Yet, defining species-typical norms or determining tipping points seems somewhat arbitrary and provides no clear-cut answers. Even so, the approach offers workable insights that contribute to the debate about enhancements and appropriate policies.

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[58] Paul R. Wolpe, "Treatment, Enhancement, and the Ethics of Neurotherapeutics," *Brain and Cognition* 50, no. 3 (2002): 387–395.

[59] Mehlman, Lin, and Abney, "Enhanced Warfighters: Risk, Ethics, and Policy," 15.

3. Improvement of General Abilities Approach

Menuz et al. describe their third approach *"*as the result of the application of emerging technologies to individuals to improve their body, mind, or any ability beyond the "species-typical normal functioning" of a human being."[60] Although this approach does not focus on the distinction between health and treatment, but on the purpose and the outcome of the intervention instead, drawing the line for species-typical normal functioning again proves challenging.

The more radical the outcome of an intervention, the easier it is to classify it as an enhancement. Yet, the closer we get to the mean, the more vague the concept becomes. This makes both approaches susceptible to the Sorites paradox.[61] This philosophical dilemma, also known as the paradox of the heap, describes the problem of distinguishing sharp lines of precise definitions where vagueness seems to reign. For example, when do we distinguish a heap of sand from a non-heap? Let us assume that removing one single grain does not alter the preconditions of a heap. This seems plausible as it seems counter-intuitive to think that just a single grain of sand can make the difference between something being a heap or not. Yet, as we repeat the process, at some point the heap will become less than a heap. But, at what point exactly? Where this boundary lies seems impossible to ascertain.

Indeed, as with a species-typical norm of functioning, there is no straight answer with this approach either. To avoid the dilemma presented by the heaps, one might simply decide to say that a certain number of grains make a heap, and anything less than that number is not a heap. Although this might not seem to help much since drawing a line is arbitrary and therefore misleading, we also cannot say that there is no distinction between an enhancement and a non-enhancement. Instead, we should probably simply acknowledge that vagueness is endemic to the human condition and that outcomes always depend on given thresholds.

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[60] Menuz, Hurlimann, and Godard, "Is Human Enhancement Also a Personal Matter?," 168.

[61] Jon Moline, "V.—Aristotle, Eubulides and the Sorites," *Mind* 78, no. 311 (1969): 393–407.

4. The Welfarist Approach

Individual wellbeing, or the "welfarist approach," is Menuz et al.'s final approach and focuses on "the improvement of individual wellbeing."[62] Savulescu describes human enhancement as "any change in the biology or psychology of a person which increases the chances of leading a good life."[63] His ideas are based on the conception that an intervention is an enhancement if it increases "the value of a person's life."[64]

This person-centric approach cleverly avoids the dilemma of determining the species-typical normal functioning level, but replaces it with something else: what constitutes a "good" life and what criteria do we use to determine when an intervention improves one's wellbeing? These questions are difficult to answer. Moreover, our personal choices are closely linked to cultural pressures. The SOF environment, for example, is highly competitive, focused as it is on individual and group performance. "Being the best" or "it pays to be a winner" are common themes during selection, training, and even during missions. This competitive environment creates a degree of passive coercion, which most likely influences a soldier's perceptions of what constitutes a "good life," and subsequently influences his personal choices. Another interesting insight concerns the expected impact that an intervention will have on a person's welfare. According to the person-centric approach, a potential increase of wellbeing is considered an enhancement. What if the intervention, although intended to enhance a "good life," has undesired side effects? Or, what if those side effects only became apparent much later? Should the intervention still be considered an enhancement?

Given the difficulty in addressing questions like these, the welfarist approach does not seem to fit the military environment. Nevertheless, it does raise important considerations about individual wellbeing, personal interests, cultural effects, and group dynamics. Especially in a highly competitive environment, as is the military, we cannot neglect the impact that culture and peer pressure have on an individual's perspective on the ethical norms of using PES/Ds.

[62] Menuz, Hurlimann, and Godard, "Is Human Enhancement Also a Personal Matter?," 168.

[63] Savulescu, "Justice, Fairness, and Enhancement," 325.

[64] Ibid.

B. OTHER CONSIDERATIONS

Beyond the previously mentioned approaches are further important considerations. For example, one distinction centers on enhancements by natural versus artificial aids. Anything that is not manipulated by humans is often considered natural. Yet, by this definition, a fisherman using a net to catch fish or an Inuit wearing a thick jacket to protect his body against hypothermia would be using artificial enhancements. This proposition is of course shortsighted and does not bring us closer to consensus. However, claiming that humans are "natural beings" and therefore *any* intervention is natural is equally problematic.

The debate over internal versus external enhancements is somewhat more helpful. Patrick Lin, for instance, compares a smartphone to a computer chip that is implanted in the brain. Although both interventions aim to improve the capability of accessing information, the smartphone is typically considered a tool whereas the brain chip is regarded as an enhancement. The distinction here is not based on what they enable you to do, but on the accessibility of the aid. The brain chip is always accessible and is more or less integrated to the human system. The smartphone, on the other hand, is only accessible and beneficial once it is within reach, activated, and properly used. Another example of the external/internal distinction is a groundbreaking aerodynamic racing bike versus the use of Erythropoietin (rHuEPO). Both aim to improve performance in cycling. But, the aerodynamic bicycle only improves the cyclist's performance when he uses the aerodynamic bicycle. In contrast, rHuEPO aims to have the same effects by pushing the cyclist's physical limits, on any racing bike and at any time. While the therapeutic use of pharmaceuticals like Erythropoietin seems an exception to the rule, the distinction between internal and external interventions is a useful reference point.

C. OUR DEFINITION

So, where do we stand in this thesis? All four of the approaches just reviewed offer useful elements, but are in themselves inconclusive. The implicit approach offers probably the quickest way to set up a framework for an enhancement program. Nevertheless, tailoring a program to a specific working environment is too limited since current and future developments will push the bounds of human limitations; what will be required instead is a holistic understanding of the challenges to come. One of these challenges is that we may not agree upon a species-typical norm of functioning. The therapy-enhancement distinction and the improvement of general abilities approach are both built around this vague rule of thumb principle. Agreeing on norms of functioning cross-culturally and internationally is probably one of the most interesting but complicated themes in the debate about human enhancement. The welfarist approach concentrates on the potential impact an intervention has on a person's ability to lead a good life, which is useful but will also always be contingent on the environment in which the individual is living. This interpretation underestimates the impact of cultural influences and peer pressure. In the SOF environment especially, peer pressure affects a person's view on leading a "good" life.

The takeaway from all of these approaches is that human enhancement involves a technological intervention that increases human abilities beyond a species-typical norm of functioning. The problem is that whether this norm should be generated by a shortlist, is culturally dependent, or is based on one's personal wellbeing is still subject to debate. Thus, considering the previously mentioned arguments, we prefer as our definition of enhancement: *"any medical or biological intervention that aims to temporarily or permanently improve current performance, appearance, or capabilities besides what is necessary to achieve, sustain or restore health."*[65] The intervention is artificial, internal, or non-therapeutic in nature.

This definition excludes improvements caused by natural, external, or therapeutic aids. A groundbreaking training technique that enables athletes to run faster, the use of a laptop to quickly access information, or medication that helps a patient to recover from an illness should all be considered non-enhancements in our view. But, a drug that improves an athlete's endurance, a chip implanted in the eye that enables infrared vision, or a medication that negates the effects of sleep deprivation and extends the employability of soldiers in combat are all to be regarded as artificial, internal, or non-therapeutic interventions. They *are* enhancements.

[65] Eric Juengst, "The Meaning of Enhancement," 29–47; Mehlman, Lin, and Abney, "Enhanced Warfighters: Risk, Ethics, and Policy," (Emphasis ours).

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IV. CATEGORIZING PERFORMANCE-ENHANCING SUPPLEMENTS OR DRUGS

To understand the military usefulness of performance enhancers it is important to know what they are, what they aim to do, and what unintended consequences they could potentially cause. This chapter explains the characteristics of classes and subclasses of performance-enhancing substances by examining various medical studies on their intended and unintended effects. We have divided the drugs into cognitive and physical enhancers and, based on their chemical structure, clustered them into subcategories accordingly. What we present is limited to the accessible literature about the use and misuse of performance enhancers and to those compounds that have had historical or appear to have future military relevance.

A. COGNITIVE ENHANCERS

The psychologist Ulric Neisser defines cognition as "those processes by which the sensory input is transformed, reduced, elaborated upon, stored, recovered, and used."[66] Cognition concerns higher-level functions of the brain that encompass language, imagination, perception, and planning.[67] This includes how we think, understand, judge, learn, concentrate, reason, solve problems, plan, and make decisions. Cognitive enhancers aim to promote these functions and control emotions like fear, anger, excitement, or stress. These compounds can be differentiated as stimulants, nootropics, and adaptogens, as explained in the ensuing paragraphs. Classifications are based on the drug's chemical structure and the effects it has on different parts of the brain.

1. Stimulants

Cognitive stimulants or psychostimulants are chemical compounds that increase activity in the brain. They affect the central nervous system (CNS) by enhancing specific body

[66] Ulric Neisser, *Cognitive Psychology: Classic Edition* (New York: Psychology Press, 2014), 4.

[67] Kendra Cherry, "What Exactly Is Cognition?," *Verywell*, September 5, 2016, accessed November 14, 2016, https://www.verywell.com/what-is-cognition-2794982.

functions like alertness, wakefulness, memory, and locomotion. There are three classes of cognitive stimulants: ampakines, amphetamines, and eugregorics.

Ampakines are compounds that stimulate neurotransmission via AMPA (α-amino-3hydroxy-5methyl-4isooxalopropionic acid) receptor activation. These so-called AMPA receptors act as control channels to regulate and oversee synaptic transmissions and activities throughout the CNS.[68] They have been shown to promote long-term and short-term spatial (sense of locality) and olfactory (sense of smell) memory in rats, and enhanced spatial memory in nonhuman primates.[69] Human testing suggests that ampakines may affect visual recognition, motor performance, and general intellectual functioning.[70] Yet, different studies show different results, varying from improved short-term memory and weakened episodic (autobiographical) memory to fatigue prevention and performance maintenance traits after extended wakefulness.[71] The varying test results are in part explained by the novelty of the drug.

Ampakines are rather new, and scientists and researchers are continuing to learn more about the action and possible consequences of using these substances. It appears that further research will not only increase our understanding of the substance, but may also help with mapping human brain functioning, particularly with respect to memory and cognitive abilities.

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68 Julia Boyle et al., "Acute Sleep Deprivation: The Effects of the AMPAKINE Compound CX717 on Human Cognitive Performance, Alertness and Recovery Sleep," *Journal of Psychopharmacology* 26, no. 8 (2012): 1047–1057, doi:10.1177/0269881111405353.

69 Ursula Stäubli et al., "Centrally Active Modulators of Glutamate Receptors Facilitate the Induction of Long-Term Potentiation in Vivo," *Proceedings of the National Academy of Sciences* 91, no. 23 (1994): 11158–11162; Robert E. Hampson, et al., "Facilitative Effects of the Ampakine CX516 on Short-Term Memory in Rats: Enhancement of Delayed-Nonmatch-to-Sample Performance," *Journal of Neuroscience* 18, no. 7 (1998): 2740–2747; Linda J. Porrino et al., "Facilitation of Task Performance and Removal of the Effects of Sleep Deprivation by an Ampakine (CX717) in Nonhuman Primates," ed. Richard Morris, *PLoS Biology* 3, no. 9 (2005): e299, doi:10.1371/journal.pbio.0030299.

70 Martin Ingvar et al., "Enhancement by an Ampakine of Memory Encoding in Humans," *Experimental Neurology* 146, no. 2 (1997): 553–559, doi:10.1006/exnr.1997.6581.

71 Elke Wezenberg et al., "Acute Effects of the Ampakine Farampator on Memory and Information Processing in Healthy Elderly Volunteers," Neuropsychopharmacology 32, no. 6 (2007): 1272–1283; Nancy J. Wesensten, Rebecca M. Reichardt, and Thomas J. Balkin, "Ampakine (CX717) Effects on Performance and Alertness During Simulated Night Shift Work," Aviation, Space, and Environmental Medicine 78, no. 10 (2007): 937–43, doi:10.3357/ASEM.2055.2007; Julia Boyle et al., "Acute Sleep Deprivation: The Effects of the Ampakine Compound CX717 on Human Cognitive Performance, Alertness and Recovery Sleep," 1047–1057.

The second class of stimulants is **amphetamines**. Amphetamines share the same chemical structure as the body's own hormone, adrenaline, and are agents that stimulate the sympathetic nervous system, thereby inducing euphoria, alertness, emotions, aggression, self-esteem, and arousal.[72] Amphetamines were discovered in 1887 and introduced on the market as Benzedrine in 1935.[73] At the time, Benzedrine was freely available and used to treat a variety of over 40 diseases and disorders, including attention deficit hyperactivity disorder (ADHD), narcolepsy, epilepsy, Parkinson's disease, fatigue, depression, obesity, and alcoholism.[74] The broad usefulness of the drug combined with its highly addictive traits and initial unrestricted access caused an outbreak in substance abuse.[75] Researchers discovered that misuse could lead to extreme aggression, depression, lassitude, anxiety, nervousness, irritability, restlessness, tremors, sleeplessness, hallucinations, panic states, and suicidal tendencies.[76] These extreme side effects caused many countries to ban, legislate, or highly restrict the use of amphetamine-based medicines.[77]

Today, amphetamine-based medications like Adderall and Dexedrine are used to treat attention deficit disorder (ADD), ADHD, narcolepsy, and depression disorder. The side effects seem manageable, even though these drugs can also cause anorexia, weight loss, nausea, vomiting, abdominal cramps, increased heart rate and blood pressure, and

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72 Harvey Marcovitch, *Black's Medical Dictionary* (London: A. & C. Black, 2005), 31; F. H. Gawin and E. H. Ellinwood Jr., "Cocaine and Other Stimulants: Actions, Abuse, and Treatment," *New England Journal of Medecine* 318 (1988): 1173–1182.

73 Erich Guttmann and William Sargant, "Observations on Benzedrine," *British Medical Journal* 1, no. 3984 (1937): 1013.

74 W. R. Bett, "Benzedrine Sulphate in Clinical Medicine," 205; Guttmann and Sargant, "Observations on Benzedrine," 1013.

75 Nicolas Rasmussen, "America's First Amphetamine Epidemic 1929–1971," *American Journal of Public Health* 98, no. 6 (2008): 974–85.

76 P. S. Cathcart, "The Emotions in Gastro-Intestinal Disturbances," *Canadian Medical Association Journal* 55, no. 5 (1946): 465; Rasmussen, "Medical Science and the Military: The Allies' Use of Amphetamine during World War II," 205–233.

77 Steven M. Berman, et al., "Potential Adverse Effects of Amphetamine Treatment on Brain and Behavior: A Review," *Molecular Psychiatry,* no. 14 (2009): 123−142.

insomnia.[78] Controlled short-term usage by healthy people can indeed have enhancing effects on several cognitive functions. The compounds may counter fatigue and promote focus and task performance, but the fast-acting effects of amphetamines also make them highly addictive and could pose significant health risks.

The third class of cognitive stimulants is **Eugregorics**. Eugregorics are psychoactive agents that promote wakefulness and alertness, and reduce fatigue and the need for sleep. One of the best-known Eugregorics is Modafinil. Modafinil, which is prescribed for the treatment of narcolepsy and excessive lethargy, is a synthetic molecule that simulates amphetamines by producing high quality wakefulness without the negative side effects.[79] It is less addicting, without the highs and lows of amphetamines.[80] As a result, Modafinil is referred to as "a molecule of military interest."[81]

In research funded by USSOCOM, the United States Air Force Research Laboratory tested Modafinil's ability to counter the effects of extreme long-duration missions by maintaining, "alertness and performance over several days of reduced sleep in a field environment."[82] The scientists concluded that Modafinil is a "promising drug with

[78] William E. Pelham, et al., "A Comparison of Morning-Only and Morning/Late Afternoon Adderall to Morning-Only, Twice-Daily, and Three Times-Daily Methylphenidate in Children with Attention-Deficit/Hyperactivity Disorder," *Pediatrics* 104, no. 6 (1999): 1300–1311; David W. Goodman et al., "An Interim Analysis of the Quality of Life, Effectiveness, Safety, and Tolerability (QU. EST) Evaluation of Mixed Amphetamine Salts Extended Release in Adults with ADHD," *CNS Spectrums* 10, no. 20 (2005): 26–34; Lenard A. Adler et al., "Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of Lisdexamfetamine Dimesylate in Adults with Attention-Deficit/Hyperactivity Disorder," *Journal of Clinical Psychiatry* 69, no. 9 (2008): 1364; Richard Weisler et al., "Long-Term Safety and Effectiveness of Lisdexamfetamine Dimesylate in Adults with Attention-Deficit/Hyperactivity Disorder," *CNS Spectrums* 14, no. 10 (2009): 573−586.

[79] D. Lagarde et al., "Interest of Modafinil, a New Psychostimulant, During a Sixty-Hour Sleep Deprivation Experiment," *Fundamental & Clinical Pharmacology* 9, no. 3 (1995): 271−279.

[80] Thomas A. Rugino and Teresa C. Copley, "Effects of Modafinil in Children with Attention-Deficit Hyperactivity Disorder: An Open-Label Study," *Journal of the American Academy of Child & Adolescent Psychiatry* 40, no. 2 (2001): 230–235.

[81] C. Piérard, *Modafinil: A Molecule of Military Interest,* (Br6tigny-sur-Orge Cedex, France: Institut De Medecine Aerospatiale Du Service De Sante Des Armees Cedex) Dept. of Physiology, 2001, http://oai.dtic.mil/oai/oai?verb=getRecord&metadataPrefix=html&identifier=ADP011050.

[82] Jeffery Whitmore et al., *The Efficacy of Modafinil as an Operational Fatigue Countermeasure over Several Days of Reduced Sleep during a Simulated Escape and Evasion Scenario*, *Air Force Research Lab Brooks Afb Tx Human Effectiveness Dir/Biodynamics And Protection Div*, No. Afrl-He-Br-Tr-2002-0021, 2004, accessed December 18, 2016, http://oai.dtic.mil/oai/oai?verb=getRecord&metadataPrefix=html&identifier=ADA422857.

little side effects that helps maintaining alertness and performance."[83] The participants even pointed out the operational relevancy of Modafinil, recommending its use in the field.[84] The researchers suggested that the Air Force consider "incorporating Modafinil into various operational domains, especially those where sleep is often not an option allowed to the warfighter."[85]

In a similar study, the Canadian Defense and Civil Institute of Environmental Medicine investigated "the effects of Modafinil on the ability to self-monitor cognitive performance during 64 hours of sleep deprivation."[86] The tests showed that Modafinil promotes wakefulness and reduces fatigue, but also induces euphoria and overconfidence, particularly during the first few hours.[87] The researchers acknowledged its enhancing effects on cognitive performance under conditions of sleep deprivation and they encourage a better understanding of the side effects before recommending Modafinil as a safe and reliable sleep countermeasure.[88]

So far, Modafinil has been tested as a replacement for amphetamine. Although the results appear promising, the general problem with sleep-replacing supplements is the need to also maintain mental functioning during prolonged wakefulness.

2. Nootropics

Nootropics are compounds that act on the CNS to facilitate learning and memory or prevent cognitive impairments induced by diseases and brain damage.[89] This category consists of synthetic and natural compounds and includes non-sedative agents of various

[83] Whitmore et al., "The Efficacy of Modafinil as an Operational Fatigue Countermeasure over Several Days of Reduced Sleep during a Simulated Escape and Evasion Scenario."

[84] Ibid.

[85] Whitmore et al., "The Efficacy of Modafinil as an Operational Fatigue Countermeasure over Several Days of Reduced Sleep during a Simulated Escape and Evasion Scenario."

[86] Joseph Baranski and Ross Pigeau, "Self-Monitoring Cognitive Performance during Sleep Deprivation: Effects of Modafinil, D-Amphetamine and Placebo," *Journal of Sleep Research* 6, no. 2 (1997): 84–91.

[87] Baranski and Pigeau, "Self-Monitoring Cognitive Performance during Sleep Deprivation: Effects of Modafinil, D-Amphetamine and Placebo," 84−91.

[88] Ibid. 84−91.

[89] U. Schindler, D. K. Rush, and S. Fielding, "Nootropic Drugs: Animal Models for Studying Effects on Cognition," *Drug Development Research* 4, no. 5 (1984): 567−576.

types. Nootropics are used to improve concentration, memory, motivation, attention, and perception, or to treat brain disorders such as Alzheimer's and Parkinson's disease, brain trauma, stroke, and dyslexia.[90] Nootropics are referred to as smart drugs, memory enhancers, or cognitive enhancers. Nonetheless, these terms are not interchangeable. To be recognized as a nootropic the drug should:

> (1) enhance memory and learning abilities; (2) promote resistance to impairing agents (function under disruptive conditions like hypoxia and electroconvulsive shock); (3) protect the brain against various physical or chemical injuries; (4) increase the efficacy of neuronal firing control mechanisms in cortical and sub-cortical regions of the brain; (5) and possess very few side effects and have low toxic levels.[91]

Piracetam, a synthetic agent that was invented in the 1960s, is considered the prototype synthetic nootropic.[92] The compound acts on cognitive function without causing sedation or stimulation and is used for the treatment of age-related cognitive dysfunction, vertigo (dizziness), cortical myoclonus (involuntary twitching of muscles), dyslexia, and sickle cell anemia (a type of blood disorder).[93] Due to Piracetam's assumed limited side effects its use has expanded to the over-the-counter use by healthy individuals.

Pharmacologist Ornella Corazza and her team who research new drug trends and cultural/lifestyle issues behind risky behaviors, analyzed the misuse of Piracetam and noted that this synthetic nootropic "is widely used by healthy individuals to enhance cognitive functioning and performance in study and work, and as a recreational drug for its psychedelic properties."[94] Most users claim "improvement in learning, memory,

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[90] Ruchi Malik et al., "Towards Better Brain Management: Nootropics," *Current Medicinal Chemistry* 14, no. 2 (2007): 123–131; Olga Benešová, "Neuropathobiology of Senile Dementia and Mechanism of Action of Nootropic Drugs," *Drugs & Aging* 4, no.4 (1994): 285−303; J. Kessler et al., "Piracetam Improves Activated Blood Flow and Facilitates Rehabilitation of Poststroke Aphasic Patients," *Stroke* 31, no. 9 (2000): 2112–2116.

[91] Corneliu Giurgea and M. Salama, "Nootropic Drugs," *Progress in Neuro-Psychopharmacology* 1, no. 3 (1977): 235−247.

[92] Corneliu Giurgea, "Pharmacology of Integrative Activity of the Brain. Attempt at Nootropic Concept in Psychopharmacology," *Actualités Pharmacologiques* no. 25 (1972): 115.

[93] Bengt Winblad, "Piracetam: A Review of Pharmacological Properties and Clinical Uses," *CNS Drug Reviews* 11, no. 2 (2005): 169–182.

[94] Ornella Corazza et al., "The Diffusion of Performance and Image-Enhancing Drugs (PIEDs) on the Internet: The Abuse of the Cognitive Enhancer Piracetam," *Substance Use & Misuse* 49, no. 14 (2014): 1849–1856, doi:10.3109/10826084.2014.912232.

concentration, and 'verbal intelligence.'"[95] Recreational users state that Piracetam "has hallucinogenic and mood-improving effects and enhances dream experiences."[96] Recreational users often combine this nootropic with other recreational drugs.[97] In some cases, the combination of Piracetam with other drugs caused "hallucinations, psychomotor agitation, dysphoria, tiredness, dizziness, memory loss, headache, and severe diarrhoea."[98]

Natural or herbal nootropics represent the second type of nootropics. These compounds consist of nutraceuticals, functional foods, or plant extracts and are proven to enhance brain functions while also making the brain healthier. Natural nootropics increase blood circulation to the brain and transport nutrients.[99] Examples of natural nootropics are nicotine and Panax ginseng. Nicotine is a psychoactive alkaloid that is found in the leaves of the tobacco plant.[100] It has been shown to stimulate receptors that are responsible for the release of neurotransmitters that enhance memory function and learning, and reduce memory impairment.[101] Yet, the addictive potential and adverse health effects from tobacco products overshadow the beneficial effects of nicotine. Panax Ginseng, also known as the king herb, is an important traditional Chinese medicine.[102] The non-toxic herb is claimed to increase neurotransmitters in the brain, resulting in enhanced memory and cognitive

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[95] Corazza et al., "The Diffusion of Performance and Image-Enhancing Drugs (PIEDs) on the Internet: The Abuse of the Cognitive Enhancer Piracetam," 1849–1856.

[96] Corazza et al., "The Diffusion of Performance and Image-Enhancing Drugs (PIEDs) on the Internet: The Abuse of the Cognitive Enhancer Piracetam," 1849–1856.

[97] Ibid.

[98] Corazza et al., "The Diffusion of Performance and Image-Enhancing Drugs (PIEDs) on the Internet: The Abuse of the Cognitive Enhancer Piracetam," 1849–1856. Corazza's et al. open source study provides no conclusive answers and shows little evidence of cognitive improvements of Piracetam use by healthy individuals. It also lacks distinction in the doses taken compared to occurred side effects. It is, however, one of the few studies on the non-prescriptive use of the nootropic that shows its potential for abuse.

[99] J. Kessler et al., "Piracetam Improves Activated Blood Flow and Facilitates Rehabilitation of Poststroke Aphasic Patients," *Stroke* 31, no. 9 (2000): 2112–16, doi:10.1161/01.STR.31.9.2112.

[100] Kenneth G. Lloyd and Michael Williams, "Neuronal Nicotinic Acetylcholine Receptors as Novel Drug Targets," *Journal of Pharmacology and Experimental Therapeutics* 292, no. 2 (2000): 461.

[101] Noor A. Suliman et al., "Establishing Natural Nootropics: Recent Molecular Enhancement Influenced by Natural Nootropic," *Evidence-Based Complementary and Alternative Medicine* (2016): 1−12, doi:10.1155/2016/4391375; Timothy J. Greenamyre et al., "Dementia of the Alzheimer's Type: Changes in Hippocampal L-[3H] Glutamate Binding," *Journal of Neurochemistry* 48, no. 2 (1987): 543−551.

[102] Jing-Tian Xie, Sangeeta Mehendale, and Chun-Su Yuan, "Ginseng and Diabetes," *American Journal of Chinese Medicine* 33, no. 3 (2005): 397–404.

properties.[103] The antioxidant property of the herb is also assumed to suppress Alzheimer's-like pathology and improve memory performance, as well as speed attention processes in healthy individuals.[104]

Even so, the Cochrane Collaboration, an independent non-profit organization involved in organizing medical research information, in its review of the efficacy and adverse effects of Panax ginseng on healthy participants and participants with cognitive impairments or dementia, concluded "there is a lack of convincing evidence to show a cognitive enhancing effect of Panax ginseng in healthy participants and no high quality evidence about its efficacy in patients with dementia."[105] While the compound has been studied for a variety of uses, it appears there is a lack of evidence to conclusively support the health claims associated with the herb.

3. Adaptogens

Adaptogens are medical plants that improve the body's adaptability to stress and enhance concentration and endurance during fatigue.[106] Herbal expert Alexander Panossian and his co-authors describe adaptogens as "a new class of metabolic regulators (of a natural

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[103] J. T. Zhang, Z.W. Qu, Y. Liu, and H. L. Deng, "Preliminary Study on the Antiamnestic Mechanism of Ginsenoside Rg1 and Rb1," *European Journal of Pharmacology* 183, no. 4 (1990): 1460−1461; D. Tsang et al., "Ginseng Saponins: Influence on Neurotransmitter Uptake in Rat Brain Synaptosomes," *Planta Medica* 51, no. 3 (1985): 221−224.

[104] Santo-Neto dos Leopoldo et al., "The Use of Herbal Medicine in Alzheimer's Disease—A Systematic Review," *Evidence-Based Complementary and Alternative Medicine* 3, no. 4 (2006): 441–45, doi:10.1093/ecam/nel071; David O. Kennedy and Andrew B. Scholey, "Ginseng: Potential for the Enhancement of Cognitive Performance and Mood," *Pharmacology Biochemistry and Behavior* 75, no. 3 (2003): 687–700, doi:10.1016/S0091-3057(03)00126-6; David O. Kennedy, Andrew B. Scholey, and Keith A. Wesnes, "Modulation of Cognition and Mood Following Administration of Single Doses of Ginkgo Biloba, Ginseng, and a Ginkgo/Ginseng Combination to Healthy Young Adults," *Physiology & Behavior* 75, no. 5 (2002): 739–751; Jonathon L. Reay, Andrew B. Scholey, and David O. Kennedy, "Panax Ginseng (G115) Improves Aspects of Working Memory Performance and Subjective Ratings of Calmness in Healthy Young Adults," *Human Psychopharmacology: Clinical and Experimental* 25, no. 6 (2010): 462–71, doi:10.1002/hup.1138; S. I. Sünram-Lea et al., "The Effect of Acute Administration of 400 mg of Panax Ginseng on Cognitive Performance and Mood in Healthy Young Volunteers," *Current Topics in Nutraceutical Research* 3, no. 1 (2005): 65−74.

[105] J. Geng et al., "Ginseng for Cognition," *Cochrane Library* 12, no. CD007769 (2010), doi/10.1002/14651858.CD007769.pub2.

[106] I.I. Brekhman and I V Dardymov, "New Substances of Plant Origin which Increase Nonspecific Resistance," *Annual Review of Pharmacology* 9, no. 1 (1969): 419–30, doi:10.1146/annurev.pa.09.040169.002223; Alexander Panossian, G. Wikman, and H. Wagner, "Plant Adaptogens III. Earlier and More Recent Aspects and Concepts on Their Mode of Action," *Phytomedicine* 6, no. 4 (1999): 287–300.

origin) which have been shown to increase the ability of the organism to adapt to environmental factors and to avoid damage from such factors."[107] Adaptogens increase our tolerance to environmental changes such as cold, heat, and high altitude hypoxia, and promote our resistance to pain and infectious organisms.[108] Adaptogens are non-toxic, have a non-specific response, and a normalizing influence on physiology.[109] Under stressful conditions, adaptogens allow the human body to handle situations in a more resourceful manner. Adaptogens' ability to increase mental performance, attention, and concentration during fatigue is supported by several clinical studies.[110]

A much-researched adaptogen is Rhodiola Rosea*,* a plant that grows at high altitudes and is known to increase resistance to a variety of biological, chemical, and physical stressors. It is frequently used in traditional medicine for decreasing depression, countering fatigue, enhancing work performance, and preventing altitude sickness.[111] Its benefits are said to include anti-cancer, cardio-protective, and CNS enhancement.[112] A study done on the effects of the substance in students during demanding examinations showed improvement in psychomotor function, mental fatigue, wellbeing, and work

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[107] Panossian, Wikman, and Wagner, "Plant Adaptogens III. Earlier and More Recent Aspects and Concepts on Their Mode of Action," 287–300.

[108] Shalini Saggu and Ratan Kumar, "Stress Management and Herbal Adaptogens," *Chemistry Medicinal Value* 25 (2009): 253–271.

[109] David Winston and Steven Maimes, *Adaptogens: Herbs for Strength, Stamina, and Stress Relief* (Rochester: Healing Arts Press, 2007), 18.

[110] Jonathon L Reay, David O. Kennedy, and Andrew B. Scholey, "Single Doses of Panax Ginseng (G115) Reduce Blood Glucose Levels and Improve Cognitive Performance during Sustained Mental Activity," *Journal of Psychopharmacology* 19, no. 4 (2005): 357–65, doi:10.1177/0269881105053286; Erik Olsson, Bo von Schéele, and Alexander Panossian, "A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of the Standardized Extract SHR-5 of the Roots of *Rhodiola Rosea* in the Treatment of Subjects with Stress-Related Fatigue," *Planta Medica* 75, no. 2 (2009): 105–112, doi:10.1055/s-0028-1088346; V. Darbinyan et al., "Rhodiola Rosea in Stress Induced Fatigue—A Double Blind Cross-Over Study of a Standardized Extract SHR-5 with a Repeated Low-Dose Regimen on the Mental Performance of Healthy Physicians during Night Duty," *Phytomedicine* 7, no. 5 (2000): 365−371; A.A. Spasov et al., "A Double-Blind, Placebo-Controlled Pilot Study of the Stimulating and Adaptogenic Effect of Rhodiola Rosea SHR-5 Extract on the Fatigue of Students Caused by Stress during an Examination Period with a Repeated Low-Dose Regimen," *Phytomedicine* 7, no. 2 (2000): 85−89.

[111] R.A. Aksenova et al., "Comparative Characteristics of the Stimulating and Adaptogenic Effects of Rhodiola Rosea Preparations," *Stimulants of the Central Nervous System* 2 (1968): 3−12.

[112] Gregory S. Kelly, "Rhodiola Rosea: A Possible Plant Adaptogen," *Alternative Medicine Review: A Journal of Clinical Therapeutic* 6, no. 3 (2001): 293−302.

capacity.[113] A more recent study about the effectiveness of the plant in the treatment of individuals suffering from stress-related fatigue, revealed improvement in cognitive function and enhancing effects on fatigue levels, attention, and response to inducing stress.[114] Both studies confirmed beneficial properties in healthy individuals and patients suffering from stress-induced fatigue.

In addition, Rhodiola rosea has very low toxicity levels and few side effects. Clinical trials indicated a complete absence of side effects.[115] Because adaptogens appear to be powerful compounds with diverse beneficial traits in stress-related situations, to have low toxicity and no adverse effects, this should make them an interesting drug for potential military application.[116]

Table 1 provides a summary of cognitive enhancing supplements or drugs and their various effects, both intended and unintended.

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[113] Spasov et al., "A Double-Blind, Placebo-Controlled Pilot Study of the Stimulating and Adaptogenic Effect of Rhodiola Rosea SHR-5 Extract on the Fatigue of Students Caused by Stress During an Examination Period with a Repeated Low-Dose Regimen," 85−89.

[114] Erik M.G. Olsson, Bo von Schéele, and Alexander G. Panossian, "A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of the Standardized Extract SHR-5 of the Roots of *Rhodiola Rosea* in the Treatment of Subjects with Stress-Related Fatigue," *Planta Medica* 75, no. 2 (2009): 105−112.

[115] Kelly, "Rhodiola Rosea: A Possible Plant Adaptogen," 293−302.

[116] Although early clinical studies indicate that some individuals might experience an increase in irritability and insomnia, the adverse effects are typically caused by high dose intakes. Administering smaller quantities with a gradual dose increase dissipates these reactions.

Table 1. Overview of cognitive performance enhancers

Class	Type	Effects	Unwanted effects
Stimulants Chemical agents that produce a transient increase in psychomotor activity by affecting the central nervous system, enhancing specific body functions like alertness, wakefulness, memory, and locomotion.	**Ampakines** (e.g., CX517, CX717)	• Promotes attention span, alertness, and learning and memory abilities • Increases tolerance to cold and stress	• Possible headache, sleepiness, nausea, and impaired episodic memory (memory loss)
	Eugrogerics (e.g., Modafinil, Adrafinil)	• Promotes alertness, wakefulness, and arousal • Reduces tiredness and drowsiness	• Excitation or agitation, anxiety, insomnia, irritability, nervousness, aggressiveness, tremor, nausea, and sleep disturbance
	Amphetamines (e.g., Methylphenidate, Pemoline)	• Promotes attention, arousal, mood, and wakefulness • Reduces anxiety, rebound depression, and fatigue	• Highly addictive • Insomnia, agitation, dry mouth, dizziness, tremors, restlessness, increased hearth rate, loss of appetite, aggressiveness, and irritability
Nootropics Compounds that act on the CNS to facilitate learning and memory or prevent cognitive impairments induced by diseases and brain damage.[117]	**Synthetic** (e.g., Piracetam, Oxiracetam)	• Promotes memory functions, learning, and memory restoration • Reduces stress, drug addiction, cholesterol levels, and pain	• Excitation, depression, dizziness, and sleep disturbance • Psychomotor agitation, dysphoria, tiredness, memory loss, headache, and diarrhea
	Natural (e.g., nicotine, Panax ginseng)	• Promotes memory functions and learning • Reduces memory impairment	• Unknown
Adaptogens Medical plants that improve the body's adaptability to stress and enhance concentration and endurance during fatigue.[118]	**Natural** (e.g., Rhodiola rosea)	• Increases tolerance to environmental changes such as cold, heat, and high altitude hypoxia • Promotes resistance to pain, infectious organisms, and stress • Promotes attention and concentration during fatigue	• Increase in irritability and insomnia (caused by high dose intake)

[117] Schindler, Rush, and Fielding, "Nootropic Drugs: Animal Models for Studying Effects on Cognition," 567−576.

[118] Brekhman and Dardymov, "New Substances of Plant Origin Which Increase Nonspecific Resistance," 419–30, See also: Panossian, Wikman, and Wagner, "Plant Adaptogens III. Earlier and More Recent Aspects and Concepts on Their Mode of Action," 287–300.

B. PHYSICAL ENHANCERS

The second group of enhancers is physical enhancers. These compounds aim to improve endurance, strength, recovery, and pain resistance. We subcategorized physical enhancers into supplements, anabolics, blood doping, and gene doping. This classification is based on the substance's chemical structure and the effects it has on physical human functions.

1. Supplements

The United States Dietary Supplement, Health and Education Act defines dietary supplements as the following substances that are added to the diet: vitamins, minerals, amino acids, herbs or botanicals, and metabolites/constituents/extracts or a combination of any of these ingredients.[119] There are hundreds of legal supplements available on the market. For the sake of brevity, we will only discuss the most common supplements, which the sport and medical industries have found to yield the best results with minimal side effects and thus could possibly be useful (and acceptable for use) by the military. Research suggests that the best selling supplements legally available for purchase and use are creatine and protein supplements.[120]

Creatine is a non-essential amino acid that is naturally formed in the liver via a two-step process from metabolizing arginine and glycine.[121] It is also organically found in some meats and dairy products, and absorbed through digestion.[122] Creatine was originally discovered in 1830 by a French chemist and is one of the most widely studied ergogenic acids.[123] Supplemental creatine is popular among athletes and used as a therapy for patients

[119] Bernd Wollschlaeger, "The Dietary Supplement and Health Education Act and Supplements: Dietary and Nutritional Supplements Need No More Regulations," *International Journal of Toxicology* 22, no. 5 (2003): 387–390.

[120] Anthony Lattavo, Andrew Kopperud, and Peter D. Rogers, "Creatine and Other Supplements," *Pediatric Clinics of North America* 54, no. 4 (2007): 735–760, doi:10.1016/j.pcl.2007.04.009.

[121] Lattavo, Kopperud, and Rogers, "Creatine and Other Supplements," 735−760.

[122] Robin P. da Silva et al., "Creatine Synthesis: Hepatic Metabolism of Guanidinoacetate and Creatine in the Rat in Vitro and in Vivo," *American Journal of Physiology - Endocrinology and Metabolism* 296, no. 2 (2009): E256–261, doi:10.1152/ajpendo.90547.2008.

[123] Bernd Wollschlaeger, "The Dietary Supplement and Health Education Act and Supplements: Dietary and Nutritional Supplements need no more Regulations," *International Journal of Toxicology* 22, no. 5 (2003): 387−390.

suffering from neurological and neuromuscular disorders.[124] Creatine is vital to cellular function; it serves as a pH buffer, and plays an important role in the energy conversion process within cells of the brain and muscle tissues.[125] It facilitates the movement of high-energy phosphates from mitochondrial sites to cytoplasmic sites to convert fuel into energy.[126] Although crucial for brain function, creatine is naturally expelled from the body through the urine and therefore needs to be continuously replaced either through synthesis in the liver and kidneys or via diet.[127] Natural synthesis of creatine is more difficult for the body because it requires the cells to metabolize two other amino acids; absorbing creatine via the diet is easier.[128]

Despite its wide use, it is unclear whether creatine's performance enhancement effect is direct or indirect. Creatine in the body allows for better muscle function, which in turn facilitates greater performance during physical exertion. Higher performance subsequently enables physical adaptations such as increased lean muscle mass. Increases in lean muscle mass allow for more vigorous exercise, and are also associated with improvements in other biological mechanisms such as metabolism of carbohydrates for energy and oxidization of fat (necessary for transforming fat into a useful fuel source).[129]

Experiments suggest that use of creatine combined with resistance training leads to more muscle fiber.[130] Consequently, creatine could prove highly beneficial during military train-up phases, to build strength so that the body becomes more resilient to injury associated with heavy loads. But, it should not be expected to improve performance during

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124 John T. Brosnan and Margaret E. Brosnan, "Creatine: Endogenous Metabolite, Dietary, and Therapeutic Supplement," *Annual Review of Nutrition* 27, no. 1 (2007): 241–261, doi:10.1146/annurev.nutr.27.061406.093621.

125 Brosnan and Brosnan, "Creatine,," 241–261.

126 Ibid.

127 Ibid.

128 Creatine supplementation enables some water retention, which in turn reduces the natural expulsion of creatine through the urine. However, to absorb creatine consumed through supplementation into the muscle, physical exertion is required. Once absorbed, creatine has marked effects on the performance and strength capacity in short duration high intensity physical exertion less than 30 seconds, but virtually no effect on efforts that last longer than 150 seconds.

129 Brosnan and Brosnan, "Creatine," 241–261.

130 Ibid.

extended operations. There is some potential for negative side effects as well. Creatinine is a natural by-product of the consumption of creatine in the muscles during heavy exertion.[131] Creatinine must then be filtered out of the body by the kidneys. If creatinine is not adequately filtered out of the blood and expelled through urine, a condition called uremia may result. Uremia can eventually lead to renal failure.[132]

Creatine is well studied and its effects, both positive and negative, are manageable with proper administration, and should be considered of potential use in the military.

Another popular supplement that is considered safe and effective is **protein supplement powder**. Protein powders are derived from a variety of natural foods. Today, you can find protein powders ranging from plant-based formulas (such as soy), to whey and casein protein (derivatives of dairy products), to egg protein-based powders. Dietary protein supplements provide 20 essential and nonessential amino acids.[133] There appears to be some consensus that physically active individuals have a need for increased dietary protein. This is due to protein catabolism which occurs during high intensity training or endurance exercise.[134] This is particularly prevalent in those individuals who are consistently in a state of over-training, as are SOF operators on extended missions in austere environments. In such cases, the body is subject to a constant state of protein metabolism or ketosis. Because ketone bodies are also highly acidic, they can eventually lead to acidemia of the blood (pH less than 7.35). Irreversible cell damage and organ failure may result from prolonged states of acidemia.[135]

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[131] Da Silva et al., "Creatine Synthesis: Hepatic Metabolism of Guanidinoacetate and Creatine in the Rat in Vitro and in Vivo," E256–261.

[132] Michael L. Bishop, Edward P. Fody, and Larry E. Schoeff, *Clinical Chemistry: Principles, Techniques, and Correlations* (Philadelphia: Lippincott Williams & Wilkins, 2013), 583. The amount of creatine ingested must be extremely high to cause this disorder, and theoretically could also result from excessive digestion of protein, as creatine and creatinine are natural by-products of metabolizing these structures. However, individuals with reduced kidney function may experience detrimental side effects from protein or creatine intake, because the kidneys are not excreting the waste products. In conditions where soldiers either have naturally reduced kidney function or experience reduced kidney function because of dehydration from prolonged exertion in military operations or training, creatine intake should be avoided.

[133] Melvin H. Williams, "Facts and Fallacies of Purported Ergogenic Amino Acid Supplements," *Clinics in Sports Medicine* 18, no. 3 (1999): 633–649, doi:10.1016/S0278-5919(05)70173-3.

[134] Williams, "Facts and Fallacies of Purported Ergogenic Amino Acid Supplements," 633–649.

[135] Sheila Jennett, *Churchill Livingstone's Dictionary of Sport and Exercise Science and Medicine*, (New York: Elsevier Health Sciences, 2008) 6−7.

A functioning natural metabolic process is important for many other processes, such as regulating body temperature, sleep cycles, and reproduction. Under extreme conditions and instances of over-training, dietary supplementation can improve the body's metabolic function to sustain prolonged high intensity work outputs. Nonetheless, just as with prescription medications, supplements need to be taken according to stipulated protocols. Most problems or negative side effects associated with dietary supplements occur when they are not taken as prescribed. This seems to be a matter of education. For instance, taking twice as much does not mean you benefit twice as much. In fact, taking more than the recommended dose creates more waste by-products, which your body then must eliminate. A constant cycle of taxing your body's filtration system can have lasting effects.[136] Proper education is vital for appreciating how supplements should be used.

In sum, supplements can be highly beneficial if they are taken as recommended, but alone they will not produce performance-enhancing results. For any of these natural supplements to affect performance, proper diet and exercise is still needed to create physiological changes in strength, endurance, lean muscle mass, and metabolic efficiency. In the remaining subsections, we examine some synthetic physical enhancers, which have been used to try to boost performance.

2. Anabolics

Anabolic-androgenic steroids (AAS) are "synthetic derivatives of testosterone with potent anabolic effects on the musculoskeletal system, influencing lean body mass, muscle size, strength, protein metabolism, bone metabolism, sex drive, and collagen synthesis."[137] Beyond increasing body mass and strength, it improves tolerance to extreme exercise and strain by guarding the body against damage to muscle fibers, and during recovery there is an increase in protein synthesis.[138] AAS also has behavioral effects like

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[136] Bishop, *Clinical Chemistry: Principles, Techniques, and Correlations*, 14.

[137] Herbert A. Haupt and George D. Rovere, "Anabolic Steroids: A Review of the Literature," *American Journal of Sports Medicine* 12, no. 6 (1983): 469–484; Shalender Bhasin et al., "Testosterone Dose-Response Relationships in Healthy Young Men," *American Journal of Physiology-Endocrinology and Metabolism* 281, no. 6 (2001): E1172–E1181.

[138] Tetsuro Tamaki et al., "Anabolic Steroids Increase Exercise Tolerance," *American Journal of Physiology-Endocrinology And Metabolism* 280, no. 6 (2001): E973–E981.

euphoria, increased energy, and sexual arousal.[139] Most adverse effects from the non-medical use of AAS result in minor and reversible complications like the shrinking of testicles, the swelling of the breast tissue, or stretch marks.[140] With prolonged use, AAS could lead to cardiovascular disease, liver failure, or dermatologic changes.[141]

In their article "Effects of Androgenic-Anabolic Steroids in Athletes*,"* sports medicine specialist Fred Hartgens and physiologist Harm Kuipers review the effects of AAS on body composition and performance and the adverse effects on health status in athletes.[142] They conclude that both short- and long-term AAS use affects body dimensions and increases lean body mass, muscle mass, and strength.[143] Improvements, however, largely depend on dose levels, as well as the duration of use. Whether endurance is enhanced is unclear. Although few studies claim AAS are able to improve endurance performance, most indicate that AAS do not have endurance enhancing effects.[144] According to Hartgens and Kuipers, adverse effects include both minor and serious health risks.

Studies about self-monitoring high dose usage of AAS by athletes report increased sexual drive, occurrence of acne, an increase in body hair, and an increase in aggressive behavior.[145] Other untoward effects include elevated blood pressure, sleeplessness, loss of head hair, increased irritability, decreased feeling of wellbeing, decreased libido, increased appetite, growth of male breast tissue, and a decrease in quality and quantity of semen

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[139] Tung-Ping Su et al., "Neuropsychiatric Effects of Anabolic Steroids in Male Normal Volunteers." *Journal of the American Medical Association* 269, no.21 (1993): 2760–2764.

[140] Nick. A. Evans, "Current Concepts in Anabolic-Androgenic Steroids," *American Journal of Sports Medicine* 32, no. 2 (2004): 534, doi:10.1177/0363546503262202.

[141] Eric C. Kutscher, Brian C. Lund, and Paul J. Perry, "Anabolic Steroids," *Sports Medicine* 32, no. 5 (2002): 285–296; Todd E. Schroeder et al., "Effects of an Oral Androgen on Muscle and Metabolism in Older, Community-Dwelling Men," *American Journal of Physiology - Endocrinology And Metabolism* 284, no. 1 (2003): E120–28, doi:10.1152/ajpendo.00363.2002; S. Shuster, "The Cause of Striae Distensae," *Acta Dermato-Venereologica. Supplementum* 59, no. 85 (1978): 161−169.

[142] Fred Hartgens and Harm Kuipers, "Effects of Androgenic-Anabolic Steroids in Athletes," *Sports Medicine* 34, no. 8 (2004): 516.

[143] Hartgens and Kuipers, "Effects of Androgenic-Anabolic Steroids in Athletes," 527.

[144] Hartgens and Kuipers, "Effects of Androgenic-Anabolic Steroids in Athletes," 534.

[145] Ibid., 535.

production in male athletes that may lead to infertility.[146] AAS abuse can also induce liver disorders, have profound effects on mental state and behavior, and can lead to cardiovascular events, including acute heart failure or cardiac sudden death.[147]

Recently, the U.S. military has shown renewed interest in testosterone's effects on military performance. According to an article in *The Military Times*, the U.S. Department of Defense is studying whether "a boost of testosterone can keep military muscle and brains operating in top form during long periods of combat."[148] The Optimizing Performance in Soldiers Study involves 50 men of military service age. The participants are on calorie-restricted diets and put through combat-like physical activities. The researchers are examining the effect of testosterone on muscle mass when calories are restricted. According to the lead investigator, Jennifer Rood, the study is not aimed to see if soldiers, in general, can be turned into super warriors, but rather what effect being engaged in prolonged warfare has on SOF personnel and combat arms troops.[149] Regardless of the outcome, it will be interesting to see whether this leads to additional research or opens doors to examining a broader range of anabolic steroids.

3. Blood Doping

Blood doping or blood boosting aims to increase the number of red blood cells in circulation in order to enhance aerobic capacity and endurance.[150] Because red blood cells carry oxygen to the muscle with higher concentrations of red blood cells, the increase in oxygen concentration to the muscles increases athletic performance in the body.[151] There are three techniques to increase red blood cell levels: (1) blood transfusion, which involves

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146 Ibid.

147 Ibid., 536−543.

148 Patricia Kime, "Can Testosterone Boost Combat Performance? Pentagon Studies Hormone's Role in Fitness," *Military Times*, September 23, 2016, accessed January 12, 2017, http://www.militarytimes.com/articles/can-testosterone-boost-combat-performance-military-study-examines-hormones-role-in-fitness.

149 Kime, "Can Testosterone Boost Combat Performance? Pentagon Studies Hormone's Role in Fitness."

150 Mario Zorzoli, "Blood Monitoring in Anti-Doping Setting," *Recent Advances in Doping Analysis: Sport Und Buch Strauss. Edition Sport, Koln* (2005): 255–264; Daniel A. Smith and Paul J. Perry, "The Efficacy of Ergogenic Agents in Athletic Competition Part I: Androgenic-Anabolic Steroids," *Annals of Pharmacotherapy* 26, no. 4 (1992): 520−528.

151 Zorzoli, "Blood Monitoring in Anti-Doping Setting," 255–264

the infusion of blood from donors (heterologous) or a subject's own stored blood (autologous); (2) injections of synthetic oxygen carriers; and (3) injections of recombinant human erythropoietin (rHuEPO) to stimulate red blood cell production.

The utility of the first method, blood transfusion, depends largely on how the blood is stored (either conventionally or by high glycerol freezing). The conventional method includes adding preservatives and refrigerating the blood at 4°C.[152] The disadvantage of this technique is how limited the use of the blood is after it is stored. Conventional stored blood deteriorates progressively and becomes less flexible and more fragile, resulting in a loss of one percent of the stored red blood cells every day.[153] After three or four weeks, about 30 to 40 percent of the red blood cells are lost or have no practical use when reinfused.[154] Since it takes about eight to twelve weeks to fully recover from donating blood, conventionally blood storage can be beneficial for heterologous blood boosting but is of no use for autologous blood doping.[155] Yet, greater risks are associated with heterologous blood transfusion, such as the transmission of infectious diseases like hepatitis and HIV.[156]

The only way to benefit from autologous blood doping is by high glycerol freezing. This technique enables red blood cells to be stored for up to ten years and ensures an adequate interval between blood donation and reinfusion.[157] The blood is centrifuged and glycerol is added before storage in liquid nitrogen at -80°C.[158] Before reinfusion, the cells

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[152] M. Jones and D.S. Tunstall Pedoe, "Blood Doping–a Literature Review," *British Journal of Sports Medicine* 23, no. 2 (1989): 84–88.

[153] I.L. Kanstrup and B. Ekblom, "Blood Volume and Hemoglobin Concentration as Determinants of Maximal Aerobic Power," *Medicine and Science in Sports and Exercise* 16, no. 3 (1984): 256−262.

[154] Norman Gledhill, "Blood Doping and Related Issues: A Brief Review, "*Medicine and Science in Sports and Exercise* 14, no. 3 (1981): 183−189.

[155] Edward R. Eichner, "Blood Doping: Results and Consequences from the Laboratory and the Field," *Physician and Sportsmedicine* 15, no. 1 (1987): 120−22. In Jones and Tunstall, "Blood Doping–a Literature Review," 84–88.

[156] Jones and Tunstall, "Blood Doping–a Literature Review," 84–88.

[157] Ibid.

[158] Ibid.

undergo a series of washes to remove the glycerol. Over the course of the process, only 15 percent of the red blood cells are lost.[159]

The adverse effects of blood reinfusion are the same as with any intravenous infusion the possibility of allergic reactions, bacterial contamination, venous thrombosis, inflammation of veins, and blood poisoning.[160] An important step in limiting the risks and ensuring the safety of transfused blood is by screening it for infectious diseases. To date, however, and even when transfusions are conducted according to standard hospital procedures, there is no adequate method that eliminates all risks.

The second method for enhancing the uptake, transport, and delivery of oxygen to the blood is by using hemoglobin-based oxygen carriers (HBOC). HBOCs are artificial blood replacement products that perform the oxygen-carrying functions of red blood cells.[161] Although most of these compounds are still under development or in clinical trials, their effects on endurance performance seem promising and include increased serum iron (iron circulating in the blood), ferritin (proteins that functions as iron carriers), and erythropoietin.[162] Furthermore, HBOCs increase oxygen diffusion and exercise capacity by 20 percent; they also promote carbon dioxide production and lower lactate levels.[163] Beyond the general risks associated with intravenous infusion, HBOCs could cause the

[159] Gledhill, "Blood Doping and Related Issues: A Brief Review," 183−189.

[160] Jones and Tunstall, "Blood Doping–a Literature Review," 84–88; Nick A. Ghaphery, "Performance-Enhancing Drugs," *Orthopedic Clinics of North America* 26, no. 3 (1995): 433−442.

[161] Thomas Chang and Ming Swi, *Blood Substitutes: Principles, Methods, Products and Clinical Trials Vol. 1* (Basel: Karger Landes Systems, 1997), 9−18.

[162] G. S. Hughes Jr. et al., "Hematologic Effects of a Novel Hemoglobin-Based Oxygen Carrier in Normal Male and Female Subjects," *Journal of Laboratory and Clinical Medicine* 126, no. 5 (1995): 444−451.

[163] George E. J. Hughes Jr. et al.,"Pharmacokinetics of a Novel Hemoglobin-Based Oxygen Carrier in Humans," *Critical Care Medicine* 23, no. 1 (1995): A257. In Giuseppe Lippi et al., "Biochemistry, Physiology, and Complications of Blood Doping: Facts and Speculation," *Critical Reviews in Clinical Laboratory Sciences* 43, no. 4 (2006): 349–91, doi:10.1080/10408360600755313; George S. Hughes et al., "Hemoglobin-Based Oxygen Carrier Preserves Submaximal Exercise Capacity in Humans," *Clinical Pharmacology & Therapeutics* 58, no. 4 (1995): 434−443. In Giuseppe et al., "Biochemistry, Physiology, and Complications of Blood Doping: Facts and Speculation," 349–91.

narrowing of blood vessels, high blood pressure, gastrointestinal dysfunction, marked flatulence and meteorism (accumulation of gas in the abdomen), and renal toxicity.[164]

The third technique is to inject of rHuEPO. Human erythropoietin or endogenous erythropoietin (EPO) is a hormone produced by the liver and kidney that regulates red blood cell production.[165] Like EPO, rHuEPO promotes red cell production and is used to treat anemia, related to kidney failure, HIV, blood cancer, chemotherapy, and premature birth.[166] rHuEPO stimulates several physiological processes like the regulation of blood pressure, neuroprotection, and maximum oxygen uptake.[167] Moderate rHuEPO use has been shown to have beneficial effects on the quality of life by increasing happiness, wellbeing, sexual satisfaction, and sex drive.[168]

A study on the psychological effects of rHuEPO misuse by endurance athletes revealed that while self-esteem, self-perception, energy levels, and libido improved (along with their physical conditioning and endurance),[169] rHuEPO injections also caused hedonic

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164 York O. Schumacher and Michael Ashenden, "Doping with Artificial Oxygen Carriers," *Sports Medicine* 34, no. 3 (2004): 141−150. In Giuseppe, "Biochemistry, Physiology, and Complications of Blood Doping: Facts and Speculation," 349–91.

165 James W. Fisher, "Erythropoietin: Physiology and Pharmacology Update," *Experimental Biology and Medicine* 228, no. 1 (2003): 1−14.

166 Evanthia Diamanti-Kandarakis et al., "Erythropoietin Abuse and Erythropoietin Gene Doping," *Sports Medicine* 35, no. 10 (2005): 831–840.

167 Faqi Li, Zhao Zhong Chong, and Kenneth Maiese, "Erythropoietin on a Tightrope: Balancing Neuronal and Vascular Protection between Intrinsic and Extrinsic Pathways," *Neurosignals* 13, no. 6 (2004): 265–89, doi:10.1159/000081963; Kåre I. Birkeland et al., "Effect of rhEPO Administration on Serum Levels of sTfR and Cycling Performance," *Medicine and Science in Sports and Exercise* 32, no. 7 (2000): 1238−1243; B. Berglund and B. Ekblom, "Effect of Recombinant Human Erythropoietin Treatment on Blood Pressure and some Haematological Parameters in Healthy Men," *Journal of Internal Medicine* 229, no. 2 (1991): 125−130.

168 Roger W. Evans, Barbara Rader, and Diane L. Manninen, "The Quality of Life of Hemodialysis Recipients Treated with Recombinant Human Erythropoietin," *Journal of the American Medical Association* 263, no. 6 (1990): 825−830. In Center for Food Safety and Applied Nutrition, "Dietary Supplements," accessed April 19, 2017, https://www.fda.gov/Food/DietarySupplements/default.htm; J. Bommer et al., "Recombinant Human Erythropoietin Therapy in Haemodialysis Patients—dose Determination and Clinical Experience," *Nephrology Dialysis Transplantation* 2, no. 4 (1987): 238–242; J. Trembecki, et al., "[Improvement of Sexual Function in Hemodialyzed Male Patients with Chronic Renal Failure Treated with Erythropoietin (rHuEPO)]," *Przeglad Lekarski* 52, no. 9 (1994): 462–466. In Grégory Ninot, Philippe Connes, and Corrine Caillaud Connes, "Effects of Recombinant Human Erythropoietin Injections on Physical Self in Endurance Athletes," *Journal of Sports Sciences* 24, no. 4 (2006): 383−391.

169 Trembecki et al.,"[Improvement of Sexual Function in Hemodialyzed Male Patients with Chronic Renal Failure Treated with Erythropoietin (rHuEPO)]," 462−466. In Ninot, "Effects of Recombinant Human Erythropoietin Injections on Physical Self in Endurance Athletes," 383−391.

behavior. Although expectations about physical performance rose in tandem with fitness improvements, they ultimately did not result in greater feelings of satisfaction.[170] The study did not point to any physical side effects, but there are several risks to be aware of. Between 1987 and 2000, 23 elite cyclists who used rHuEPO died from stroke, heart attack, pulmonary embolism, or unexplained reasons.[171] Additional research on this form of doping is therefore needed.

The U.S. Army Research Institute of Environmental Medicine (USARIEM) has conducted several studies on the military applications of blood boosting. In 1986, researchers measured the physical exercise capabilities of U.S. Army Special Forces soldiers to determine the subsequent performance enhancing influence of autologous blood reinfusion.[172] The researchers examined 12 male soldiers, all of whom were members of the same team and met high aerobic fitness standards. Six team members were infused with 600 ml autologous blood and compared to the control group. The soldiers who were reinfused with autologous blood showed an increase in their red cell volume of 11 percent.[173] The control group, on the other hand, displayed a decrease in red cell volume of 3 percent.[174] The researchers concluded that blood reinfusion increased maximal aerobic power for at least ten days after infusion.[175]

Another study by USAREIM done in conjunction with the Naval Blood Research laboratory, examined "the effects of autologous erythrocyte infusion on blood volume and thermoregulation during exercise in the heat."[176] The researchers infused nine acclimated male subjects with blood supplements to measure their oxygen uptake during exercise-

[170] Trembecki et al.,"[Improvement of Sexual Function in Hemodialyzed Male Patients with Chronic Renal Failure Treated with Erythropoietin (rHuEPO)]," 462−466. In Ninot, "Effects of Recombinant Human Erythropoietin Injections on Physical Self in Endurance Athletes," 383−391.

[171] J. M. Tokish, "Ergogenic Aids: A Review of Basic Science, Performance, Side Effects, and Status in Sports," *American Journal of Sports Medicine* 32, no. 6 (2004): 1543–53, doi:10.1177/0363546504268041.

[172] Stephen R. Muza et al., "Elite Special Forces: Physiological Description and Ergogenic Influence of Blood Infusion," *Army Research Inst of Environmental Medicine Natick Ma,* no. USARIEM-M-41/86 (1986).

[173] Muza et al., "Elite Special Forces."

[174] Ibid.

[175] Ibid.

[176] Michael N. Sawka et al., "Influence of Polycythemia on Blood Volume and Thermoregulation during Exercise-Heat Stress," *Journal of Applied Physiology* 62, no. 3 (1987): 912−918.

induced heat stress. The test results indicated an increase in oxygen uptake of 11 percent as well as more maximal strength and a small thermoregulatory advantage.[177] The researchers considered "autologous erythrocyte infusion [to be] a powerful tool to further our understanding of physiological control mechanisms in response to exercise-heat stress."[178]

Other studies show that blood transfusion, in general, can have major effects on oxygen carriage and endurance capacity. When sufficient red blood cells are transfused, a definite improvement can be seen in endurance performance. However, blood transfusion may be risky. One method for limiting risks is hypoxic training. In 2007, the USARIEM studied the military applications of hypoxic training for high-altitude operations in situations where rapid deployment is involved and soldiers do not have the opportunity to fully acclimatize.[179] The researchers used a technique called intermittent hypoxic exposures (IHE) to simulate high altitude conditions. For one and a half hours a day for over a week, the participants were exposed to simulated altitudes above 4000 meters. The researchers concluded that IHE-induced altitude acclimatization appears to increase oxygen levels in the blood. "IHE is a promising approach to provide the benefits of altitude acclimatization to low altitude-based soldiers prior to their deployments to high mountainous regions."[180]

4. Gene Doping

Gene therapy is the modification of human DNA to fix a genetic problem at the source.[181] **Gene doping** aims to manipulate DNA to improve aspects of athletic performance, such as speed, power, or endurance. In sports, gene doping is defined as "transfer of nucleic acid sequences or the use of normal or genetically modified cells to

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177 Ibid.

178 Ibid.

179 Stephen R. Muza, "Military Applications of Hypoxic Training for High-Altitude Operations," *Medicine & Science in Sports & Exercise* 39, no. 9 (2007): 1625–1631, doi:10.1249/mss.0b013e3180de49fe.

180 Muza, "Military Applications of Hypoxic Training for High-Altitude Operations," 1625–1631.

181 H. J. Haisma and O. de Hon, "Gene Doping," *International Journal of Sports Medicine* 27, no. 4 (2006): 257–266, doi:10.1055/s-2006-923986.

enhance sports performance."[182] Depending on the effects desired, gene doping can boost oxygen supply, muscle mass, and pain tolerance, or it can delay the sense of fatigue. Examples of potential proteins for gene doping are rHuEPO, insulin-like growth factor, and myostatin.

As discussed in the previous section, rHuEPO stimulates endurance capacity by improving maximum oxygen uptake. In gene doping, rHuEPO is injected. Once cells incorporate it, specific gene sequences are copied, resulting in an increased production of proteins similar to rHuEPO.[183] In one study on mice and monkeys, the volume of blood was increased by 80 percent.[184] By contrast, in some animals the opposite occurred, causing anemia due to an autoimmune response.[185] Although these unexpected reactions have not been uniformly observed, they may pose serious problems should they occur in human trials.[186]

Another form of gene doping involves Insulin-like Growth Factor-1 (IGF-1). IGF-1 is a protein that has anabolic effects and is made in the liver and muscles.[187] Concentrated IGF-1 is used in the treatment of degenerative muscle conditions by targeting those specific muscles. Trials in mice injected with IGF-1 resulted in an increase in muscle mass of 15 percent and a 14 percent increase in strength without any specific training.[188] When resistance training was added, a similar study saw a significant increase in the mass of the

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[182] Toon van der Gronde et al., "Gene Doping: An Overview and Current Implications for Athletes," *British Journal of Sports Medicine* 47, no. 11 (2013): 670–678, doi:10.1136/bjsports-2012-091288.

[183] Giuseppe Fischetto and Stéphane Bermon, "From Gene Engineering to Gene Modulation and Manipulation: Can We Prevent or Detect Gene Doping in Sports?," *Sports Medicine* 43, no. 10 (2013): 965–77, doi:10.1007/s40279-013-0075-4.

[184] S. Zhou, J. E. Murphy, J. A. Escobedo, and V. J. Dwarki, "Adeno-Associated Virus-Mediated Delivery of Erythropoietin Leads to Sustained Elevation of Hematocrit in Nonhuman Primates," *Gene Therapy* 5, no. 5 (1998).

[185] Guangping Gao et al., "Erythropoietin Gene Therapy Leads to Autoimmune Anemia in Macaques," *Blood* 103, no. 9 (2004): 3300–3302.

[186] Gao et al., "Erythropoietin Gene Therapy Leads to Autoimmune Anemia in Macaques," 3300–3302.

[187] Haisma and de Hon, "Gene Doping," 257–266.

[188] Elisabeth R. Barton-Davis et al., "Viral Mediated Expression of Insulin-Like Growth Factor I Blocks the Aging-Related Loss of Skeletal Muscle Function," *Proceedings of the National Academy of Sciences* 95, no. 26 (1998): 15603−15607.

targeted muscles by up to 23 percent.[189] So far, these research results appear promising since there have been few side effects. Strengthening specific muscles according to the type of military mission to be undertaken might lead to improved performance. Yet, because IGF-1 is a relatively new protein, it requires additional testing before it can be studied in human clinical trials.

The third protein potentially useful for gene doping is Myostatin. Myostatin regulates muscle formation.[190] Since it appears to inhibit muscle cell growth and differentiation, blocking this activity can "result in dramatic and widespread increase in skeletal muscle mass."[191] A case study of a former professional athlete, who gave birth to an extraordinarily muscular boy, revealed a link between the absence of myostatin production and muscle mass development.[192] Genetic analysis of relatives who were likewise reported to be unusually strong, revealed a mutation in the myostatin gene.[193] This mutation resulted in a lack of myostatin production, which subsequently caused the unusual growth in muscle mass and muscle strength. Blocking the production of myostatin production is therefore expected to increase muscle mass and muscle strength and may have military potential.

Gene doping is a relatively new form of performance enhancement. So far, clinical studies have proven to be relatively safe.[194] Nonetheless, the risks may be substantial and are in many cases similar to those of other forms of doping. As with blood doping, boosting rHuEPO levels in healthy people will increase their chances of heart attack and stroke. Furthermore, the expression of rHuEPO that is delivered by gene therapy is difficult to

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[189] S. Lee, "Viral Expression of Insulin-like Growth Factor-I Enhances Muscle Hypertrophy in Resistance-Trained Rats," *Journal of Applied Physiology* 96, no. 3 (2003): 1097–1104, doi:10.1152/japplphysiol.00479.2003.

[190] Haisma and de Hon, "Gene Doping," 257–266.

[191] Yun-Sil Lee, Thanh V. Huynh, and Se-Jin Lee, "Paracrine and Endocrine Modes of Myostatin Action," *Journal of Applied Physiology* 120, no. 6 (2016): 592–98, doi:10.1152/japplphysiol.00874.2015.

[192] Markus Schuelke et al., "Myostatin Mutation Associated with Gross Muscle Hypertrophy in a Child," *New England Journal of Medicine* 350, no. 26 (2004): 2682–2688.

[193] Schuelke et al., "Myostatin Mutation Associated with Gross Muscle Hypertrophy in a Child," 2682–2688.

[194] J. Kimmelman, "Recent Developments in Gene Transfer: Risk and Ethics," *BMJ* 330, no. 7482 (2005): 79–82, doi:10.1136/bmj.330.7482.79.

control and may lead to overexpression that could reach toxic levels.[195] Another health risk is the autoimmune response to injected proteins, which may lead to the destruction of endogenous proteins. The autoimmune response in monkeys that caused severe anemia serves as a good example.

Table 2 provides a summary of physical enhancing supplements or drugs and their various effects, both intended and unintended.

195 Van der Gronde et al., "Gene Doping: An Overview and Current Implications for Athletes," 670–678.

Table 2. Physical performance enhancers

Class	Type	Effects	Unwanted effects
Supplements A product intended for ingestion that contains a dietary ingredient intended to add further nutritional value to the diet.[196]	**Creatine and Protein powders** (e.g., vitamins, minerals, herbs, amino acids, metabolite).	• Increases lean body mass, muscle size and strength • Promotes energy cycle within the cells	• Water retention • Creatinine by-product may produce acidemia • Waste by-product can stress the kidneys • Gastro-intestinal discomfort • Constipation
Anabolic Synthetic derivatives of testosterone with potent anabolic effects on the musculoskeletal system, influencing lean body mass, muscle size, strength, protein metabolism, bone metabolism, sex drive, and collagen synthesis.[197]	**Anabolic-androgenic steroids**	• Increases lean body mass, muscle size, and strength. • Promotes protein metabolism, bone metabolism, and collagen synthesis. • Promotes, sex drive, exercise tolerance, and recovery	• Cardiovascular o Elevated blood pressure, irregular heartbeat, thrombosis • Liver failure • Dermatologic o Acne, cutaneous striae, alopecia • Behavioral o Mood swings, aggression, depression • Male-specific o Libido changes, subfertility, testicular atrophy, impotence • Female-specific o Hirsutism/masculinization, menstrual irregularities, reduced breast size
Blood Doping Blood boosting aims to increase the number of red blood cells in circulation in order to enhance aerobic capacity and endurance.[198]	**Blood transfusion** (e.g., autologous, heterogolous)	• Promotes aerobic capacity and endurance • Promotes exercise recovery	• Infectious diseases like hepatitis and AIDS • Allergic reactions, bacterial contamination, blood poisoning • Venous thrombosis • Inflammation of veins
	Synthetic oxygen carriers (e.g., HBOCs)	• Promotes aerobic capacity and endurance • Promotes exercise recovery • Promotes oxygen diffusion and carbon dioxide production	• Allergic reactions, bacterial contamination, blood poisoning • Venous thrombosis • Inflammation of veins • Narrowing of blood vessels • Meteorism
	Erythropoietin (e.g., rHuEPO)	• Promotes aerobic capacity and endurance • Promotes exercise recovery • Increased red blood cell production • Promotes self-esteem, libido, and energy levels	• Increased risk of blood viscosity • Increased risk of stroke or heart attack • Allergic reactions, bacterial contamination, blood poisoning • Venous thrombosis • Inflammation of veins
Gene Doping Gene doping aims to manipulate DNA to improve aspects of athletic performance, such as speed, power, or endurance.[199]	**rHuEPO**	• Promotes aerobic capacity and endurance • Promotes exercise recovery • Increased red blood cell production	• Autoimmune response • Anemia
	Insulin-like growth factor	• Increases targeted muscle mass and strength	• Unknown
	Myostatin	• Leads to widespread increase in skeletal muscle mass and strength	• Unknown

[196] Wollschlaeger, "The Dietary Supplement and Health Education Act and Supplements" 387–390.

[197] Haupt and Rovere, "Anabolic Steroids," 469–484; Bhasin et al., "Testosterone Dose-Response Relationships in Healthy Young Men," E1172–E1181.

[198] Zorzoli, "Blood Monitoring in Anti-Doping Setting," 255–264; Smith and Perry, "The Efficacy of Ergogenic Agents in Athletic Competition Part I," 520–528.

[199] Gronde van der et al., "Gene Doping: An Overview and Current Implications for Athletes," 670–678.

C. CONCLUSION

One of the greatest challenges posed by PES/Ds is mapping their long-term effects on healthy individuals. Many performance enhancers spring from compounds designed to treat diseases. Healthy individuals may respond differently to these agents. The field of competitive sports is potentially an ideal environment in which to study the effects of performance enhancers on healthy individuals. Athletes present a homogeneous research population similar in many ways to the military population. Yet, experimenting with PES/Ds seems inconsistent with good sportsmanship. Therefore, it will likely be difficult to conduct long-term research on the effects of appropriate PES/Ds use on these healthy individuals, most comparable to SOF operators.

Another avenue of research could involve individuals who misuse, abuse, or take PES/Ds in a manner other than their prescribed use. Such research, however, would be anecdotal and could not include controlled experimentation. It would also rely on self-reporting, which itself can be unreliable. Baseline health conditions of the heterogeneous research population would also be unknown or undocumented by healthcare professionals. For those and other reasons, data from this population is effectively useless, especially for truly understanding the long-term effects of PES/Ds.

Militaries, on the other hand, provide ideal conditions for research. They offer almost limitless access to homogeneous research populations and their research could be tailored to the environments in which soldiers will operate and in which the PES/Ds would be utilized. Results would likely be more consistent and reliable than from other sources of research. Moreover, follow-on research would also be easy to execute. In these respects, military research seems both commonsensical and reasonable. However, although the military provides what may be the most reliable environment for PES/D research, any activity involving human enhancement has to be congruent with existing regulations and policies. In the next chapter, we review the current protocols on PES/Ds.

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V. REGULATIONS

Constitutional law and legislation on food supplements, medication, and gene therapy aim to protect individual rights, contribute to a person's health, and prevent unintended harmful effects. Using or testing PES/Ds is therefore restricted to those compounds that fall within regulations. Regulations vary from nation to nation; there is no international consistency. Different cultures and experiences naturally shape ethical norms, which likely explains the differences we see in regulation. Military law tends to be based on shared human values and internationally agreed upon human rights, which most Western cultures share. Military regulations regarding PES/Ds follow many of these principles (and in some cases add even greater restrictions); however, the legal position of the military does create a unique situation in which policies are subject to other considerations, like military effectiveness, mission success, or operational risks.

This chapter compares European, U.S., and Dutch regulations with current military regulations.

A. GOVERNMENTAL LEGISLATION

Since there are no laws specifically designed for PES/Ds, we fall back on legislation regulating food supplements, medication, and gene therapy.

1. Supplements

Nutritional additives like vitamins, minerals, proteins, and amino acids are concentrated sources of nutrients that are used as an addition to a normal diet. In the Netherlands, the regulations for legal nutritional additives are outlined in the Food Additives (Commodities Act) Decree of 2003, which is based on Directive 2002/46/EC of the European Parliament.[200] According to this decree, food supplements include only vitamins and minerals that "supplement the normal diet, are concentrated sources of nutrients or other substances with a nutritional or physiological effect, and are marketed in

[200] Ministerie van Volksgezondheid, Welzijn en Sport, *Warenwetbesluit Voedingssupplementen*, AMvB BWBR0014814, 's Gravenhage: Ministerie van Volksgezondheid, Welzijn en Sport (2003), accessed March 16, 2017, http://wetten.overheid.nl/BWBR0014814/2014-12-13.

dose form designed to be taken in measured small unit quantities."[201] Food supplements that comply with the legislation on food additives can be legally possessed, used, and commercially sold. While most food supplements claim to have enhancing effects on specific physical or cognitive functions, some supplements also claim to have medicinal properties. These products, even if they are not officially recognized as medicines, automatically fall under the Dutch Medicine Act of 2007.

Conversely, U.S. regulations prohibit a manufacturer of supplements from making any statement or specific medicinal claims. In the United States, the Food and Drug Administration (FDA) enforces regulations on products containing dietary supplements as well as their ingredients. Dietary supplements belong to a category of regulations separate from ordinary foods and drug products. Under the Dietary Supplement Health and Education Act of 1994, the FDA makes a clear delineation among dietary ingredients, supplements, and drugs. As with the European definition of supplements, the FDA states: "A dietary ingredient is defined as a vitamin; mineral; herb or other botanical; amino acid; dietary substance for use by man to supplement the diet by increasing the total dietary intake; or a concentrate, metabolite, constituent, extract, or combination of the preceding substances."[202] Any manufactured substance that meets these criteria will then fall into the category of "supplements" and is subsequently handled differently from drugs.

Under FDA regulation, a "supplement is not intended to treat, diagnose, prevent, or cure diseases."[203] Consequently, no such claims can be made in marketing them. The FDA in conjunction with the Fair Trade Commission can have products removed from the market if such products are considered unsafe or misbranded. Nonetheless, the FDA does not regulate supplements in the same manner as it does drugs, and supplements on the market are not as well researched as drugs.

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[201] European Parliament and of the Council, *Approximation of the Laws of the Member States Relating to Food Supplements*, Directive 2002/46/EC, Luxembourg: European Parliament and of the Council, 2002, accessed March 8, 2017, http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32002L0046.

[202] U.S. Code: Title 21 - Food and Drugs, *LII / Legal Information Institute*, accessed April 14, 2017, https://www.law.cornell.edu/uscode/text/21.

[203] "Laws Enforced by FDA," U.S. Food & Drug Administration, last modified July 2, 2015, https://www.fda.gov/RegulatoryInformation/LawsEnforcedbyFDA/default.htm.

2. Drugs

In the Netherlands, legislation is stricter about medicine than food supplements. Rules are applied to a medicine's composition, production, storage, and distribution. Additionally, only authorized medical institutions and persons are allowed to prescribe medical products. According to the Dutch Medicine Act of 2007 and Directive 2001/83/EC of the Community Code relating to medicinal products for human use, medical products are:

> any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.[204]

As long as medicines meet these criteria and are prescribed according to regulations, their use is considered legitimate.

In contrast, legislation in the United States applies the same guidelines and regulations to medicine as to food and food supplements. The FDA is responsible for ensuring "the safety of all food except for meat, poultry and some egg products; ensuring the safety and effectiveness of all drugs, biological products (including blood, vaccines and tissues for transplantation), medical devices, and animal drugs and feed; and ensuring that cosmetics and medical and consumer products that emit radiation do no harm."[205]

Compounds that are illegal to use in the Netherlands are listed in the Dutch Opium Act. The Act covers drugs that are addictive or prone to being abused as well as those that are physically harmful. The act distinguishes between hard and soft drugs, like cocaine, heroine, amphetamines, and morphine, and hashish, sedatives, and marijuana[206] It is

[204] European Parliament and of the Council, *Community Code Relating to Medicinal Products for Human Use,* Directive 2001/83/EC, Brussels: European Parliament and of the Council, 2001, accessed March 8, 2017, http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32001L0083.

[205] "Laws Enforced by FDA."

[206] "Difference between Hard and Soft Drugs," *Government of the Netherlands*, accessed January 12, 2017, https://www.government.nl/topics/drugs/contents/difference-between-hard-and-soft-drugs; Thomas Nordegren, *The A−Z Encyclopedia of Alcohol and Drug Abuse* (Universal-Publishers, 2002), 327.

prohibited to manufacture, prepare, process, sell, deliver, provide, or transport either type of drugs unless they are used for medical or scientific purposes and only under strict monitoring.[207] The sanctions on soft drugs are less severe and possession of a small quantity of soft drugs for personal use is even tolerated.[208]

Similarly, the United States categorizes drugs by their effects and use. Section 812 of Title 21 U.S. Code Controlled Substance Act categorizes drugs into "schedules." There are five established schedules, which are delineated by the potential for drug abuse, the acceptable medical use of the drug, the safety of the drug under medical supervision, and the potential for physical or psychological dependence.[209]

3. Gene Therapy

The United States' Public Health Service Act and the Federal Food, Drug, and Cosmetic Act serve as the catch-all for any products intended to prevent, treat, or diagnose diseases or injuries. Therefore, just as the FDA has authority to regulate dietary supplements and drugs, the FDA also has the obligation to provide guidance, oversight, and ultimately regulate the practices surrounding gene therapy. Here, too, the FDA's focus is to enforce a set of standards to ensure the continued safety, purity, and potency of products created for medical use.[210]

Current guidelines in the United States concern the unknown risks or delayed adverse events following exposure to Gene Transfer Technology. To address these issues, the FDA convened the Biological Response Modifiers Advisory Committee to solicit advice regarding long-term risks to subjects in gene therapy clinical trials. On the committee's recommendations, the FDA requires that sponsors of gene therapy studies

[207] Ministerie van Volksgezondheid, Welzijn en Sport, *Opiumwet*, Wet BWBR0001941, s' Gravenhage: Ministerie van Volksgezondheid, Welzijn en Sport, 2001, accessed March 16, 2017, http://wetten.overheid.nl/BWBR0001941/2009-07-01.

[208] "Difference between Hard and Soft Drugs."

[209] "Title 21 United States Code (USC) Controlled Substances Act - Section 812," accessed April 14, 2017, https://www.deadiversion.usdoj.gov/21cfr/21usc/812.htm

[210] Michael S. Labson, Krista Hessler Carver, and Marie C. Boyd, "FDA Regulation of Biological Products," in *The Pharmaceutical Regulatory Process, Second Edition* (New York: CRC Press, 2008), 103–129.

engage in long-term follow-up observations for "a 15-year period, including at least five years of annual examinations followed by ten years of annual queries of study subjects."[211]

In the Netherlands, legislation regarding research on genetically modified organisms (GMO) is still in development. Regulatory organizations that monitor nascent research are the Central Committee on Research Involving Human Subjects (CCMO) and the Ministry of Housing, Spatial Planning, and the Environment (VROM). The CCMO evaluates the medical, ethical, and scientific aspects of gene therapy research protecting participants who volunteer for medical trials. The agency evaluates whether research proposals meet the requirements of the Central Assessment of Medical Research (Human Subjects) Decree. The Ministry of Health, Welfare, and Sport must also approve clinical gene therapy trials. Their approval depends on whether there will likely be adverse effects and risks to the human subjects. The Ministry of VROM is responsible for assessing the environmental and human health risks of GMO activities and developing policies and regulations that protect against these risks. Evaluation of clinical gene therapy trials is based on EU Directive 2001/18/EC (which governs the deliberate release into the environment of GMOs).[212] The environmental risk assessment and subsequent permission for production and use is based on the Genetically Modified Organisms Decree.[213]

Ratifying gene therapy for enhancing human performance seems a complicated and lengthy process that would involve the cooperation of several agencies. The fact that the primary goal is to improve the capabilities of already healthy individuals instead of discovering new treatments or protection against diseases makes ratification even less likely.

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[211] U.S. Food & Drug Administration, *Cellular & Gene Therapy Guidances - Guidance for Industry: Gene Therapy Clinical Trials - Observing Subjects for Delayed Adverse Events,* U.S. Department of Health and Human Services, Center for Biologics Evaluation and Research, accessed April 14, 2017, https://www.fda.gov/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/cellularandgenetherapy/ucm072957.htm.

[212] Commission of the European Communities, *Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the Deliberate Release into the Environment of Genetically Modified Organisms and Repealing,* Council Directive 90/220/EEC, *Official Journal L 106, 17/4/2001* (2001), 1–39.

[213] Ministerie van Infrastructuur en Milieu, *Besluit Genetisch Gemodificeerde Organismen Milieubeheer 2013*, AMvB BWBR0035090, Wassenaar, Ministerie van Infrastructuur en Milieu, 2014, accessed March 16, 2017,. http://wetten.overheid.nl/BWBR0035090/2015-03-01.

Worth noting is that, overall, the Netherlands seems to place significant emphasis on regulating who can participate in research studies, while the United States has more detailed regulations on follow-up research to determine long-term effects.

B. MILITARY LEGAL POSITION

In the United States, health care is not a right.[214] Yet, as outlined in DOD Directive 6205.02, Policy and Program for Immunizations to Protect the Health of Service Members and Military Beneficiaries, the services are required to provide healthcare and immunization services in accordance with the most recent medical recommendations.[215] In accordance with U.S. Army Regulation 40–562, military personnel are required to receive certain vaccinations. The authority to enforce these regulations comes from the U.S. Congress. Under Article 1, section 8 of the U.S. Constitution, Congress has the right to create regulations for the land and naval forces via the Uniformed Code of Military Justice (UCMJ). The UCMJ provides Commanders with punitive authority over service members who do not obey lawful orders (Article 92), comply with procedural rules (Article 98) or neglect the good order and discipline of the unit (Article 134).[216]

Perhaps not surprisingly, for reasons of operational employability, servicemen must comply with taking vaccines.[217] Despite the rigidity of U.S. immunization law as well as the DODD 6205.02E, certain health conditions warrant medical waivers. Administrative waivers can be granted on religious grounds and according to time remaining in service; however, both require a command decision and once granted can be revoked at any time.[218]

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[214] Jody Heymann, Adele Cassola, Amy Ruab, and Lipa Mishra, "Constitutional Rights to Health, Public Health and Medical Care: The Status of Health Protections in 191 Countries," in *Global Health an International Journal for Research, Policy and Practice* 8, issue 6 (2013), 639‒653.

[215] DODD 6205.02. *Policy and Program for Immunizations to Protect the Health of Service Members and Military Beneficiaries* (2006).

[216] "Title 21 United States Code (USC) Controlled Substances Act - Section 812."; Certain civilians are also subject to this regulation, e.g., contractors, family members accompanying service members, etc. Furthermore, civilian employees working under DOD contracts are subject to the Occupational Safety and Health Administration standards outlined in 29 CFR 1910.1030.

[217] Ministerie van Defensie, *Wet Immunisatie Militairen*, Wet BWBR0002117, Soesdijk: Ministerie van Defensie, 1953, accessed March 16, 2017, http://wetten.overheid.nl/BWBR0002117/1998-01-01.

[218]Army Regulation 40–562, *Immunizations and Chemoprophylaxis for the Prevention of Infectious Disease* (2013), Chapters 2–6.

Several individual rights covered by Dutch law affect the legal viability of human enhancement. These fundamental rights limit state power over human dignity and freedom.[219] Article 109 of the Constitution for the Kingdom of the Netherlands, guides the policies to protect these rights.[220] For example, it helps shape articles 92 and 93 of Dutch military law regarding healthcare. Article 11 of the Constitution for the Kingdom of the Netherlands also impacts the military's treatment of those in uniform by protecting the sanctity of the human body while article 3 of the European Constitutional law describes the right of the integrity of the human.[221] Article 3 identifies the following rights:

> (1) Everyone has the right to respect for his or her physical and mental integrity; (2) In the fields of medicine and biology, the following must be respected in particular: (a) the free and informed consent of the person concerned, according to the procedures laid down by law, (b) the prohibition of eugenic practices, in particular those aiming at the selection of persons, (c) the prohibition on making the human body and its parts as such a source of financial gain, (d) and the prohibition of the reproductive cloning of human beings.[222]

In essence, given Dutch rules and regulations, Dutch soldiers are allowed to use legitimate food supplements, but at the same time cannot be forced to use them. The use of illegal supplements or supplements that negatively affect military employability is prohibited. With the exception of prescription drugs, use of compounds that are listed in the Opium Act is forbidden. Servicemen are permitted and, in some cases, obligated to use prescription medication. But, unless there is a medical need, they cannot be forced to take anything. Regulations on gene therapy are rather new and still under development. Yet, any form of interference with someone's physical integrity requires his explicit approval. And, even when approval has been given, the individual never gives up his individual rights.

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[219] P. J. J. Van der Kruit, "Handboek militair recht.-2e dr.," (2009).

[220] Ibid.

[221] G. J. Leenknegt, "The Protection of Fundamental Rights in a Digital Age," *Electronic Journal of Comparative Law,*(2002*)*, https://www.ejcl.org//64/art64-19.txt; Steve Peers et al., eds. *The EU Charter of Fundamental Rights: A Commentary* (Bloomsbury Publishing, 2014).

[222] Peers et al., eds. *The EU Charter of Fundamental Rights: A Commentary, 2014.*

U.S. regulations on this point are similar. Legitimate food supplements are authorized for use, but cannot be forced upon an individual. U.S. regulation does, however, enable military commanders to be more restrictive. For example, the SOCOM Chief of Staff issued a memorandum in 2008 (Policy Memorandum 08–01) prohibiting certain supplement use. In both the United States and the Netherlands, military personnel must comply with the taking of medications and vaccines for the sake of protecting their health and that of others in accordance with medical advice from appropriate medical authorities. Again, however, there must always be a medical need to enforce the use of medication.

C. RESPONSIBILITIES

The military has a responsibility to respect and protect the individual rights of its members. At the same time, it is also accountable for being ready to serve the nation wherever it is needed. This conflict of interest forces the military to occasionally impose exceptions to existing legislation and regulations. Nevertheless, to do so, in both the Netherlands and the United States., the Minister or Secretary of Defense has to request the exception from the legislature and this exception cannot be used for other situations.

The military also has a responsibility to keep its personnel healthy over the long-term, even after they have departed from active duty service. Therefore, when it issues products or techniques that contribute to their immediate good health, it must also protect them from harmful long-term effects. Since the effects of long-term use of many PES/Ds remain largely unknown or have been shown to be potentially harmful, it makes sense that the military remains cautious in providing such products or techniques.

D. CONCLUSION

There are specific laws and regulations that govern the composition, production, and use of food supplements and medicines. To conduct gene therapy research and implementation requires approval from several committees and requires extensive follow-up research. The fact that the military must respect soldiers' individual rights places certain limitations on what can be done with enhancements. The military is responsible for protecting its servicemen against the dangers of drug use. If the military enabled unregulated PES/D use, the individual would then be held responsible for his own welfare. The military, by serving as a tacit “pusher” would absolve itself from the responsibility of putting soldiers at risk with potentially harmful substances. Should the military do this, it would lose accountability over soldiers’ health and welfare. In either case, whether PES/Ds were issued or merely available, the military would find itself confronting numerous challenges.

How to best balance responsibility and regulation when it comes to PES/Ds *is* something the military could begin to tackle now, before availability outstrips control. Because rules of conduct are rooted in ethics, evaluating the ethics of enhancement and medical research in a military context should shed light on this critical tension between what might be good for the military and what might be helpful or harmful to the individual. In the following chapter, we evaluate the ethical arguments.

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VI. ETHICAL IMPLICATIONS AND INSIGHTS

Military effectiveness, mission success, and operational risks influence how militaries view the use of PES/Ds. As we have shown, present policy and regulations surrounding the potential use of such drugs are complex and, at times, not yet fully formed. However, we can and should push the debate beyond the mere legality of such use, or the formal ability to implement substances beneficial to the military, to consider the actual ethical permissibility of doing so. In our view, the ethical permissibility of such use will hinge primarily on necessity in a given context relative to the moral stakes involved. Of course, finding a balance between what is considered necessary and what is not depends largely on the demands of the particular situation and is usually affected by national or organizational interests, and the personal (to include cultural or religious) views of the individuals involved. As such, the normative opinions of the individuals who would potentially be taking PES/Ds should be prominently factored into this debate.

This chapter reviews the ethical arguments and counter-arguments regarding particular situations or contexts in which it could be morally acceptable to use PES/Ds. In Chapter VII, we examine survey results about the opinions about PES/D use by military members themselves. This information is important because it adds context about current beliefs and concerns regarding the topic and, more importantly, help us to determine how well the ethical arguments made in the current chapter align with attitudes of those who could potentially be asked to use PES/Ds.

First, we outline what we have found to be the central ethical concerns surrounding PES/D usage. These consist of two primary over-arching moral issues: worries surrounding the potential side effects of some PES/Ds, and apprehensions over the consent given by individuals who might be instructed to use such drugs in a military setting. We explore these arguments at some length and find that they are plausible concerns. However, we further find that the particular context of warfare can lead people to want to support the use of PES/Ds by military members. Namely, when the stakes are high enough, the use of PES/Ds may be justified by the nature of combat such that the ethical concerns against their use are overcome by mere immediate life and death concerns. If this argument holds, then the next step is to consider when such PES/Ds could be permissibly introduced or what criteria would have to be met to make the PES/Ds available. Lastly, we discuss concerns surrounding human testing, which would need to be implemented during training, to better understand how to safely utilize PES/Ds to optimize real world mission success. This need for greater testing, in turn, raises its own set of ethical concerns and moral tensions.

A. ETHICAL CONCERNS

Ethical dilemmas are inherent to the military profession. The modern military attempts to provide conceptual frameworks of codes and standards designed to help military members understand how they are expected to act morally. From a military perspective, the ethical solution to any problem varies depending on a wide variety of situational conditions. What seems morally wrong in one situation may be permissible in another. For example, deciding whether and to what extent the military could use PES/Ds depends on the context of the situation. Nonetheless, current regulations do not reflect this complexity. Policies are too rigid and do not provide enough flexibility. Paradoxically but tellingly, SOF encourages its soldiers to think “outside the box” and creatively operate within the confines of policy and regulation. Why not also adjust the policies and regulations?

To argue that PES/D use under certain conditions is ethically justifiable requires that we first lay out the primary moral concerns against PES/D use by the military. These have to do with potential side effects and long-term harms, and related demands for rigorous and careful testing. Second are ethical concerns over the autonomy of and consent by individual soldiers who are asked (or commanded) to take PES/Ds.

1. Side-effects and Potential Harms

As we saw in the previous chapter, militaries are charged with the moral responsibility of respecting the rights of individuals in military service and to caring for their wellbeing. As such, there is a moral imperative to not have them take PES/Ds that could cause harmful side effects. Consider for instance, a PES/D that enabled a SOF member to run faster and recover more quickly while under heavy stress in combat, but one that had a serious long-term debilitating effect on lung capacity. Such a side effect presents a clear moral impediment to the wanton use of such a drug, even if it provided certain gains, or even if the individual soldier wanted to take the drug. Indeed, one could conclude that giving a military member any PES/D, because of its potential negative side effects and other harms associated with its use, provides a clear ethical objection to such use.

Yet, sacrifices are sometimes necessary. For example, using a grenade could result in hearing loss, but this option will sometimes ensure mission success and therefore the risk of hearing loss becomes an acceptable cost to bear for the tactical advantage the grenade offers. Of course, the effects of a grenade are well known. Because they are well known, the risks can also be mitigated and that helps make their use more acceptable. Similarly, some PES/Ds may greatly benefit the mission. So then, why are we so reluctant to accept PES/Ds? Essentially, the stakes of the mission *and* the effects of the drugs are two variables that determine the acceptability threshold.

When we speak of thresholds we are referencing a specific moral calculus that weighs the potential harms to specific individuals, and their corollary rights to be respected as individuals, against a certain consequentialist demand for a high-stakes 'over-ride' that might necessitate the acceptance of those harms for the 'greater good.' This could be taken to be a version of what is sometimes called 'threshold deontology,' a normative approach that aims to respect the rights and wellbeing of individuals in all cases and follows normative principles that are independent of, and not derived from, consequentialist calculations. Even threshold deontology, though, recognizes that there are conditions under which consequentialist considerations can become so great—the stakes at hand so dire—that the non-consequentialist principles cross a threshold whereby they must be overridden by necessity.

This threshold depends on the level of harm to the individuals in question, the risks and importance of the particular mission, or the broader risk to the force as a whole. There is a point at which survivability becomes more important than the side effect risks involved with a particular tactic. Essentially, the only way to ensure that soldiers survive a given mission is to accept certain severe side effects of PES/Ds, the decision becomes one about their life or death. Again, consider the example of a hand grenade. Imagine a case where the commander of a small unit knows that his soldiers must use a grenade in a particular combat scenario or they will not survive. Even so, the commander also knows that given the conditions of the melee, the use of the grenade will almost certainly result in significant hearing loss for the soldier who employs it. The commander, of course, wants to respect that soldier's rights and cares about his long-term health, to include his hearing. However, the stakes of all of his soldiers' actual lives are such that they override concern for the one soldier's hearing and, in such circumstances, make the use of the grenade morally permissible.

The same could be said of the use of PES/Ds *under certain circumstances*. Even rather dire side effects of PES/Ds could be justified if their use could plausibly make the difference between life or death or, depending on the criticality of the mission, mission success or mission failure. Worth noting is that the context here is war. That is critical. Were the use of the grenade to result in long-term hearing loss in a mere training environment, the use of the grenade would not be justified; the corresponding stakes would not be high enough, nor would the use be necessary to fend off correspondingly high moral stakes.

2. Consent and Authority

Along with the long or short-term side effects possible from PES/D use, another key ethical concern revolves around individual consent and command authority. Respecting the consent of another individual is often the bedrock basis of respecting them as an autonomous agent with individual human rights. Forcing something upon someone against that individual's consent is often taken as a paradigmatic example of failing to respect the rights and moral worth of another.

To give consent, requires that you understand what it is that you are giving consent to. In the case of PES/Ds, giving consent implies understanding the consequences of taking PES/Ds. But, what is the purpose of giving or obtaining consent in the first place? Seeking consent is typically necessary when a decision maker does not have the authority to make such a decision by himself. Consent generates mutual understanding and an acceptance of the variables at hand. It is synonymous with approval or permission, which is the basis of cooperation. In order for teams or organizations to cooperate effectively, there must be some level of approval among the members of the group. Securing consent in a military context, however, is not always feasible or necessary. Indeed, consent as a normative concept is treated differently in many military contexts than it is elsewhere. Military leaders make decisions all the time without informing subordinates of all the potential consequences. In fact, it is quite often inefficient to seek consent from all soldiers within a given unit for each command decision. Militaries function because soldiers trust leaders to make the best decisions they can. Thus, in the military, it is often *trust,* and not explicit consent, that becomes the basis of cooperation.

Again, the reason for needing command trust in the military is because of the life and death circumstances encountered in warfare. If people's lives are directly on the line, a commander cannot—by moral necessity—await individual consent from each member of the group before committing them to action, and particularly not if that action is critical to their continued survival. Consequently, service members must often make decisions that would be considered unacceptable in other contexts. These decisions may result in the individual's wellbeing being sacrificed for the "greater good." In essence, there are occasions when the success of a military operation is more important, morally, than the wellbeing of the members carrying out that mission.

Sacrifice is inherent to military service. When weighing risks, decision makers have to consider sacrifices to men versus the significance of the mission. This is an important process in mission planning. If we regard PES/Ds as a potentially useful tool in the kit bag, then the willingness or reluctance to use PES/Ds becomes just another planning factor. They offer yet another option for helping to meet challenges and have to be weighed accordingly. Decisions involving difficult trade-offs are made in battle all the time.

To fully appreciate the argument we are making here, it is helpful to compare both of these moral concerns—side-effect harms and consent issues in a military context—with decisions where there are no life and death (or notional security) consequences. Imagine if an athlete, or a team of athletes, was making the kinds of decisions we are discussing, in a particular sporting event. No matter what the stakes in a sporting event might be, most athletes would quickly reject the risk of known long-term, permanent harm, just to possibly win that single event. Similarly, precisely because the stakes of sporting competitions are, by comparison to those in military missions, so low, we cannot fathom a plausible moral justification for overriding the consent of an individual athlete and forcing him or her to take PES/Ds against his or her will for the good of the team winning. Yet, in the life-and-death realm of warfare, this moral justification is often sound. Even then, however, when the stakes are at their highest, compulsion is only justified when it is both necessary and when a commander fully understands the stakes involved.

3. Moral Demand for Testing

In order to determine whether taking PES/Ds will enable mission success, even in the face of competing harms or consent concerns, we should first understand their likely effects in military and battlefield settings. Just as with any other tool, soldiers must also learn how to use PES/Ds effectively. Unlike grenades, however, effects of PES/Ds have been insufficiently researched in military settings. When researching the utility of any capability, unknown factors and conditions create challenges. In this case, the unknowns make ethical judgments about whether their use could be justified in particular cases all the more hazy.

Meanwhile, the more control we have over conditions, the better we can manage and minimize risks. Further, the more specificity we develop about both advantages and potential side effects, the better informed and more ethical, decision-making will be. Such knowledge can only come through testing. Thus, the potentiality that inheres in PES/Ds does not merely create corollary demand for far greater testing, but testing specifically within and for the military.

Here, we are not advocating for indiscriminate exploration of PES/Ds. Just because we have identified a need for testing does not mean that the ethical issues that testing itself raises can be ignored. Testing needs to be conducted under the supervision of qualified healthcare professionals, in accordance with medical ethical standards, in compliance with all regulations, and under proper oversight. The specific procedures and ethical concerns surrounding human testing are beyond the scope of this thesis, but it is nonetheless important to highlight how essential these are. For instance, in 1943, the U.S. Navy tested mustard gas on conscientious objectors in preparation for World War II. The test subjects did not know what they were volunteering for and experimenters used their authority to gain the participants' consent.[223] As reported by National Public Radio, subjects were "sworn to secrecy about the tests under threat of dishonorable discharge and military prison time."[224] Worse yet, follow-up research was not conducted, and sailors were not provided appropriate treatment for their injuries resulting from the experiments. This example illustrates the importance of maintaining a moral commitment to the subjects of experiments. Although this testing did provide valuable insights, individuals continued to suffer as a result. Understanding the importance of maintaining ethical integrity cannot be overstated.

4. Availability and Approach

Because lack of precision is a common element of war, we should want to understand how to use PES/Ds under a variety of situations. If their effects are ambiguous, it will be difficult to make decisions to justify their use. Human field-testing conducted under realistic conditions can provide the details service members need to make informed decisions about their own choices. The same holds for commanders who must make decisions for their operators. In addition, as with a weapon system or specific piece of equipment, testing under a variety of conditions is paramount.

In Chapter II we introduced neuroscientist Michael Russo's five guidelines for determining the conditions that would eventually justify PES/D use. His first guideline states that individuals' use of the compound should be truly informed. This, too, is why we urge gaining a better understanding of PES/Ds through testing and training. According to his first guideline, the use must also be voluntary. Here we differ because as we have pointed out, in the military consent is not always feasible; trust becomes a stand-in instead. Russo's third guideline states that the medication itself must be "safe for the individual and

[223] Caitlin, Dickerson, "Secret World War II Chemical Experiments Tested Troops by Race," *NPR.org*, accessed May 5, 2017, http://www.npr.org/2015/06/22/415194765/u-s-troops-tested-by-race-in-secret-world-war-ii-chemical-experiments.

[224] Dickerson, "Secret World War II Chemical Experiments Tested Troops by Race."

can be safely used within the context of the environment."[225] Because much of what the military is expected to do is considered unsafe, the term "safe" has to be considered relative given the context of the situation. To return to our example of throwing a grenade, the grenade itself is unsafe, but a degree of safety is built around it via proficiency. This comes from testing and training under a variety of conditions. According to Russo's third guideline, too, "the intended use of the cogniceutical is consistent with its dosage and pharmacological function."[226] Again, this determination can only come through testing and training. His fourth guideline stipulates, "the cogniceutical is used with appropriate medical supervision."[227] We agree; to optimize the utility of the PES/Ds requires proper supervision in the military. Finally, Russo advocates that non-pharmacological alternatives be fully utilized. This echoes our understanding that a threshold exists for when PES/D use is acceptable.

As should be clear by now, there will be instances when it will be impossible to determine what the consequences will be if we do *not* make drugs available for use on the battlefield and in specific circumstances. Consequently, it is unrealistic to expect that Russo's five conditions can always be met.

At the same time, if any argument is equipped to tackle the ethical issues surrounding PES/D use in the military, it is SOF. SOF is asked to test new and advanced equipment and provide feedback on a regular basis. This is part of their role in the broader military community. Their opinion and perspective is valued on everything else, so why should we not include their opinion or perspective on something as edgy as PES/Ds?

5. The Soldier's View

Operators within Special Operations undergo several forms of assessment and selection to determine their capacity and ability to serve in SOF. These tests do not merely gauge strength and physical endurance, but also moral standards, mental maturity, and overall professionalism. SOFs hold their soldiers and leaders to a higher standard because

[225] Russo et al., "Ethical Use of Cogniceuticals in the Military of Democratic Nations," 39–41.

[226] Ibid.

[227] Ibid.

they will be expected to make snap decisions that could have strategic impacts. Much responsibility is placed in the hands of a young captain or junior non-commissioned officer. So, given that we entrust these soldiers and officers with making tactical decisions that could have strategic impact, why would we not want to take into account their opinions and thoughts when creating policies and regulations that will directly affect their performance, health, and welfare? After all, the military already accepts that these individuals are fully capable of making well-informed tough decisions.

This thesis would not have been complete had we not asked SOF operators for their thoughts about the moral acceptability of using PES/Ds. We were also interested in what their biggest ethical concerns are. Our methodology does not include hard empirical data, but rather is primarily anecdotal with the aim of gaining some initial insights into where some in this community stand. We turn now to their perspective.

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VII. SURVEY AND RESULTS

Our survey consisted of two sections, totaling 75 statements about PES/Ds to which we sought scaled responses. A copy of the survey in its entirety is found in Appendix A. The survey was designed to assess attitudes regarding the use of PES/Ds from an operational perspective. We were also interested in the military utility and applicability of PES/Ds. Attitudes about side effects, confidence in the military's administering of PES/Ds, individual willingness to use PES/Ds, and views about cultural/group norm/team dynamics.

A. SURVEY DESIGN

In the first section of 54 questions, our statements were relatively generic. Then the survey included a summary of several adverse effects associated with PES/Ds. In the following section of 20 questions we repeated some of the earlier statements to see if and to what extent attitudes toward using PES/Ds changed once additional information about side effects was available. The survey ended with two open-ended questions that asked for participants to express what they believe are acceptable conditions under which to use PES/Ds and what most concerns them. The open-ended questions are included in Appendix C. The survey did not identify specific substances or situations but rather concentrated on specific purposes. We recognize this limits our ability to define acceptance thresholds for specific types of performance enhancers. It also prevents us from perfectly correlating the data here with the threshold justification arguments presented in the previous chapter. However, our approach reveals operators' overall attitude regarding PES/Ds and the concerns they have with them, and shows to what extent their attitudes align, or fail to align, with the moral arguments we present in this thesis.

A survey of this kind is new; therefore, the survey instrument used has not yet been validated. The survey results (depicted in Appendix B) serve an anecdotal purpose and cannot be considered as hard empirical social science data. Yet, again, the results provide valuable insights that help improve our understanding of the issue. As such, our survey venture should be considered merely an initial step in unpacking the complexity of attitudes surrounding PES/Ds.

B. PARTICIPANTS

Why the SOF community? As discussed previously, Special Operations Forces are tasked with mission sets that make high physical and mental demands. Teams of special operators work autonomously, with limited resupply, and in austere environments. Moreover, special operations are ad hoc, and can be frequent, long-lasting, and irregular. These dynamics not only require a high state of readiness, but also put the SOF population typically at a greater risk for injuries. The SOF population could thus benefit from the enhancing effects PES/Ds have on physical and mental capabilities, as well as recovery.

We obtained survey data from SOF members of the Royal Netherlands Marine Corps, and the U.S. military. The sample size for our Dutch population represents about 25 percent of the Netherlands SOF Marines. The U.S. SOF sample, on the other hand, represents only about one percent of the force. This disparity in sample size is due to the difference in overall population size of each SOF.

1. Demographics

The demographics are uniquely different for each sample. The U.S. sample represents all services, which provides a better representation of the joint SOF population, but all respondents were of the same rank. The international sample, on the other hand, consists only of Dutch Marine SOF members but includes more demographic variety (e.g., age, rank, and education levels). With the Dutch Marine SOF sample the cross-tabulation test demonstrates weak correlations between openness to performance enhancers and age, rank, and educational level. There is only a slight positive relationship between rank and acceptability of the use of PES/Ds. By contrast, when we evaluate the relationship between rank and overall acceptability attitudes, senior non-commissioned officers (Sr. NCOs) prove to be outliers. Otherwise, in what may be a surprising finding to most people, our statistical tests show that, with the exception of Sr. NCOs, the higher the rank the more positive the normative attitudes regarding the use of PES/Ds. On the other hand, the acceptability among Sr. NCOs is split nearly 50/50 between agreeing and disagreeing that PES/Ds are acceptable for military operations.

2. Overall Results

Overall, participants demonstrate a favorable normative attitude toward the acceptability of PES/D use. In general, there is a 67 percent favorable attitude toward the acceptability of PES/Ds. Only 15 percent report unfavorable attitudes, while the remaining 18 percent are undecided. Additionally, 74 percent responded favorably to the statement that it is acceptable to explore the use of PES/Ds to maintain a military advantage over our adversaries. Only 10 percent expressed an unfavorable attitude and 16 percent were undecided. Initially it appears that, on average, SOF soldiers display an accepting attitude toward the use of PES/Ds. If such findings bear out, it would correspond well to the moral arguments for the justification of PES/D use we offered in Chapter VI.

Even so, the willingness or acceptance to use PES/Ds is highly dependent on the terms involved. For instance, 93 percent of our participants agreed to accept the use of PES/Ds only if they were fully informed about all side effects, while 83 percent would refuse PES/D use if not fully informed. Overall, participants preferred to have a choice about whether or not to use PES/Ds, which is congruent with the moral argument for in-depth testing of PES/Ds. Notably too, the preference for having a choice about whether or not to use PES/Ds does appear to strengthen the ethical concerns regarding consent and authority covered in the previous chapter.

Another interesting observation comes from the respondents' attitudes about the reasons to use PES/Ds. We asked about their willingness to use PES/Ds for specific purposes—such as to improve physical performance, strength, endurance, cognitive performance, alertness, memory, to counter fatigue, reduce stress, improve learning abilities, improve courage, and increase tolerance to pain. The highest approval rating, 64 percent, went to improving alertness. However, all responses about these kinds of enhancements were favorable (with favorability ranging from 51 to 64 percent). With an average of 24 percent undecided that leaves about 19 percent of participants who seem opposed the use of PES/Ds.

SOF soldiers are not without concerns about PES/Ds' side effects, legal consequences, or the social stigma associated with them. Despite operators' seemingly positive attitudes, our respondents maintain consistent concern about their health and the welfare of their units. The results show an 84 percent positive response rate for being very concerned about long-term side effects. On the other hand, the response for short-term side effects was not as strong: only 64 percent expressed strong concerns. This suggests that some SOF members might identify some instances in which mission success outweighs short-term side effects.

Despite the concerns about potential adverse effects, however, operators seem to favor the need to conduct human subjects testing. Notably, 74 percent of our respondents agreed that it is acceptable to explore the use of PES/Ds and 63 percent also agreed that human testing is acceptable in order to explore the utility of PES/Ds for military use. Moreover, 54 percent agreed that human subject testing is necessary. Again, this correlates well with the moral demand for testing that, we argue, derives from the use of PES/Ds being justified in some situations (e.g., in extremis).

Interestingly, too, after being provided additional information about potential adverse effects, the operators seemed to accept the use of PES/Ds *more*. This result is both unexpected and surprising. Based on the current survey design, we cannot explain why acceptability levels rose. The topic of PES/Ds is relatively new. It is possible that attitudes about the military use of performance enhancers changed as respondents went through the survey and as they were asked to think about the possible opportunities and consequences. Explaining this further is just one of the many areas that merits additional research.

3. Differences between Dutch and U.S. Results

The attitudes of Dutch and U.S. participants towards PES/Ds are comparable with some exceptions. Overall, acceptability of PES/Ds among the U.S. participants was higher. U.S. operators also gave greater weight to mission success than to short-term side effects. Additionally, they agreed more strongly that PES/Ds should be used consistently. The Dutch participants were less willing to use PES/Ds for any purpose. However, the Dutch attitudes mirror the U.S. attitudes in that cognitive enhancement and alertness are considered the most acceptable rationales for PES/D use. Dutch operators seem to be less affected by peer pressure; on average, the Dutch participants disagreed more strongly that if their teammates used PES/Ds they would also use PES/Ds. U.S. operators, for their part, objected more strongly to the military having the authority to order service members to take PES/Ds.

Because our U.S. sample exclusively consisted of officers, we separated the Dutch officers' responses to compare them to U.S. officers' attitudes. A comparative examination between the two groups reveals significant congruence. This suggests that cultural differences may not be present; rather bigger differences may be associated with rank. This suggests the need to further refine the survey instrument or to administer the survey by rank, by year group, and by other factors.

C. CONCLUSION

So, what do these results suggest and what should be the next step? Overall, soldiers are moderately accepting of the prospect of PES/D use for military purposes. Soldiers are concerned mostly about potential risk factors that include side effects, dependency, and substance abuse. Soldiers strongly feel the need to be fully informed about all potential effects, and they want and would demand proper administration of the substances. Risk mitigation is extremely important, primarily because SOF operators seem so concerned with long-term effects and health concerns associated with PES/Ds.

These opinions and attitudes will not shape policies and regulations, but they are an important factor to take into account when considering whether PES/D use is ethically acceptable. Our survey research suggests that the average soldier and officer are amenable to the idea of using PES/Ds for military operations; therefore, the next steps will be to figure out where the threshold is in terms of what should and should not be considered acceptable for future development and possible use.

Perhaps the most useful information gleaned from the survey is the overall positive attitude towards human testing. This observation may be especially useful to practitioners devising future medical studies. Given recent interest in this topic by USSOCOM, it is our hope that this conversation continues and the community pushes forward in analyzing all advances, not just in the hard technologies, but also in human optimization and performance enhancement of biological systems.

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VIII. CONCLUSION

We have reviewed specific PES/Ds the regulations surrounding these substances, and examined the moral concerns and ethical realities that pertain to their potential use in the military. This thesis concludes that there *are* ethically permissible uses for PES/Ds within the military, and by SOF, in particular. Moreover, our examination of a sampling of SOF attitudes toward such use likewise supports our conclusion. Based on our findings, we assess that the broader SOF community should be open and willing to engage in the research and testing necessary to see whether such a conclusion deserves to stand. To that end, the type of PES/Ds, the extent of their use, and the conditions under which they would be utilized need to be explored through more rigorous testing—under safe but realistic conditions. It is only after more knowledge is gained about the specific combat advantages certain PES/Ds can offer, and more importantly about the particular risks operators who take them will run, that the actual thresholds of justifiable use on any given military mission can be defined.

Our survey results indicated that operators themselves are likely to welcome a more proactive approach on the part of the military. Over the course of our research, we have found that there has been little military experimentation with PES/Ds outside of wartime conditions. Furthermore, in these cases, experimentation was halted due to extremely negative short-term side effects. Yet, drugs and supplements have evolved greatly since the world wars. Short-term testing of some newer supplements and drugs have resulted in minimal side effects. Even so, approval for long-term human testing is extremely restrictive due to past experiments, heightened concerns about human rights, and greater sensitivity to bioethical concerns.

This creates a knowledge gap that our survey participants recognized as a major shortfall in advancing human performance science and technology. For instance, operators we surveyed responded favorably to exploring potential performance boosting substances that will reduce the risks associated with SOF's increased operational tempo, and that will increase physical advantages over adversaries to enable greater mission success. However, despite their overall positive attitude, our participants were also not without concerns, and rightly so. These concerns revolved around the long-term side effects of taking PES/Ds, along with concerns about addiction, reliability, and the natural physical limitations of the human body. These concerns can only be allayed or confirmed through testing.

Finding a balance between what is considered necessary and what is not will always depend on the situation and will be affected by many variables. Based on the findings discussed throughout this thesis, it is our recommendation that the medical community spare no effort to help determine safe practices and proper utilization of PES/Ds designed to not only benefit the mission, but also the individual warfighter. At this point, it appears that the possibilities are limitless.

Our research was guided by the initial thesis question: Could conditions be met such that it is morally justifiable to allow Special Operations Forces to use performance-enhancing supplements or drugs to improve individual capabilities, develop greater resiliency, and expand the overall performance of SOF units and, if so, what are the implications? Our thorough consideration of the ethical question led us to understand that it is indeed justifiable to allow SOF to use PES/Ds. The next step is to fill in a more detailed picture of the conditions under which it would be morally justifiable to do so, which requires additional human subjects testing. Furthermore, our survey data suggest that SOF operators themselves support this notion and agree that testing is vital. Still, it is not enough to end by saying that to answer this initial research question the military needs to conduct tests. Rather the military has a moral obligation to do so. Otherwise, tomorrows' soldiers may find themselves being drugged to ill effect in a future war, such as happened in the past when testing was not conducted timely in advance of critical need. The tragedy will be that today we have the will (in the guise of SOF operators) and the way, thanks to bio-ethically informed research models. Consider this: the time to experiment and determine the usefulness of PES/Ds is not in combat.

APPENDIX A. SURVEY QUESTIONNAIRE

Performance-enhancing Drugs Survey

You are invited to participate in a survey for a research study on regulating the use of performance-enhancing drugs (PEDs) within the Special Operations Forces (SOF).

This survey is designed to provide information to help evaluate the current knowledge and attitudes towards PEDs and shall contribute in the development of guidelines for PED use. These results may also benefit other units in the NATO special operations community.

The survey should take about 20-25 minutes to complete. Please note that all survey records and data collected are confidential: individuals who participate will not be identified. Your input is important for establishing a roadmap for the use of PEDs in a military context. We hope you will choose to participate in this survey. However, you are free to stop participating at any time or to skip survey questions without penalty.

If you have any questions regarding this study, please contact the principal investigator, Dr Bradley Strawser, bjstrawser@nps.edu, or the researchers, MAJ CGJ Wigger, cwigger@nps.edu or CPT Patricia Oelschlager, pjoelsch@nps.edu.

Demographics

Age	<25	25-30	31-35	36-40	41-45	>45
	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ	Ⓕ
Rank	Soldier	Corporal	Sergeant	Senior NCO	Officer	
	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ	
Educational level	< High school	High School	College	University		
	Ⓐ	Ⓑ	Ⓒ	Ⓓ		

Introduction

PEDs are substances that aim to temporarily or permanently improve your current cognitive capabilities and physical performance beyond your natural limitations. Cognitive enhancers focus on promoting learning abilities and memory; increasing alertness, wakefulness, and concentration; and controlling emotions like fear, anger, excitement, or stress. Physical enhancers aim to improve endurance, strength, and pain resistance. PEDs have the potential to enhance our mental and physical limitations and could benefit overall performance of SOF units. But the use of PEDs raises many questions about moral responsibilities, short- and long-term effects for the individual using the drugs in relation to mission success, and the role of the military as a "pusher".

This section is designed to assess your attitude regarding the use of PEDs from an operational perspective.	**Strongly disagree**	**Disagree**	**Neutral**	**Agree**	**Strongly agree**
1. When PEDs contribute to mission success, it should be acceptable to use them.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
2. When PEDs contribute to mission success, it would be wrong not to use them.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
3. To maintain military superiority, it is necessary to use PEDs.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
4. To maintain military superiority, it is acceptable to use PEDs.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
5. (Possible) short-term side effects from PEDs are more important than mission success.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
6. (Possible) long-term side effects from PEDs are more important than mission success.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
7. The use of PEDs is only acceptable during missions.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ

This section is designed to assess your attitude toward military utility of PEDs and exploration of implementation.	**Strongly disagree**	**Disagree**	**Neutral**	**Agree**	**Strongly agree**
8. To maintain military superiority, it is necessary to explore PEDs' potential.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
9. To maintain military superiority, it is acceptable to explore PEDs' potential.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
10. To improve SOF performance, it is important to explore the use of PEDs.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
11. To explore the effects PEDs have on performance, they should be used in training.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
12. To explore the effects PEDs have on performance, they should be used repeatedly.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
13. To explore the potential of PEDs, it is necessary to do military human testing.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
14. To explore the potential of PEDs, it is acceptable to do military human testing.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ

This section is designed to assess your attitude regarding the side effects PEDs could cause.	**Strongly disagree**	**Disagree**	**Neutral**	**Agree**	**Strongly agree**
15. I am concerned about PEDs' short-term side effects.	A	B	C	D	E
16. I am concerned about PEDs' long-term side effects.	A	B	C	D	E
17. I am concerned about PEDs that could cause behavioral problems (e.g. depression, aggression, irritability, nervousness).	A	B	C	D	E
18. I am concerned about PEDs that could cause minor physical pain or discomfort (e.g. vomiting, cramps, sleeplessness, dizziness, tiredness, headache, diarrhea).	A	B	C	D	E
19. I am concerned about PEDs that could decrease the quality and quantity of semen production, or infertility.	A	B	C	D	E
20. I am concerned about PEDs that could cause serious health risks (e.g. increased blood pressure, heart disease, liver disorders, cancer).	A	B	C	D	E

This section is designed to assess your confidence in the military when it comes to administering PEDs.	**Strongly disagree**	**Disagree**	**Neutral**	**Agree**	**Strongly agree**
21. I have confidence in the military, *in general*, when it comes to administering PEDs.	A	B	C	D	E
22. I have confidence in the military, *in general*, when it comes to testing PEDs.	A	B	C	D	E
23. I have confidence in military *medical institutions* when it comes to administering PEDs.	A	B	C	D	E
24. I have confidence in military *medical institutions* when it comes to testing PEDs.	A	B	C	D	E
25. I have confidence in the likelihood of commanding officers when it comes to administering PEDs.	A	B	C	D	E
26. When PEDs increase mission success, the military must have the authority to order servicemen to use them.	A	B	C	D	E
27. I will only use PEDs when ordered to.	A	B	C	D	E
28. I want to decide for myself whether or not I use PEDs.	A	B	C	D	E
29. It is important to be fully informed about the effects and adverse effects of PEDs before using them.	A	B	C	D	E
30. As a commanding officer, I am confident about ordering my team members / unit to use PEDs (if applicable).	A	B	C	D	E
31. If I am not fully informed about the effects and adverse effects of PEDs, I refuse to use them.	A	B	C	D	E

This section is designed to assess your willingness to use / preferences regarding specific PEDs.

		Strongly disagree	Disagree	Neutral	Agree	Strongly agree
32.	I am willing to use PEDs that improve physical performance.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
33.	I am willing to use PEDs that improve physical strength.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
34.	I am willing to use PEDs that improve physical endurance.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
35.	I am willing to use PEDs that increase tolerance to pain.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
36.	I am willing to use PEDs that improve cognitive performance.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
37.	I am willing to use PEDs that counter fatigue.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
38.	I am willing to use PEDs that improve courage.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
39.	I am willing to use PEDs that improve alertness.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
40.	I am willing to use PEDs that reduce stress.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
41.	I am willing to use PEDs that improve learning abilities.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
42.	I am willing to use PEDs that improve memory.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ

		YES	**NO**
43.	Do you think your spouse will agree to your one-time/short-time/long-time use of PEDs if the military deemed these as mission essential?	Ⓨ	Ⓝ
44.	Do you think your spouse's views on PEDs use would affect your willingness to use them?	Ⓨ	Ⓝ

This section is designed to assess cultural differences within countries or SOF units regarding the use of PEDs.

		Strongly Disagree	Disagree	Neutral	Agree	Strongly agree
45.	Physical performance is an important aspect of operating in the SOF community.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
46.	Mental performance is an important aspect of operating in the SOF community.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
47.	If my team members use PEDs, I am willing to use them too.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
48.	PEDs are only effective if everyone uses them.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
49.	When PEDs improve performance, and the military administers them, it should be allowed to set new physical standards.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
50.	A team member who underperforms, because he refuses to use PEDs, has a negative effect on team cohesion.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
51.	A team member, who underperforms because he refuses to use PEDs and thereby impacts team performance, should be expelled from the team.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
52.	I am capable of self-administering PEDs.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
53.	I would tell my friends/family when I am using PEDs.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
54.	Militaries that use PEDs are cheating.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ

Understanding several adverse effects

This section provides two examples of PEDs and its side effects. After reading the examples you are asked to answer additional questions.

Amphetamine-based medications like Adderall, Generic, and Dexedrine are fast-acting compounds that may counter fatigue and promote focus and task performance. The side effects seem manageable, even though use of these PEDs can cause anorexia, weight loss, sickness, vomiting, stomach cramps, increase in heart-rate and blood-pressure, and sleeplessness.

Anabolic-androgenic steroids (AAS) increase body mass, muscle-mass, and strength; improve exercise tolerance and recovery; and have behavioral effects that can induce euphoria, increase energy, and increase sexual arousal. Adverse effects include both minor and serious health risks. Studies about self-monitoring high dose usage of AAS by athletes indicate increased sexual drive, occurrence of acne, an increase in body hair, and an increase in aggressive behavior. Other untoward effects include: elevated blood pressure, sleeplessness, loss of head hair, increased irritability, increased feelings of well-being, decreased libido, growth of male breast tissue, and a decrease in quality and quantity of semen production that may lead to infertility. AAS abuse may also induce liver disorders, have profound effects on an individual's mental state and behavior, and can lead to cardiovascular events, including acute heart failure or cardiac sudden death.

This section is designed to assess your attitude regarding the use of PEDs from an operational perspective, knowing that there could be side effects involved.	**Strongly Disagree**	**Disagree**	**Neutral**	**Agree**	**Strongly Agree**
55. Despite the possibilities of side effects, we should allow to use of PEDs that will contribute to mission success.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
56. Despite the possibilities of side effects, when PEDs contribute to mission success, it would be wrong not to use them.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
57. Despite the possibilities of side effects, maintaining military superiority requires the use of PEDs.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
58. Despite the possibilities of side effects, it should be acceptable to use PEDs in order to maintain military superiority.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
59. To better understand the effects PEDs have on performance and to better control the side effects, PEDs should be used *during training*.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
60. To better understand the effects PEDs have on performance and to better understand and control the side effects, PEDs should be used *repeatedly*.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
61. Possible short-term side effects from PEDs are more important than mission success.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
62. Possible long-term side effects from PEDs are more important than mission success.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ

This section is designed to assess your attitude regarding testing PEDs in order to better understand their effects and military utility, knowing that there could be side effects involved.	**Strongly Disagree**	**Disagree**	**Neutral**	**Agree**	**Strongly Agree**
63. Despite the possibilities of side effects, to maintain military superiority, it is necessary to explore PEDs' potential.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
64. Despite the possibilities of side effects, to maintain military superiority, it is acceptable to explore PEDs' potential.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
65. Despite the possibilities of side effects, to improve SOF performance, it is important to explore the use of PEDs.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
66. Despite the possibilities of side effects, to explore the effects PEDs have on performance, they should be used in training.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
67. Despite the possibilities of side effects, to explore the effects PEDs have on performance, they should be used repeatedly.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
68. Despite the possibilities of side effects, to explore PEDs' potential, it is necessary to do military human testing.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
69. Despite the possibilities of side effects, to explore PED's potential, it is acceptable to do military human testing.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ

This section is designed to assess your attitude regarding the side effects PEDs could cause.	**Strongly Disagree**	**Disagree**	**Neutral**	**Agree**	**Strongly Agree**
70. I am concerned about the short-term side effects of PEDs.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
71. I am concerned about the long-term side effects of PEDs.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
72. I am concerned about PEDs that could cause behavioral problems (e.g. depression, aggression, irritability, nervousness).	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
73. I am concerned about PEDs that could cause minor physical pain or discomfort (e.g. vomiting, cramps, sleeplessness, dizziness, tiredness, headache, diarrhea).	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
74. I am concerned about PEDs that could decrease quality and quantity of semen production, or infertility.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ
75. I am concerned about PEDs that could cause serious health risks (e.g. increased blood pressure, heart disease, liver disorders, cancer).	Ⓐ	Ⓑ	Ⓒ	Ⓓ	Ⓔ

This section is an opportunity for you to express in your own words your opinions and concerns regarding the use an implementation of PEDs. Do not include any information that could potentially contain Personally Identifiable Information (PII). Do not disclose any incriminating information or experience with PED use.

76. Under what conditions do you feel that it would be acceptable to use PEDs for operational purposes? **Do not include any information that could potentially contain Personally Identifiable Information (PII). Do not disclose any incriminating information or experience with PED use.**

77. What concerns you the most about the use and implementa**tion of PEDs for operational** purposes? **Do not include any information that could potentially contain Personally Identifiable Information (PII). Do not disclose any incriminating information or experience with PED use.**

Thank you for participating!

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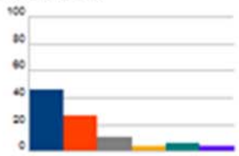
APPENDIX B. SURVEY RESULTS

Item Analysis Graph Report

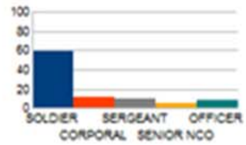
AGE DEMO



Response	Percent
LESS THAN 25	46.30
25-3-	26.85
31-35	11.57
36-40	4.63
41-45	6.48
OVER 45	4.17

Mean: 2.11

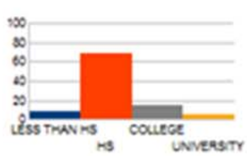
RANK



Response	Percent
SOLDIER	60.19
CORPORAL	12.96
SERGEANT	10.65
SENIOR NCO	6.94
OFFICER	9.26

Mean: 1.92

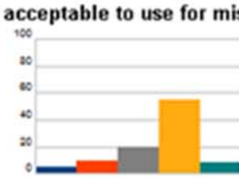
EDUCATION LEVEL



Response	Percent
LESS THAN HS	9.72
HS	68.98
COLLEGE	15.28
UNIVERSITY	5.56

Mean: 2.17

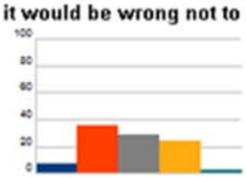
acceptable to use for mission success



Response	Percent
Strongly Disagree	5.56
Disagree	9.72
Neither Agree or Disagree	20.37
Agree	55.56
Strongly Agree	8.80

Mean: 3.52

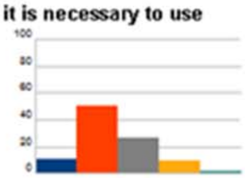
it would be wrong not to use



Response	Percent
Strongly Disagree	7.41
Disagree	35.65
Neither Agree or Disagree	29.17
Agree	24.54
Strongly Agree	2.78

Mean: 2.80

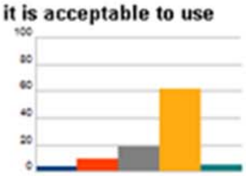
it is necessary to use



Response	Percent
Strongly Disagree	10.65
Disagree	50.93
Neither Agree or Disagree	26.39
Agree	9.72
Strongly Agree	2.31

Mean: 2.42

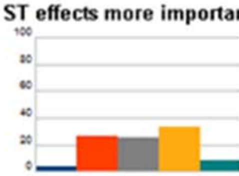
it is acceptable to use



Response	Percent
Strongly Disagree	4.17
Disagree	10.19
Neither Agree or Disagree	18.52
Agree	61.57
Strongly Agree	5.09

Mean: 3.53

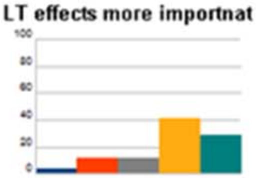
ST effects more important the MS



Response	Percent
Strongly Disagree	4.17
Disagree	27.31
Neither Agree or Disagree	25.46
Agree	33.80
Strongly Agree	9.26

Mean: 3.17

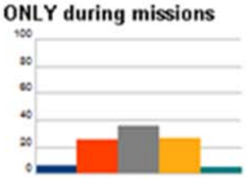
LT effects more importnat than Mission



Response	Percent
Strongly Disagree	4.63
Disagree	12.04
Neither Agree or Disagree	12.04
Agree	41.20
Strongly Agree	29.63

Mean: 3.80

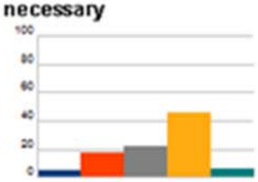
ONLY during missions



Response	Percent
Strongly Disagree	6.02
Disagree	25.46
Neither Agree or Disagree	35.65
Agree	26.85
Strongly Agree	5.56

Mean: 3.00

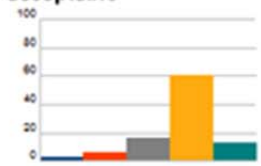
necessary



Mean: 3.31

Response	Percent
Strongly Disagree	5.56
Disagree	18.06
Neither Agree or Disagree	22.69
Agree	46.76
Strongly Agree	6.94

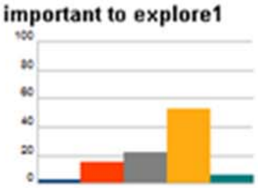
acceptable



Mean: 3.75

Response	Percent
Strongly Disagree	2.78
Disagree	6.94
Neither Agree or Disagree	16.20
Agree	61.11
Strongly Agree	12.96

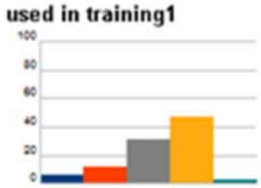
important to explore1



Mean: 3.43

Response	Percent
Strongly Disagree	3.70
Disagree	15.28
Neither Agree or Disagree	21.76
Agree	53.24
Strongly Agree	6.02

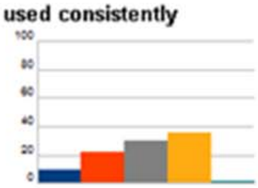
used in training1



Mean: 3.30

Response	Percent
Strongly Disagree	6.02
Disagree	12.04
Neither Agree or Disagree	31.48
Agree	47.22
Strongly Agree	3.24

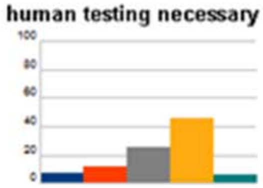
used consistently



Mean: 2.98

Response	Percent
Strongly Disagree	9.72
Disagree	22.22
Neither Agree or Disagree	30.56
Agree	35.65
Strongly Agree	1.85

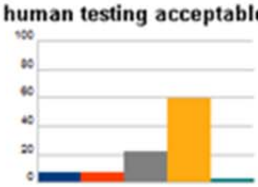
human testing necessary



Mean: 3.33

Response	Percent
Strongly Disagree	7.87
Disagree	12.04
Neither Agree or Disagree	25.93
Agree	46.76
Strongly Agree	6.94

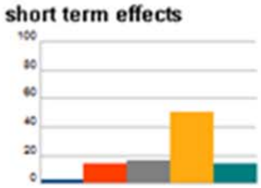
human testing acceptable



Mean: 3.44

Response	Percent
Strongly Disagree	7.41
Disagree	7.41
Neither Agree or Disagree	22.22
Agree	59.26
Strongly Agree	3.70

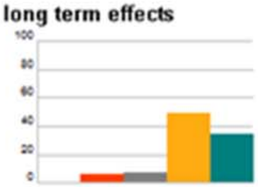
short term effects



Mean: 3.57

Response	Percent
Strongly Disagree	3.70
Disagree	14.35
Neither Agree or Disagree	16.67
Agree	50.93
Strongly Agree	13.89

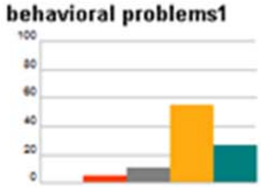
long term effects



Mean: 4.11

Response	Percent
Strongly Disagree	1.39
Disagree	6.02
Neither Agree or Disagree	7.87
Agree	49.07
Strongly Agree	35.19

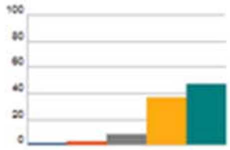
behavioral problems1



Mean: 4.01

Response	Percent
Strongly Disagree	1.39
Disagree	5.09
Neither Agree or Disagree	11.11
Agree	55.09
Strongly Agree	26.39

want the choice



Mean: 4.27

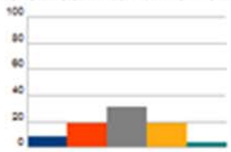
Response	Percent
Strongly Disagree	1.85
Disagree	3.24
Neither Agree or Disagree	8.80
Agree	37.50
Strongly Agree	47.22

inform on side effects

Mean: 4.64

Response	Percent
Strongly Disagree	0.93
Disagree	0.46
Neither Agree or Disagree	5.09
Agree	19.44
Strongly Agree	71.30

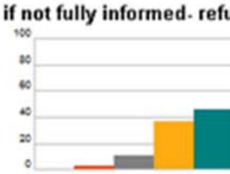
As CO confident in ordering team



Mean: 2.88

Response	Percent
Strongly Disagree	9.26
Disagree	19.44
Neither Agree or Disagree	31.02
Agree	18.52
Strongly Agree	4.63

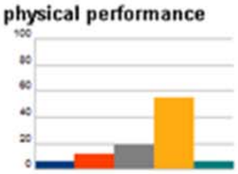
if not fully informed- refuse



Mean: 4.25

Response	Percent
Strongly Disagree	1.39
Disagree	3.24
Neither Agree or Disagree	11.11
Agree	36.57
Strongly Agree	46.76

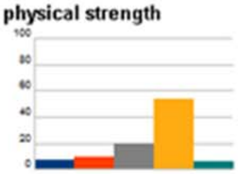
physical performance



Mean: 3.42

Response	Percent
Strongly Disagree	6.94
Disagree	12.04
Neither Agree or Disagree	18.52
Agree	55.56
Strongly Agree	6.02

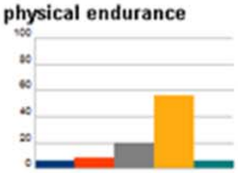
physical strength



Mean: 3.44

Response	Percent
Strongly Disagree	7.41
Disagree	10.19
Neither Agree or Disagree	19.91
Agree	54.63
Strongly Agree	6.94

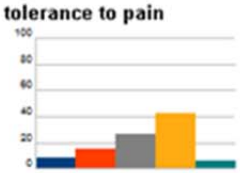
physical endurance



Mean: 3.48

Response	Percent
Strongly Disagree	6.94
Disagree	8.80
Neither Agree or Disagree	19.91
Agree	56.48
Strongly Agree	6.94

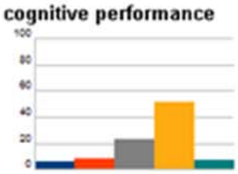
tolerance to pain



Mean: 3.21

Response	Percent
Strongly Disagree	8.80
Disagree	15.74
Neither Agree or Disagree	26.39
Agree	42.59
Strongly Agree	6.02

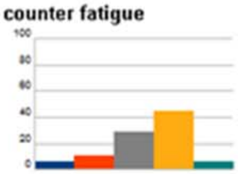
cognitive performance



Mean: 3.46

Response	Percent
Strongly Disagree	6.48
Disagree	8.80
Neither Agree or Disagree	23.61
Agree	51.85
Strongly Agree	7.41

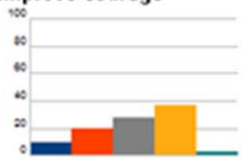
counter fatigue



Mean: 3.34

Response	Percent
Strongly Disagree	6.48
Disagree	10.65
Neither Agree or Disagree	29.63
Agree	44.91
Strongly Agree	6.02

improve courage



Mean: 3.02

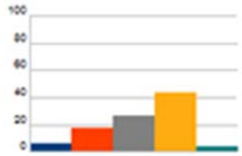
Response	Percent
Strongly Disagree	10.19
Disagree	20.37
Neither Agree or Disagree	28.24
Agree	37.50
Strongly Agree	2.78

improve alertness

Mean: 3.50

Response	Percent
Strongly Disagree	6.94
Disagree	8.33
Neither Agree or Disagree	19.44
Agree	57.41
Strongly Agree	6.94

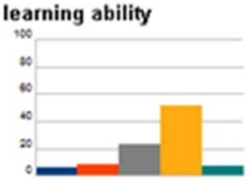
reduce stress



Mean: 3.21

Response	Percent
Strongly Disagree	6.48
Disagree	18.06
Neither Agree or Disagree	26.39
Agree	43.98
Strongly Agree	4.17

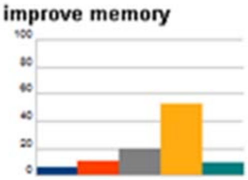
learning ability



Mean: 3.47

Response	Percent
Strongly Disagree	6.48
Disagree	8.80
Neither Agree or Disagree	23.61
Agree	52.31
Strongly Agree	7.87

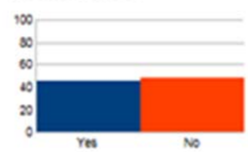
improve memory



Mean: 3.50

Response	Percent
Strongly Disagree	6.02
Disagree	10.65
Neither Agree or Disagree	19.91
Agree	53.24
Strongly Agree	9.72

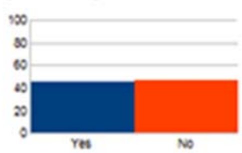
spouse agree?



Mean: 0.48

Response	Percent
Yes	45.83
No	49.07

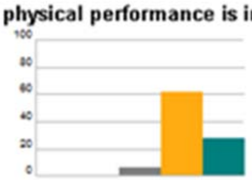
spouses opinion affect?



Mean: 0.50

Response	Percent
Yes	46.76
No	47.22

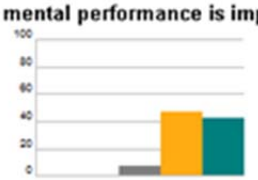
physical performance is important



Mean: 4.16

Response	Percent
Strongly Disagree	0.93
Disagree	1.39
Neither Agree or Disagree	6.48
Agree	61.57
Strongly Agree	28.24

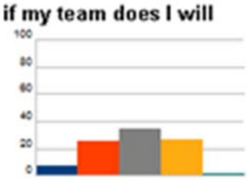
mental performance is important



Mean: 4.32

Response	Percent
Strongly Disagree	0.93
Disagree	0.00
Neither Agree or Disagree	7.87
Agree	47.22
Strongly Agree	42.13

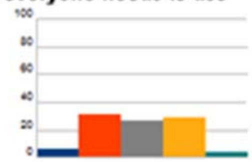
if my team does I will



Mean: 2.90

Response	Percent
Strongly Disagree	7.87
Disagree	25.93
Neither Agree or Disagree	35.19
Agree	26.85
Strongly Agree	2.31

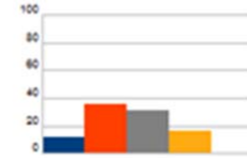
everyone needs to use



Mean: 2.95

Response	Percent
Strongly Disagree	6.48
Disagree	31.02
Neither Agree or Disagree	26.39
Agree	29.63
Strongly Agree	4.63

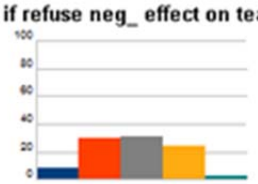
set new standards



Mean: 2.57

Response	Percent
Strongly Disagree	12.50
Disagree	36.11
Neither Agree or Disagree	31.02
Agree	17.13
Strongly Agree	0.93

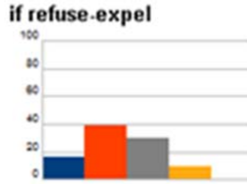
if refuse neg_ effect on team



Mean: 2.83

Response	Percent
Strongly Disagree	8.33
Disagree	30.56
Neither Agree or Disagree	31.48
Agree	25.00
Strongly Agree	2.78

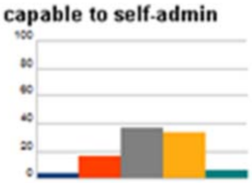
if refuse-expel



Mean: 2.39

Response	Percent
Strongly Disagree	16.67
Disagree	39.81
Neither Agree or Disagree	30.09
Agree	10.19
Strongly Agree	1.39

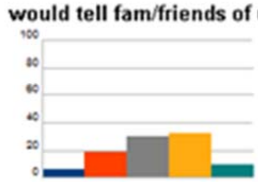
capable to self-admin



Mean: 3.21

Response	Percent
Strongly Disagree	4.63
Disagree	16.20
Neither Agree or Disagree	37.04
Agree	33.80
Strongly Agree	6.02

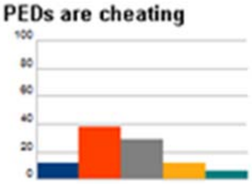
would tell fam/friends of use



Mean: 3.22

Response	Percent
Strongly Disagree	6.02
Disagree	18.98
Neither Agree or Disagree	30.09
Agree	32.87
Strongly Agree	9.72

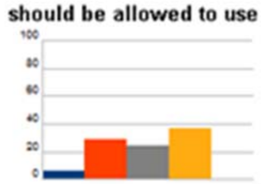
PEDs are cheating



Mean: 2.62

Response	Percent
Strongly Disagree	12.04
Disagree	38.43
Neither Agree or Disagree	29.63
Agree	12.50
Strongly Agree	6.02

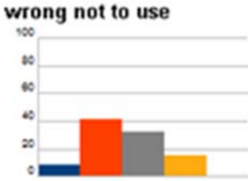
should be allowed to use



Mean: 2.98

Response	Percent
Strongly Disagree	6.94
Disagree	28.70
Neither Agree or Disagree	25.00
Agree	37.50
Strongly Agree	1.39

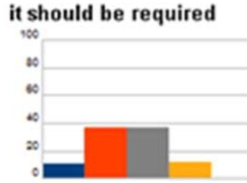
wrong not to use



Mean: 2.58

Response	Percent
Strongly Disagree	9.26
Disagree	41.20
Neither Agree or Disagree	32.41
Agree	15.74
Strongly Agree	0.93

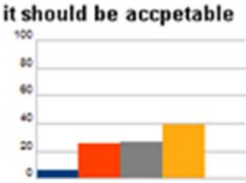
it should be required



Mean: 2.52

Response	Percent
Strongly Disagree	11.57
Disagree	37.04
Neither Agree or Disagree	37.04
Agree	12.04
Strongly Agree	0.46

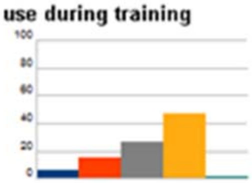
it should be accpetable



Response	Percent
Strongly Disagree	6.94
Disagree	25.93
Neither Agree or Disagree	26.85
Agree	39.35
Strongly Agree	0.46

Mean: 3.00

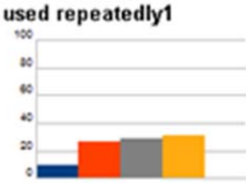
use during training



Response	Percent
Strongly Disagree	6.94
Disagree	15.74
Neither Agree or Disagree	26.85
Agree	47.69
Strongly Agree	2.31

Mean: 3.23

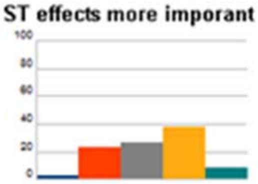
used repeatedly1



Response	Percent
Strongly Disagree	10.19
Disagree	26.85
Neither Agree or Disagree	29.17
Agree	31.94
Strongly Agree	1.39

Mean: 2.87

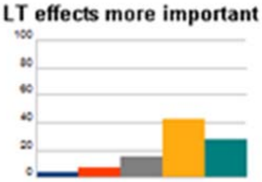
ST effects more imporant than MS



Response	Percent
Strongly Disagree	2.78
Disagree	23.15
Neither Agree or Disagree	26.39
Agree	38.43
Strongly Agree	8.80

Mean: 3.27

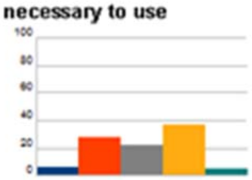
LT effects more important than MS



Response	Percent
Strongly Disagree	4.63
Disagree	7.87
Neither Agree or Disagree	15.74
Agree	43.06
Strongly Agree	28.24

Mean: 3.83

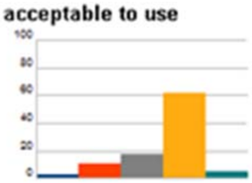
necessary to use



Response	Percent
Strongly Disagree	6.02
Disagree	27.78
Neither Agree or Disagree	22.22
Agree	37.50
Strongly Agree	5.56

Mean: 3.09

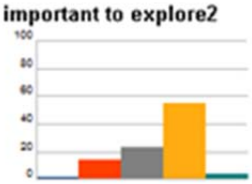
acceptable to use



Response	Percent
Strongly Disagree	3.24
Disagree	10.65
Neither Agree or Disagree	18.06
Agree	61.57
Strongly Agree	5.56

Mean: 3.56

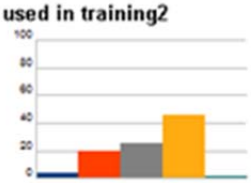
important to explore2



Response	Percent
Strongly Disagree	1.85
Disagree	14.35
Neither Agree or Disagree	23.15
Agree	55.09
Strongly Agree	4.17

Mean: 3.46

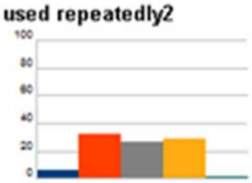
used in training2



Response	Percent
Strongly Disagree	4.63
Disagree	19.91
Neither Agree or Disagree	25.93
Agree	46.30
Strongly Agree	1.85

Mean: 3.21

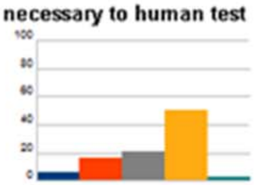
used repeatedly2



Response	Percent
Strongly Disagree	6.94
Disagree	32.41
Neither Agree or Disagree	27.31
Agree	29.63
Strongly Agree	1.85

Mean: 2.87

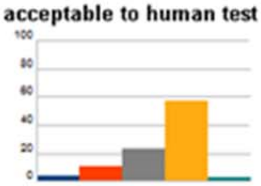
necessary to human test



Mean: 3.27

Response	Percent
Strongly Disagree	6.94
Disagree	16.67
Neither Agree or Disagree	21.30
Agree	50.46
Strongly Agree	3.24

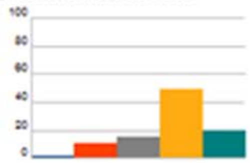
acceptable to human test



Mean: 3.44

Response	Percent
Strongly Disagree	4.63
Disagree	10.65
Neither Agree or Disagree	23.15
Agree	57.41
Strongly Agree	2.78

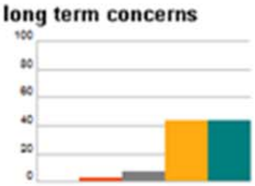
short term concerns



Mean: 3.76

Response	Percent
Strongly Disagree	1.85
Disagree	11.57
Neither Agree or Disagree	15.28
Agree	50.00
Strongly Agree	20.37

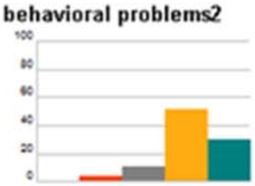
long term concerns



Mean: 4.29

Response	Percent
Strongly Disagree	0.00
Disagree	3.70
Neither Agree or Disagree	7.41
Agree	43.98
Strongly Agree	43.52

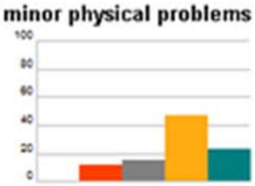
behavioral problems2



Mean: 4.10

Response	Percent
Strongly Disagree	0.00
Disagree	4.17
Neither Agree or Disagree	11.57
Agree	52.31
Strongly Agree	30.09

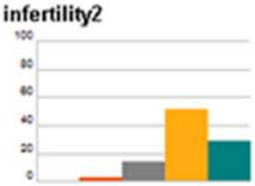
minor physical problems



Mean: 3.82

Response	Percent
Strongly Disagree	0.00
Disagree	12.50
Neither Agree or Disagree	15.74
Agree	47.69
Strongly Agree	23.15

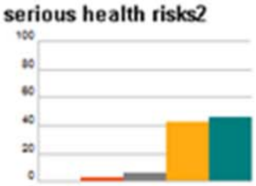
infertility2



Mean: 4.06

Response	Percent
Strongly Disagree	0.46
Disagree	3.70
Neither Agree or Disagree	13.89
Agree	51.85
Strongly Agree	28.70

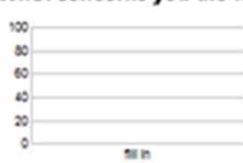
serious health risks2



Mean: 4.32

Response	Percent
Strongly Disagree	0.00
Disagree	3.70
Neither Agree or Disagree	6.48
Agree	43.06
Strongly Agree	45.83

What concerns you the most



Mean: -

Response	Percent
fill in	0.00

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APPENDIX C. ANSWERS TO THE OPEN-ENDED QUESTIONS

Following is an overview of the answers to the open-ended questions. Participants were asked to describe their main concerns with using PES/Ds or situations in which it is acceptable to use them. Similar type answers are clustered. The figures represent the number of times participants gave similar type of answers. Participants were allowed to describe multiple conditions or concerns.

1. Under what conditions do you feel it would be acceptable to use PES/Ds for operational or medical purposes?	
When in life-threatening circumstances, as a last resort	28
When it is thoroughly tested	25
When it has significant operational benefits/during missions	24
During high-risk/highly important missions	20
When one can freely choose whether to use PES/Ds or not	19
Under no circumstances is it acceptable to use PES/Ds	15
When it has no side effects	13
When PES/Ds cause only small side effects	11
When it improves performance	10
Fully informed about the effects	10
When it is controlled by the medical authorities	10
During training	8
In a World War III scenario. When the survival of the nation is at stake	6
When it improves recovery	6
Only certain PES/Ds like food supplements	3
When it decreases pain	2
When it has no long-term side effects	2
When the military takes full responsibility for the actions of servicemen using PES/D	1
When in combat situations and it helps preventing PTSD-like symptoms	1

2. What concerns you the most about the use or implementation of PES/Ds for operational or medical purposes	
Side effects in general	67
Long-term side effects	50
Behavioral side effects	14
Dependency or addiction in order to normal functioning	13
Creating new physical and mental standards	7
Crossing an ethical line	5
Sort-term side effects	3
The reputation of the military	3
Acceptance of PES/Ds in relation to illicit drugs	2
Unnecessary use	2
Determining the necessity when to take PES/Ds	2
Side effects in relation to career possibilities	2
The military taking advantage of its personnel	2
Uncontrolled use, no adequate control mechanisms	2
Increased intake to get the same results	1
The legal position of the servicemen when committing behavioral missteps related to PES/Ds	1

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