

# Challenges in Reporting Adverse Events From Dietary Supplements

Rebecca B. Costello, PhD  
Andrea T. Lindsey, MS  
Patricia A. Deuster, PhD, MPH

In 2008, the Institute of Medicine Committee on Dietary Supplement Use by Military Personnel recommended the development of service-wide military policies (eg, education or regulations) to guide commanders in management practices for safe use of dietary supplements (DSs). This review summarizes the activities the military has undertaken to advance the safe use of DSs by service members and develop best practices on reporting adverse events across the Department of Defense (DoD). In March 2022, the Department of Defense issued a DoD Instruction (DoDI) regarding the use of DSs by members of the US military. This DoDI provides guidelines to establish an official list of prohibited substances. The DoDI also identifies Operation Supplement Safety at CHAMP as DoD's "go-to" program for DS use and information about DSs and ingredients. Noted are a number of gaps in the reporting of adverse events from DSs that need to be addressed by multiple constituencies. *Nutr Today* 2023;58(1):34–38

In 2008, the Institute of Medicine Committee on Dietary Supplement Use by Military Personnel recommended the development of service-wide military policies (eg, education or regulations) to guide commanders in manage-

**Rebecca B. Costello, PhD**, is a scientific consultant for the Office of Dietary Supplements at the National Institutes of Health and is an adjunct professor at the Uniformed Services University, Bethesda, Maryland.

**Andrea T. Lindsey, MS**, is director of Operation Supplement Safety and Senior Nutrition Scientist for the Henry M. Jackson Foundation for the Advancement of Military Medicine, in support of the Consortium for Health and Military Performance (CHAMP), Bethesda, Maryland.

**Patricia A. Deuster, PhD, MPH**, is a professor in the Department of Military and Emergency Medicine at the Uniformed Services University and Executive Director of the Consortium for Health and Military Performance (CHAMP), Bethesda, Maryland.

This work was supported by the National Institutes of Health Office of Dietary Supplements and the Department of Defense, and Uniformed Services University. This is a US Government work and is in the public domain in the United States.

The authors have no conflicts of interest to disclose.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the National Institutes of Health, Uniformed Services University, or the Department of Defense.

**Correspondence:** Rebecca B. Costello, PhD, Office of Dietary Supplements, National Institutes of Health, 6705 Rockledge Dr (Rockledge 1), Room 730, MSC 7991, Bethesda, MD 20817 (costellb@od.nih.gov).

Copyright © 2023 Wolters Kluwer Health, Inc. All rights reserved.

DOI: 10.1097/NT.0000000000000587

ment practices for safe use of dietary supplements (DSs).<sup>1</sup> The lack of consistent policies for the safe use of DSs has raised concerns owing to the vulnerabilities of some military subpopulations. However, this is not a problem unique to the military as many young, physically active, and/or weight-conscious individuals strive on a daily basis to have a competitive edge in sports or improve their physical looks and well-being. This review summarizes the activities the military has undertaken to advance the safe use of DSs by service members and develop best practices on reporting adverse events (AEs) across the Department of Defense (DoD).

It is recognized that service members are under pressure to meet body composition and physical fitness standards, and these factors may contribute to use of DSs by service members. Based on the 2015 DoD Survey of Health-Related Behaviors, 32% of service members report using at least 1 DS daily, and 13% of males report using body-building supplements each day. Women use body-building supplements less frequently (4.5% daily) but are more likely to use weight-loss supplements (8.6%) than men (6.3%).<sup>2</sup> Although service members are concerned about weight status or "popping positive" on a routine military drug test, their family members may also use DSs for health-related reasons. It is clear that multi-ingredient, adulterated (eg, steroids, stimulants, prescription drugs, heavy metals),<sup>3</sup> and contaminated DSs pose a significant risk to our military population and compromise military readiness.<sup>4–7</sup> A recent review of the US Food and Drug Administration (FDA) Tainted Dietary Supplement Database for the years 2007 through 2021 revealed 1068 unique DS products adulterated with active pharmaceutical ingredients.<sup>8</sup> Although this is a mere fraction of the more than 100 000 DSs currently on the market, only a small fraction of DSs were even tested. The majority of the identified products were for sexual enhancement and weight loss.<sup>8</sup> Other investigators have also published articles on DS adulteration with various controlled substances and pharmaceuticals.<sup>4,5,9–11</sup> The potential to scan and pair problematic DS ingredients with likely and known AEs by using the FDA CFSAN Adverse Event Reporting System database with signal detection methodology was recently demonstrated.<sup>12</sup> The database of detected ingredient-AE and product-AE associations is available at <https://github.com/zhang-informatics/DDSAE>.

Not only do adulterated products pose a risk to military readiness, but inappropriate use of DSs can be problematic. A convenience sample conducted in 2010–2011 of service members noted that combination product users were more than two times more likely to self-report experiencing abnormal heartbeats, stomach pain, dizziness, tremors, and numbness/tingling.<sup>13</sup> Users of purported steroid analogs were more than 2.5 times more likely than nonusers to report experiencing dizziness.<sup>13</sup> Of great concern, however, are the deaths of several service members potentially associated with DS use and others who were hospitalized with hepatic injury or suffered other AEs from taking DSs containing harmful ingredients.<sup>14–18</sup> Although the evidence is limited, even excessive use of some vitamin and mineral supplements may be associated with higher risk of serious harms (hip fracture [vitamin A], hemorrhagic stroke [vitamin E], and kidney stones [vitamin C, calcium]).<sup>18</sup> Therefore, identifying supplements that are safe to consume and have scientifically validated efficacy is critical for sustaining military health and performance.

## HOW BEST TO CAPTURE USE OF DIETARY SUPPLEMENTS?

Since the publication of the Institute of Medicine Report in 2008, the DoD, primarily by the Consortium for Health and Military Performance at the Uniformed Services University and the DoD Dietary Supplement and Other Self-care Products Subcommittee, has sought to address the issue of how best to capture AEs from DSs by service members to inform leadership of potential problems and to mitigate future AEs. From 2008 to 2022, multiple activities and actions were taken to encourage and adopt an AE reporting system military-wide. Many of these activities either failed to be acted on or were short-lived. One action taken in 2017 was to propose *International Classification of Diseases (ICD), Tenth Revision* codes that could be developed and implemented within the DoD electronic health record (EHR) to simplify and enhance the capture of DSs. The codes were categorized by the intended use and/or composition of the DSs as shown below:

T43.615X: Caffeine and other dietary stimulant-containing supplements	T50.4 × 5: Protein supplements (protein, creatine, amino acids)
T45.2 × 5: Vitamins and/or mineral supplements	T50.5 × 5: Weight loss supplements
T50.0 × 5: Health supplements (joint, heart, brain, gut, immune health)	T50.7 × 5: Androgenic/anabolic and/or anabolic-like substances
T50.1 × 5: Other types of supplements (unclear as to intended use and/or ingredients)	T50.995X: Herbals and other botanical supplements
T50.3 × 5: Sexual enhancement	

For example, under the code, T43.615X: Caffeine and other dietary stimulant-containing supplements/products, the following DS ingredients and products could further be described in the EHR.

- Stimulant ingredients: DMAA, DMBA, DMHA, ephedra, higenamine, hordenine, methylsynephrine, octopamine, rauwolscine
- Examples of preworkout products: Cellucor C4 Original, Condemned Labz Arsynist, Insane Labz Psychotic Gold, Metabolic Nutrition Synedrex, Muscletech #Shatter SX-7, ProSupps Mr. Hyde, Beyond Raw Lit, BSN N.O.-Xplode
- Examples of energy drinks products: Monster, Red Bull, Rockstar, Amp, Full Throttle, Venom, Xyience, Rip It, NOS High Performance Energy Drink
- Examples of energy shot products: 5-Hour Energy, MTN OPS, Rip It Energy Shot

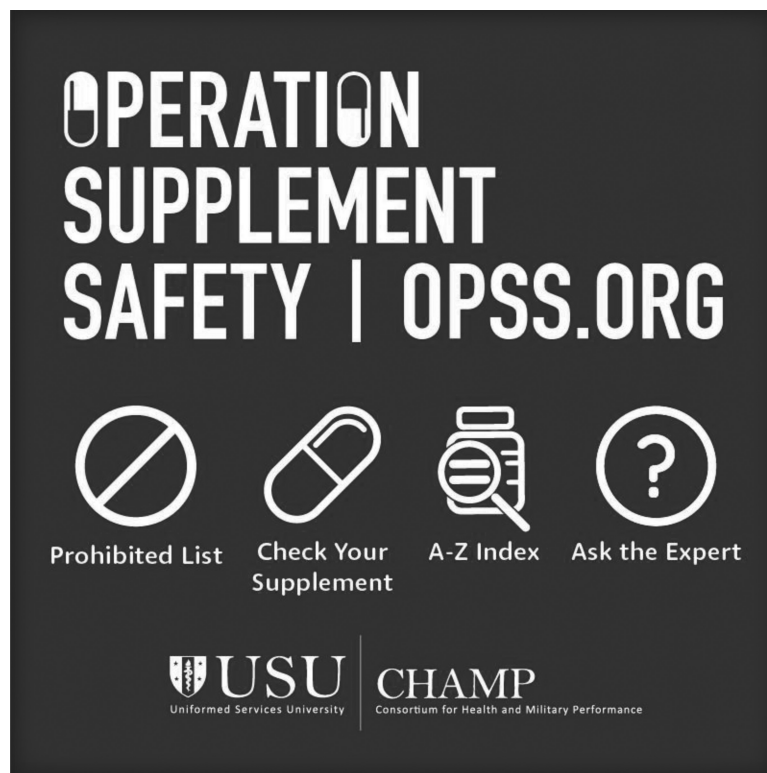
## Can Electronic Health Records Facilitate Capture of Dietary Supplement Use?

In many EHRs, DSs are recorded in the medications list, a structured field within the record to facilitate uniformity of recording and provide for the ability to retrieve data. Use of *ICD* codes, also presented in a structured format, allows for greater interoperability of the EHR so DSs recorded in the medications list could be linked to *ICD* codes and the reporting of AEs. Within the current DoD EHR, this feature is not available. This interoperability gap was also pointed out in a survey of EHR systems and practices within 4 federal agencies: DoD (Army and Air Force, Indian Health Service, Department of Veterans Affairs, and the National Institutes of Health Clinical Center), which deliver clinical services.<sup>19</sup> The following is a list of what would be needed for a robust EHR for collecting DSs and AEs:

- Uniform reporting of DSs in a structured field and format
- Built-in functionality to implement drug-drug and drug-allergy interaction checks with automatic real-time notifications to the healthcare provider (HCP)
- A DS-drug interaction check as many DSs have multiple active ingredients that increase the likelihood of an AE
- Full listing of available DSs in drug-knowledge software programs
- Instructions and training on processes
- Ease of automatic filing reports with US Department of Health and Human Services/FDA Safety Reporting Portal

## How the DoD Instruction Can Promote Capture of the Use of DSs by Service Members?

Another action of a long-awaited approval and enforcement was a new DoD Instruction (DoDI), signed and issued on March 9, 2022, regarding the use of DSs by members of the US military. It was signed: DoDI 6130.06: Use of Dietary Supplements in the DoD (referred to below as just “the DoDI”; <https://www.esd.whs.mil/Directives/issuances/dodi/>). This DoDI provides guidelines to establish an official list of prohibited substances. The DoDI also identifies Operation Supplement Safety (OPSS) at the Consortium for Health and Military Performance as DoD’s “go-to” program for DS use and information about DSs and ingredients. The OPSS website (OPSS.org) (Figure) hosts the official “DoD



**FIGURE.** The Operation Supplement Safety (OPSS) program at the Consortium for Health and Military Performance at the Uniformed Services University of the Health Sciences. Materials posted on the OPSS website (opss.org) are free and available to military service members, federal agencies, healthcare professionals, and consumers.

Prohibited Dietary Supplement Ingredients list.” This list will be updated when an FDA action occurs, or new scientific information becomes available regarding DS ingredients. Service members are not allowed to use any product with an ingredient on the DoD Prohibited Dietary Supplement Ingredients list.

The policy applies to the Office of the Secretary of Defense, the Military Departments, the Office of the Chairman of the Joint Chiefs of Staff and the Joint Staff, the Combatant Commands, Office of the Inspector General of the DoD, the Defense Agencies, the DoD Field Activities, and other organizations within DoD. DoDI 6130.06 also explicitly states that “No retail facility on a military installation can sell products containing ingredients on the DoD Prohibited Dietary Supplement Ingredients list on the OPSS website.” Dietary supplement education is required for all service members and those who provide health-related services to military members. This includes healthcare personnel, health promotion specialists, fitness leaders, athletic trainers, and strength-and-conditioning specialists. The DoDI also requires DoD HCPs to document the use of all DSs in the service member's EHR and to report “suspected serious adverse events resulting from use of dietary supplements” both via the AEs button on the main page of the OPSS website and in the user's EHR.

## GAPS IN AE REPORTING THAT NEED TO BE FILLED

The DoDI 6130.06 is a major accomplishment to ensure the health and safety of service members and their families. However, a number of gaps remain in the full implementation of the DoDI. As demonstrated, enhancements to the EHR are needed, followed by implementation and then a mechanism whereby the information would automatically go to FDA. In addition, DoD needs support from Federal Partners and outside collaborators to ensure the safety of our service members. Currently, the FDA has neither the authority nor the resources to limit what comes on the market, and although it has an Adverse Event Reporting System, it is not possible within the system to identify service members, what service, and other information needed to track within the DoD. What we do know is that most HCPs have seen AEs in association with DSs. Published reports indicate that 60% to 81% of HCPs have encountered an AE in association with a DS.<sup>20–22</sup> Despite observing such events, most HCPs report lacking the knowledge as to where and how to report such AE.<sup>20–22</sup> Interestingly, many do report the observed AE (10%–41%), but to various sources, including the hospital database, other specialists, Poison Control Center, and the like. The FDA's Safety Reporting Portal is intended to streamline

the process of reporting product safety issues to the FDA and the National Institutes of Health. However, when data from the various studies are combined, estimates for reporting AEs to FDA's Safety Reporting Portal range from 0% to 15%.<sup>20–23</sup> Most of the AEs submitted to the FDA are not voluntary, but rather related to the postmarket surveillance requirement for manufacturers to report all serious AEs to the agency within 15 business days of receipt.<sup>24</sup> Also, if one wanted to review a FDA case record, a request must be filed under the Freedom of Information Act. Finally, the FDA reporting system was not designed to accommodate the workflow of busy HCPs, so it is not surprising that voluntary reporting rates are so low. Healthcare providers need to be educated on the importance of AE reporting, but the process must be simple—a coding and note in the EHR, extract data, and have it submitted to the FDA. Only when the process is simple for reporting AEs will they become useful as signals for action. If DoD had such a system, they would be able to calculate the costs of lost duty time, medevacating from theater, and both short- and long-term healthcare costs associated with treating AEs associated with DSs.<sup>25</sup>

A simple process is within reach, as the mechanism is there. The Operation Supplement Safety started as an educational campaign back in 2012 because of several deaths and other AEs in service members taking products containing DMAA (1,3-dimethylamylamine).<sup>15</sup> Now an established program, with the DoD Prohibited Dietary Supplement Ingredients list containing more than 800 ingredients, it is time to ensure all service members and HCPs are adequately educated on the risks and benefits of DSs. We need to work together to find a practical way to report AEs from DSs within the EHR to ensure DoD can identify any pertinent signals, in cooperation with the FDA so they can take action.

Lastly, industry continues to show it does not have the will to self-regulate and strives to control what happens in the DS world, even when some DSs are a threat to force readiness. Exploitation of the unique health needs of military personnel with misleading and irresponsible marketing claims and misbranded and adulterated products is both reprehensible and frequently illegal. At least one dietary supplement trade association has gone on record by stating that responsible industry has “a role for ensuring that supplements are safe for all consumers,” and this would include military personnel and supports FDA enforcement against violative products.<sup>26</sup> Other trade associations and businesses selling DSs should also demand such practices be stopped. Service members should feel assured that the products they purchase will not cause them an adverse health event or a positive drug test. It is time for service members and the public to have access to only safe DS products.


## REFERENCES

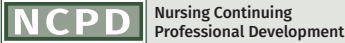
1. Institute of Medicine Committee on Dietary Supplement Use by Military P, Greenwood MRC, Oria M, eds. Use of dietary supplements


- by military personnel. In: *Use of Dietary Supplements by Military Personnel*. Washington, DC: National Academies Press; 2008.
2. Deuster PA, Lindsey AT, Scott JM. Dietary supplements: regulatory challenges and issues in the Department of Defense. *Mil Med*. 2018; 183(3–4):53–55.
  3. Pomeranz JL, Barbosa G, Killian C, Austin SB. The dangerous mix of adolescents and dietary supplements for weight loss and muscle building: legal strategies for state action. *J Public Health Manag Pract*. 2015;21(5):496–503.
  4. Crawford C, Boyd C, Avula B, Wang YH, Khan IA, Deuster PA. A public health issue: dietary supplements promoted for brain health and cognitive performance. *J Altern Complement Med*. 2020; 26(4):265–272.
  5. Crawford C, Walter AR, Avula B, et al. Relative safety and quality of various dietary supplement products U.S. service members ask about. *Clin Toxicol (Phila)*. 2022;60(6):737–744.
  6. Deventer K, Roels K, Delbeke FT, Van Eenoo P. Prevalence of legal and illegal stimulating agents in sports. *Anal Bioanal Chem*. 2011;401(2):421–432.
  7. Judkins CMG, Teale P, Hall DJ. The role of banned substance residue analysis in the control of dietary supplement contamination. *Drug Test Anal*. 2010;2(9):417–420.
  8. White CM. Continued risk of dietary supplements adulterated with approved and unapproved drugs: assessment of the US Food and Drug Administration's tainted supplements database 2007 through 2021. *J Clin Pharmacol*. 2022;62:928–934.
  9. Cohen PA, Travis JC, Vanhee C, Ohana D, Venhuis BJ. Nine prohibited stimulants found in sports and weight loss supplements: deterenol, phenpromethamine (Vonedrine), oxilofrine, octodrine, beta-methylphenylethylamine (BMPEA), 1,3-dimethylamylamine (1,3-DMAA), 1,4-dimethylamylamine (1,4-DMAA), 1,3-dimethylbutylamine (1,3-DMBA) and higenamine. *Clin Toxicol (Phila)*. 2021;59(11): 975–981.
  10. Cohen PA, Zakharevich I, Gerona R. Presence of piracetam in cognitive enhancement dietary supplements. *JAMA Intern Med*. 2020;180(3):458–459.
  11. Avula B, Chittiboyina AG, Bae JY, et al. The power of hyphenated chromatography—time of flight mass spectrometry for unequivocal identification of spirostanes in bodybuilding dietary supplements. *J Pharm Biomed Anal*. 2019;167:74–82.
  12. Vasilakes JA, Rizvi RF, Zhang J, Adam TJ, Zhang R. Detecting signals of dietary supplement adverse events from the CFSAN Adverse Event Reporting System (CAERS). *AMIA Jt Summits Transl Sci Proc*. 2019;2019:258–266.
  13. Austin KG, Farina EK, Lieberman HR. Self-reported side-effects associated with use of dietary supplements in an armed forces population. *Drug Test Anal*. 2016;8(3–4):287–295.
  14. Whaley D, Sylvester JE, Deuster PA. A threat to military combat power: dietary supplements. *Am J Med*. 2021;134(12):1560–1563.
  15. Eliason MJ, Eichner A, Cancio A, Bestervelt L, Adams BD, Deuster PA. Case reports: death of active duty soldiers following ingestion of dietary supplements containing 1,3-dimethylamylamine (DMAA). *Mil Med*. 2012;177(12):1455–1459.
  16. Hughes JR, Shelton B, Hughes T. Suspected dietary supplement injuries in special operations soldiers. *J Spec Oper Med*. 2010; 10(3):14–24.
  17. Bridwell RE, Yoo MJ, Grove JJ, Ng PC. Chest pain from supplement use in an active duty soldier: a case report. *Mil Med*. 2020;185(9–10): e1857–e1859.
  18. O'Connor EA, Evans CV, Ivlev I, et al. Vitamin and mineral supplements for the primary prevention of cardiovascular disease and cancer: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2022;327(23): 2334–2347.
  19. Costello RB, Deuster PA, Michael M, Utech A. Capturing the use of dietary supplements in electronic medical records: room for improvement. *Nutr Today*. 2019;54(4):144–150.

20. Rittenhouse M, Scott J, Deuster P. Dietary supplements: knowledge and adverse event reporting practices of Department of Defense health care providers. *Mil Med.* 2020;185(11–12):2076–2081.
21. Cellini M, Attipoe S, Seales P, et al. Dietary supplements: physician knowledge and adverse event reporting. *Med Sci Sports Exerc.* 2013;45(1):23–28.
22. Pascale B, Steele C, Attipoe S, O'Connor FG, Deuster PA. Dietary supplements: knowledge and adverse event reporting among American medical Society for Sports Medicine Physicians. *Clin J Sport Med.* 2016;26(2):139–144.
23. Timbo BB, Chirtel SJ, Ihrle J, et al. Dietary supplement adverse event report data from the FDA Center for Food Safety and Applied Nutrition Adverse Event Reporting System (CAERS), 2004–2013. *Ann Pharmacother.* 2018;52(5):431–438.
24. Schmitz SMMDMPH, Lopez HLMDMS, Mackay DND, Nguyen HBS, Miller PEBS. Serious adverse events reported with dietary supplement use in the United States: a 2.5 year experience. *J Diet Suppl.* 2020;17(2):227–248.
25. Deuster PA. Dietary supplements and adverse events. *Mil Med.* 2020;185(9–10):e1381–e1382.
26. Mister S. CRN Steadfast to Secure Responsible Mandatory Product Listing for Dietary Supplements: Council for Responsible Nutrition; 2022.

For more than 90 additional continuing education articles related to Nutrition topics, go to [NursingCenter.com/CE](http://NursingCenter.com/CE).







**INSTRUCTIONS**

**Challenges in Reporting Adverse Events From Dietary Supplements**

**TEST INSTRUCTIONS**

- Read the article. The test for this nursing continuing professional development (NCPD) activity is to be taken online at [www.nursingcenter.com/CE](http://www.nursingcenter.com/CE). Tests can no longer be mailed or faxed.
- You'll need to create an account (it's free!) and log in to access My Planner before taking online tests. Your planner will keep track of all your Lippincott Professional Development online NCPD activities for you.
- There's only one correct answer for each question. A passing score for this test is 7 correct answers. If you pass, you can print your certificate of earned contact hours and access the answer key. If you fail, you have the option of taking the test again at no additional cost.
- For questions, contact Lippincott Professional Development: 1-800-787-8985.
- Registration deadline is December 5, 2025

**CONTINUING EDUCATION INFORMATION FOR REGISTERED DIETICIANS AND DIETETIC TECHNICIANS, REGISTERED:**

The test for this activity for dietetic professionals is located online at <http://alliedhealth.ceconnection.com>. Lippincott Professional Development (LPD) is a Continuing Professional Education (CPE) Accredited Provider with the Commission on Dietetic Registration (CDR), provider number L1001. Registered dietitians (RDs) will receive

1.0 continuing professional education units (CPEUs) for successful completion of this program/material, CPE Level 2. Dietetics practitioners may submit evaluations of the quality of programs/materials on the CDR website: [www.cdrnet.org](http://www.cdrnet.org). LPD is approved as a provider of continuing education for the Florida Council for Dietetics and Nutrition, CE Broker # 50-1223.

**PROVIDER ACCREDITATION**

Lippincott Professional Development will award 1.5 contact hours for this for this nursing continuing professional development activity.

Lippincott Professional Development is accredited as a provider of nursing continuing professional development by the American Nurses Credentialing Center's Commission on Accreditation.

This activity is also provider approved by the California Board of Registered Nursing, Provider Number CEP 11749 for 1.5 contact hours. Lippincott Professional Development is also an approved provider of continuing nursing education by the District of Columbia, Georgia, West Virginia, New Mexico, South Carolina, and Florida, CE Broker #50-1223. Your certificate is valid in all states.

**Payment:** The registration fee for this test is \$17.95.

**Disclosure Statement:** The author and planners have disclosed no potential relevant financial relationships or otherwise.