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Division of Dockets Management
Food and Drug Administration
Room 1061, HFA-305
5630 Fishers Lane
Rockville, MD 20852

CITIZEN PETITION TO FIND ELYSIUM HEALTH, INC.'S
BASIS PRODUCT TO BE ADULTERATED

Petitioner, ChromaDex, Inc. ("ChromaDex")[1], respectfully submits this petition, pursuant to 10 C.F.R. §§ 10.25 and 10.30, to request that the Commissioner of Food and Drugs ("the Commissioner") at the Food and Drug Administration ("FDA") investigate and take appropriate remedial action against Elysium Health, Inc. ("Elysium"), which has made, offers for sale and sells, as a dietary supplement, a product named "Basis."[2]

Elysium's Basis product is a composition of nicotinamide riboside chloride and pterostilbene. ChromaDex is the **only** supplier of nicotinamide riboside chloride, called NIAGEN®, sold under a New Dietary Ingredient Notification filed with the FDA and has been generally recognized as safe ("GRAS"). In the past, ChromaDex supplied Elysium with NIAGEN® for use in its Basis product. However, Elysium is now using a new supplier(s) for the ingredients in Basis, the identity of which is currently unknown. ChromaDex discovered, as shown in the laboratory report attached as Exhibit 1, that Elysium's new Basis product is contaminated with toluene (CAS No. 108-88-3), an industrial solvent used in such things as paint thinners, fingernail polish, lacquers, and adhesives. In addition, Elysium is now using a nicotinamide riboside chloride ingredient in its product for which no New Dietary Ingredient Notification has been filed with the FDA and which does not have GRAS status. As such, Elysium's Basis product should be found to be adulterated and the FDA should take prompt remedial action to protect public health and safety.

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[1] ChromaDex discovers, acquires, develops, and commercializes patented and proprietary ingredient technologies in the dietary supplement, food, beverage, skin care, and pharmaceutical markets.

[2] Elysium is a Delaware corporation with its principal place of business located at 594 Broadway, Suite 707, New York, New York. It describes itself as a company that utilizes science and technology to create consumer health products.

A. Action Requested

ChromaDex specifically requests the following actions take place:

I. Make a determination that Elysium's Basis product is adulterated under 21 U.S.C. § 342(a) and (f) based on the undeclared presence of toluene in the product at a level of **96-144 mg/kg** and to take all appropriate remedial action, including that Elysium cease distribution of its Basis product and take other appropriate enforcement action, including seizure of violating products and an injunction against the manufacturers and distributors under 21 U.S.C. §§ 332 and 334.

II. Make a determination that Elysium's Basis product contains a new dietary ingredient under 21 U.S.C. § 350b and that Elysium has not submitted a NDI notification for the NR ingredient in its new Basis product, thereby rendering the product adulterated under 21 U.S.C. § 342(f)(1)(B). As such, Basis should be found to be adulterated under §§ 342(f)(1)(B) and 350b(a), and FDA should take all appropriate remedial action, including that Elysium cease distribution of its Basis product and take other appropriate enforcement action, including seizure of violating products and an injunction against the manufacturers and distributors under 21 U.S.C. §§ 332 and 334.

B. Statement of Grounds

BACKGROUND

- *ChromaDex*

ChromaDex makes and sells NIAGEN®, a patented, proprietary health ingredient that is comprised of nicotinamide riboside chloride ("NR"). NR is a form of vitamin B3. NR is a precursor to Nicotinamide Adenine Dinucleotide ("NAD+"), which is an essential molecule found in every living cell. ChromaDex® also makes pTeroPure®, a patented, proprietary health ingredient made of pterostilbene.[3]

NIAGEN® was generally recognized as safe by an independent panel of expert toxicologists, and in August 2016, the FDA issued a GRAS No Objection Letter. In addition, on August 20, 2015, ChromaDex submitted a New Dietary Ingredient Notification ("NDIN") to FDA covering its NIAGEN® product. The NDIN documentation included detailed technical and manufacturing information defining the purity, impurities, residual solvents, and contaminants that may be present within defined limits for commercial NR under the brand name NIAGEN®.[4] In the regulatory filing, ChromaDex informed FDA that it proposed to use NIAGEN® as a sole active ingredient in a dietary supplement capsule formulation. Excipients will be approved food additives, Generally Recognized As Safe (GRAS) ingredients or listed in "Capsule and Tablet

[3] Pterostilbene is an antioxidant found in blueberries and some grape varieties.
[4] ChromaDex submitted additional information to FDA on October 13 and 30, 2015.

Ingredients" of "NNFA List of Dietary Supplement Ingredients In Use Before October 15, 1994."

On November 3, 2015, FDA notified ChromaDex of acceptance of the NDIN for NIAGEN® in accordance with 21 C.F.R. § 190.6 (c). This regulatory procedure established that ChromaDex has defined the identity of, and manufacturing process for, commercial NR.

NIAGEN® is manufactured by the method described in NDIN 882. The NR product conforming to its specifications was subject to a comprehensive toxicology program that included genotoxicity and mutagenicity studies, acute toxicity, a 14-day dose range finding study, subchronic toxicity (90-day rodent study), and a human study. These studies were conducted in accordance with good laboratory practices (GLP) and preclinical studies following accepted OECD protocols. ChromaDex employs a comprehensive quality assurance program that is intended to ensure that its commercially available nicotinamide riboside conforms to the specifications defined in NDIN 882, thereby assuring that all product released into commerce is safe for intended use.

- *Elysium and its Basis Product*

Elysium sells one product called "Basis." It represents to the public that Basis is "[d]esigned with over 25 years of aging research, Basis is clinically proven to increase NAD+ levels."[5] According to Elysium, "Basis is a clinically-validated formulation designed to support well-being at the cellular level." The two active ingredients in Basis are NR (250 mg) and pterostilbene (50 mg) per serving.

Elysium's website states that nicotinamide riboside is: "A direct precursor to the coenzyme NAD+, which the body uses to power metabolism." As to pterostilbene, Elysium states: "A powerful and bioavailable polyphenol similar to resveratrol, but more bioavailable. Pterostilbene is created by plants to protect against internal and external stresses." Elysium represents that Basis contains others ingredients, namely Microcrystalline Cellulose, Hypromellose, Vegetable Magnesium Stearate and Silica. Elysium's website includes a link to its label for Basis. The supplement facts panel directs users to take two vegetarian capsules per day. Elysium represents that Basis contains no animal products and that the product is vegetarian, vegan, gluten-free, nut-free, and contains no artificial colors or flavors. Finally, Elysium represents to the public that:

> Exceeds FDA Recommendations
>
> The ingredients in Basis have been tested for safety and are produced in facilities that meet FDA requirements. Basis also undergoes rigorous third party purity testing.

The "purity testing" link allegedly reflects purity information for lot number 0271-6170.

[5] *See* Elysium's website, https://www.elysiumhealth.com (last accessed August 18, 2017).

Elysium's website also emphasizes the "purity" of its supply chain: "During the course of manufacturing Basis there are a total of five quality and purity audits before a batch is shipped. All manufacturing facilities are located in the US and are compliant with the cGMP regulations as stipulated by the FDA." Elysium does not disclose that Basis contains toluene, a residual solvent.

In 2014, ChromaDex entered into certain agreements to supply Elysium with the NIAGEN® and pTeroPure® products as the two active ingredients in Basis. ChromaDex has not supplied Elysium with additional NIAGEN® or pTeroPure® since August 2016.

ChromaDex recently learned that Elysium is no longer using NIAGEN® as the NR ingredient in Basis. In order to investigate concerns about a counterfeit product, ChromaDex, obtained commercially available Basis products from multiple sources for product testing. A series of analyses were performed on eight Elysium Basis product samples received from various persons in July and August 2017. A copy of the testing report is attached as Ex. 1 and incorporated by reference.

The report shows there were visually observed differences in both product color and statements made on the packaging containers. The Elysium Basis that arrived in July 2017 had a tan to brown color, which is consistent with the color of ChromaDex's NIAGEN® product. The August samples, however, were white and homogenous in color, which indicates a difference in the formulation. Further, the packaging on the samples had different lot numbers (July – 0278 6170, August – 0711 7150). The lid of the containers had a foil seal for lot 0278 6170 and a white seal for lot 0711 7150. There were other packaging differences – the containers received in August removed patent markings, the printing font of the lot code and expiration date on the bottom of the containers were different, and the label was changed from "Metabolic Repair & Optimization" to "Cellular Health and Optimization." The July and August samples also had different expiration dates.

There were multiple chemical differences observed in the data between the samples obtained in July and those that arrived in August. The testing shows that the July samples were made with NIAGEN® supplied to Elysium by ChromaDex. The August samples, however, contain ingredients from a source other than ChromaDex.

The NR potency analysis indicated the NR present in the lots of Elysium Basis met Label claims of 250 mg/serving. The NR and nicotinamide impurity evaluation indicated the presence of a new unknown impurity in all four samples received in August that is not significantly present in the NR ingredient lots ChromaDex sold to Elysium. Further, the absence of the NR monoacetate peak, which is a known minor compound in ChromaDex's product is not present in the four samples received in August.

The pterostilbene potency analysis indicated the pterostilbene present in the lots of Basis met label claims of 50 mg/serving.

The residual solvents analysis indicated the presence of four solvents in the August samples that are not found in the July samples. The solvents detected in the August samples

include ethanol, ethyl acetate, dichloromethane (DCM), and toluene. While ethanol, ethyl acetate and DCM were present in trace concentrations, toluene was present at 96-144 mg/kg, which renders Elysium's product adulterated, as further discussed below.

The NMR analysis confirmed the eight Elysium Basis product samples were structurally the beta form of NR. There was a slight variation in the ^{1}H NMR peak intensity and presence at ~2 ppm between the Elysium samples that were received in July as opposed to those in August. This variation further supports the lack of the NR monoacetate peak in the Elysium Basis samples received in August that is consistent with the NR analysis by HPLC. The ^{19}F NMR spectrums confirm the product is not the triflate salt form and does not contain any other fluorine salts.

The metals analysis indicated a different metals composition between the July and August Basis samples. Lead, molybdenum, and zinc were not detected in the July samples but were detected in the August samples.

Thus, the report concludes, the Basis product samples received in July were different from those received in August. The compositional differences in the product point to a different source of NR that was not supplied by ChromaDex in the samples received in August. The impurity differences, solvents present, metals composition and NMR spectra all support the conclusion that a new source of NR must be present in the formulation currently being sold by Elysium. Elysium's new source of ingredients is currently unknown to ChromaDex.

ARGUMENT

I. Elysium's New Basis Product Is Adulterated With Toluene.

A food shall be deemed to be adulterated, among other things, if "it bears or contains any poisonous or deleterious substance which may render it injurious to health; but in case the substance is not an added substance such food shall not be considered adulterated under this clause if the quantity of such substance in such food does not ordinarily render it injurious to health." 21 U.S.C. § 342(a)(1).

The evidence shows that Elysium's new Basis product, containing ingredients from an unknown source other than ChromaDex, contain a deleterious substance that renders it injurious to health. The residual solvents analysis using GC-MS shows the presence of different solvents in the July and August samples. *See* Ex. 1 Tables 5 and 6. ChromaDex's NR does not contain toluene and the solvent is not detected in the July samples.[6] Toluene was affirmatively detected in the August 2017 samples.[7] The laboratory report shows that the August 2017 samples showed toluene present in an amount ranging from **96-144 mg/kg**. FDA has not set any allowed level of exposure to toluene through oral ingestion of a dietary supplement. Toluene is not listed as a solvent permitted in food for human consumption. 21 C.F.R. 173 Subpart C.

[6] Toluene was absent from ChromaDex's NDIN 882.

[7] The laboratory report shows that the August samples also contained other solvents in trace concentrations – ethanol, ethyl acetate and DCM.

The presence of a toxic industrial solvent in Basis raises health and safety concerns. Toluene ingestion is injurious to health. In September 2015, the Center for Disease Control issued a Public Health Statement warning of a "serious health concern" that toluene may have an effect on the nervous system (brain and nerves).

> Nervous system effects can be temporary, such as headaches, dizziness, or unconsciousness. However, effects such as incoordination, cognitive impairment, and vision and hearing loss may become permanent with repeated exposure, especially at concentrations associated with intentional solvent abuse. High levels of toluene exposure during pregnancy, such as those associated with solvent abuse, may lead to retardation of mental abilities and growth in children. Other health effects of potential concern may include immune, kidney, liver, and reproductive effects.

Available at https://www.atsdr.cdc.gov/ToxProfiles/tp56-c1-b.pdf (last accessed Aug. 18, 2017).

Because Elysium's new Basis product is adulterated, FDA should immediately require that Elysium cease distribution of its Basis product and take other appropriate enforcement action, including seizure of violating products and an injunction against the manufacturers and distributors under 21 U.S.C. §§ 332 and 334.

II. Elysium's Basis Product Contains A New Dietary Ingredient And Is Adulterated.

Under 21 U.S.C. § 350b, a dietary supplement that contains a new dietary ingredient shall be deemed adulterated under 21 U.S.C. § 342(f)(1)(B) unless it meets one of two requirements:

1. The dietary supplement contains only dietary ingredients that have been present in the food supply as an article used for food in a form in which the food has not been chemically altered; or

2. There is a history of use or other evidence of safety establishing that the dietary ingredient when used under the conditions recommended or suggested in the labeling of the dietary supplement will reasonably be expected to be safe and, at least 75 days before being introduced or delivered for introduction into interstate commerce, the manufacturer or distributor of the dietary ingredient or dietary supplement provides FDA with information, including any citation to published articles, which is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such dietary ingredient will reasonably be expected to be safe.

As discussed above, ChromaDex's NIAGEN®, is the only source of NR that has sufficient preclinical and clinical safety data to establish that it is reasonably expected to be safe and the only source of NR that has an NDIN filed by the FDA.

Based on the results of the testing, the new Basis product contains counterfeit (i.e., non-NIAGEN®) material. ChromaDex last supplied NIAGEN® to Elysium in 2016. The laboratory report demonstrates both visual and chemical difference between the samples received in July and August 2017.

To the best of ChromaDex's knowledge, there is no information demonstrating that NR was lawfully marketed as a dietary ingredient in the United States before October 15, 1994, nor is there information demonstrating that this ingredient has been present in the food supply as an article used for human food in a form in which the food has not been chemically altered. Further, ChromaDex submitted NDIN 882 for its NR product, NIAGEN®. On November 3, 2015, FDA notified ChromaDex of acceptance of the NDIN for NIAGEN® in accordance with 21 C.F.R. § 190.6 (c). To the best of ChromaDex's knowledge, Elysium has not submitted a NDI notification for the NR ingredient in its new Basis product in compliance with 21 U.S.C. § 350b(a)(2) and 21 C.F.R. § 190.6. As such, Basis should be found to be adulterated under §§ 342(f)(1)(B) and 350b(a).

FDA should immediately require that Elysium cease distribution of its Basis product and take other appropriate enforcement action, including seizure of violating products and an injunction against the manufacturers and distributors under 21 U.S.C. §§ 332 and 334.

CONCLUSION

For the foregoing reasons, the petition should be granted.

C. Environmental Impact

The action requested in this petition is subject to categorical exclusion under 21 C.F.R. § 25.32.

D. Economic Impact

Pursuant to 21 C.F.R. § 10.30(b), ChromaDex would be willing, only when requested by the Commissioner and following review of the petition, to submit additional economic impact information on the effect of this requested action.

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to ChromaDex that are unfavorable to the petition.

Sincerely,

Frank Jaksch
Founder and CEO
ChromaDex, Inc. (NASDAQ: CDXC)