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Dietary Supplements And FDA: Potential For Partnership?

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On Aug. 18, 2017, dietary supplement ingredient supplier ChromaDex filed a citizen petition requesting that the U.S. Food and Drug Administration "investigate and take appropriate remedial action" against Elysium Health Inc., which markets the dietary supplement Basis. The petition, filed against a backdrop of bicoastal litigation between Elysium and ChromaDex, alleges that samples of Elysium's Basis dietary supplement contained an industrial solvent, toluene, at 94-144 milligrams per kilogram (mg/kg), and also contained lead and molybdenum.[1] The citizen petition and its assertions were surprising and unexpected, especially given Elysium's history and prominence in the dietary supplement industry.

Elysium is, by all accounts, a superbly successful dietary supplement manufacturer. Elysium's website showcases eight Nobel Laureates[2] that sit on Elysium's scientific advisory board, as well as several science and medical advisers who may one day become Noble Prize winners.[3] Elysium's dietary supplement, Basis, was featured in a recent Time magazine article.[4] Elysium's Basis is targeted as: "The one daily supplement your cells need."[5] Elysium's advertising hints at the benefits that may come from regularly ingesting Basis: "Basis is clinically proven to increase [nicotinamide adenine dinucleotide] NAD+, levels, which decline with age. NAD+ is required for energy creation, regulating circadian rhythms and maintaining healthy DNA."[6] Results from a Basis clinical trial were published in "Nature Partner Journals: Aging and Mechanisms of Disease."[7]

In essence, Basis is marketed toward health conscious consumers who are concerned about healthy aging. If the positions taken in ChromaDex's citizen petition are true,[8] then at least some of these health conscious consumers may have been unknowingly and concomitantly micro-dosing with toluene when ingesting Basis.

Elysium's response was swift and strident. First, Elysium, through counsel, asserted that ChromaDex was, in effect, using the citizen petition as a vehicle to improperly "mislead FDA and the public solely for a competitive advantage."[9] Elysium also noted that "the level of toluene ChromaDex alleges to be present in Basis is far below the level established by the International Conference on Harmonisation

(ICH) in its guidelines for acceptable amounts of residual solvents in pharmaceuticals"; and that "FDA has adopted these guidelines for pharmaceuticals and has accepted submissions from dietary supplement manufacturers that rely on these guidelines."[10]

Put differently, Elysium characterized toluene, not as a "toxic industrial solvent," but as a "residual solvent" that was routinely used in manufacturing pharmaceuticals (and dietary supplements). And, even if toluene was present in the levels alleged, said Elysium, those levels were far below the acceptable levels established by the ICH in its guidelines. In essence, no harm, no foul.

In a subsequently and recently filed comment, Elysium, again through counsel, noted that had "ChromaDex retested Basis before filing its supplemental petition, it would have discovered that the toluene has been removed from Basis so that it currently is at or below non-detect levels for numerous forms of testing."[11] The comment further stated that although "Elysium believes that the ICH guidelines establish safety of toluene at the minimal levels previously found in Basis, Elysium elected to eliminate the presence of toluene from Basis as part of its continuing efforts to ensure superior product quality."[12]

How this turns out is anyone's guess. But, several points are worth noting. First, the citizen petition and its aftermath present an opportunity for FDA to clarify acceptable levels of routinely used solvents in dietary supplements. Clarification at this juncture could be useful to a growing dietary supplement industry.

Second, what solvent levels in dietary supplements are acceptable to consumers? And will consumers accept solvent levels set by the FDA, or will consumers be more demanding? Consumers will vote with their wallets.

Third, if you are a dietary supplement manufacturer, the FDA and the Federal Trade Commission are not the only policing entities. Competitors, looking to take market share and embarrass your company, will also be monitoring your product(s).

Fourth, building and maintaining consumer trust is key to a successful dietary supplement company. The dietary supplement industry is unique in its regulatory structure. Under the Dietary Supplement Health and Education Act of 1994 (DHSEA), manufacturers of dietary supplements are prohibited from marketing misbranded or adulterated dietary supplements. Importantly, dietary supplement manufacturers have initial responsibility to make sure that their dietary supplements are safe and correctly labeled before commencing marketing. After a dietary supplement is marketed, FDA is responsible for acting on any misbranded or adulterated dietary supplement.[13]

The dietary supplement industry is large, and growing larger. One estimate is that the dietary supplement market will be worth about $278 billion by 2024.[14] For those keeping score in the pharmaceutical industry, that is the equivalent of 278 billion dollar drugs.

And dietary supplements are widely used, including at the highest levels of the FDA. At his confirmation hearing, FDA Commissioner Scott Gottlieb stated "As someone who uses dietary supplements every day, I believe they serve an important role in health promotion for millions of Americans, and I support consumer access to these products."[15]

In large part, the dietary supplement industry is rising to the challenge and opportunity of self-regulation. For example, the Council for Responsible Nutrition cites data showing that more than 170

million Americans take dietary supplements every year, and 87 percent say they have confidence in their safety, quality and effectiveness.[16] FDA warning letters are relatively rare given the size of the dietary supplement industry, although those relative few warning letters that the FDA issues often allege worrisome violations of adulteration[17] or misbranding.[18]

But the continued growth of the dietary supplement industry, in one important sense, will depend on trust built and maintained with supplement consumers. And dietary supplement companies that work to earn and maintain consumer trust will be big winners in the marketplace.

Toward this end, there are industry proposed initiatives such as the Seal of Quality Assurance. And while these have value, we ask a different question, which leads to our fifth point: Is this the time for a voluntary, higher level of partnership with the FDA?

Since the passage of the DSHEA, the dietary supplement industry has been subject to additional regulations, for example, GMP manufacturing and adverse event reporting requirements.[19] And the industry has adjusted to, and thrived under, the added regulatory burden.

Having a higher level of voluntary regulation — a voluntary partnership with the FDA — could be acceptable to the industry[20] and the FDA. And there are precedents in the U.S. and Europe that point to how such a partnership might work.

For example, in Europe, medical devices must be certified and bear the CE mark. Certain medium-risk medical devices can be certified by notified bodies. Notified bodies — which are private entities — work with private medical device companies to review technical dossiers. The National Competent Authority periodically audits the notified bodies and reports their audit findings to the European Commission.

A similar scheme could work for dietary supplements in the U.S. The FDA could certify private entities to participate in a voluntary program with the dietary supplement industry. These private entities would act as liaisons between dietary supplement manufacturers and the FDA. Participating dietary supplement manufacturers would fund the program. This would have the advantage of not significantly diverting resources from the FDA, while helping the FDA with its oversight duties. These private entities could periodically inspect manufacturing facilities and randomly analyze dietary supplements — reporting their findings to both the dietary supplement company and the FDA.

The dietary supplement analyses would, at minimum, check for the presence and proper amounts of the active ingredients in dietary supplements. The presence or absence of other molecules that could adulterate dietary supplements — such as drugs that have previously appeared in some dietary supplements — could be checked for, as well as heavy metals, polychlorinated biphenyls (PCBs), and the presence and levels of common residual solvents. Indeed, the analytical piece is already significantly in place, as shown by entities like Labdoor Inc., and would likely require minimum adaptation.

Dietary supplement companies participating in the program, who remain in good standing, would be able to affix a mark — for example a QE mark (for quality evaluated) — to their products that certifies their dietary supplement meets the program's standards. Such a program would give consumers a higher level of confidence, and help keep the many good dietary supplement manufacturers from being tarred by the negative publicity generated by the few industry bad actors. And the mark could convey significant market advantage to discriminating, health conscious consumers. All of this would raise the confidence level of consumers of these companies' products, and potentially give participating companies a competitive edge in a growing marketplace.

So is this the time for a voluntary, higher level of partnership with the FDA?

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[1] "Citizen Petition to Find Elysium Health Inc.'s Basis Product to be Adulterated," ChromaDex, Aug. 18, 2017, at 5.

[2] See https://www.elysiumhealth.com/science, last accessed Feb. 27, 2018.

[3] Id.

[4] A. Sifferlin, "Is an Anti-Aging Pill on the Horizon?", Time, Feb. 28, 2018, available at: http://time.com/5159879/is-an-anti-aging-pill-on-the-horizon/, last accessed Feb. 27, 2018.

[5] See https://www.elysiumhealth.com/, last accessed Feb. 27, 2018.

[6] Id.

[7] Id.

[8] The authors of this article are not in a position to judge the accuracy of the allegations in ChromaDex's citizen petition, and therefore take no position on the petition's contents or accuracy.

[9] "Comment on Citizen Petition from ChromaDex Inc.", Sept. 22, 2017, at 3.

[10] Id. at 1.

[11] "Comment on ChromaDex Inc.'s, Supplemental Citizen Petition dated Jan. 16, 2018," Jan. 25, 2018.

[12] Id.

[13] The Federal Trade Commission regulates dietary supplement advertising.

[14] "Dietary Supplements Market Size Worth $278.02 Billion By 2024," Grand View Research, available at: https://www.grandviewresearch.com/press-release/global-dietary-supplements-market, last accessed Feb. 27, 2018.

[15] See, e.g., H. Schultz, "FDA nominee strongly affirms DSHEA during hearing," Nutra, April 24, 2017.

[16] See https://www.crnusa.org/, last accessed Feb. 27, 2018.

[17] E.g., dietary supplements containing prescription drugs with no warning to the consumer.

[18] One dietary supplement manufacturer was alleged to promote daily taking about 30 different dietary supplements as part of a cancer cure protocol.

[19] See, e.g., 21 U.S.C. § 379aa-1(b)(1).

[20] Major players in other regulated areas, such as cosmetics, have supported and voluntarily sought a higher level of nonvoluntary regulation (see, e.g., the Personal Care Products Safety Act).