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# Ethical, Legal, Social, and Policy Issues in the Use of Genomic Technology by the U.S. Military

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# ETHICAL, LEGAL, SOCIAL, AND POLICY ISSUES IN THE USE OF GENOMIC TECHNOLOGY BY THE U.S. MILITARY<sup>1</sup>

*Maxwell J. Mehlman<sup>2</sup> & Tracy Yeheng Li*

*Advances in genomic science are attracting the interest of the U.S. military for their potential to improve medical care for members of the military and to aid in military recruitment, training, specialization, and mission accomplishment. While researchers have explored the ethical, legal, and social issues raised by the use of genomic science in a wide variety of contexts, there has been virtually no examination of these issues in connection with the use of genomics by the military. This article identifies potential uses of genomic science by the military, proposes an applicable ethical and legal framework, and applies the framework to provide ethical and legal guidance for military decision-makers.*

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I. INTRODUCTION

The U.S. military is beginning to employ genetic and genomic science to achieve military objectives, and is planning to expand these efforts in the future. In December 2010, JASON, a group of scientific advisors to the military, issued a report entitled “The \$100 Genome: Implications for the Department of Defense” that outlined an ambitious plan to employ genomic technologies to “enhance medical status and improve treatment outcomes,” enhance “health, readiness, and performance of military personnel,” and “know the genetic

identities of an adversary.”<sup>3</sup> The report also called for the Department of Defense (DoD) to take advantage of its “large, well-defined population in generally good health, together with their medical records” to “facilitate valuable longitudinal studies correlating genotype and phenotype.”<sup>4</sup> The report went on to recommend that DoD:

[D]etermine which phenotypes that might reasonably be expected to have a genetic component have special relevance to military performance and medical cost containment. These phenotypes might pertain to shortand long-term medical readiness, physical and mental performance, and response to drugs, vaccines, and various environmental exposures, all of which will have different features in a military context. More specifically, one might wish to know about phenotypic responses to battlefield stress, including post-traumatic stress disorder, the ability to tolerate conditions of sleep deprivation, dehydration, or prolonged exposure to heat, cold, or high altitude, or the susceptibility to traumatic bone fracture, prolonged bleeding, or slow wound healing.<sup>5</sup>

The JASON report also included in its “major recommendation” that DoD establish “policies that result in . . . the resolution of ethical and social issues that arise from these activities.”<sup>6</sup> Since the inception of the Human Genome Project in 1990, the Ethical, Legal, and Social Implications (ELSI) Research Program within the National Human Genome Research Institute at the National Institutes of Health (NIH) has funded a substantial body of research on the ethical, legal, social, and policy implications of this scientific initiative and subsequent scientific developments. However, virtually none of this research has addressed issues raised by the use of genomic technology by the military. Moreover, in view of differences between the military and civilian realms, the extent to which the insights from the ELSI program would apply to the military is unclear.

This paper is an effort to adapt the knowledge generated by the ELSI program to the U.S. military. It begins by describing current and potential uses of genomic technology<sup>7</sup> by the military. It then

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3. JASON PROGRAM, THE \$100 GENOME: IMPLICATIONS FOR THE DOD 1 (Dec. 2010), *available at* <http://www.fas.org/irp/agency/dod/jason/hundred.pdf> (accessed May 2, 2014) [hereinafter, JASON Report].
  4. *Id.* at 43.
  5. *Id.*
  6. *Id.* at 50.
  7. Technically, the term “genetic” refers to a particular gene while “genomic” refers to the entire genome. *See Talking Glossary of Genetic Terms*, NAT’L HUM. GENOME RES. INST., <http://www.genome.gov/>

describes how civilian norms and values are a poor fit with the military, and how this limits the application of existing ELSI findings to the military. The paper next describes the ethical, legal, social, and policy issues that would be raised by military genomics, and after explaining how these issues would be resolved according to the lessons learned in the ELSI program, it proposes how the issues should be handled in the military.<sup>8</sup>

## II. USES OF GENOMIC TECHNOLOGY BY THE MILITARY

### A. Biobanks and Geno-Phenobanks

The major current use of genomic technology by the military is collecting DNA from present and former members of the military in order to facilitate the identification of remains. The collection, called a biobank or biorepository, is the Armed Services Repository of Specimen Samples for the Identification of Remains (AFRSSIR), which was established in 1993. Every member of the military is required to submit a blood sample to the repository upon enlistment, and as of 2012, over 6.5 million blood samples have been collected and stored on bloodstain cards similar to those used for newborn screening.<sup>9</sup> Under current policy, AFRSSIR can retain the samples for up to 50 years.<sup>10</sup> Aside from being used to identify remains, DNA collected by the military can be decoded or sequenced, and the results linked to medical and personnel information obtained from service members or extracted from existing records. This results in the creation of a “geno-phenobank,” which enables genetic and genomic variations to be correlated with medical, physical, and other characteristics and was one of the recommendations in the JASON report. Several military geno-phenobanks are under construction. In

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glossary/index.cfm?id=532 (last visited May 2, 2014). The remainder of this paper uses the terms interchangeably unless the discussion requires that either genetic or genomic technologies be addressed specifically.

8. The JASON report also notes that “it may be beneficial to know the genetic identities of an adversary and, conversely, to prevent an adversary from accessing the genetic identities of U.S. military personnel.” JASON Report, *supra* note 1, at 1. The report does not elaborate, but the authors arguably have in mind the use of genetic information in the development of weaponry. Although the ethical, legal, and policy issues raised by the prospect of genetic weaponry are beyond the scope of this paper, the paper considers the need to keep genomic information about our own personnel from being used as a weapon by adversaries as a factor in its analysis.
9. Donna Miles, *DNA Registry Unlocks Key to Fallen Servicemembers’ Identities*, U.S. ARMY (Jan. 25, 2007), [http://www.army.mil/article/1508/DNA\\_Registry\\_Unlocks\\_Key\\_to\\_Fallen\\_Servicemembers\\_039\\_Identities/](http://www.army.mil/article/1508/DNA_Registry_Unlocks_Key_to_Fallen_Servicemembers_039_Identities/).
10. *Mayfield v. Dalton*, 109 F.3d 1423, 1426 (9th Cir.1997).

2009, in collaboration with the National Institute of Mental Health, the U.S. Army began a \$65 million, 6-year “Army Study to Assess Risk and Resilience in Servicemembers” (STARRS) to identify risk factors for military suicides. One component of the research, the New Soldier Study which started in February, 2011, asks new enlistees to volunteer to complete surveys and to undergo neurological and DNA testing to identify genetic and other risk factors.<sup>11</sup> As of November, 2012, 34,851 blood samples have been obtained.<sup>12</sup> In 2012, the U.S. Air Force Office of the Surgeon General established the “Patient-Centered Precision Care Research (PC2-Z) Program,” which collects and sequences DNA from saliva samples provided by volunteers from the Air Force Medical Service and matches the results with their medical information and family history.<sup>13</sup> The purpose of the project is to create a “personalized medicine profile” that identifies genomic risks for “clinically actionable, common complex diseases that are traditionally treated in the primary care setting,” and to determine the impact of this information on the health of the volunteers.<sup>14</sup> Finally, in 2011, the US Department of Veterans Affairs (VA) established the Million Veteran Program, a geno-phenobank that collects DNA and health information from veterans and combines it with their VA medical records for research purposes. As of March 2014, over 240,000 veterans have enrolled.<sup>15</sup>

In the future, the military may want to use the AFRSSIR DNA samples for research purposes rather than just for the identification of remains. The results of DNA sequencing could be combined with medical and personnel records for present and former members of the military to form a very large geno-phenobank. Aside from ELSI concerns discussed below, such an effort may be limited by the degree to which past records have been converted to an electronic format, which would be necessary in order to facilitate the research project.

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11. *Army STARRS New Soldier Study (NSS): The First Days of Service*, NAT’L INST. MENTAL HEALTH, <http://www.nimh.nih.gov/health/topics/suicide-prevention/suicide-prevention-studies/army-starrs-new-soldier-study-nss-the-first-days-of-service.shtml> (last visited May 2, 2014).
  12. ARMY STARRS, ARMY STARRS BY THE NUMBERS: QUARTER 4, 2013, available at <http://www.armystarrs.org/sites/default/files/By%20the%20numbers%20Web%202013Q4%20.pdf>.
  13. Christopher E. Bradburne et al., *Implementing Genome-Informed Personalized Medicine in the U.S. Air Force Medical Service via the Patient-Centered Precision Care Research (PC2-Z) Program*, 31 *JOHNS HOPKINS APL TECHNICAL DIGEST* 4, 333 (2013), [http://techdigest.jhuapl.edu/TD/td3104/31\\_04-Bradburne.pdf](http://techdigest.jhuapl.edu/TD/td3104/31_04-Bradburne.pdf) (accessed May 2, 2014).
  14. *Id.* at 337.
  15. *AKESOgen and the VA Million Veteran Program to Collaborate on Genotyping 105,000 Veterans*, U.S. DEP’T VET. AFF. (Mar. 5, 2014), <http://www.research.va.gov/MVP/media.cfm>.

### *B. Genomic Testing*

As noted earlier, the JASON report calls for DoD to create phenobanks to “determine which phenotypes that might reasonably be expected to have a genetic component have special relevance to military performance and medical cost containment.” Once these genetic and genomic components are identified, genetic tests can be developed to identify which individuals possess genotypes that contain these components.

Currently, the U.S. military tests enlistees for sickle cell anemia and Glucose 6-phosphate dehydrogenase deficiency.<sup>16</sup> As the field of personalized genomic medicine expands, military physicians can be expected to use newly developed genomic tests in the same ways as their civilian medical colleagues, namely, to identify individual genomic characteristics associated with the prevention, diagnosis, and treatment of disease. For example, genetic testing can identify individuals with genetic disorders that will not become symptomatic until some point in the future, such as Alzheimer’s or Huntington’s disease. In some cases, there may be steps that can be taken to prevent or mitigate the symptoms. Genomic testing also may be able to make or to help confirm a clinical diagnosis; the Air Force, for example, is reported to be developing a genetic test for colorblindness that improves upon existing detection methods.<sup>17</sup> As the JASON report recognized, military physicians also increasingly will practice pharmacogenomics, in which genomic tests help determine the appropriate drugs to prescribe for specific patients based on their genomic profiles.<sup>18</sup> Like their civilian counterparts, moreover, military physicians might use genomic testing to identify individuals who were at risk for genetic disorders such as breast and colorectal cancers that can be prevented or mitigated by early detection and intervention.

Military interest in genomic testing will extend beyond the prevention, diagnosis, and treatment of disease. The JASON report anticipates that tests will identify individuals who have genetic profiles that are of “special relevance to military performance and medical cost containment.” Depending on whether test results revealed that individuals possessed desirable or undesirable genomes, the military could consider the results in deciding whether to incentivize or block enlistment, or to advance or curtail military careers, and the test results also could be useful in making duty,

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16. Susannah Baruch & Kathy Hudson, *Civilian and Military Genetics: Nondiscrimination Policy in a Post-GINA World*, 83 AM. J. HUM. GENET. 435, 439 (2008).

17. *Genevolve to Launch Military Grade DNA Test for Color Blindness*, PRWEB (May 4, 2012), <http://www.prweb.com/releases/2012/5/prweb9471028.htm>.

18. JASON Report, *supra* note 1, at 43.

specialization, and geographic assignments. The National Cancer Institute, for instance, describes a young woman found to carry a mutation in a gene that increases the risk of breast cancer who may not be considered eligible for deployment for a 12to 15-month period because access to recommended health care, such as MRI screening, may not be easily accessible.<sup>19</sup> In 2010, a former military physician described an officer with a family history of Huntington's disease who was tested to see if he had inherited the disease gene before being promoted to flag rank, and a female pilot who was grounded after she developed a deep vein thrombosis and genetic testing revealed that she had a genetic mutation called Factor V Leiden polymorphism that increases the risk of such life-threatening blood clots.<sup>20</sup>

The military will be interested in identifying individuals with genomic variations of general medical interest, but also mutations that affect physical attributes that are of particular significance in military operations. The JASON report, for example, mentions the value of genetic testing for susceptibility to traumatic bone fracture, prolonged bleeding, or slow wound healing.<sup>21</sup> In 2009, a group of researchers published an updated human gene map for "performance and health-related fitness phenotypes" containing over 214 entries that may be of interest to the military.<sup>22</sup> The JASON report also describes future genetic testing that would provide information about "the ability to tolerate conditions of sleep deprivation, dehydration, or prolonged exposure to heat, cold, or high altitude."<sup>23</sup>

Researchers already have developed and marketed a genetic test that identifies one variant of the ACTN3 gene in humans, called R577X, which codes for a protein called  $\alpha$ -actinin-3. Individuals with this genetic variation tend to have an abundance of slowtwitch muscles, which are associated with activities such as long-distance running that require endurance, while individuals who do not have this variant of the ACTN3 gene have more fast-twitch muscles, which are associated with activities requiring shorter bursts of energy such as sprinting and weightlifting. Recruiters and training and assigning

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19. *Cancer Genetics Risk Assessment and Counseling*, NAT'L CANCER INST., <http://www.cancer.gov/cancertopics/pdq/genetics/risk-assessment-and-counseling/HealthProfessional/page6> (last visited May 2, 2014).
  20. Genetics and Public Policy Center, *Genetics Perspectives on Policy Seminar—Genes in Uniform: Don't Test, Don't Tell*, GENETICS & PUB. POL'Y CTR. (Jan. 10, 2006), [http://www.dnapolicy.org/news.past.php?action=detail&past\\_event\\_id=25](http://www.dnapolicy.org/news.past.php?action=detail&past_event_id=25).
  21. JASON Report, *supra* note 1, at 43.
  22. Molly S. Bray et al., *The Human Gene Map for Performance and Health-related Fitness Phenotypes: The 2006–2007 Update*, 41 *Med. Sci. Sports Exercise* 35 (2009).
  23. JASON Report, *supra* note 1, at 43.



officers might be interested in knowing which of these variations their potential enlistees or trainees possessed.

Genomic testing for mental as well as physical traits will attract the military's attention. A considerable amount of research on genetic variants associated with mental illness already is underway. For example, geneticists are searching for mutations that predispose warfighters to or protect them from post-traumatic stress disorder (PTSD) and have identified several genes, such as *FKBP5*, *PACAP*, *TLL1*, rs263232 in *ADCY8*, and rs71534169 in *DPP6*, as susceptibility genes for PTSD.<sup>24</sup> Researchers also are seeking genomic mutations that are associated with superior mental abilities, and although claims of success are often met with skepticism, many geneticists are confident that genomic tests for superior mental capabilities eventually will be developed. Scientists at the University of Pennsylvania, for example, have created a strain of "smart" mice that produce more of a protein called NR2B, giving them superior memory and learning abilities.<sup>25</sup> Studies in humans have identified a gene called dysbindin on chromosome 6 and another called SNAP-25 on chromosome 20 that are associated with cognitive ability.<sup>26</sup> Genetic researchers have demonstrated in mice that a genetic mutation of the *eIF2 $\alpha$*  gene and genetic manipulation of the *Lynx1* gene could achieve enhancements in synaptic plasticity, learning, and memory.<sup>27</sup> Studies funded by the NIH found that people with a certain variant of the gene catecholamine-*O*-methyltransferase can improve both memory

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24. See, e.g., *Post-Traumatic Stress Disorder (PTSD) Risk Prediction, Meeting Summary*, NAT'L INST. MENTAL HEALTH (Nov. 2, 2011), <http://www.nimh.nih.gov/research-funding/scientific-meetings/2011/ost-traumatic-stress-disorder-ptsd-risk-prediction/index.shtml>; Marilyn C. Connelly et al., *Genetics of Post-Traumatic Stress Disorder: Review and Recommendations for Genome-Wide Association Studies*, 12 CURR. PSYCHIATRY REP. 313 (2012); Alicia Chang, *Military Experiment Seeks to Predict PTSD*, U.S. NEWS & WORLD REP. (Nov. 20, 2009), <http://www.usnews.com/science/articles/2009/11/20/military-experiment-seeks-to-predict-ptsd>
  25. Ya-Ping Tang et al., *Genetic Enhancement of Learning and Memory in Mice*, 401 NATURE 63 (1999).
  26. Katherine E. Burdick et al., *Genetic Variation in DTNBP1 Influences General Cognitive Ability*, 15 HUM. MOLECULAR GENET. 1563 (2006); M. F. Gosso et al., *Common Variants Underlying Cognitive Ability: Further Evidence for Association between the SNAP-25 Gene and Cognition Using a Family-Based Study in Two Independent Dutch Cohorts*, 7 GENES, BRAIN BEHAV. 355 (2008).
  27. Mauro Costa-Mattioli et al., *eIF2 $\alpha$  Phosphorylation Bidirectionally Regulates the Switch from Short- to Long-Term Synaptic Plasticity and Memory*, 129 CELL 195 (2007); Julie M. Miwa & Andreas Walz, *Enhancement in Motor Learning through Genetic Manipulation of the Lynx1 gene*, PLOS ONE (Nov. 5, 2012), <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0043302>.

and problem solving by taking a drug called tolcapone, which is prescribed for patients with Parkinson's disease, and exogenous medication may overcome a type of genotype-associated trait under which genetic variation can be associated with reduced dopamine neurotransmission to impair learning and cognitive performance.<sup>28</sup> Finally, a Chinese research institute located in Hong Kong has purchased more than \$90 million worth of advanced genetic sequencing machines and is using them, among other things, to sequence the DNA of 2000 Chinese school children to search for genes that correlate with educational testing scores.<sup>29</sup> Again, recruiters and trainers can be expected to want to use tests such as these in recruitment, training, and assignment.

### *C. Gene-Based Therapeutics*

Like their civilian colleagues, military physicians will develop and employ genomic technology not only to diagnose and predict but to prevent and treat both genomic and non-genomic diseases. A detailed description of the prospects for gene-based preventive measures and treatments is beyond the scope of this paper, but they include (1) the use of techniques such as recombinant DNA to manufacture drugs; (2) gene therapy, or the introduction or modification of endogenous or exogenous human DNA to provide an increased ability to combat injury or illness (for example, Jonathan Moreno cites the interest of the Defense Advanced Research Projects Agency in using genetic manipulation to improve the immune system<sup>30</sup>) or to correct or compensate for genomic abnormalities; and (3) altering the composition or characteristics of the microbiome, the non-human organisms found in the human digestive system and elsewhere that play a significant role in metabolism and human health. An especially controversial subject is germ line therapy, which entails making therapeutic alterations in an individual's DNA at such an early stage of development that the changes will be incorporated into eggs or sperm and therefore can be inherited by the individual's descendants. The military may be interested in germ line therapy, for example, in order to reduce the frequency and costs of care for heritable genomic disorders in military families.

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28. José A. Apud et al., *Tolcapone Improves Cognition and Cortical Information Processing in Normal Human Subjects*, 32 *NEUROPSYCHOPHARMACOLOGY* 1011 (2007); Kristin M. Pearson-Fuhrhop et al., *Genetic Variation in the Human Brain Dopamine System Influences Motor Learning and Its Modulation by L-Dopa*, 8 *PLOS ONE* e61197 (2013), <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0061197>.
29. JASON Report, *supra* note 1, at 21.
30. JONATHAN MORENO, *UNDUE RISK: SECRET STATE EXPERIMENTS ON HUMANS* 291 (2001).

*D. Genomic Enhancements*

The military will be intensely interested in exploiting the association between genomics and human capabilities and performance. In 2001, the Committee on Opportunities in Biotechnology for Future Army Applications of the Board on Army Science and Technology at the National Research Council called on the Army to “lead the way in laying ground-work for the open, disciplined use of genomic data to enhance soldiers’ health and improve their performance on the battlefield.”<sup>31</sup> A 2002 report by DoD Information Assurance and Analysis Center observed that “because genomics [sic] information offers clues to improving human performance it could provide the Army with means of increasing combat effectiveness.”<sup>32</sup> The JASON report notes that “both offensive and defensive military operations may be impacted by the applications of personal genomics technologies through enhancement of the . . . readiness, and performance of military personnel.”<sup>33</sup>

One way that genomic science can improve military effectiveness has been mentioned earlier: using genomic testing to sort individuals based on how they were expected to function in various military environments. In addition, the same genomic modification techniques described in the previous section on gene-based therapeutics could be used to actively improve warfighting ability. For example, until recently, one company, 23andMe, offered direct-to-consumer genetic testing for a number of nondisease traits including avoidance of errors, eating behavior, food preference, measures of intelligence, memory, muscle performance, and pain sensitivity. The company acknowledged that the ability of the tests to actually measure these traits has not been established, but if the genomic variations could in fact be identified, it might be possible to manipulate them directly or by administering drugs that affected the proteins for which they coded. Conceivably, then, warfighters could be made smarter and less error-prone, given better memories and muscles, or have their metabolisms altered to enable them to function with fewer calories or on unusual diets.

More fancifully, perhaps, warfighters could be genomically reengineered to need less sleep. A study published in February 2013 and financed by the U.S. Air Force Office of Scientific Research

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31. NAT’L RES. COUNCIL, OPPORTUNITIES IN BIOTECHNOLOGY FOR FUTURE ARMY APPLICATIONS 64 (2001).
  32. Ashley R. Melson, *Bioterrorism, Biodefense, and Biotechnology in the Military: A Comparative Analysis of Legal and Ethical Issues in the Research, Development, and Use of Biotechnological Products on American and British Soldiers*, 14 ALB. L. J. SCI. TECH. 497, 506 n.41 (2004).
  33. JASON Report, *supra* note 1, at 1.

reported that sleep deprivation disrupted the functioning of over 700 genes.<sup>34</sup> In the future, these genes might be able to be reprogrammed so that they were not as affected by sleeplessness, enabling warfighters to carry out missions despite lack of sleep. A 2008 JASON report predicted that, in contrast to elite sports, small improvements in warfighter performance would not have a dramatic effect on the outcome of military engagements; a major breakthrough in the need for sleep, however, “could seriously alter the balance of engagement.”<sup>35</sup>

### III. LIMITATIONS ON THE USE OF CIVILIAN APPROACHES IN THE MILITARY

The uses of genomic technology by the military described in the previous section raise a host of ELSI issues. How should the military, for example, conduct genomic research? What types of genomic testing are appropriate in the military and how should the results be used? What rules should govern how the military provides genomic therapeutics and enhancement technologies to its personnel?

Similar questions arise in the civilian sector, and the ELSI program at the NIH has attempted to articulate solutions. However, the suitability of these civilian solutions in the military is limited by differences in core values. In his landmark work *Moral Issues in Military Decision Making*, Anthony Hartle articulates freedom, equality, individualism, and democracy as the core American values.<sup>36</sup> For the military on the other hand, Hartle identifies “honor”, “duty”, and “country”.<sup>37</sup> In contrast to the civilian notion that the welfare of the individual is paramount, in the military it is subservient to the unit, mission, and country. In contrast to the civilian values of freedom, equality, and democracy, members of the military are obliged to obey lawful orders. The military also emphasizes taking responsibility for one’s decisions and actions, and an obligation to promote the welfare of subordinates to the extent consistent with the welfare of the unit, the accomplishment of the mission, and the safeguarding of the state.

In a separate paper,<sup>38</sup> I argue that these differences in core values require a different set of principles to govern bioethics in the military.

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34. *Id.*

35. JASON PROJECT, HUMAN PERFORMANCE 76 (Mar. 2008), <https://www.fas.org/irp/agency/dod/jason/human.pdf>.

36. ANTHONY E. HARTLE, MORAL ISSUES IN MILITARY DECISION MAKING 136–141, 173 (2004).

37. *Id.* at 57–60.

38. Maxwell J. Mehlman & Stephanie O. Corley, *A Framework for Military Bioethics*, 13 J. MIL. ETHICS 331 (2014).

The focus on the welfare of the individual patient in the clinical application of the civilian principle of beneficence, which stands in sharp contrast to the military value of selflessness, should be replaced in the military by the principle of *proportionality*. According to the principle of proportionality, a biomedical risk can be imposed on a warfighter only when there is no less risky alternative to accomplish a legitimate military objective, and the nature and degree of the risk are outweighed by the military advantage sought to be gained. In view of the lack of individual autonomy in the military, it also makes sense to downplay the civilian emphasis on voluntary choice reflected in the principle of “respect for persons” by substituting instead the principle of *paternalism*. Combining the principles of paternalism and proportionality, military commanders have a duty to ensure that the biomedical risks that they impose on their subordinates are proportionate. These twin principles also guide privacy and confidentiality: commanders have a duty to protect their subordinates’ privacy and confidentiality unless and to the extent that it is outweighed by military necessity. Commanders likewise have a duty to protect warfighters’ dignity by avoiding exposing them to biomedical risks that humiliate or demean them. Finally, the principle of *fairness* should replace the civilian principle of justice and require members of the military to give their consent when commanders impose a biomedical risk only on a subgroup of subordinates or when the risk is especially great. Fairness also precludes using biomedical risks as a punishment for bad behavior or imposing the risks in a discriminatory manner or on warfighters who are less able to bear them than others, such as physically weaker members of a unit.

Not only do basic principles of bioethics differ in civilian and military life, but several laws that play an important role in civilian genomics do not apply to service members, including the Genetic Information Nondiscrimination Act (GINA)<sup>39</sup> and, according to the so-called Feres doctrine, the common law doctrine that provides damages for victims of medical malpractice.<sup>40</sup> These legal differences must be taken into account in analyzing the ELSI issues that arise in military genomics.

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39. See, e.g., *Genetic Discrimination*, NAT’L HUM. GENETIC RES. INST., <http://www.genome.gov/10002077> (last visited May 2, 2014); Kathy L. Hudson et al., *Keeping Pace with the Times—The Genetic Information Nondiscrimination Act of 2008*, 358 NEW ENG. J. MED. 2661 (2008); Susannah Baruch & Kathy Hudson, *Civilian and Military Genetics: Nondiscrimination Policy in a Post-GINA World*, 83 AM. J. HUM. GENET. 435 (2008).

40. See, e.g., *Feres v. United States*, 340 U.S. 135 (1950); *Lanus v. U.S.*, 133 S. Ct. 2731 (2013); *Major v. United States*, 835 F.2d 641 (6th Cir. 1987), *cert. denied*, 487 U.S. 1218 (1988); *Connell v. Copeland*, 417 Fed. Appx. 3 (D.C. Cir. 2011).

The sections that follow identify the ELSI challenges raised by military genomics explain how similar issues have been addressed by the civilian ELSI program, and consider whether the civilian approaches are appropriate in the military due to their different bioethical and legal frameworks, and, if not, how these approaches should be adjusted to meet the needs of the military in an ethically, legally, and socially appropriate manner. The challenges can be grouped into several broad categories. One set of concerns pertains to military human subjects research.<sup>41</sup> A related set of issues involve the military operation of DNA biobanks and geno-phenobanks and the commercialization of research discoveries. A third series of issues relates to clinical and enhancement uses of genomic technologies by the military.<sup>42</sup>

#### IV. RESEARCH ISSUES

Military research with human subjects can be conducted in three settings. One is intramural research, where the subjects are members of the military. The second is extramural research, where the military sponsors research that is conducted in civilian institutions such as hospitals and universities.<sup>43</sup> The third setting is research conducted by the VA on veterans who are receiving medical care from the VA. Each of these settings raises different ELSI issues and therefore will be discussed separately.

##### *A. Intramural Clinical Research*

As discussed earlier, the military may wish to conduct genomic research to obtain general information relating to human health or to obtain information of particular relevance to the military. There are two types of genomic research involving human subjects: clinical research, in which experiments are conducted on live humans, and non-clinical research, which is conducted on human biological material such as DNA samples. (DoD calls clinical research “research involving a human being as an experimental subject” to distinguish it from “research involving human subjects,” which includes both clinical and

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41. Issues are also raised by experiments on non-human subjects, especially other primates, but are beyond the scope of this paper.
  42. As noted in an earlier footnote, military genomics also potentially involves the development of genomic weaponry, a topic that is beyond the scope of this paper.
  43. A study also might be conducted on both military and civilian subjects, which will not be discussed specifically because the issues that it raises are addressed by the discussion of the separate use of these study populations.

non-clinical research.<sup>44</sup>) The following discussion concerns clinical genomic research; a discussion of non-clinical genomic research appears in *Balancing Risks and Benefits* below.

### 1. Informed Consent

It might be thought that, under the principles of proportionality and paternalism, clinical research can take place without the informed consent of military subjects when the research is important enough to the unit, mission, or nation. An argument can be made that one major philosophical justification for informed consent, Immanuel Kant's deontological "categorical imperative" that individuals should be treated as ends rather than as means, has little application in the military. Military bioethicist Michael Gross asserts that, at least in wartime, "human life is of but instrumental value", and observes that "Kant's maxim to treat others as ends guides bioethics. But it does not guide war. During armed conflict, there is very little compunction about using persons as means."<sup>45</sup> No doubt based in part on this reasoning, the military gave soldiers lysergic acid diethylamide and other hallucinogens without telling them that they were being given the drugs<sup>46</sup> but instead that they were participating in a study on the effectiveness of protective clothing and equipment against chemical warfare agents.<sup>47</sup> Similarly, voluntary consent was not always obtained from military personnel involved in radiation experiments that were conducted as part of atomic bomb testing.<sup>48</sup>

Despite doubts about the applicability of a Kantian perspective to the military, at least since the trials of Nazi war criminals and the promulgation of the Nuremberg Code, which makes no distinction between civilian and military subjects, it is generally accepted that competent adults must give their informed consent to serve as subjects in biomedical research, and this consensus has long been

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44. Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research, Department of Defense Instruction (DoDI) No. 3216.02, Glossary at 38 (2011) [hereinafter DoDI. 3216.02], *available at* <http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf> (accessed May 2, 2014).
  45. MICHAEL GROSS, *BIOETHICS AND ARMED CONFLICT: MORAL DILEMMAS OF MEDICINE AND WAR* 171–72 (2006). Gross's emphasis on wartime suggests that warfighters should not be regarded as means to the military's ends in peacetime or in non-combat operations, but the principle of proportionality applies in all phases of military life, and therefore individual welfare always can be sacrificed for military necessity so long as the sacrifice is proportionate.
  46. H. R. REP. NO. 106–556, at 111, 185 (2010) [hereinafter *Radiation Report*].
  47. *U.S. v. Stanley*, 483 U.S. 669, 671 (1987).
  48. *Radiation Report*, *supra* note 44, at 484.

reflected in official military policy.<sup>49</sup> Moreover, if the risks to subjects are more than minimal, it is required under the military bioethical principle of fairness since only a subset of the force is likely to be enrolled as participants. Informed consent also has practical value in military research; failure to obtain informed consent could discourage individuals from serving as research subjects, thereby reducing the amount of beneficial research that can be conducted, and even could discourage individuals from serving in the military in the first place. A 2000 congressional report on the DoD's mandatory anthrax vaccine program, for example, was especially concerned about the effect of the program on retention in reserve units, and noted that half of the air crew in one Air National Guard unit had resigned as a result.<sup>50</sup>

There is no reason to waive or weaken the requirement of informed consent for biomedical research employing military personnel as subjects when the research involves genomic science. Informed consent is a central focus in the government's efforts to protect human subjects in genetic and genomic research.<sup>51</sup> Indeed, it has been

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49. Troops in Cuba who participated in Walter Reed's yellow fever experiments signed forms indicating that they understood the risk and freely consented to be enrolled as subjects. Radiation Report, *supra* note 44, at 97; Arthur O. Anderson, *A Brief History of Military Contributions to Ethical Standards for Research Involving Human Subjects*, ARTNSCIENCE, [http://artnsience.us/Med\\_Ethics/index.html](http://artnsience.us/Med_Ethics/index.html) (last visited May 4, 2014) [hereinafter Anderson History]. In 1953, the Secretary of Defense, Charles E. Wilson, distributed a memorandum throughout the military that permitted Armed Services personnel to serve as research subjects only if they gave their voluntary consent. Radiation Report, *supra* note 44, at 105; Anderson History, at 11. Although the Wilson Memorandum was classified top secret until 1975 for reasons that are not entirely clear (*see* Radiation Report, *supra* note 44, at 107), the Army chief of staff issued a non-classified version of the memorandum in 1954 as Army Directive CS:35 (*see* Radiation Report, *supra* note 44, at 107) and incorporated CS:35 into Army regulations as AR 70-25 in 1962. Radiation Report, *supra* note 44, at 182; Anderson History at 11, 16. The Air Force issued the Wilson Memorandum as a regulation in 1965, and the Navy included a requirement of voluntary research consent in its Medical Department Manual in 1967. Radiation Report, *supra* note 44, at 183. In addition, the Navy made it clear in 1969 that the requirement of voluntary consent applied both to patients and healthy subjects, and the Army followed suit in 1973 in Army Regulation 40-38. Radiation Report, *supra* note 44, at 183. In 1984, Congress enacted legislation prohibiting DoD from conducting human subjects research without informed consent (10 U.S.C. § 980). (As discussed below, however, the Secretary of Defense may waive the requirement of informed consent in certain circumstances.) DoD also has issued Directive 3216.2, which, among other things, states that informed consent is a requirement of DoD policy.

50. Radiation Report, *supra* note 44, at 46.

51. *See, e.g., Informed Consent for Genomics Research*, NAT'L HUM. GENOME RES. INST., <http://www.genome.gov/27026588> (last visited May



argued that genomic research requires even stronger protections for subjects than many other types of human experimentation because of the sensitive nature of personal genomic information that a study may uncover, such as predictive data about future illnesses for which the subject or the subject's family members are at risk<sup>52</sup> or misattributed paternity and maternity, that is, the discovery that a person's presumed father or mother is not in fact biologically related.<sup>53</sup>

One reason to conduct genomic research on military personnel without informed consent might be to help preserve secrecy so that adversaries were not alerted to the production of information that might help them construct genomic weapons or defenses.<sup>54</sup> For example, the military may feel the need to conceal the fact that it is obtaining genomic information about members of the same genomically differentiated subpopulation as enemy combatants.<sup>55</sup> National security arguments have been put forth on behalf of military experiments conducted without consent in the past, such as atomic radiation experiments during the Manhattan Project and the Cold War. Although critics of those experiments argue that a measure of voluntary consent could have been sought from subjects, for example, by using the term "dangerous radioactive substance" in place of the classified word "plutonium",<sup>56</sup> it may not always be possible to use obfuscating terminology and still provide sufficient information to

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2, 2014); *ELSI Research Priorities and Possible Research Topics*, NAT'L HUM. GENOME RES. INST., <http://www.genome.gov/27543732> (last visited May 2, 2014).

52. *Protecting Human Research Subjects, National Institutes of Health Office for Protection from Research Risks (OPRR) 1993 Institutional Review Board Guidebook*, NAT'L HUM. GENOME RES. INST., <http://www.genome.gov/10001752> (last visited May 2, 2014).
53. Jean McEwen, *Genetic Information, Ethics, and Information Relating to Biological Parenthood*, in 1 *ENCYCLOPEDIA OF ETHICAL, LEGAL, AND POLICY ISSUES IN BIOTECHNOLOGY* 356 (Thomas H. Murray & Maxwell J. Mehlman eds., 2000).
54. Another reason to permit human subjects research to proceed without informed consent is to facilitate research on emergency treatments for patients who cannot give consent because of their condition and where there is no time to obtain legally authorized consent from someone else, such as a family member. Congress in 2001 enacted a provision permitting this type of emergency research to be conducted on warfighters. 10 USC § 980(b). In 2006, Food and Drug Administration (FDA) adopted a regulation permitting emergency research to be conducted outside of the military as well. 21 CFR § 50.24.
55. Victor W. Sidel & Barry S. Levy, *Physician-Soldier: A Moral Dilemma?* in 1 *TEXTBOOKS OF MILITARY MEDICINE: MILITARY MEDICAL ETHICS* (Edmund D. Pellegrino, Anthony E. Hartle, Edmund G. Howe & Walter Reed eds., 2004), at 293-312.
56. Radiation Report, *supra* note 44, at 205-207.

subjects to enable them to give informed consent. The solution would seem to be to enroll only those subjects who held security clearances high enough to permit them to be given the classified information.

A requirement that members of the military give their informed consent to serve as subjects in genomic research does not mean that they actually can do so, however. In order for individuals to give informed consent, they first must have adequate information about the nature, potential benefits, and risks of the experiment, and they must be able to understand the information to a reasonable degree.<sup>57</sup> Serious doubts have been expressed about prospective subjects' ability to comprehend and absorb the information they are given.<sup>58</sup> There is little reason to expect members of the military to do better than other subjects; on average, for example, they are less well educated than the general public.<sup>59</sup>

Members of the military may also feel pressured to consent. Indeed, a strong argument can be made that warfighters should be regarded as a "vulnerable" study population, despite not being formally listed as vulnerable in the Common Rule.<sup>60</sup> It was not until 1981 that Army regulations were changed to prohibit penalties under the Uniform Code of Military Justice from being imposed on warfighters who refused to volunteer or withdrew from participating in military research.<sup>61</sup> Even without the prospect of formal punishment, warfighters may feel that they have no choice but to acquiesce when they are invited to serve as subjects. As Victor Sidel and Barry Levy explain in the *Textbook of Military Medicine*, "because they cannot simply "quit their jobs" "file a grievance" with a union, government agency, or professional organization, military personnel may not believe that they can truly refuse to participate in these experiments. They may feel more like a "captive audience" than like "volunteers."<sup>62</sup> Moreover, as the House Committee on Government Reform pointed out in its critique of DoD's mandatory anthrax vaccination program, "in a culture based on a chain of command and the power to compel, attempts at persuasion and education often devolve into intimidation."<sup>63</sup> Superiors may make

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57. *Canterbury v. Spence*, 464 F.2d 772 (D.C. Cir. 1972).

58. See James Flory & Ezekiel Emanuel, *Interventions to Improve Research Participants' Understanding in Informed Consent for Research*, 292 JAMA 1593 (2004).

59. Efthimios Parasidis, *Justice and Beneficence in Military Medicine and Research*, 73 OHIO ST. L. J. 723, 765–66 (2012).

60. *Id.* at 775; John McManus et al., *Informed Consent and Ethical issues in Military Medical Research*, 12 ACAD. EMER. MED. 1120 (2005).

61. Anderson, *supra* note 47.

62. Sidel & Levy, *supra* note 53, at 297.

63. Radiation Report, *supra* note 44, at 46.

subordinates' willingness to serve as subjects a condition for allowing them to undertake certain attractive missions, for example, missions to test exciting new technologies such as genomic enhancements.<sup>64</sup> Unit cohesion and comradeship may lead warfighters to agree to be subjects if other members of their unit already have.<sup>65</sup> Warfighters may also feel that it is their patriotic duty to participate in research,<sup>66</sup> a notion that some commentators are pushing in the civilian sector.<sup>67</sup>

DoD is well aware of the risk that warfighters asked to give their informed consent to serve as research subjects will feel that they have no choice but to accede. DoD rules prohibit superiors from "influencing" the decisions of their subordinates regarding participation as subjects and specifically forbid superiors from being present when informed consent is being sought.<sup>68</sup> Moreover, except for a payment of \$50 in return for having blood withdrawn, military personnel on duty may not be compensated for serving as subjects.<sup>69</sup>

Warfighter's limited autonomy requires a shift in emphasis in military clinical research away from the reliance on informed consent as a primary protection for subjects in the civilian model and toward a reliance on paternalism. Civilian research ethics contain a strong element of paternalism; subjects are only asked to give their consent to participate in research after experts, in the form of institutional review boards, sponsors, government regulators, and the investigators themselves, are satisfied that the potential benefits of a study outweigh the risks. Given the limits on warfighter autonomy, the need for paternalism in the military is more pronounced, however, and ensuring proportionality must be viewed as the primary responsibility of research directors, institutional review boards, and subjects' commanders rather than the subjects themselves. To that end, DoD rules require the appointment of an "ombudsman" and a "research

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64. See Jennifer Siegel, *Advancing Ethical Research Practices in the Military*, 24 ABA HEALTH SECTION, THE HEALTH LAWYER 1 (2012).

65. *Id.*

66. *Id.*

67. See G. Owen Schaefer, Ezekiel J. Emanuel & Alan Wertheimer, *The Obligation to Participate in Biomedical Research*, 302 JAMA 67 (2009). Warfighter's rights are also limited by the *Feres* doctrine, which prohibits warfighters from suing the military for damages for medical malpractice, including when they have been harmed by researcher negligence. The staff of the Senate Committee on Veterans Affairs in 1994 therefore recommended that the doctrine be deemed inapplicable if military personnel are injured in experiments in which they were forced to serve as subjects. U.S. SENATE CMTE. ON VET. AFF., IS MILITARY RESEARCH HAZARDOUS TO VETERANS' HEALTH? LESSONS SPANNING HALF A CENTURY 44 (1994).

68. DoDI 3216.02, *supra* note 42, at §§ 7(e)(1)(b) and (c).

69. *Id.* at § 11(a)(1)(a).

monitor” (who may be the same person) to oversee the informed consent process when the research presents more than minimal risk (and, in the case of an ombudsman, when the recruitment of subjects takes place in a “group setting”).<sup>70</sup> Individual services have added additional oversight in certain cases in the form of a requirement for a second level of protocol review in addition to review by an institutional review board (IRB).<sup>71</sup> One approach that the military has taken to promote voluntary participation in research is to establish special units from which to draw subjects, beginning with Operation Whitecoat, in which 2,300 Seventh-Day Adventist Church conscientious objectors between 1954 and 1973 participated in 137 protocols to develop vaccines and treatments for Q fever, tularemia, various viral encephalitides, Rift Valley fever virus, sand fly fever and plague,<sup>72</sup> and continuing with the Medical Research Volunteer Subjects program using the US Army Medical Research Institute of Infectious Diseases (USAMRIID) troops recruited from “Medic School 91B” at Fort Sam Houston, Texas.<sup>73</sup> Although concerns have been voiced in connection with Operation Whitecoat that Seventh-Day Adventist church officials endorsed the program, with one subject later pointing out that “we grew up to trust the church,”<sup>74</sup> the head of USAMRIID emphasizes that participation in research among members of these units is voluntary, with only about eighty percent of the troops consenting to serve as subjects in any one year.<sup>75</sup> This has led some commentators to suggest that similar units should be the

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70. *Id.* at §§ 7(e)(1)(d), 8(a).

71. The Army requires second-level review by the Human Research Protection Office, a part of the Office of Research Protections, US Army Medical Command Medical Research and Materiel Command. U.S. Army Regulation 40–38 (1989) and 70–25 (1990). The Navy requires second-level review by the Director, Defense Research and Engineering, for clinical studies and the Secretary of the Navy must review research involving “severe or unusual intrusions, either physical or psychological, on human subjects” including “consciousness-altering drugs or mind-control techniques,” (p. 9) and research on ‘potentially or inherently controversial topics (such as those likely to attract significant media coverage or that might involve challenge by interest groups).’ SECNAVINST 3900.39D (2006). The Air Force Surgeon General’s Research Oversight Committee reviews protocols involving greater than minimal risk and investigational drugs, etc. AFI40–402, § 2.2.2 (2005).

72. Anderson, *supra* note 47.

73. *Id.*

74. Mark D. Somerson, *Church Blessed Germ Experiments; Army’s Biological Warfare Research Used Seventh-Day Adventist Volunteers*, COLUMBUS DISPATCH, Nov. 8, 2001, at 1A.

75. *Id.*

primary if not the exclusive source of military research subjects.<sup>76</sup> But it is still unclear if the members of these units would feel sufficiently free to decline to participate in research, and specialized groups of subjects may not be representative of the troops who actually would be exposed to the instrumentalities being tested.

## 2. Balancing Risks and Benefits

An axiom of research ethics is that a study may proceed only if the risks are outweighed by the potential benefits. In balancing research risks and benefits, civilian and military principles of bioethics function almost identically. In both regimes, the risks to the subjects can be outweighed either by the benefits to the subjects themselves or by the benefits, in the form of the knowledge gained, to others. Civilian research thus employs an approach similar to the military principle of proportionality in which the welfare of the individual can be subordinated to a greater good in appropriate circumstances. Civilian research also embraces the military principle of paternalism; as mentioned earlier, the balancing of risks and benefits is entrusted first to institutional review boards, study sponsors, government regulators, and the investigators themselves, and only after they have satisfied themselves that the benefits outweigh the risks are subjects asked to make their own assessment in giving their informed consent to participate.

Balancing research risks and benefits in the military raises certain questions, however. Warfighters may be subjected to grave personal risks in order to achieve a military objective; as Bill Rhodes, president of the International Society for Military Ethics, states, “a military member is expected to serve the state unto maiming, capture, or death.”<sup>77</sup> Accordingly, a research risk that would be deemed excessive for civilian subjects, such as a significant likelihood of serious harm in a study intended to produce knowledge to benefit others but with no direct benefit to the subjects, might be deemed acceptable for military subjects, under the principle of proportionality if the military objectives were sufficiently important. In other words, while the risks might be greater than for civilians, so might be the corresponding benefits to the unit, mission, or country.<sup>78</sup> Along this line, military

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76. Parasidis, *supra* note 57, at 778.

77. BILL RHODES, AN INTRODUCTION TO MILITARY ETHICS 50–51 (2009).

78. Military research rules incorporate the civilian concept of ‘no more than minimal risk’, which relaxes certain human subjects’ protections in certain civilian studies. However, the meaning of the concept in the military is unclear. DoD regulations use the same definition of ‘minimal risk’ as civilian regulations (no more than those risks ‘ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests’) (32 CFR § 219.102(i)); and DoD Instruction 3216.02 states that ‘the phrase “ordinarily encountered in

subjects ought to be allowed to participate in studies intended to produce information of special relevance to the military, such as tests of genomic interventions to treat PTSD, that posed greater risks than studies aimed at developing genomic interventions of no special value to the military.

Another question is how to weigh the risks and benefits of research on genomic enhancements, such as interventions to increase “the ability to tolerate conditions of sleep deprivation, dehydration, or prolonged exposure to heat, cold, or high altitude” mentioned in the JASON report.<sup>79</sup> Although as discussed later, the distinction between enhancements and other types of biomedical interventions is not always easy to make,<sup>80</sup> some commentators believe that enhancement benefits are less worthwhile than medical benefits and therefore that a risk that might be acceptable in a medical trial would be unethical in an enhancement experiment. One bioethicist states, for example, that:

[t]he cost/benefit analysis is different for enhancement. While those who are experimenting with treatments for serious diseases may only succeed in substituting one kind of misery for another, those experimenting on human enhancement are likely to substitute a miserable life for a happy one.<sup>81</sup>

As my colleague Jessica Berg and I have argued, however, the value of a benefit clearly depends on the nature of the benefit;<sup>82</sup> an enhancement that potentially increased cognitive function

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daily life or during the performance of routine physical or physiological examinations or tests” in the definition of minimal risk . . . shall not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, *soldier in a combat zone*) or having a medical condition (e.g., frequent medical tests or constant pain)’ [DoD Instruction 3216.02, Encl. 3(6)(b)(emphasis added)]. This language suggests that the risks of ordinary daily life for warfighters should be deemed the same as those for civilians. On the other hand, the DoD Instruction could be interpreted to mean that, while ordinary daily risks for warfighters are understood to be greater than for civilians, “minimal risk” should not be evaluated in terms of warfighters in especially dangerous units or locations, such as combat. Clarification of the DoD Instruction would be helpful.

79. JASON, *supra* note 1, at 43.

80. See text accompanying notes 180–182, *infra*.

81. NICHOLAS AGAR, LIBERAL EUGENICS: IN DEFENCE OF HUMAN ENHANCEMENT 167–68 (2004).

82. Jessica Berg & Maxwell Mehlman, *Human Subjects Protections in Biomedical Enhancement Research: Assessing Risk and Benefit and Obtaining Informed Consent*, 36 J. L. MED. ETHICS 546 (2008).

substantially, for example, might be deemed more valuable than a treatment, say, for nail fungus. In both health-oriented and enhancement research, therefore, the potential benefit necessary to justify a set of risks will depend on the specifics of the study in question. Moreover, it is difficult to distinguish between enhancement and other types of biomedical research in the military; a study of a genomic intervention to provide combat troops with better-than-normal vision, hearing, or cognition, or a greater-than-normal ability to tolerate conditions of sleep deprivation, dehydration, or prolonged exposure to heat, cold, or high altitude, for example, could be regarded as the study of how to prevent injury as well as an enhancement study. In short, there is no reason to treat an enhancement experiment differently than a treatment study when it comes to balancing risks and benefits.

### 3. Return of Research Results

A particularly controversial topic in genomic research is whether researchers have a duty to provide study findings to the subjects if the information could provide health benefits to the subjects. The issue arises especially when researchers are examining large amounts of genomic information on large numbers of subjects, such as searching a collection of DNA samples for variations associated with particular disease risks or traits. As noted earlier, for example, military researchers are hunting for genomic variations that predispose warfighters to PTSD. If they discover such variations, should they inform those subjects who have them?

The answer might seem to be “of course”, since individuals generally have a right to receive their personal biomedical information. But some geneticists worry that, since genomic information is often difficult to understand, subjects may misinterpret it and be harmed. Genomic findings often are probabilistic, and the average person has difficulty understanding probabilities. The effect of a genomic variation may be small; the genetic variation APOE4, for example, is found in forty percent of persons with late-onset Alzheimer’s disease but also in twenty-five to thirty percent of the general population.<sup>83</sup> Many disease genes vary greatly in how they are “expressed” and in their degree of “penetrance”, so that individuals may never show symptoms or may only experience a mild form of the illness. Since physicians may be uncertain about how to interpret genomic test results, one suggestion is to rely on specially trained experts called genetic counselors to convey results to subjects, but this requires more time and adds to the cost. Another complication is that

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83. *Alzheimer’s Disease Fact Sheet*, NAT’L INST. ON AGING, <http://www.nia.nih.gov/alzheimers/publication/alzheimers-disease-genetics-fact-sheet> (last visited May 2, 2014).

some diseases such as Alzheimer's cannot now be prevented or treated, and some commentators question the value of informing subjects about risks for those kinds of disorders.<sup>84</sup> Furthermore, the Clinical Laboratories Improvement Act (CLIA) requires laboratories that test DNA to be "CLIA-certified" if the results are reported to diagnose, prevent, or treat disease or to assess health,<sup>85</sup> and obtaining and maintaining CLIA certification is burdensome and expensive. Finally, commentators argue that researchers do not have the same obligations to subjects that physicians have to their patients, in particular, a duty to look after the subjects' health needs.<sup>86</sup>

Some of these objections do not apply in the military as much as they do in civilian research. The military is responsible for service members' health, so military researchers, like other superiors, have an obligation to look out for the well-being of their subordinates under the principle of paternalism. Moreover, military laboratories are not driven by the same profit motive as private civilian laboratories, and therefore may be less burdened by having to comply with CLIA requirements.

But military researchers still need to carefully consider the pros and cons of returning results to subject. They should have the same compunctions about how well subjects understand study results as their civilian brethren, especially since they are held accountable for the welfare of subjects under the principle of paternalism. Furthermore, there may be special considerations that justify withholding genomic information from military subjects. For example, if the military eventually discovers genomic variations closely associated with certain desirable or undesirable traits, it may decide to test prospective enlistees and use the results in making service assignments, but may not want to disclose the results to warfighters because of military exigencies. Warfighters told that they were at increased risk for certain types of battlefield injuries, for example, they might lose effectiveness if military necessity required them to participate in combat missions. The need for security to keep sensitive

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84. See, e.g., Sanford C. Gordon & Dimitri Landa, *Disclosure of the Genetic Risk of Alzheimer's Disease*, 362 NEW ENG. J. MED. 181 (2010); Rosalie A. Kane & Robert L. Kane, *Effect of Genetic Testing for Risk of Alzheimer's Disease*, 361 NEW ENG. J. MED. 298 (2009).

85. 42 C.F.R. § 493 (2003).

86. See, e.g., Ellen W. Clayton & Amy L. McGuire, *The Legal Risks of Returning Results of Genomics Research*, 14 GENET. MED. 473 (2012); Pilar Ossorio, *Taking Aims Seriously: Repository Research and Limits on the Duty to Return Individual Research Findings*, 14 GENET. MED. 461 (2012); Leslie A. Meltzer, *Undesirable Implications of Disclosing Individual Genetic Results to Research Participants*, 6 AM. J. BIOETHICS 28 (2006).



genomic information out of the hands of adversaries also might justify withholding test results from warfighters in certain circumstances.

Another question is whether researchers who disclose results to patients to improve their health should also disclose the results to family members who may also be at risk for the same genomic conditions, and if so, should they do so only with the subjects' permission. The question has been addressed mainly in the context of the relationship between patients and physicians rather than subjects and researchers, and there is a split of opinion. Many prominent groups say that doctors may override the patient's wishes if the physician has made a reasonable effort to obtain the patient's consent, there is a high probability that imminent, serious harm will occur if the information is not disclosed, and only information necessary for the diagnosis or treatment of disease is disclosed.<sup>87</sup> (The Institute of Medicine goes further and says that the information *must* be disclosed.<sup>88</sup>) However, some physician groups maintain that notifying family members is the patient's responsibility rather than the physician's, and point out that laws in Illinois, Massachusetts, and New York prohibit any disclosure of genetic information without the patient's consent.<sup>89</sup> Whatever the eventual consensus, the only reason for the rules governing disclosure of research to family members to differ between military and civilian life would be if the disclosure would pose a significant threat to national security or the successful completion of a military mission.

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87. See, e.g., U.S. PRESIDENT'S COMMISSION FOR THE STUDY OF ETHICAL PROBLEMS IN MEDICINE AND BIOMEDICAL AND BEHAVIORAL RESEARCH, SCREENING AND COUNSELING FOR GENETIC CONDITIONS: A REPORT ON THE ETHICAL, SOCIAL, AND LEGAL IMPLICATIONS OF GENETIC SCREENING, COUNSELING, AND EDUCATION PROGRAMS (1983); B.M. Knoppers et al., *ASHG Statement: Professional Disclosure of Familial Genetic Information*, 62 AM. J. HUM. GENET. 474 (1998), available at <http://www.ashg.org/pdf/pol-29%20.pdf> (accessed May 5, 2014); Ruth Macklin, *Privacy Control of Genetic Information*, in GENE MAPPING: USING LAW AND ETHICS AS GUIDES 157–72, (George J. Annas & Sherman Elias eds., 1992); Kenneth Offit et al., *The "Duty to Warn" a Patient's Family Members About Hereditary Disease Risks*, 292 JAMA 1469 (2004); Dorothy C. Wertz, John C. Fletcher & Kare Berg, *Review of Ethical Issues in Medical Genetics*, WORLD HEALTH ORG. HUM. GENETICS PROGRAMME (2003), <http://www.who.int/genomics/publications/en/ethicalissuesinmedgenetics%20report.pdf> (last visited May 5, 2014).
88. INST. MED., ASSESSING GENETIC RISKS: IMPLICATIONS FOR HEALTH AND SOCIAL POLICY (Lori B. Andrews et al. eds., 1994).
89. See, e.g., Mark E. Robson et al., *American Society of Clinical Oncology Policy Statement Update: Genetic Testing for Cancer Susceptibility*, 21 J. CLINICAL ONCOLOGY 2397 (2003); Am. Med. Ass'n, Proceedings of the 2013 Annual Meeting of the House of Delegates, *Reports of the Council on Science and Public Health* (Nov. 17, 2013), available at <http://www.ama-assn.org/assets/meeting/2013a/a13-csaph-reports.pdf>.

#### 4. Incidental and Unintended Findings

A topic that is closely related to the return of research results is how researchers should handle information about subjects that is outside of the scope of the study, called “incidental” or “unintended” findings.<sup>90</sup> (A similar issue arises when a physician examining a patient’s genome for certain clinically relevant information discovers other medically relevant findings.<sup>91</sup>) Researchers searching for genomic mutations that made subjects susceptible to PTSD, for example, inadvertently might discover mutations that placed certain subjects at risk for other diseases. The question is whether the researchers should disclose the incidental information. Again, the answer might seem clear that they should, since doing so could alert subjects to the need for future vigilance and beneficial medical care. But this raises concerns similar to those raised by returning results in general. Is the medical risk reflected by the incidental information sufficiently important to outweigh the chance that subjects will misunderstand it? How clear is it that the individual will show symptoms of the genomic disease or will experience a serious form of the illness? What if little or nothing can be done to reduce or eliminate the health risk? One particularly troublesome type of unintended finding, which can occur when both parents and offspring are studied in “pedigree” research, is that a parent is not biologically related to a child; how should researchers handle this result, which can be extremely disruptive to the family unit?

For these reasons, some commentators maintain that researchers have no obligation to inform subjects about incidental findings.<sup>92</sup> A growing consensus seems to be emerging, however, that researchers should disclose incidental findings that are sufficiently important for the subjects’ health, or at least that subjects should be asked during the informed consent process if they wish to receive this information.<sup>93</sup>

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90. See PRESIDENTIAL COMMISSION FOR THE STUDY OF BIOETHICAL ISSUES, ANTICIPATE AND COMMUNICATE: ETHICAL MANAGEMENT OF INCIDENTAL AND SECONDARY FINDINGS IN THE CLINICAL, RESEARCH, AND DIRECT-TO-CONSUMER CONTEXTS (2013), <http://bioethics.gov/sites/default/files/FINALAnticipateCommunicate PCSBI0.pdf>.
91. See, eg, Robert C. Green et al., *American College of Medical Genetics and Genomics Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing*, 15 GENET. MED. 565 (2013).
92. Joanna S. Forsberg, Mats G. Hansson & Stefan Eriksson, *Changing Perspectives in Biobank Research: From Individual Rights to Concerns About Public Health Regarding the Return of Results*, 17 EUR. J. HUM. GENET. 1544 (2009).
93. See, e.g., Susan M. Wolf, *The Past, Present, and Future of the Debate over Return of Research Results and Incidental Findings*, 14 (4) GENETICS IN MED. 355 (2012); James P. Evans & Barbra B. Rothschild, *Return of Results: Not That Complicated?* 14 (4) GENETICS IN MED. 358

There is no reason to assume that military researchers have a lesser obligation regarding disclosure of incidental findings than civilian researchers. In fact, an argument can be made that military researchers have a greater obligation than their civilian counterparts to consider returning incidental findings to subjects because military personnel have less ability than civilians to obtain genomic testing outside of the military.

#### 5. Follow-Up with Subjects

Another research controversy concerns whether researchers have a duty to contact subjects after a study is over to ascertain whether they are suffering any long-term or latent adverse effects, and to alert them to new information bearing on their health, such as the discovery of genomic risks that were not known at the time of the study or the availability of new treatments or preventive measures. The military has been criticized, for example, for not adequately following up with subjects in the “man-break” experiments on mustard gas during World War II.<sup>94</sup> Civilian researchers object that they should not have a long-term obligation to follow up with subjects because of the difficulties of keeping track of their whereabouts, but military researchers should be better able to keep track of military subjects, who may still be in the military or receiving care from the VA. In addition, the Army maintains a Volunteer Registry for all subjects in more-than-minimal-risk studies, one of the purposes of which is to enable the military to “exercise its obligation to ensure research volunteers are adequately warned of new risks and to provide new information as it becomes available,”<sup>95</sup> and the US Army Medical Research and Materiel Command (USAMRMC) stores the information for a minimum of 75 years. In sum, the military should

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(2012); Susan M. Wolf et al, Managing Incidental Findings and Research Results in Genomic Research Involving Biobanks and Archived Data Sets, 14 (4) *Genetics in Med.* 361 (2012); Isaac S. Kohane et al, Taxonomizing, Sizing, and Overcoming the Incidentalome, 14 (4) *Genetics in Med.* 399 (2012); Robert C. Green et al, Exploring Concordance and Discordance for Return of Incidental Findings from Clinical Sequencing, 14 (4) *Genetics in Med.* 405 (2012); Michael Ferriere and Brian Van Ness, Return of Individual Research Results and Incidental Findings in the Clinical Trials Cooperative Group Setting, 14 (4) *Genetics in Med.* 411 (2012).

94. Radiation Report, *supra* note 44; INST. MED., VETERANS AT RISK: THE HEALTH EFFECTS OF MUSTARD GAS AND LEWISITE 50–52 at Summary (Constance M. Pechura & David P. Rall eds., 1993).

95. U.S. Army, Guidelines for Investigators: Requirements for U.S. Army Medical Research and Materiel Command (USAMRMC) Headquarters Review and Approval of Research Involving Human Volunteers, Human Anatomical Substances, and/or Human Data, § III(G)(2).

endeavor to contact subjects about future developments of significance to their health.

#### 6. Paying for Participation in Research

Bioethicists are concerned that offering people substantial amounts of money or other items of economic value in return for serving as research subjects could compromise the voluntariness of informed consent,<sup>96</sup> but this is less of a concern in the military because DoD rules forbid paying research subjects on active duty except for drawing a blood sample, for which they may receive \$50.<sup>97</sup> (Off-duty personnel may receive compensation comparable to civilian subjects,<sup>98</sup> which under Health and Human Services (HHS) rules must be approved by an IRB and be a reasonable amount in accordance with prevailing local rates.<sup>99</sup>) Military IRBs must be on guard however against offering troops non-monetary benefits for enrolling in research studies, such as desirable assignments or commendations. DoD rules prohibit superiors “from influencing the decisions of their subordinates . . . regarding participation as subjects”,<sup>100</sup> but the rules could be more specific by defining what counts as “influence”. Moreover, the prohibition against paying military subjects emphasizes the need to protect them from being exploited by being pressured to participate in disproportionately risky research.

Another financial issue that arises in civilian biomedical research is whether subjects are entitled to a portion of the financial benefits that accrue to sponsors of studies that lead to the commercialization of a lucrative new medical product. Although withholding compensation has been criticized as unfair, there is a general consensus that sponsors can avoid compensating subjects if they disclose their policy to subjects during the informed consent process.<sup>101</sup>

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96. Neal Dickert & Christine Grady, *Incentives for Research Participation*, in THE OXFORD TEXTBOOK OF CLINICAL RESEARCH ETHICS c. 36 (Ezekiel J. Emanuel et al. eds., 2008).
97. DoDI. 3216.02, *supra* note 42, at § 11(a)(1).
98. *Id.* at § 11(a)(2).
99. *When Does Compensating Subjects Undermine Informed Consent or Parental Permission?*, U.S. DEP’T HEALTH & HUM. SERVS., <http://answers.hhs.gov/ohrp/questions/7251> (last visited May 5, 2014).
100. DoDI. 3216.02, *supra* note 42, at § 7(e)(1)(b).
101. *See, e.g.*, William J. Curran & S. M. Hyg, *Scientific and Commercial Development of Human Cell Lines—Issues of Property, Ethics, and Conflict of Interest*, 324 NEW ENG. J. MED. 998 (1991); Charlotte H. Harrison, *Neither Moore nor the Market: Alternative Models for Compensating Contributors of Human Tissue*, 28 AM. J. L. MED. 77, 80 (2002); Russell Korobkin, “No Compensation” or “Pro Compensation”: *Moore v. Regents and Default Rules for Human Tissue Donations*, 40 J. HEALTH L. 1, 23 (2007); Natalie Ram, *Assigning Rights and Protecting*

The argument for rewarding military subjects is weakened by their obligation to serve the national interest, but the issue is complicated by the fact that a substantial amount of the fruits of military research often redounds to the benefit of private enterprises that commercialize the resulting discoveries, including prostheses<sup>102</sup> and thermal imaging devices.<sup>103</sup> A solution might be for DoD to ensure that genomic discoveries with important medical value derived from research on military subjects were available to current and former members of the military through military medical services and the VA.

#### 7. Compensating Subjects for Experimental Injury

The Common Rule governing human subjects research does not require researchers to compensate civilian subjects for injuries sustained as a result of their participation,<sup>104</sup> but subjects who have been injured by negligent investigators may recover monetary damages in a tort action. For example, the father of an 18-year-old subject who died in a University of Pennsylvania experiment aimed at developing a gene therapy for a genetic disease called ornithine transcarbamylase sued the investigators for negligently enrolling his son without proper safety testing. (The case was eventually settled for an undisclosed sum.<sup>105</sup>) No such remedy is available to military subjects, however, as a result of the so-called *Feres* doctrine.<sup>106</sup> DoD rules require researchers “to establish procedures to protect human

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*Interests: Constructing Ethical and Efficient Legal Rights in Human Tissue Research*, 23 HARV. J. L. TECH. 119, 121 (2009).

102. *Troops' New Bionic Leg Now for Civilians, Too*, CBS NEWS (Jun. 16, 2011), <http://www.cbsnews.com/news/troops-new-bionic-leg-now-for-civilians-too/>.
103. See, e.g., Tom A. Peter, *Military Inventions Hit the Civilian Market*, CHRIST. SCI. MONITOR (Jun. 19, 2008), <http://www.csmonitor.com/Innovation/Tech-Culture/2008/0619/built-for-battle-but-perfect-in-peacetime>; Josh Kulla, *FLIR Introduces Products for the Civilian Market*, PAMPLIN MEDIA GRP. (Jan. 22, 2014), <http://www.pamplinmedia.com/wsp/139-business/207955-63820-flir-introduces-products-for-the-civilian-market>; Matthew Peach, *IR Imaging Market Shifting from Military to Civilian*, OPTICS.ORG (Sept. 13, 2013), <http://optics.org/news/4/9/16>.
104. U.S. DEP'T HEALTH & HUM. SERVS., OFC. FOR HUM. RES. PROT., INSTITUTIONAL REVIEW BOARD GUIDEBOOK, c. 3 (1993), available at [http://www.hhs.gov/ohrp/archive/irb/irb\\_chapter3.htm](http://www.hhs.gov/ohrp/archive/irb/irb_chapter3.htm).
105. Mary R. Anderlik & Nanette Elster, *Currents in Contemporary Ethics*, 29 J. L. MED. ETHICS 220 (2001); Frances H. Miller, *Trusting Doctors: Tricky Business When it Comes to Clinical Research*, 81 B.U. L. REV. 423, 426 (2001); Robin F. Wilson, *The Death of Jesse Gelsinger: New Evidence of the Influence of Money and Prestige in Human Research*, 36 AM. J. L. MED. 295 (2010).
106. *Stanley v. CIA*, 639 F.2d 1146 (1981).

subjects from medical expenses (not otherwise reimbursed)” that directly result from participation in more-than-minimal-risk military research, whereas civilian subjects may receive compensation for losses such as pain and suffering and reduced future earnings.<sup>107</sup>

The application of the *Feres* doctrine in military research has been criticized.<sup>108</sup> It also runs counter to the principle of paternalism insofar as it shields the military from having to fully redress superiors’ mistakes. But Congress has not seen fit to modify the doctrine to permit injured subjects to receive compensation, the courts have consistently given the doctrine a broad interpretation on the premise that immunity from suit is essential to maintain military discipline, and even some of the critics only want soldiers to be able to sue for intentional rather than merely negligent research misconduct.<sup>109</sup>

## 8. Privacy and Confidentiality

Protecting the privacy and the confidentiality of subjects’ personal health information has long been a priority in civilian research, and its importance has been reinforced by the adoption of the privacy and security provisions of the Health Insurance Portability and Accountability Act (HIPAA) and its accompanying regulations. One of the requirements of informed consent under the Common Rule, for example, is giving potential subjects “a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained,”<sup>110</sup> and the government recently has proposed strengthening data security and information protection requirements for federally sponsored research.<sup>111</sup> In addition, the GINA specifies that genetic information is protected under HIPAA.<sup>112</sup>

As noted earlier, DoD has adopted the Common Rule/It also has subjected itself to HIPAA.<sup>113</sup> However, the privacy and confidentiality

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107. DoDI. 3216.02, *supra* note 42, at § 10(b).

108. Parasidis, *supra* note 57, at 790–91; Siegel, *supra* note 62, at 4; Jaffee v. U.S., 663 F.2d 1226, 1249–1250 (3d Cir. 1981) (Gibbons, J., dissenting).

109. Parasidis, *supra* note 57, at 791.

110. 42 C.F.R. § 46.116(a)(5).

111. Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators, 76 Fed. Reg. 44,512, 44,525 (July 26, 2011) (to be codified at 45 C.F.R. pts. 46, 164 and 21 C.F.R. pts. 50, 56) (hereinafter HHS, ANPRM).

112. 42 USC § 1320d–9.

113. 42 USC § 1171(5)(I), (J) (HIPAA), U.S. Department of Defense, Reg. 6025.18-R, DoD Health Information Privacy Regulation (2003) (hereinafter DODR 6025.18-R).

of members of the military is subordinate to military necessity. Michael Gross observes, for example, that “among one’s own soldiers, the scope of the private sphere decreases and that of the public expands as collective welfare takes precedence over an individual’s private good.”<sup>114</sup> DoD rules accordingly permit commanders to obtain health information “to assure the proper execution of the military mission”,<sup>115</sup> and while service members have the right to an accounting of disclosures, there is no such right for disclosures for national security or intelligence purposes.<sup>116</sup>

One of the chief reasons for protecting privacy and confidentiality in regard to genomic information is to prevent stigma and discrimination. The legal protections against workplace discrimination for civilian federal employees in the Rehabilitation Act of 1973 and GINA do not apply to uniformed members of the military.<sup>117</sup> Once warfighters leave the military, however, they come under GINA’s protections against employment discrimination on the basis of genomic information. Furthermore, DoD policies implementing the National Defense Authorization Act of 2008 changed a previous policy that had denied health and disability benefits to service members who experienced injuries or illnesses during their time of service if the condition was “congenital or hereditary.”<sup>118</sup> Now, service members are entitled to compensation and benefits so long as they do not have a disability that was noted at the time of enlistment, unless there is “compelling evidence or medical judgment” that the disability existed prior to enlistment.<sup>119</sup> However, United States Army Special Operations Command (USASOC) found that the two strongest fears among service members with respect to behavioral health treatment, including PTSD, were confidentiality, fear of being labeled, and negative impact on career.<sup>120</sup> As shown in Part I.B., the most recent

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114. Gross, *supra* note 43, at 121.

115. DODR 6025.18-R, *supra* note 111, at § C7.11.1.1.

116. DODR 6025.18-R, *supra* note 111, at § C13.1.1.5.

117. *Rehabilitation Act/GINA: Confidentiality of Medical/Genetic Information*, U.S. EQUAL EMP’T OPP. COMM’N (Dec. 12, 2012), <http://www.eeoc.gov/eeoc/foia/letters/2012/ginaconfidentialityofmedicalgeneticinformation2.html>; Susannah Baruch & Kathy Hudson, *Civilian and Military Genetics: Nondiscrimination Policy in a Post-GINA World*, 83 AM. J. HUM. GENET. 435 (2008). It is not clear, however, at what point enlistees lose the protection of GINA.

118. Disability Evaluation System, DoD Directive 1332.38 (Aug. 5, 2014), § E.3.P.4.5.2.2.

119. Hereditary and/or Genetic Diseases, Revised DoD Instruction E3.P4.5.2.2 (2008).

120. Lt. Col. Paul Dean & Lt. Col. Jeffrey McNeil, *Breaking the Stigma of Behavioral Healthcare*, 25 SPECIAL WARFARE 6 (2012).

research has shown a genetic contribution to PTSD and some scholars have raised concerns regarding “the display of pertinent genetic information . . . may also generate stigma and affect individual career outcomes.”<sup>121</sup>

How should the status of subjects as members of the military affect the privacy and confidentiality of identifiable genomic information obtained in the course of military human subjects research? One approach might be that, given the reduced privacy and confidentiality within the military, the military should be able to use identifiable genomic information obtained in the course of conducting human subjects research on military subjects without the subjects’ informed consent, so long as the information is used for a legitimate military purpose. But this approach conflicts with the spirit of the military’s policy of requiring military subjects to give their informed consent to serve as research subjects. Another approach would be for IRBs to give the potential loss of privacy and confidentiality less weight when balancing risks and benefits in research on military subjects than in research on civilians. But the federal government is contemplating removing privacy and confidentiality concerns altogether as matters for IRB review and instead imposing mandatory data security rules on all human subjects research.<sup>122</sup> The best approach therefore is to rely on the principles of proportionality and paternalism described earlier and place the responsibility on commanders, including those overseeing research programs and the researchers themselves, to protect subordinates against inappropriate disclosures of identifiable genomic information.

In summary, using members of the military as subjects raises many of the same ethical issues as employing civilian subjects, but there are several notable differences. Due to limitations on warfighter autonomy, members of the military need special protection from coercion and undue influence during the informed consent process, and the principles of proportionality and paternalism require commanders to assure themselves that the potential benefits of the study outweigh the risks rather than relying on individual subjects to make this judgement for themselves in uncertain cases. At the same time, risks that would be excessive for civilian subjects might be acceptable in the military if the military’s need for the research were sufficiently compelling. Finally, the fact that the military is responsible for the health of its members and the relative ease with which it can keep track of warfighters, including after they are discharged, argue in favor of imposing a clearer obligation on military

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121. Megan Allyse, Lauren C. Milner & Mildred K. Cho, *Ethics Watch: The G.I. Genome: Ethical Implications of Genome Sequencing in the Military*, 12 NATURE REV. GENET. 589 (2011).

122. HHS, ANPRM, *supra* note 109.



researchers than on civilian researchers to follow up with subjects and to return results and incidental and unintended findings to them in appropriate cases.

*B. Extramural Clinical Research*

DoD spends approximately seventy-five percent of its outlay for research and development on extramural research, that is, research conducted at civilian institutions.<sup>123</sup> The allocation of such a large portion of the defense R&D budget to civilian researchers results from the need to fund industrial contractors that develop weapon systems and the desire to nourish a broad science base at U.S. academic institutions. Some of this DoD sponsored research—there are no published estimates of how much—involves the use of live human subjects. Some of these studies may involve genomic science, and the amount of genomic human subjects research can be expected to increase if DoD follows the recommendations in the JASON report described earlier.

Extramural studies of human subjects must be approved by IRBs at the civilian institutions conducting the research as well as by internal military IRBs. The Army requires an additional layer of protocol review by the USAMRMC Commanding General's Human Subjects Research Review Board for studies involving "gene transfer".<sup>124</sup>

Although commentators have noted the potential for conflict between internal military and external civilian IRBs,<sup>125</sup> there is no information on how they interact, for example, how they resolve disagreements. Nor is there an understanding of how the members of civilian IRBs decide whether to approve protocols for military sponsored research. They may not be clear on how to weigh risks to subjects against military necessity and national security. On the one hand, they may feel that it is inappropriate for them to reject military studies that pose risks to subjects that would be unacceptable in purely civilian research. On the other hand, some IRB members may be critical of military research for various reasons, leading them to block or unreasonably delay studies that should go forward. In addition, both DoD and HHS regulations forbid IRBs from

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123. AM. ASS'N FOR ADV'T SCI., AAAS REPORT XXXVII: RESEARCH AND DEVELOPMENT FY 2013, c. 5, p. 61 (2013).

124. U.S. Army Medical Department Medical Research and Materiel Command, Guidelines for Investigators: Requirements for U.S. Army Medical Research and Materiel Command (USAMRMC) Headquarters Review and Approval of Research Involving Human Volunteers, Human Anatomical Substances, and/or Human Data, § IV(A) (2007).

125. Paul J. Amoroso & Lynn L. Wenger, *The Human Volunteer in Military Biomedical Research*, in II MILITARY MEDICAL ETHICS 563-660 (Thomas E. Beam and Linette R. Sparacino eds., 2003).

considering “possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility,”<sup>126</sup> and IRBs may not know how this restriction should affect their consideration of the long-range effects of military research.

A special set of problems arises with classified extramural military research. Bioethicist Jonathan Moreno notes the difficulties raised by conducting classified military research outside of the military, including requiring IRB members and potential subjects to have security clearances.<sup>127</sup> (DoD rules, for example, require IRBs to determine if potential subjects “need access to classified information to make a valid, informed consent decision.”<sup>128</sup>) The Advisory Committee on Human Radiation Experiments evaluated human subjects protections in classified government research and identified a number of shortcomings in written informed consent forms.<sup>129</sup> Academics describe resistance among academics and universities to conducting classified government research due to concerns about infringement of academic freedoms, including the freedom to publish research results.<sup>130</sup> Nineteen of thirty-nine universities she studied had policies prohibiting either classified or non-publishable research. (Eisenberg notes, however, that in some cases faculty researchers at these institutions may be affiliated with off-campus laboratories that do not have similar restrictions.) In addition, Eisenberg reports that a number of other universities do not consider classified research for purposes of promotion, tenure, or academic credit.

DoD has adopted special protections for subjects in classified experiments regardless of whether the subjects are military personnel or civilians: the protocol must be approved by the Secretary of Defense; the fact that the study is sponsored by DoD and that the research is classified must be disclosed as part of the informed consent process, unless the Secretary of Defense makes an exception because “providing this information could compromise intelligence sources or

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126. 32 CFR § 219.11(a)(2); 45 CFR § 46.111(a)(2).

127. Jonathan D. Moreno, *Bioethics and the National Security State*, 32 J. L. MED. ETHICS 198 (2004).

128. DoDI 3216.02, *supra* note 42, at § 13(d)(4) (2011).

129. Nancy E. Kass & Jeremy Sugarman, *Are Research Subjects Adequately Protected? A Review and Discussion of Studies Conducted by the Advisory Committee on Human Radiation Experiments*, 6 KENNEDY INST. ETHICS J. 271 (1996).

130. Maxwell Gregg Bloche, *Review Essay: Rogue Science: Science in the Service of Human Rights. By Richard Pierre Claude*, 91 GEO. L. J. 1257, 1274 (2003); Rebecca S. Eisenberg, *Academic Research and Academic Values in Sponsored Research*, 66 TEX. L. REV. 1363 (1988).

methods;" IRBs must do a full rather than "expedited" review; and an IRB member who disagrees with a majority decision approving the study may appeal to the Secretary.<sup>131 132,</sup>

The foregoing concerns about extramural military research raise the question of whether and in what circumstances it should take place at all. An argument can be made that all military human subjects research, including genomic research, should take place intramurally using members of the military as subjects. By being in the military, they have agreed to subordinate their interests to those of the military, and therefore seem more appropriate to bear research risks than civilians, especially in experiments that offer no prospect of direct benefit to subjects. Furthermore, military subjects are protected by the principle of paternalism and therefore, at least in theory, commanders who expose them to disproportionate experimental risks are accountable and subject to punishment. In civilian bioethics, on the other hand, there is a dispute over how much of a duty civilian researchers owe to protect the interests of their subjects, with some commentators asserting that the investigators' duty to subjects is superseded by their duty to the study sponsor.<sup>133</sup> On the other hand, certain types of genomic studies may be more difficult to conduct in a military environment. For example, genome-wide association studies may need to use large civilian DNA repositories in order to have the power to discover variations that account in small ways for phenotypes of military interest. Moreover, the importance of maintaining the quality of U.S. science argues in favor of continuing to use military research funding to support civilian research institutions. Finally, requiring military research to be conducted on military personnel could lead to public perceptions that they were being used as human guinea pigs, especially if the research was not on a topic primarily of military interest.

### *C. VA Clinical Research*

The VA has already staked a claim to genomic research by launching its Million Veteran Program in May, 2011, which collects voluntary donations of DNA from veterans along with permission to correlate their genetic data with information in their medical and

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131. DoDI 3216.02, *supra* note 42, at § 13.

132. In addition, in classified extramural research, at least one member of the IRB must be a non-federal employee. DoDI 3216.02, *supra* note 42, at § 13 (d)(2).

133. *See, e.g.,* E. Haavi Morreim, *Medical Research Litigation and Malpractice Tort Doctrines: Courts on a Learning Curve*, 4 HOUS. J. HEALTH L. POL'Y 1, 41-46 (2003).

personnel records in order to establish a geno-phenobank.<sup>134</sup> (The program is described further below in the section on biobanks.) In addition, the VA conducts genomic research on amyotrophic lateral sclerosis, bipolar disorder and schizophrenia, and PTSD.<sup>135</sup> In 2006, it established a Genomic Medicine Program Advisory Committee to guide the start of a new Genomic Medicine Program, and it also conducts pharmacogenomic research.<sup>136</sup> (All VA research is intramural.<sup>137</sup>)

The VA, like DoD, has adopted the Common Rule to govern live human subjects research.<sup>138</sup> However, VA patients asked to participate as subjects, like other civilian patients, may fear that they will be denied health care if they refuse. VA researchers are required to make “every reasonable effort” to provide patients with an informational brochure called “Volunteering in Research—Here Are Some Things You Need To Know” which states that they have a right to say “no” and that refusing to participate “will not affect your VA health care or benefits.”<sup>139</sup> Beyond that, the agency has no special human subjects’ protections. For example, it does not recognize veterans as a vulnerable research population. While it is true that they are not among the groups formally designated as vulnerable subjects, they resemble those groups in their dependence on government-provided health care, and the fact that they served in the military may make them feel that they have a duty to participate in research whenever they are asked. These considerations require the VA to employ a heightened degree of paternalism to protect veterans against disproportionate research risks.

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134. Joel Kupersmith, *The Million Veterans Program: Building VA’s Mega-Database for Genomic Medicine*, HEALTH AFF. BLOG (Nov. 19, 2012), <http://healthaffairs.org/blog/2012/11/19/the-million-veteran-program-building-vas-mega-database-for-genomic-medicine/print/>.

135. *Genomics*, U.S. DEP’T VETS. AFF., OFC. RES. & DEV., <http://www.research.va.gov/researchtopics/genomics.cfm#.Ud8Nhqz7Yhg> (last visited May 5, 2014).

136. Ronald Przygodski, *Genomic Medicine Program*, VETS. HEALTH ADMIN. OFC. RES. & DEV., <http://www.cdc.gov/genomics/translation/GAPPNet/meeting/file/print/slides/Przygodzki.pdf> (last visited May 5, 2014).

137. *Veterans Health Administration Research and Development Program*, U.S. DEP’T VETS. AFF., VETS. HEALTH ADMIN. (Jul. 9, 2009), <http://www.va.gov/vhapublications/ViewPublication.asp?pub ID=2043>.

138. 38 CFR § 16.101 ff.

139. U.S. Department of Veterans Affairs Office of Research and Development, *Volunteering in Research—Here Are Some Things You Need To Know*, U.S. DEP’T VETS. AFF. OFC. RES. & DEV., <http://www.research.va.gov/programs/pride/veterans/trifold.pdf> (last visited May 5, 2014).

*D. Geno-Phenobanks*

While the foregoing sections discuss the ethical, legal, and policy issues raised by clinical genomic research using human subjects, this section discusses another type of genomic research that uses DNA samples rather than living human subjects.

As noted earlier, the military currently possesses millions of DNA samples from current and former service members, and the Army, Air Force, and VA are collecting additional samples for research purposes. The resulting biorepositories can be linked to the medical and personnel records of the individuals who contribute the DNA to create geno-phenobanks, enabling researchers to discover links between DNA variants and physical and mental conditions and characteristics.

Geno-phenobank research raises many of the same types of ethical, legal, and policy concerns as clinical research, including the need to obtain consent from DNA contributors to use their DNA for research, return of results and incidental findings, shared benefit, and maintaining the privacy and confidentiality of research results. In regard to consent, some commentators have suggested that, based on traditional research ethics, individuals whose DNA is proposed to be used for research should be re-contacted and asked to give consent for each new research project.<sup>140</sup> Other commentators propose that, at the time that their DNA is obtained, individuals should give “multi-layered” consent which would enable them to specify their wishes on a detailed form, such as giving consent to future research on specific diseases or being re-contacted and asked to consent to any future research.<sup>141</sup> However, under increasing recognition that recontacting participants to obtain their specific informed consent for every future research project may be impractical, expensive, and possibly impede socially valuable research,<sup>142</sup> there has been a growing movement away from the model of specific informed consent. Alternatives that have been put forward include (1) permitting human research ethics committees to waive individual consent under circumstances where obtaining consent is impracticable and there is a strong public interest in the research;<sup>143</sup> (2) “broad” consent that allows samples to be used for one or more general purposes, such as biomedical research in

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140. See, e.g., Bernice S. Elger & Arthur L. Caplan, *Consent and Anonymization in Research Involving Biobanks: Differing Terms and Norms Present Serious Barriers to an International Framework*, 7 EMBO REPS. 661 (2006); Margaret F. A. Otlowski, *Tackling Legal Challenges Posed by Population Biobanks: Reconceptualizing Consent Requirements*, 20 MED. L. REV. 191 (2012).

141. *Id.*

142. *Id.*

143. *Id.*

general, or research on one or more specific diseases<sup>144</sup>; and (3) “blanket” consent that allows for unrestricted use of samples.<sup>145</sup>

To understand the issues involving consent, it is important to distinguish between research on existing DNA samples and research on newly acquired samples. Suppose DoD wanted to combine existing DNA samples in the AFRSSIR with digitalized medical and personnel records of service members in order to conduct biomedical research. Would DoD have to obtain the consent of the DNA contributors, and if so, what kind of consent?

On the one hand, it might be argued that consent is unnecessary. The DoD policy that requires informed consent from military research subjects only applies to “research involving a human being as an experimental subject,” which DoD defines as involving “an intervention or interaction with a living individual,”<sup>146</sup> and therefore the policy does not apply to research on ex vivo DNA samples. Moreover, providing DNA to the AFRSSIR is mandatory; warfighters have been court-martialed for refusing,<sup>147</sup> and their courts-martial have been upheld by the courts.<sup>148</sup> Furthermore, having to obtain consent could be burdensome in the case of individuals who are no longer in the service, who might be difficult to locate. The argument for proceeding without consent is especially strong in regard to research with distinct military applications, for example, on gene variants associated with coolness under fire, or genomic therapies that speed trauma recovery.

On the other hand, the consensus in the civilian sector is that research on DNA samples requires the consent of the contributors if their identity is revealed or can be determined from the data, which, as mentioned earlier, would be the case with a military genobank.<sup>149</sup> Furthermore, the mandatory nature of the AFRSSIR

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144. Otlowski, *supra* note 138, at 225.

145. Mats G. Hansson et al., *Should Donors Be Allowed to Give Broad Consent to Future Biobank Research*, 7 LANCET ONCOLOGY 266 (2006).

146. DoDI. 3216.02, *supra* note 42, at Glossary.

147. LORI ANDREWS & DOROTHY NELKIN, BODY BAZAAR: THE MARKET FOR HUMAN TISSUE IN THE BIOTECHNOLOGY AGE 113–114 (2001).

148. *Mayfield v. Dalton*, 901 F. Supp. 300 (D. Haw. 1995), *vacated as moot*, 109 F.3d 1423 (9th Cir. 1997).

149. The Department of Health and Human Services (DHHS) is proposing to revise the rules for civilian research to require consent for any research with human DNA or with biospecimens from which DNA may be extracted, even if the researchers attempt to ‘de-identify’ their data. HHS, ANPRM, *supra* note 109. Moreover, there is a considerable doubt about whether genomic data can ever truly be de-identified. *See, e.g.*, Jean E. McEwen, Joy T. Boyer & Kathie Y. Sun, *Evolving Approaches to the Ethical Management of Genomic Data*, 29 TRENDS IN GENET. 375 (2013) (“[B]ecause of its comprehensiveness, genomic information, even

program has been criticized,<sup>150</sup> and in any event, DoD currently permits AFRRSSIR samples to be used for purposes other than identification of remains only with the consent of the donor or the surviving primary next-of-kin.<sup>151</sup> Finally, the whereabouts of personnel who have left the service may not be that difficult to determine since they may be obtaining health care from the Veterans Administration.

If the consent of warfighters to use existing DNA samples is necessary, what kind of consent must be obtained? Specifically, can warfighters be asked to consent to *any* research use of their DNA (referred to as “broad” or “general” consent), or must they give specific consent for each particular research project, including for different projects undertaken in the future? This is the subject of controversy in the civilian sector, but there appears to be a growing consensus, reinforced by changes in consent rules proposed by DHHS,<sup>152</sup> that broad consent is acceptable, and the reasoning supporting the consensus suggests that broad consent also should be sufficient for military research.

If the military must obtain consent for research using existing DNA, all the more reason that it should obtain consent for research on newly acquired specimens, since this can be done easily when the specimen is obtained. Again, the consent could be broad. Indeed, this is the approach followed by current military genomic research projects.<sup>153</sup> Additional issues arise in connection with the use of DNA

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when stripped of traditional identifiers, has, at least in some sense, the potential to re-identify the individual from whom it was obtained.”).

150. Steven C. Hendricks, *A Fourth Amendment Privacy Analysis of the Department of Defense’s DNA Repository for the Identification of Human Remains: The Law of Fingerprints Can Show Us the Way*, 181 MIL. L. REV. 69 (2004); Patricia A. Ham, *Army of Suspects: The History and Constitutionality of the U.S. Military’s DNA Repository and Its Access for Law Enforcement Purposes*, 2003 ARMY L. 1 (2003); Kelly S. Erbes, *Identification of the Unknown Soldier and the Fight for the Right to Anonymity: The Human Genome Project and Implications of a National DNA Database*, 47 CLEV. ST. L. REV. 443 (1999); Elizabeth Reiter, *The Department of Defense DNA Repository: Practical Analysis of the Government’s Interest and the Potential for Genetic Discrimination*, 47 BUFF. L. REV. 975 (1999); Sarah Gill, *The Military’s DNA Registry: An Analysis of Current Law and a Proposal for Safeguards*, 44 NAVAL L. REV. 175 (1997); Robert Craig Scherer, *Mandatory Genetic Dogtags and the Fourth Amendment: The Need for a New Post-Skinner Test*, 85 GEO. L. J. 2007 (1997).
151. Armed Forces Institute of Pathology Operations, DoD Instruction 5154.30, § E2.5.4.4 (Mar. 18, 2003) at E2.5.
152. HHS, ANPRM, *supra* note 109.
153. ARMY STARRS, <http://www.armystarrs.org> (last visited May 5, 2014); *Informed Consent Session—U.S. Air Force Medical Service PC2-Z Study*, CORIELL PERSONALIZED MED. COLLAB., <http://www.cpmc>.

samples from deceased individuals. The Common Rule that governs civilian research does not apply to deceased persons, who are not deemed to be “human subjects.”<sup>154</sup> However, some commentators have argued that researchers should honor preferences that a deceased person made known while alive,<sup>155</sup> and that consent should be obtained from the next-of-kin.<sup>156</sup> In the case of the military, when they submit samples to AFRSSIR, enlistees could be asked to give their consent to posthumous research using their DNA.

As noted earlier, the VA operates the Million Veteran Program, a geno-phenobank that collects DNA and health information from veterans and combines it with their VA medical records for research purposes. Veterans at participating VA medical centers are sent a letter asking if they would like to participate. If they opt in, they fill out a brief health survey and make an appointment at the medical center to accompany their next medical visit.<sup>157</sup> During this visit, they are counseled about the program, given the opportunity to consent to be placed in the database and to make their medical records available for research, and asked to give a blood sample. The consent is broad, as the veteran is asked to consent to a general program of genetic research, and the sample is kept indefinitely. As of October, 2012, over 100,000 veterans had enrolled.<sup>158</sup> As noted earlier, the VA does not return any results to the donors, claiming that it is barred from doing so because the DNA is not analyzed at a CLIA-certified laboratory. Given the public nature of VA funding and the relative ease in locating participating veterans, an argument can be made that

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coriell.org/Sections/Membership/EnrollmentConsent.aspx?CoriellReg=Y &PgId=9&id=38 (last visited May 5, 2014).

154. 45 C.F.R. § 46.102(f).

155. Mark Wicclair & Michael DeVita, *Oversight of Research Involving the Dead*, 14 KENNEDY INST. ETHICS J. 143 (2004). *See also* WORLD HEALTH ORG. (WHO), GENETIC DATABASES: ASSESSING THE BENEFITS AND THE IMPACT ON HUMAN AND PATIENT RIGHTS (2003) (“The death of an individual who has provided a genetic sample or genetic information does not represent the end of the ethical responsibilities that are owed in respect of the samples or information.”).

156. U.N. EDUC., SCI. & CULTURAL ORG. (UNESCO), HUMAN GENETIC DATA: PRELIMINARY STUDY BY THE IBC ON ITS COLLECTION, PROCESSING, STORAGE AND USE 18, *available at* [http://portal.unesco.org/shs/en/files/2138/10563744931Rapfinal\\_gendataen.pdf/Rapfinalgendata\\_en.pdf](http://portal.unesco.org/shs/en/files/2138/10563744931Rapfinal_gendataen.pdf/Rapfinalgendata_en.pdf).

157. *Million Veteran Program*, U.S. DEP’T VETS. AFF. <http://www.research.va.gov/mvp/> (last visited May 5, 2014).

158. Joel Kupersmith, *The Million Veterans Program: Building VA’s Mega-Database for Genomic Medicine*, HEALTH AFF. BLOG (Nov. 19, 2012), <http://healthaffairs.org/blog/2012/11/19/the-million-veteran-program-building-vas-mega-database-for-genomic-medicine/print/>.



the cost concerns raised by requiring samples to be analyzed at CLIA-certified laboratories are outweighed by the potential health benefits of returning results that are medically significant.

## V. GENOMIC TESTING

Testing in aid of medical diagnosis or treatment raises ethical and legal concerns. Whether physicians can order HIV tests and drug screens without patient consent has been especially contentious, but objections also have been made to the widespread physician practice of ordering other “routine” medical tests without informing patients of the nature of the tests and obtaining their consent.<sup>159</sup>

When the testing in question is genomic, special concerns arise because the testing laboratory obtains access to the patient’s DNA, which contains the patient’s entire genetic code rather than just information about the targeted illness. One issue that has been discussed earlier, for example, is whether the physician has a duty to inform the patient about “incidental” findings relevant to the patient’s health.

When addressing ethical and legal concerns of genomic testing, it is common to distinguish between predictive genomic testing, which aims to ascertain if a person is at risk for a genomic illness in the future, and non-predictive testing, that is, testing to diagnose or aid in treating a manifested illness. As discussed earlier, military physicians can be expected to employ genomic testing for non-predictive purposes in the same manner as their civilian colleagues, that is, to help diagnose and treat illness in their military patients. Non-predictive genomic testing generally has been less controversial, since it tends to be viewed as analogous to other types of medical testing. For example, a provision in Massachusetts state law prohibiting genetic testing without informed consent excludes “any test for the purpose of diagnosing or detecting an existing disease, illness, impairment or disorder” from its definition of “genetic test.”<sup>160</sup> But even when it is performed for non-predictive purposes, genomic testing can yield information about the patient’s risks for future illnesses, which can lead to social stigma if it becomes known to others and discrimination if it gets into the hands of employers or health insurers. From an ethical and legal standpoint, then, there is no meaningful difference between predictive and non-predictive genomic testing, and in the civilian sector, there is a clear consensus

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159. See, e.g., Clarence H. Braddock III et al., *Informed Decision Making in Outpatient Practice*, 282 JAMA 2313 (1999); Clarence H. Braddock III et al., *How Doctors and Patients Discuss Routine Clinical Decisions*, 12 J. GEN. INT. MED. 339 (1997).

160. Mass. Gen. laws, c. 111, § 70G(a) (2013).

that no genomic testing should be performed without an individual's informed consent.<sup>161</sup>

As discussed previously, however, the bioethical principles that govern military life are different from those that apply to civilians. The health status of warfighters not only affects their well-being, but the well-being of the unit, the success of the mission, and the security of the state. Unlike civilians, therefore, warfighters are not free to refuse necessary medical care, including medical testing.<sup>162</sup> Should the fact that a test is genomic change this rule, that is, should warfighters be able to refuse a genomic test, and should the answer be the same when the genomic test is predictive rather than in aid of diagnosis or treatment? Finally, should warfighters be able to refuse genomic testing that pertains to non-disease characteristics, such as physical and mental abilities?

Despite the special concerns raised by genomic testing, a strong argument can be made that it should be subject to the same rules as other types of military medical testing, meaning that warfighters cannot refuse to submit to genomic testing, including when it is predictive rather than in aid of treatment and diagnosis. As noted earlier, providing a blood sample for DNA testing under AFRRSSIR

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161. See, e.g., *Genetic Testing by Employers, Opinion 2.132(2)(e)*, AM. MED. ASS'N (Jun. 1991), <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion2132.page>, *Ethical Issues in Carrier Screening of Genetic Disorders, Opinion 2.137*, AM. MED. ASS'N (Jun. 1994), <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion2137.page>, and *Multiplex Genetic Testing, Opinion 2.139*, AM. MED. ASS'N (Jun. 1998), <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion2139.page>; Lois Snyder, American College of Physicians Ethics, Professionalism, and Human Rights Committee, *American College of Physicians Ethics Manual: Sixth Edition*, 156 ANNALS INT. MED. 73 (2012); ARIZ. REV. STAT. ANN. § 12-2803 (a health care provider shall not conduct a genetic test on a person unless the health care provider first obtains written informed consent from the person to be tested or from the person's authorized representative); FLA. STAT. ANN. § 760.40(2)(a) (DNA analysis may be performed only with the informed consent of the person to be tested); NEV. REV. STAT. § 629.151(1) to (6) (It is unlawful to obtain any genetic information of a person without first obtaining the informed consent of the person or the person's legal guardian); N.M. STAT. ANN. § 24-21-3(A) (no person shall obtain genetic information or samples for genetic analysis from a person without first obtaining informed and written consent from the person or the person's authorized representative); VT. STAT. ANN. tit. 18, § 9332(d) (no genetic testing shall be performed on any individual or body parts of any individual nor shall any bodily materials be released for purposes of genetic testing without the prior written authorization and informed consent of the individual to be tested).

162. U.S. Army Regulation 600-20 (2012).

is mandatory, and its mandatory nature has been upheld by the courts. Furthermore, the Military Rules of Evidence governing proceedings under the Uniform Military Code of Justice provide that, while communications between a patient and psychotherapist—arguably the most sensitive type of medical information—are privileged, the privilege does not apply when the information is “necessary to ensure the safety and security of military personnel . . . or the accomplishment of a military mission.”<sup>163</sup> Moreover, although the military in a sense is an employer of its personnel, it is not subject to the prohibition in GINA against requiring employees to undergo genomic testing. In any event, there is some sentiment that GINA should be amended to allow employers to use genomic testing that could identify job applicants who might pose a threat to the safety of others as a result of their genomic endowment.<sup>164</sup>

At the same time, however, military genomic testing is subject to the principles of proportionality and paternalism that govern military bioethics generally, so it may only be undertaken if accountable superiors determine that the risks, including loss of privacy and potential breaches of confidentiality, are outweighed by military necessity. This is especially important in the case of genomic testing for non-disease characteristics. The military has a legitimate interest in obtaining information about warfighters’ physical and mental abilities, including genomic information, but only if the genomic test is a valid indicator of what it purports to show and the information is necessary in order to carry out the mission. Furthermore, as noted earlier, the military has adopted the privacy rules of HIPAA, including the limitation on disclosure of protected health information to the minimum necessary to accomplish the purpose of the disclosure,<sup>165</sup> and the requirement that the information must be kept secure.

Finally, the military must be mindful of relying too heavily on the results of genomic tests that have not been adequately validated. The popular press is quick to tout purported links between genomic factors and traits or conditions that often turn out to be false or overstated.<sup>166</sup> Although military exigencies may create a compelling need for genomic data, the data must be viewed with caution until they are adequately confirmed. This raises the question of under what circumstances the military is entitled to rely on genomic technologies that have not yet been fully tested, discussed in the following section.

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163. Manual for Courts-Martial United States, Rule 513(d)(6) (2012).

164. Noah Levin, *A Defense of Genetic Discrimination*, 43 HASTINGS CTR. REP. 33 (2013).

165. DODR 6025.18-R, *supra* note 109, at § C8.2.1.

166. *See, e.g.*, Joel N. Hirschhorn, *A Comprehensive Review of Genetic Association Studies*, 4 GENET. MED. 45 (2002).

## VI. DEPLOYMENT USE OF UNPROVEN GENOMIC TECHNOLOGIES

As described earlier, the military has an interest in giving troops gene-based technologies that could help protect them, treat injury and illness, and improve their performance. Earlier, this article discussed ethical and legal issues surrounding the testing of these interventions in military and civilian subjects. But the military might not want to pass up the opportunity to provide a promising genomic intervention to warfighters, especially those in harm's way, even though the intervention had not undergone complete testing for safety and efficacy.

A similar situation, although not involving genomic technologies, arose with the distribution of pyridostigmine bromide (PB) and botulinum toxoid (BT) vaccine to troops during the Gulf War, and with the DoD's Anthrax Vaccine Immunization Program (AVIP), which began in 1998. These modalities were given to troops to protect against chemical and biological weapons rather than solely to determine whether or not they actually worked. In other words, they were deployment uses rather than formal research studies. At the time, the Food and Drug Administration (FDA) had approved PB for treatment of myasthenia gravis, but not for protection against nerve agents,<sup>167</sup> while at the start of the AVIP Program, the anthrax vaccine was approved by the FDA to protect against cutaneous exposure but not against the airborne exposure that DoD expected. (The FDA approved anthrax vaccine for all routes of exposure in 2004.<sup>168</sup>) Therefore, these were "off-label" or "unapproved" uses, a common medical practice. The FDA had not approved BT vaccine for any use at the time of the Gulf War, but the vaccine had an odd history; it was the only vaccine available against botulinum toxin, had been used by doctors to protect people against it for years, and was manufactured for that purpose by the Centers for Disease Control and Prevention under an investigational new drug exemption,<sup>169</sup> the

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167. William J. FitzPatrick & Lee L. Zwanziger, *Defending Against Biochemical Warfare: Ethical Issues Involving the Coercive Use of Investigational Drugs and Biologics in the Military*, 3 J. PHIL. SCI. L. 1 (2003).

168. Parasidis, *supra* note 57.

169. *Statement of Randolph E. Wykoff, Assoc. Comm'r for Ops, Food & Drug Adm., on Medical, Chemical, and Biological Warfare Preparedness before the Senate Committee on Veterans Affairs*, FOOD & DRUG ADM. (Mar. 17, 1998), <http://www.fda.gov/NewsEvents/Testimony/ucml115125.htm>.

FDA's mechanism for allowing unapproved products to travel legally across state lines.<sup>170</sup>

These deployment uses generated controversy over whether they should be voluntary, that is, whether troops should be allowed to refuse to take the drug and the vaccines. One concern was that making deployment use mandatory would encourage the military to use it to circumvent the informed consent requirements of formal research. Ultimately, Congress decided that drugs could be given to troops off-label only if a waiver of informed consent was issued by the President<sup>171</sup> or under an Emergency Use Authorization (EUA) granted by the FDA during a national emergency, and then not to all members of the armed forces but only to troops "in a particular military operation."<sup>172</sup> The same legal restrictions currently would apply to the deployment use of unapproved or off-label genomic technologies. In addition, the military should only seek a Presidential waiver or an EUA when the use of these genomic technologies would

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170. Some sources including the FDA and DoD itself described the Gulf War use of these drugs as "investigational." FitzPatrick & Zwanziger, *supra* note 165. But this is a misnomer. FDA regulations define 'investigational' as a drug or biological drug "that is used in a clinical investigation," (21 C.F.R. § 312.3(b)) that is, in a safety and efficacy study conducted with human subjects. Neither PB nor BT vaccine was being studied in a formal clinical investigation; no manufacturer was conducting studies at the time, and most commentators do not consider the Gulf War use to be formal research, since although the DoD clearly was interested in seeing what effect PB and BT vaccines had on the troops who took them, the primary intent was to protect troops against attack rather than to produce generalizable knowledge. DoD evidently called the Gulf War uses "investigative" because it felt that its actions sufficiently resembled human subjects research that, under current law, the troops would need to give their informed consent before taking them. DoD deemed this to be impractical under combat conditions, but was concerned that proceeding without informed consent would be illegal and appear to violate the Nuremberg Code. It therefore asked the FDA to establish a special procedure whereby troops could be given the products without their consent. RICHARD A. RETTIG, *MILITARY USE OF DRUGS NOT YET APPROVED BY THE FDA FOR CW/BW DEFENSE: LESSONS FROM THE GULF WAR* (1990). The result was an "interim rule" permitting the Commissioner of the FDA to waive the need for informed consent so that DoD could use "investigational" products for military purposes. Food and Drug Administration, *Informed Consent for Human Drugs and Biologics; Determination that Informed Consent is Not Feasible*, 55 Fed. Reg. 52814 (1990). Gulf War veterans unsuccessfully challenged the interim rule in court [John Doe and Mary Doe v. Sullivan, 756 F. Supp. 12 (USDC 1991); Doe v. Sullivan, 938 F.2d 1370 (US App DC 1991)]. In 1999, Congress transferred the authority to grant the waiver from the Commission of the FDA to the President (10 U.S.C. § 1107(f) (1999)).

171. 10 U.S.C. § 1107(f) (1999).

172. Project BioShield Act of 2004 (Pub. Law 108-276).

be ethical, that is, when it would comply with the principles of proportionality, paternalism, and fairness. Commanders should carefully consider the available evidence concerning the risks and benefits of the technology in question and determine that there is no less risky alternative, so that imposing the risks on troops would be necessary in order to accomplish the mission.

## VII. THE ROLE OF MILITARY PHYSICIANS

With the possible exception of deployment uses, warfighter access to genomic technologies will be through a physician intermediary, whether as a researcher, clinician, or operator of a genomic testing program. This raises the question of what obligations military physicians owe to military personnel. Some commentators claim that physicians in the military should behave no differently than physicians in the civilian world and that the same ethical norms and legal rules should apply. The World Medical Association, for example, states that “medical ethics in times of armed conflict is identical to medical ethics in times of peace,”<sup>173</sup> bioethicist Peter Clark asserts that “the failure of medical professionals to recognize that military and civic duty can never trump medical ethical principles is clearly an injustice,”<sup>174</sup> and Sidel and Levy go so far as to claim that “it is morally unacceptable for a physician to serve as both a physician and a soldier in the United States military forces ...,”<sup>175</sup> leaving open the question of who is going to provide medical services in the military.

As noted earlier, the civilian bioethical principle that the welfare of the individual patient is the paramount is in conflict with the military principle that the welfare of the individual is subordinate to the welfare of the unit, the success of the mission, and the security of the state. As Edmund Howe emphasizes, “the military physician, at least implicitly, promises to support the mission or greater good when and if this is necessary, even if this requires subordinating the medical well-being of the individual soldier.”<sup>176</sup> If military doctors acted according to civilian principles of bioethics when they provided services to their own troops, they might find themselves having to

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173. Gross, *supra* note 43, at 101.

174. Peter Clark, *Medical Ethics at Guantanamo Bay and Abu Ghraib: The Problem of Dual Loyalty*, 34 J. L. Med. Ethics 577 (2006).

175. Victor W. Sidel & Barry S. Levy, *Physician-Soldier: A Moral Dilemma?*, in 1 TEXTBOOKS OF MILITARY MEDICINE: MILITARY MEDICAL ETHICS 312 (Edmund D. Pellegrino, Anthony E. Hartle, Edmund G. Howe & Walter Reed eds., 2004).

176. Edmund G. Howe, *Mixed Agency in Military Medicine: Ethical Roles in Conflict*, in 1 TEXTBOOKS OF MILITARY MEDICINE: MILITARY MEDICAL ETHICS 333 (Edmund D. Pellegrino, Anthony E. Hartle, Edmund G. Howe & Walter Reed eds., 2004).

violate the fundamental principle of military bioethics. Consequently, the rules governing military physicians cannot be the same as those that govern civilians.

Military physicians are still medical professionals, however, and while this status cannot relieve them of their obligations as members of the military, it imposes on them a special obligation to look out for the interests of warfighters for whom they are responsible. Due to their medical expertise, they should be in a better position than nonphysicians to assess biomedical risks and benefits, and therefore they have a duty to apply their medical expertise to determine if a genomic risk that commanders seek to impose on their subordinates is disproportionate. If physicians disagree with the commanders' judgement, they must take the matter up the chain of command until they are satisfied that their professional concerns have received due consideration. As Canadian brigadier general and former director of Canadian military health services Hilary Jaeger states, "the military physician must act as a counterweight, by being the voice of caution," and "should not hesitate to challenge when they are not satisfied."<sup>177</sup>

A prime example of the special protective role of military physicians in fact involves a genomic technology, a recombinant-DNA-manufactured clotting agent called Factor VII.<sup>178</sup> The army introduced the product into clinical practice in Iraq in 2004 before full-scale testing, which later revealed both safety problems, such as an increased risk of blot clots that could cause strokes<sup>179</sup> and a lack of efficacy.<sup>180</sup> Army physicians in Baghdad became concerned in 2006 about the safety and efficacy of the clotting agent and urged their

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177. Hillary F. Jaeger, *A Glance at the Tip of a Big Iceberg: Commentary on 'Recommendations for the Ethical use of Pharmacological Fatigue Countermeasures in the US Military'*, 78 AVIATION, SPACE ENVTL. MED. B128 (2007).

178. According to the package insert, Factor VII, brand-name NovoSeven, is produced by cloning the gene for human Factor VII, expressing it in baby hamster kidney cells, secreting it into a culture media containing newborn calf serum in its single-chain form, and then proteolytically converting it by auto-catalysis to the active two-chain form during a chromatographic purification process. See generally *NovoNordisk: NovoSeven*, FOOD & DRUG ADM. (Oct. 13, 2006), <http://www.fda.gov/downloads/biologicsbloodvaccines/bloodbloodproducts/approvedproducts/licensedproductsblas/fractionatedplasmaproducts/ucm056915.pdf>.

179. Alex Berenson, *Army's Aggressive Surgeon Is Too Aggressive for Some*, N. Y. TIMES (Nov. 6, 2007), <http://www.nytimes.com/2007/11/06/health/06prof.html?pagewanted=all>.

180. Robert Little, *Army Medicine: Untested in Battle*, BALTIMORE SUN (Mar. 29, 2009), <http://www.baltimoresun.com/news/nation-world/bal-te.militarymed29mar29,0,7320913,full.story>.

superiors in the medical chain of command to curtail its use. This led to rebukes from their superiors.<sup>181</sup>

### VIII. GENOMIC ENHANCEMENT

Ethical and legal issues raised by military human subjects research on genomic enhancements were discussed earlier in *Balancing Risks and Benefits*. This section addresses the issues raised by giving genomic enhancements to troops outside of research, such as during training or deployment. Genomic enhancement technologies raise some of the same ethical and legal concerns that have been discussed in connection with other genomic technologies, for example, whether warfighters must be asked for informed consent. The question here is whether the fact that the genomic technology is an enhancement rather than medically related calls for different treatment.

Generally speaking, the answer is no. The fact that a genomic test seeks information about a warfighter's physical or mental abilities rather than their risk for genomic disease, for example, does not alter the ground rules for military genomic testing described in *Genomic Testing*, which mandate that any risks from the testing be proportionate to the military's need for the information and that superiors protect the warfighter's welfare to the greatest extent possible. The same is true for a genomic intervention such as a recombinant-DNA-manufactured drug, an example of which would be erythropoietin, which provides greater endurance by increasing the oxygen supply to tissues, or even a direct genomic manipulation that aims to improve warfighter performance. In all these cases, the same considerations of safety, efficacy, proportionality, paternalism, and fairness obtain.

One reason for not making special rules for genomic enhancement is that the distinction between an enhancement and other sorts of genomic technologies is difficult to make. Consider a recombinant drug that improves mental ability or endurance. Is this an enhancement or a preventive medical measure that helps prevent warfighters from becoming ill or injured? Some commentators argue that an enhancement is something that enables an individual to exceed population norms for the characteristic or ability. Thus, a drug to improve cognitive function in persons with below-normal cognitive ability would not be considered an enhancement. But the concept of normality is elusive. In some cases, it refers to the frequency with which a trait or capability occurs within a population. In regard to height, the convention is to regard individuals who are more than two standard deviations below the mean height of the population as being

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181. *Id.*



of short stature.<sup>182</sup> In other circumstances, what is considered normal may have no relationship to the distribution of a trait. For example, normal eyesight is deemed to be 20/20, but only about 35 percent of adults have 20/20 vision without some form of correction.<sup>183</sup> Standards of normality also may vary from place to place and time to time, and can be expected to change as the use of enhancements increases. Body shapes that were considered healthy a 100 years ago, for instance, are now considered obese. Furthermore, the concepts of disease and disorder themselves may be hard to pin down. Before 1973, the American Psychiatric Association regarded homosexuality as a mental disorder.<sup>184</sup> Moreover, there is a tendency to regard more and more health states as diseases and more and more interventions as treatments. Instead of attempting to make a brightline distinction between enhancements and other techniques, the emphasis should be on the effect of the intervention on the well-being of the warfighters who receive the intervention, the welfare of their units, and the completion of the mission.

Are there certain types of biomedical enhancements that should be out of bounds in the military? Arguably enhancements should not compromise warfighter dignity by producing socially stigmatizing or disfiguring physical characteristics. In the debate about the ethics and legality of human genomic engineering, one technology that causes particular concern, for example, is intermixing human and animal DNA.<sup>185</sup> Critics object that even using this technology to combat disease, let alone for enhancement purposes, should be prohibited due to the risk of creating monsters<sup>186</sup> and blurring the line between humans and other animals.<sup>187</sup> On the other hand, an argument can be made that the benefits from giving warfighters an eagle's daytime vision, an owl's night vision, a dog's sense of smell, a gorilla's

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182. *Short stature: Criteria for Determining Disability in Infants and Children*, U.S. DEP'T HEALTH & HUM. SERVS. AGENCY FOR HEALTHCARE RES. & QUALITY (Mar. 2003), <http://www.ahrq.gov/clinic/epcsums/shortsum.htm>.

183. Tim Johnson, *What is 20/20 vision?*, UNIV. IOWA HOSPS. & CLINICS, <https://www.uihealthcare.org/2column.aspx?id=225702> (last visited May 5, 2014).

184. *Let's Talk Facts Brochures: Sexual Orientation*, AM. PSYCHIATRIC ASS'N, <http://www.psychiatry.org/mental-health/people/lgbt-sexual-orientation> (last visited May 5, 2014).

185. *See Organ Farms*, PBS FRONTLINE, <http://www.pbs.org/wgbh/pages/frontline/shows/organfarm/etc/faqs.html> (last visited May 5, 2014).

186. JOHN HARRIS, *ENHANCING EVOLUTION: THE ETHICAL CASE FOR MAKING BETTER PEOPLE* 38 (2007).

187. JONATHAN GLOVER, *WHAT SORT OF PEOPLE SHOULD THERE BE?* 40-41 (1984).

strength, or a cheetah's speed might be so great that they should not be ruled out of the question. From a technical standpoint, however, it may well be necessary to produce such changes at a sufficiently early stage of embryonic development that the alterations showed up in all of the resulting individual's cells, including their reproductive cells, and therefore would be passed on to their descendants.<sup>188</sup> In short, germ line genomic engineering. This is another genomic approach that meets with strong objections, including that it could cause inadvertent harm to future generations.<sup>189</sup> The question then would be whether the military ought to be allowed to produce modifications that made the offspring of their personnel especially valuable as warfighters if the same types of changes were forbidden in the general population. This scenario is sufficiently far in the future that it doesn't have to be resolved at this time, but one conclusion that seems certain even now is that such modifications would be unethical without the warfighter's informed consent.

Another ethical issue is what effect genomic enhancement use should have on promotions, commendations, and other rewards within the military. If warfighters are required to take the enhancements, then it does not seem justified to deprive them of resulting service benefits so long as access to the enhancements is fairly distributed. On the other hand, if warfighters use enhancements voluntarily, the situation might be thought to resemble enhancements in sport, where it is argued that abilities or accomplishments attributable in substantial part to enhancements do not deserve reward. As in the case of sports, however, one must inquire why from an ethical standpoint biomedical enhancements should be treated differently than permissible performance improving practices such as dietary modification and extreme training. Moreover, unlike in sport, where the use of enhancements may confer benefits on individual athletes and teams but produce little or no broader societal benefit, enhancements in the military could help protect warfighters and their comrades from harm, and aid them in accomplishing missions deemed to be in the national interest. In terms of the impact on military rewards, then, the willingness of warfighters to incur health risks from enhancements in order to benefit others as well as themselves might be deemed to be praiseworthy.

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188. See, e.g., Mark Frankel, Audrey Chapman & American Association for the Advancement of Science, *Human Inheritable Genetic Modifications: Assessing Scientific, Ethical, Religious, and Policy Issues*, AM. ASS'N FOR ADV. SCI. (2000), <http://www.aaas.org/sites/default/files/migrate/uploads/germline.pdf>.

189. Emily Marden & Dorothy Nelkin, *Displaced Agendas: Current Regulatory Strategies for Germline Gene Therapy*, 45 MCGILL L. J. 461, 468 (2000).

An additional concern is the potential for genomic enhancement technology to migrate from the military to the civilian sector. The successful development of enhancements for the military is likely to become publicly known and create pressure to make them available to civilians, including from entities that have a proprietary interest in the technologies. Warfighters also might illegally distribute enhancements that they were given for military use to family members and other civilians. Just as the military legitimately prohibits public access to properly classified information and dangerous weaponry, it would be appropriate to prevent the public from gaining access to military enhancements that were overly dangerous or that were so effective that it would threaten national security if they became available to adversaries.

A final question is whether warfighters should be allowed to benefit from being enhanced after they are discharged from the military or retire. The ability to do so, for example, might be used as a recruiting incentive, similar to being taught technical skills. A fairness issue would arise, however, if former warfighters continued to enjoy advantages from enhancements that were not readily available to civilians because they were illegal or too expensive. On the one hand, continued advantage might seem unfair to civilians who were not eligible for military service. On the other hand, enhancement advantages could be viewed as a legitimate part of warfighters' compensation package, especially if they were in combat or had been given other especially risky assignments. Similar considerations arise in connection with other veterans benefits such as government-subsidized college education, job preferences, and access to VA care; in all cases, the public must decide whether the benefits are justified based on factors such as the need for military volunteers and the value of the benefit compared to what is available to civilians. In the case of genomic enhancements, an additional issue is how difficult or dangerous it would be to remove or cancel the effect of the warfighter's enhancement.

## IX. CONCLUSION

Although genomic technologies could produce significant benefits for the military and its individual members, they must be subject to appropriate ethical and legal constraints. The bioethical principles that underlie these constraints differ between military and civilian contexts, and therefore the rules that govern the military use of genomic technologies also must be different.

Given the exigencies of military operations and national security, the military in many respects deserves to have greater freedom to conduct research using military subjects, obtain genomic information from military personnel, create and establish military genobanks, and provide genomic therapies and enhancements to warfighters than would be ethically acceptable in civilian biomedical

contexts. Nevertheless, warfighters deserve to be respected and to have their welfare maximized as much as possible under the circumstances. The essence of military bioethics is the duty of superiors to protect their subordinate's welfare and impose risks on them only to the extent that the risk is appropriate in light of the military benefits to be gained. Given the scientific uncertainty surrounding many aspects of genomics, public sensitivity to genomic misconduct, and the importance of maintaining an effective voluntary military force, adherence to these principles in the realm of genomics is especially critical.

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