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Commentary

Dietary supplements in the USA: problematic trends

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Abstract

More than 25 years have passed since the Dietary Supplement Health and Education Act of 1994 classified dietary supplements as a subcategory of food, thereby exempting manufacturers from providing premarket evidence of product safety and efficacy. In this commentary, I discuss problems in the supplement industry through an examination of cases introduced or decided in US federal courts between 2010 and 2019. More than half the cases located involved defendants charged with introducing misbranded food or drugs into interstate commerce. Contaminants included anabolic steroids, erectile dysfunction medications, weight-loss drugs, workout stimulants and mind-altering substances. As the article points out, raw powders obtained in bulk quantities facilitate the practice of 'home brewing' and the introduction of prescription drugs into dietary supplements.

Keywords
Dietary supplements
Public policy
US Food and Drug Administration

In the USA, more than 25 years have passed since the Dietary Supplement Health and Education Act of 1994 (DSHEA) classified a diverse number of health products – vitamins, minerals, herbs or other botanicals, and amino acids – as dietary supplements[1]. DSHEA placed the products in a special category of foods, as opposed to drugs, thereby exempting manufacturers from providing premarket evidence of product safety and efficacy to the US Food and Drug Administration (FDA). Ostensibly, this exemption would allow manufacturers to avoid delays in marketing supplements to consumers whose diets lacked certain nutrients. In practice, DSHEA has facilitated sales of adulterated and mislabelled products[2]. Adulterated supplements typically contain hazardous or untested ingredients, or they have been prepared, packaged or stocked in violation of good manufacturing practices[3]. Mislabelled products contain false or misleading information or do not contain required product details[3].

Since 2007, the FDA has identified more than 1050 tainted dietary supplements[4], and analyses continue to identify synthetic drugs as product adulterants[5]. An estimated 23 000 individuals visit emergency departments each year due to supplement-related adverse events[6], and even when supplements do not cause problems, their benefits appear marginal[7–12]. Nevertheless, more than 50 % of adults in the USA take at least one dietary supplement, and the industry has reached $40 billion in annual sales[2].

In this commentary, I discuss problems in the supplement industry through an examination of cases introduced or decided in US federal courts between 2010 and 2019. I gathered information about these cases from news releases archived by the FDA (www.fda.gov), focusing on product adulterants as well as charges filed against individuals and/or companies. Although every case did not fit precisely in a single category, seventeen of the fifty-seven cases I located with the search term 'dietary supplements' involved anabolic steroids or steroid precursors, eleven pertained to erectile dysfunction substances, nine involved weight-loss drugs, seven pertained to workout stimulants and three to mind-altering substances. Ten additional items involved products purporting to enhance cognition, reduce cholesterol, cure the common cold and manage diabetes, among other conditions. More than half the cases I located involved defendants charged with introducing misbranded food or drugs into interstate commerce. Other charges included mail fraud, wire fraud, money laundering, distribution of a controlled substance, conspiracy to traffic in counterfeit goods, conspiracy to defraud the FDA, smuggling misbranded substances into the USA and criminal contempt of court. While this list of charges may appear more applicable to the international drug trade than to the dietary supplement industry, defendants nevertheless faced these allegations in the past decade. Below I discuss cases that appeared especially relevant to public health.

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In the past 10 years, few supplement ingredients have caused more problems than the synthetic stimulant 1-3-dmethylhexaneamine, or DMAA[13]. Two soldiers who had taken the supplement Jack3d, which contained DMAA, suffered cardiac arrest and died during training exercises[14], and researchers linked the use of a similar product, OxyElite Pro, to at least thirty-six cases of hepatotoxicity in Hawaii[15]. DMAA has been found in party pills linked with cerebral haemorrhage[16], and as a banned substance in sport, its unlisted presence in dietary supplements has resulted in multiple athlete suspensions[17]. In 2019, five individuals and two companies associated with Jack3d and OxyElite Pro pleaded guilty in federal court to felonies associated with the introduction of misbranded food into interstate commerce with intent to defraud[18]. According to the US Department of Justice, the defendants imported DMAA from China using false certificates of analysis and false labelling, and they falsely characterised DMAA as a 'natural plant extract' when it actually came from a Chinese chemical factory[18].

In fact, cases in the federal courts showed that importation of raw powders from the Far East has been a consistent practice in recent years. In the case of workout energisers, a federal grand jury in 2017 returned indictments against five individuals and four companies from China for attempting to sell misbranded DMAA and a similar substance, 1,5-dimethylhexylamine (DMHA), in the USA[19]. The previous year, an individual received an 11-year prison sentence for selling supplements containing ephedrine[20]. FDA officials had warned the individual about the federal ban on ephedrine, but his decision to continue making false statements and selling it online eventually led to guilty verdicts on 30 felony counts[20].

Another set of cases heard in the federal courts involved 'dietary supplements' purporting to treat erectile dysfunction. Most of the cases involved the importation of substances such as sildenafil, the active ingredient in Viagra, and tadalafil, the active agent in Cialis. In 2019, an individual received a 3-year prison sentence for marketing a supplement containing sildenafil[21], and in a separate case, a defendant received a 100-month sentence after he sold $11 million worth of tadalafil[22]. Both defendants imported ingredients from China and, according to the FDA, between 2011 and 2017 the latter manufactured at least 5·5 million pills from imported powder. Some pills contained fourteen times the levels of tadalafil found in Cialis pills and left a portion of users with permanent injuries[22].

Importation of raw powders threatens public health when bulk purchasers do not verify that powders contain the ingredients they are supposed to contain. Even when products do contain legitimate ingredients, supplement purchasers must trust that bulk buyers convert powders to pills in a chemically safe manner – and do so under sanitary conditions. In 2011, a New Jersey court found a supplement-company owner and two managers guilty of criminal contempt after they continued to operate a contaminated facility closed by consent decree[23]. In a routine inspection, 'FDA investigators observed a dead rodent – cut in half – on a blender motor platform; a dead rodent, surrounded by rodent excreta pellets in an area used to store near-finished product; and on two occasions, a live rodent running through the blending room'[23]. One would hope that situation did not repeat itself, but the FDA continues to observe problems during inspections of supplement facilities[24].

Among weight-loss substances, hazardous drugs such as sibutramine, withdrawn from the US market in 2010, have continued to show up in 'natural' supplements. In 2019, an individual received 6 months of home confinement for selling sibutramine she had purchased from China[25]. Also in 2019, a federal grand jury returned an indictment against an individual who had sold weight-loss products containing sibutramine and phenolphthalein; he, too, had purchased the drugs from China[26]. Earlier in the year, an individual received a 3-year sentence for selling a weight-loss product containing 2,4-dinitrophenol, a fertiliser not approved for human consumption[27]. Although those who consumed 2,4-dinitrophenol may not have realised it, they actually may have risked their lives in using the substance.

Along with pharmaceuticals found in workout energisers and weight-loss products, anabolic steroids and steroid precursors continue to show up in dietary supplements. Naturally occurring precursors, or prohormones, have proven especially attractive to manufacturers, as policies regulating their sale lack consistency and can be challenged in court. For example, androstenedione, the steroid precursor used by now-retired baseball player Mark McGwire, is classified as a Schedule III controlled substance; DHEA, which converts to androstenedione[28], is available in retail outlets as an 'anti-ageing' product. As it happened, a US senator who championed dietary supplements insisted that DHEA receives an exemption from the list of controlled substances[29].

Among the steroid-related cases reviewed for this article, a federal court in 2019 indicted six individuals and two companies for selling dietary supplements containing anabolic steroids[30]. Prior to that, in 2017, an individual in New York pleaded guilty to selling a misbranded substance containing stanozolol, the anabolic steroid used by Canadian sprinter Ben Johnson at the 1988 Seoul Olympics[31]. In 2016, an individual pled guilty to conspiracy charges in a case involving the illegal importation of a drug powder containing methasterone, sold as Superdrol[32]. As with other substances, powders containing anabolic steroids and steroid precursors frequently came from China and were bought on the Internet.

Raw powders facilitate profit, as they can be purchased inexpensively and then mixed with fillers to increase volume. Nearly anyone can purchase a pill press, and in fact a recent report by the National Association of Boards

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of Pharmacy, the National Association of Drug Diversion Investigators and the Partnership for Safe Medicines characterised pill presses and counterfeit pill molds as an overlooked health threat[33]. The report noted that pill presses range from 'desktop' presses, which can produce 1800 pills in an hour, to much larger industrial presses, which can produce 1·6 million pills in the same time period. From 2011 to 2017, the report stated, seizures of pill presses at international mail facilities increased nineteen-fold[33]. Indeed, 'homebrewing' has become popular in the supplement industry, just as it has among those who sell recreational drugs. The practice removes 'middle men' and allows amateur manufacturers to operate in relative secrecy.

But in some instances, retail outlets also contribute to problems with dietary supplements. One might consider a situation in Maine, where an individual purchased a bottle of fish oil capsules, face cream and shampoo from a local pharmacy and then returned all three items the next day. Before returning the items, the purchaser replaced the fish oil capsules with stool softeners and Dilantin, a prescription anti-seizure drug[34]. While one might have expected the retail outlet to remove the opened bottle of supplements from the sales floor, an individual subsequently bought the returned capsules and discovered the switch. What if the substitute had been a stronger drug or toxic chemical? In 2015, an individual received more than 4 years in prison for selling 'Miracle Mineral Solution', a cure-all containing industrial bleach[35]. Also in 2015, a person received a 5-year sentence for marketing the product Potion 9, which contained the substance butanediol, an industrial solvent that metabolises into the date-rape drug gammahydroxybutyric[36]. Earlier, agents arrested a holistic healer in California for selling a flu and cold remedy that contained arsenic and the Schedule I controlled substance bufotenine, found in toad venom[37].

One can interpret the cases discussed in this commentary in at least two ways. First, one might consider them mere anecdotes and not indicative of broader industry practices. After all, not all who toil in the supplement industry possess ulterior motives, and supplements such as folic acid and Fe have proven useful in certain instances[38]. But one can also recognise that very few cases make it to federal court, and that the FDA sends hundreds of letters to companies that misbrand products. In a competitive marketplace – one containing more than 90 000 products[38] – some supplement manufacturers will almost certainly continue to exploit the weaknesses of DSHEA, gaining an edge by spiking products with actual drugs[39]. In recent years, supplement companies have actually filed lawsuits to discourage scientists from studying and reporting on adulterated dietary supplements[40].

Researchers recently compared supplement regulations across nations and observed little consistency in regulatory definitions and categorisations of products[41,42]. In the USA, problems discussed in this article will likely continue to occur until policy makers reform DSHEA and require premarket approval of dietary supplements. Without requiring premarket evidence of safety and efficacy, DSHEA effectively invites unscrupulous individuals to market adulterated products. Until policy reform occurs, supplement users might follow the lead of competitive athletes and examine labels for indications of third-party batch-testing. As FDA court cases reveal, adulterated supplements have contained substances such as anabolic steroids, ephedrine, sibutramine and DMAA, each which relates to physical training and/or physical appearance. In sport, United Kingdom Anti-Doping[43] advises athletes to visit the Informed Sport website to check on batch-testing[44], while the United States Anti-Doping Agency[45] refers athletes to NSF International[46]. Both contain lengthy lists of certified products, and one need not be a world-class athlete to obtain useful information. Individuals also might consult the FDA list of tainted products[4]. These resources do not guarantee a product is safe and efficacious, but absent policy reform, they offer helpful information about the history of certain supplements.

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References

1. US Food and Drug Administration (2019) Questions and answers on dietary supplements. https://www.fda.gov/food/information-consumers-using-dietary-supplements/questions-and-answers-dietary-supplements (accessed January 2021).
2. Cohen PA & Bass S (2019) Injecting safety into supplements – modernizing the dietary supplement law. *N Engl J Med* **381**, 2387–2389.
3. US Department of Defense Dietary Supplement Resource Operation Supplement Safety (2020) Adulterated and misbranded supplements. https://www.opss.org/article/adulterated-and-misbranded-supplements (accessed January 2021).
4. US Food and Drug Administration (2021) Tainted products marketed as dietary supplements. https://www.accessdata.fda.gov/scripts/sda/sdnavigation.cfm?sd=tainted_supplements_cder (accessed January 2021).
5. Marcus DM (2016) Dietary supplements: what's in a name? what's in a bottle? *Drug Test Anal* **8**, 410–412.
6. Geller AI, Shehab N & Weidle NJ (2015) Emergency department visits for adverse events related to dietary supplements. *N Engl J Med* **373**, 1531–1540.
7. Fortmann SP, Burda BU, Senger CA *et al.* (2013) Vitamin and mineral supplements in the primary prevention of

https://doi.org/10.1017/S1368980021000665 Published online by Cambridge University Press

cardiovascular disease and cancer: an updated systematic evidence review for the U.S. preventive services task force. *Ann Intern Med* **159**, 824–834.
8. Grodstein F, O'Brien J, Kang JH *et al.* (2013) Long-term multivitamin supplementation and cognitive function in men: a randomized trial. *Ann Intern Med* **159**, 806–814.
9. Lamas G, Boineau R, Goertz C *et al.* (2013) Oral high-dose multivitamins and minerals after myocardial infarction: a randomized trial. *Ann Intern Med* **159**, 797–804.
10. Manson JE, Cook NR, Lee I-M *et al.* (2019) Vitamin D supplements and prevention of cancer and cardiovascular disease. *N Engl J Med* **380**, 33–44.
11. Manson JE, Cook NR, Lee I-M *et al.* (2019) Marine *n*–3 fatty acids and prevention of cardiovascular disease and cancer. *N Engl J Med* **380**, 23–32.
12. Bjelakovic G, Nikolova D & Gluud C (2013) Antioxidant supplements to prevent mortality. *J Am Med Assoc* **310**, 1178–1179.
13. Cohen PA (2012) DMAA as a dietary ingredient. *Arch Intern Med* **172**, 1038–1039.
14. Eliason MJ, Eichner A, Cancio A *et al.* (2012) Case reports: death of active duty soldiers following ingestion of dietary supplements containing 1,3-dimethylamylamine (DMAA). *Mil Med* **177**, 1455–1459.
15. Johnston DI, Chang A, Viray M *et al.* (2016) Hepatoxicity associated with the dietary supplement OxyELITE Pro – Hawaii, 2013. *Drug Test Anal* **8**, 319–327.
16. Gee P, Tallon C & Long N (2012) Use of recreational drug 1,3-dimethylethylamine (DMAA) associated with cerebral hemorrhage. *Ann Emerg Med* **60**, 431–434.
17. Denham BE (2017) When contaminated dietary supplements cause positive drug tests: methylhexaneamine as a doping agent in sport. *Int J Sport Policy Politics* **9**, 677–689.
18. US Food and Drug Administration (2019) Five individuals and two companies plead guilty to felony charges in multimillion dollar scheme to fraudulently sell popular dietary supplements. https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/press-releases/march-13–2019-five-individuals-and-two-companies-plead-guilty-felony-charges-multimillion-dollar (accessed May 2020).
19. US Food and Drug Administration (2017) Five Chinese citizens and four Chinese companies indicted in scheme to sell mislabeled dietary supplements. https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/press-releases/october-25–2017-five-chinese-citizens-and-four-chinese-companies-indicted-scheme-sell-mislabeled (accessed May 2020).
20. US Food and Drug Administration (2016) New York man sentenced to lengthy prison term for selling unsafe dietary supplements online. https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/press-releases/december-19–2016-new-york-man-sentenced-lengthy-prison-term-selling-unsafe-dietary-supplements (accessed May 2020).
21. US Food and Drug Administration (2019) Former Springfield man sentenced for leading scheme to market dietary supplements. https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/press-releases/march-11–2019-former-springfield-man-sentenced-leading-scheme-market-dietary-supplements (accessed May 2020).
22. US Food and Drug Administration (2019) Man sentenced to more than 8 years in prison for illegally importing, selling male sexual enhancement pills branded as 'herbal' medicine. https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/press-releases/man-sentenced-more-8-years-prison-illegally-importing-selling-male-sexual-enhancement-pills-branded (accessed May 2020).
23. US Food and Drug Administration (2011) Two New Jersey dietary supplement companies and their principals found guilty of criminal contempt. https://www.justice.gov/opa/pr/two-new-jersey-dietary-supplement-firms-and-their-principals-sentenced-criminal-contempt (accessed May 2020.
24. Long J (2019) FDA irked with 'basic' dietary supplement manufacturing violations. Natural Products Insider. https://www.naturalproductsinsider.com/regulatory/fda-irked-basic-dietary-supplement-manufacturing-violations (accessed January 2021).
25. US Food and Drug Administration (2019) Woman sentenced for rebranding, selling prohibited weight loss drugs from China. https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/press-releases/woman-sentenced-rebranding-selling-prohibited-weight-loss-drugs-china (accessed May 2020).
26. US Food and Drug Administration (2019) Individual indicted and arrested for smuggling counterfeit and misbranded products from China. https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/press-releases/individual-indicted-and-arrested-smuggling-counterfeit-and-misbranded-products-china (accessed May 2020).
27. US Food and Drug Administration (2019) Sacramento man sentenced to 3 years in prison for selling fertilizer as a fat-burning pill. https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/press-releases/sacramento-man-sentenced-3-years-prison-selling-fertilizer-fat-burning-pill (accessed May 2020).
28. Kohut ML, Thompson JR, Campbell J *et al.* (2003) Ingestion of a dietary supplement containing dehydroepiandrosterone (DHEA) and androstenedione has minimal effect on immune function in middle-ages men. *J Am Coll Nutr* **22**, 363–371.
29. Kornblut AE & Wilson D (2005) How one pill escaped the list of controlled steroids. New York Times. https://www.nytimes.com/2005/04/17/us/how-one-pill-escaped-the-list-of-controlled-steroids.html (accessed May 2020).
30. US Food and Drug Administration (2019) Six individuals and two companies charged in illegal dietary supplement scheme. https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/press-releases/march-13–2019-six-individuals-and-two-companies-charged-illegal-dietary-supplement-scheme (accessed May 2020).
31. US Food and Drug Administration (2017) New York man pleads guilty to selling misbranded animal drugs containing steroids. http://wayback.archive-it.org/7993/20180126094553/https://www.fda.gov/ICECI/CriminalInvestigations/ucm583932.htm (accessed May 2020).
32. US Food and Drug Administration (2016) New York man pleads guilty to conspiring to illegally manufacture designer steroids. https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/press-releases/september-29–2016-new-york-man-pleads-guilty-conspiring-illegally-manufacture-designer-steroids (accessed May 2020).
33. National Association of Boards of Pharmacy, The National Association of Drug Diversion Investigator & The Partnership for Safe Medicines (2019) Illegal pill presses: An overlooked threat to American patients. https://nabp.pharmacy/wp-content/uploads/2019/03/PillPress-WhitePaper-March2019.pdf (accessed May 2020).
34. US Food and Drug Administration (2015) Westbrook woman pleads guilty to adulterating a dietary supplement. http://wayback.archive-it.org/7993/20180126095156/https://www.fda.gov/ICECI/CriminalInvestigations/ucm435500.htm (accessed May 2020).
35. US Food and Drug Administration (2015) Seller of 'Miracle Mineral Solution' sentenced to prison for marketing toxic chemical as a miracle cure. http://wayback.archive-it.org/7993/20180125150721/https://www.fda.gov/iceci/criminalinvestigations/ucm469831.htm (accessed May 2020).
36. US Food and Drug Administration (2015) Businessman sentenced to 5 years in prison for conspiracy to misbrand a product for human consumption, money laundering.

https://doi.org/10.1017/S1368980021000665 Published online by Cambridge University Press

http://wayback.archive-it.org/7993/20180126095034/https://www.fda.gov/ICECI/CriminalInvestigations/ucm457470.htm (accessed May 2020).
37. US Food and Drug Administration (2011) Holistic medicine practitioner arrested for sale of toxic drugs. http://wayback.archive-it.org/7993/20180126095800/https://www.fda.gov/ICECI/CriminalInvestigations/ucm256892.htm (accessed May 2020).
38. Manson JE & Bassuk SS (2018) Vitamin and mineral supplements: what clinicians need to know. *J Am Med* **319**, 859–860.
39. Cohen PA, Sharfstein J, Kamugisha A *et al.* (2020) Analysis of ingredients of supplements in the National Institutes of Health supplement database marked as containing a novel alternative to anabolic steroids. *JAMA Network Open* **3**, e202818.
40. Bagley N, Carroll AE & Cohen PA (2018) Scientific trials – in the laboratories, not the courts. *JAMA Intern Med* **178**, 7–8.
41. Thakkar S, Anklam E, Xu A *et al.* (2020) Regulatory landscape of dietary supplements and herbal medicines from a global perspective. *Regul Toxicol Pharmacol* **114**, 1–11.
42. Zayets V (2020) Comparing dietary supplement regulations in the U.S. and abroad. *Food Drug Law J* **74**, 613–629.
43. United Kingdom Anti-Doping (2021) Managing supplement risks. https://www.ukad.org.uk/athletes/managing-supplement-risks (accessed January 2021).
44. Informed Sport Certified products (2021). https://sport.wetestyoutrust.com/sites/default/files/generated-pdf/file.pdf (accessed January 2021).
45. United States Anti-Doping Agency (2019) Supplement risk and NSF Certified for Sport. https://www.usada.org/athlete-advisory/supplement-risk-nsf-certified-for-sport/ (accessed January 2021).
46. NSF International (2020) NSF athletics banned substances program – products certified for sport. http://info.nsf.org/Certified/NFL/DS-ABS_contacts.pdf (accessed January 2021).

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https://doi.org/10.1017/S1368980021000665 Published online by Cambridge University Press