Briefing Paper on Products Illegally Marketed as Dietary Supplements and Proposed Multi-Stakeholder Responses

More than 170 million consumers in the United States (U.S.) use dietary supplements[i] and they expect their supplements to be safe, quality products that are accurately labeled for their contents. However, unethical individuals and companies also engage in the manufacture and distribution of intentionally adulterated or misbranded products labeled as supplements that have generated significant threats to consumer health and safety. With an estimated 75,000 dietary supplements available[ii], and steady market growth into a $41 billion industry[iii], it is crucial that all stakeholders—supplement manufacturers, ingredient suppliers, distributors and retailers, consumers, healthcare practitioners, policymakers—are afforded the tools to respond to and understand the public health implications of tainted products to keep consumers safe. All these stakeholders, along with the government agencies who regulate dietary supplements, have a shared responsibility in keeping illegal, tainted products out of commerce and helping to advance a safe and transparent market.

The Problem of Tainted Illegal Products

"Tainted" products are ones that are illegally marketed as dietary supplements (usually with the FDA-mandated *Supplement Facts* labeling) but contain ingredients which may or may not be declared on the labeling, and may contain controlled substances, active ingredients found in FDA-approved or previously approved and subsequently withdrawn drugs, analogs of those active ingredients, or other compounds that FDA has determined do not qualify as dietary ingredients. Tainted products sold directly to consumers, whether online or in stores, are a serious problem that can pose dangerous, if not deadly, health risks to consumers. FDA has identified three product areas where this practice is most prevalent: sexual enhancement, weight loss, and muscle building products.[iv] According to the Federal Food, Drug & Cosmetic Act[v], these tainted products are deemed to be unapproved new drugs and illegal.

Problems with tainted products can arise during various points within the product supply chain, often starting with ingredient suppliers outside of the United States. Because the supply chain behind the manufacture and distribution of dietary supplements can involve multiple ingredient suppliers, brokers, and contract manufacturers, it can be difficult to track the lineage of ingredients and the identities of parties involved in the production of a single product. Good Manufacturing Practices (cGMPs) regulations for finished product manufacturers have been in place since 2010 to help ensure the safety and quality of dietary supplements.[vi] Such measures cannot fully curtail this problem, particularly when companies marketing these fraudulent products ignore their legal obligations and when FDA lacks the resources for more frequent inspections, substantive surveillance and enforcement of the law.

Since 2007, the U.S. Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER) has compiled a list of *tainted products* marketed as dietary supplements. To date, FDA has found over 820 products labeled and marketed as dietary supplements that contained substances such as PDE-5 inhibitors (e.g. sildenafil), sibutramine, anabolic steroids, ephedrine alkaloids or other banned ingredients. Of that list, 389 (47.4%) tainted products were intended for sexual enhancement, 322 (39.2%) for weight loss, and 90 (11.2%) for muscle building. Products outside of these three main categories account for only 2.3% of all remaining reports of tainted dietary supplement products[vii]. However, while this is a comprehensive list of tainted products identified by the agency, CDER notes that FDA is unable to test all products marketed as dietary supplements for potentially harmful ingredients and urges consumers to exercise caution around products in these categories through its Medication Health Fraud resource.[viii]

Unfortunately, a small portion of consumers may actively seek tainted products for their supposed benefits despite the health risks, creating demand for these illegal products. Social media forums as well as product marketing websites provide evidence of consumer interest in these products despite their illegal status and clear safety risks. Products marketed for weight loss, muscle building or sexual dysfunction may be laced with sibutramine, anabolic steroids or tadalafil/sildenafil (or their analogues), respectively. For some, this ability to access these medicines without seeking a doctor's prescription is desirable for a variety of reasons—yet brings with it the dangers of using these prescription ingredients without the supervision of a healthcare provider, coupled with the lack of any information about the potency or amount of these ingredients. Marketers of tainted products will tout their effects to vulnerable consumer or patient populations while falsely marketing them as "all natural" supplements.

Tainted illegal products can pose significant health risks to consumers who may be unaware of the harmful ingredients or possible interactions with other medications they are taking.[ix] Undisclosed ingredients such as tadalafil or sildenafil (the active ingredients in approved prescription drugs) could cause life-threatening problems due to explicit contraindications for interactions with other prescribed medications. Likewise, anabolic steroids added to muscle building products could lead to serious kidney or liver damage or place consumers at a greater risk for stroke or heart attacks. The extent of potential health issues related to tainted products is largely underrepresented or undocumented due to a lack of consumer awareness of the risks associated with these products.[x]

Although FDA regulates dietary supplements—under the Dietary Supplement Health & Education Act (DSHEA)[xi] as a subset of "foods" through the Center for Food Safety and Applied Nutrition (CFSAN)—those products marketed as dietary supplements that contain drug ingredients are unapproved new drugs. Once identified, these products are subject to enforcement by the Center for Drug Evaluation and Research (CDER). Irrespective of which FDA center is responsible for compliance and enforcement around these products, the agency would benefit from additional resources and tools to prioritize this critical public health issue and more effectively deter illegal products from entering the marketplace. Recent joint efforts between FDA and Federal Trade Commission (FTC), U.S. Department of Justice (DOJ), and the Drug Enforcement Administration (DEA) have helped leverage resources in support of combatting tainted products illegally marketed as supplements—and in shuttering companies involved in these criminal activities and bringing their owners to justice. However, these efforts are simply not enough to deter bad actors when marketing these products is so lucrative. The

usual compliance tools such as warning letters, while effective for getting responsible manufacturers to make corrections, are simply ineffective in the face of deliberate criminal activities. Increased penalties and disgorgement for illegal activity are necessary to ensure the safety and wellbeing of consumers nationwide. The enactment of the Designer Anabolic Steroid Control Act (DASCA) of 2014[xii], for example, is a promising new development and should provide additional tools for enforcement to the DEA.

Developing a Multi-Stakeholder Response

Just as a wide array of causes has contributed to the rise of tainted products marketed under the guise of dietary supplements, a variety of public- and private-sector efforts must be established and integrated to address problems and ensure consumer safety. These efforts should provide and support appropriate resources, processes and educational opportunities to ensure consumers have access to safe products.

U.S. Food and Drug Administration: As the agency charged with protecting the public from unsafe drugs, foods, and dietary supplements, FDA should play an integral part of policy and enforcement solutions to address the problem of tainted illegal products. Currently, FDA has enforcement authority related to unapproved new drugs, adulteration, and misbranding. However, given the scope and severity of the issue, as well as the fact that these challenges span different parts of the Agency (CFSAN and CDER) where authorities may vary as a function of product (drug and dietary supplement), FDA should be afforded additional resources to pursue these illegal products, using recalls, detentions, seizures and both civil and criminal sanctions against perpetrators. The DSQC has advocated for additional funding for CFSAN and CDER in a May 2017 letter to congressional appropriators[xiii] urging for sufficient resources for FDA to address this problem.

Other Federal & State Agencies: In conjunction with FDA, other agencies such as the DEA, FTC, U.S. Customs & Border Protection, U.S. Postal Service and DOJ should increase their use of existing authority to pursue and prosecute those who manufacture, market and distribute these tainted illegal products, and impose consequences that will serve as a strong deterrent for participation in this type of activity. State Attorneys General, consumer protection divisions, and public health agencies should all work alongside their federal partners to develop a comprehensive approach that broadens their enforcement capabilities and strengthens the deterrent message. Along with FDA, these organizations must communicate and coordinate more effectively to reduce instances of tainted products entering the marketplace and to increase the subsequent penalties and prosecution when they do. Enhanced inter-agency collaboration among all of the aforementioned federal and state agencies tasked with addressing the issue of tainted products and combatting the bad actors is critical to success.

Industry: Beyond oversight by FDA and related agencies, the dietary supplement industry, can—and should—play a more active and influential role in addressing the problem and raising awareness of bad actors and tainted products. Within the industry supply chain, ingredient providers, brokers, product manufacturers, distributors and product marketers all have the responsibility to self-regulate through qualifying and validating their suppliers, ensuring a secure supply chain, testing ingredients and finished products, identifying and removing high-risk products from product assortments, and implementing other mechanisms to assure that ingredients and final products do not contain undisclosed illegal ingredients with the potential to

harm a consumer. Manufacturers and distributors of dietary supplement products should ensure that finished products available to consumers have been produced in compliance with cGMPs and are safe for use as directed. Voluntary, self-regulatory efforts directed toward ensuring the legitimacy of the supply chain "from soil to shelf" can also play an important role in this regard.

Retailers: Retailers (both traditional and online) that stock dietary supplement products also share responsibility to perform their due diligence. Vetting of both products and vendors can help ensure that illicit products are not available at retail. Use of third-party certification programs can help assure products have been certified free of illegal substances and meet requirements for identity and purity. Online retailers should proactively monitor their sites for illicit marketers or tainted products that have been identified by FDA as containing illegal ingredients. Advertising for dietary supplements products or services should be monitored by website providers for claims that would strongly suggest the presence of illegal substances in their products.

Healthcare Providers and Other Influencers: Increased education and awareness among consumers and those who are influencers of consumer behavior with respect to supplement use are also critical. Healthcare providers, such as physicians, registered nurses, physician assistants, nurse practitioners and pharmacists stand at the front lines of healthcare and can utilize these opportunities with patients to ask questions about supplement use (especially in the aforementioned suspect categories) and to educate on the danger of tainted supplements, especially for those patients most likely to use them. Further, greater awareness of potential safety concerns or possible interactions with other drugs (prescription or over-the-counter medications) or dietary supplements will allow for practitioners to evaluate the possible role of a dietary supplement in adverse events as well as to discuss potential risks associated with concurrent use. Educating healthcare providers about the problem of tainted products will assist them to provide improved counseling and care for their patients.

Dietary supplement use by both military personnel and civilians for bodybuilding purposes is also prevalent, warranting focused education and outreach to military advisors, gyms, athletic trainers, coaches, student-athletes and others who may benefit from understanding the risks of using illegal products. In the military, dietary supplements are commonly used to maintain health, enhance performance, and reduce disease risks, and, as such, can affect force readiness. A 2013 study conducted by the U.S. Army Research Institute of Environmental Medicine[xiv] found that a significant portion of service members utilize multiple supplements on a weekly basis and are more likely than civilians to utilize dietary supplements to meet their occupational needs. Given the reliance on these products to achieve personal and professional goals, education for this subset of consumers is especially critical.

Consumer Education: Ultimately, consumers make decisions about the products they ingest. While consumers have become better informed when it comes to researching and purchasing dietary supplements, additional consumer education efforts could help increase awareness of the risks associated with tainted products and provide guidance on how to avoid them. For those purposefully seeking tainted products, education should raise their awareness about the potentially life-threatening effects caused by some of these products. Consumers should be encouraged to discuss dietary supplement use with their healthcare providers, be made aware of potential interactions with other prescription and nonprescription drugs, be instructed how to

avoid potentially tainted products, and how to report adverse events (AEs) possibly involving dietary supplement products to the FDA.

Data Collection: Beyond public- or private-sector efforts, a clear need exists for improved mechanisms for data collection between these resources. Whether it involves an industry-run registry of supplement labels[xv], the CFSAN Adverse Event Reporting System (CAERS), or a database of products identified as containing illegal ingredients,[xvi] increased collaboration among these programs will allow for all relevant stakeholders – policymakers included – to further understand the problem and the subsequent risks faced from tainted products marketed as dietary supplements.

While this *Briefing Paper* has identified numerous parties who each have a role in addressing tainted products, the DSQC believes that collaboration and cooperation among these agencies, organizations and individuals will be more effective to combat the problem. The DSQC encourages efforts to solve this problem collectively with programs utilizing the resources available through these groups.

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The Dietary Supplements Quality Collaborative
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[i] http://www.crnusa.org/newsroom/supplement-use-among-younger-adult-generations-contributes-boost-overall-usage-2016-more.
[ii] http://www.gao.gov/new.items/d09250.pdf.
[iii] http://www.newhope.com/vitamins-and-supplements/nbjs-2017-supplement-business-report.
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