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September 22, 2017

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

Re: FDA-2017-P-5082; Comment on Citizen Petition from ChromaDex, Inc.

Foley Hoag LLP, on behalf of Elysium Health, Inc. ("Elysium"), submits this comment in response to the false and misleading statements that ChromaDex, Inc. ("ChromaDex") has made to the Food and Drug Administration ("FDA") in its citizen petition ("Petition") referenced above.

ChromaDex's Petition should be denied because, as FDA has repeatedly stated, a citizen petition is a wholly inappropriate vehicle for requesting an FDA enforcement action. ChromaDex's sole purpose for submitting the Petition to FDA was not to raise any safety issue, which does not exist, but to harm Elysium, with which it is engaged in litigation and against whom it is preparing to compete.

ChromaDex's assertions that Basis is "injurious to health" are baseless. ChromaDex's allegations about the safety of Basis are founded on an incorrect and inflammatory assertion that Basis contains unsafe levels of toluene, a processing aid used in the production of pharmaceuticals. In fact, 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. The FDA has adopted these guidelines for pharmaceuticals and has accepted submissions from dietary supplement manufacturers that rely on these guidelines to support the safety of dietary supplement products.

ChromaDex knew that its claims about the safety of Basis were false and misleading. ChromaDex itself has relied on the ICH guidelines to establish the acceptable limits of solvents in its own manufacturing specifications, certificates of analysis ("COAs"), and submissions to FDA regarding the safety of its own product. ChromaDex knowingly withheld this information even though, as ChromaDex understood, it was required to provide to FDA all information unfavorable to its petition. Indeed, ChromaDex's CEO certified that

ChromaDex had complied with its disclosure obligations when bringing its Petition. This certification constitutes a false statement to a federal agency.

ChromaDex's Petition represents an abuse of the citizen petition process that FDA should not countenance. For these reasons, as explained more fully below, FDA must deny ChromaDex's petition.

False and Misleading Statements

ChromaDex's Petition is based on the false assertion that Elysium's dietary supplement product, Basis, is "contaminated" and "injurious to health" because ChromaDex's in-house laboratory tests allegedly detected between 96 and 144 mg/kg of toluene. Petition at 1 and 6. Toluene is an organic solvent that may be and is used as a processing aid in the manufacture of pharmaceuticals and dietary supplements. ChromaDex omits this fact from the Petition. By describing toluene instead as a "toxic industrial solvent" that is "used in such things as paint thinners, fingernail polish, lacquers, and adhesives," ChromaDex intentionally inflames its complaint, not for FDA review, which it knew FDA would reject, but to arouse public shock and alarm.

Indeed, in its Petition, ChromaDex creates the false and misleading impression that toluene is not permitted in *any* amount by stating that "FDA has not set any allowed level of exposure to toluene through oral ingestion in a dietary supplement," and that "[t]oluene is not listed as a solvent permitted in food for human consumption," Petition at 5. Missing from ChromaDex's Petition are several relevant facts needed for an accurate and true description of Elysium's product, as well as for ChromaDex's own product. First, ChromaDex knowingly omitted the fact that FDA adopted the ICH guidelines establishing acceptable amounts of toluene and other residual solvents in pharmaceuticals.[1] ChromaDex also intentionally omitted the fact that the ICH guidelines set an acceptable amount of toluene at 890 parts per million ("ppm"), the equivalent of 890 mg/kg.

Most importantly, ChromaDex willfully hid the fact that even the highest amount of toluene that ChromaDex supposedly found in Basis, 144 mg/kg, is significantly below the acceptable 890 mg/kg amount set forth in the ICH guidelines. Even if toluene had been present as ChromaDex alleged, between 96 and 144 mg/kg, the amount present in one daily serving of Basis would have been only between 0.0672-0.1008 mg/daily serving, a minute fraction of the 8.9 mg permitted daily exposure set by the ICH guidelines.[2] This means the amount of toluene ChromaDex alleged to be in Basis actually would have been about *88-132*

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[1] *See* FDA Guidance for Industry: Q3C Impurities: Residual Solvents (December 1997), *available at* https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073394.pdf; and FDA Guidance for Industry: Q3C – Tables and List (June 2017), *available at* https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073395.pdf.

[2] A daily serving of Basis is composed of 250 mg of nicotinamide riboside chloride and 50 mg of pterostilbene, which corresponds to two vegetarian capsules weighing a total of 700 mg, *i.e.*, 0.0007 kg. At the alleged lower level of 96 mg/kg, the daily serving would be 0.0672 mg (96 mg/kg x 0.0007 kg). At the alleged upper level of 144 mg/kg, the daily serving would be 0.1008 mg (144 mg/kg x 0.0007 kg).

times lower than the permitted daily exposure. Put differently, if toluene were present in a Basis product at the higher alleged amount, one would have to take in one sitting 176 capsules (88 daily servings) before reaching the permitted daily exposure. If toluene were present in a Basis product at the lower alleged amount, one would have to take 264 capsules in one sitting (132 daily servings) before reaching the permitted daily exposure.

There is absolutely no doubt that ChromaDex knew about the FDA-adopted ICH guidelines because ChromaDex itself had relied on these guidelines to support the safety of solvents it uses to make Niagen®, its nicotinamide riboside ("NR") supplement.[3] ChromaDex also knew that, by not revealing the existence of these guidelines, it would create the false impression that toluene is unacceptable in *any* amount. More egregious is ChromaDex's concealment of the fact that it has used toluene in the manufacture of its own supplements and sold those supplements knowing that they contained toluene in amounts similar to the amounts it alleged it found in Basis. That ChromaDex used the ICH guidelines to establish a specification for an allowable amount of toluene at 890 ppm and intentionally sold products that contained toluene is evinced by the attached ChromaDex COAs. It is indisputable that ChromaDex knew that the levels of toluene in its products were below acceptable levels and raised no safety concerns. Despite knowing that Elysium's product similarly posed no safety concerns, ChromaDex sought to mislead FDA and the public solely for a competitive advantage.

False Certification in the Citizen Petition

In compliance with the regulations governing the citizen petition procedures, 21 C.F.R. § 10.30(b)(3), the chief executive officer ("CEO") of ChromaDex, Frank Jaksch, certified in the Petition that, to his --

> *. . . best knowledge and belief . . . , 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.*

This certification is patently false.

As the CEO, Mr. Jaksch knew or should have known that FDA had adopted the ICH guidelines for residual solvents in pharmaceuticals, which set acceptable amounts for toluene at 890 mg/kg, many, many times higher than the small amounts ChromaDex alleges it found

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[3] *See* GRAS Notice No. 635 for Niagen® (nicotinamide riboside chloride), p.13 (March 9, 2016), *available at* https://www.fda.gov/downloads/food/ingredientspackaginglabeling/gras/noticeinventory/ucm505226.pdf. FDA issued a "No Objection" letter for the Niagen GRAS Notice in August 2016. On November 3, 2015, FDA accepted ChromaDex's new dietary ingredient notification for Niagen, which "defined the identity of, and manufacturing process for NR." Petition at 3. Even before then, however, ChromaDex had already commercialized Niagen, which it sold as early as 2014, to Elysium. Petition at 4.

in Basis. This is an obviously unfavorable fact, and Mr. Jaksch intentionally omitted it from the Petition.

As the CEO, Mr. Jaksch knew or should have known that FDA had not prohibited the use of toluene as a residual solvent in dietary supplements. This is an obviously unfavorable fact, and Mr. Jaksch intentionally omitted it from the Petition.

As the CEO, Mr. Jaksch knew or should have known that toluene could be used as a residual solvent in the manufacture of dietary supplements and that ChromaDex itself had used toluene in the manufacture of its supplement. These are obviously unfavorable facts, and Mr. Jaksch intentionally omitted them from the Petition.

As the CEO, Mr. Jaksch knew or should have known that ChromaDex sold supplements that contained residual amounts of toluene and raised no safety concerns and, in turn, that there were no safety concerns about Elysium's Basis. These are obviously unfavorable facts, and Mr. Jaksch intentionally omitted them from the Petition.

Abuse of Citizen Petition Process

ChromaDex submitted its intentionally false and misleading statements in a citizen petition to FDA not out of concern for public safety, but instead to disparage Elysium publicly for its own commercial gain. ChromaDex's use of the citizen petition process to incite an enforcement action was wholly inappropriate. ChromaDex of course knew it was inappropriate. FDA clearly and repeatedly has stated that requests for the agency to initiate enforcement actions are outside the scope of the citizen petition procedures.[4] Such decisions are solely within FDA's discretion and generally made on a case-by-case basis.[5] FDA has consistently denied such petitions.[6]

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[4] *See* Denial Letter from CDRH to Wood, Herron & Evans, LLP, FDA-2016-P-3195 (February 28, 2017), *available at* https://www.regulations.gov/document?D=FDA-2016-P-3195-0004. *See also* Denial Letter from Janet Woodcock, M.D. to Fluoride Action Network, FDA-2016-P-1288 (November 29, 2016) (denying citizen petition based on "an inappropriate request" to take enforcement action), *available at* https://www.regulations.gov/document?D=FDA-2016-P-1288-0020. *See* 21 C.F.R. § 10.30(k).

[5] *Id.*

[6] *See e.g.,* Denial Response from CDRH to Genentech, Inc., FDA-20087-P-0638 (July 31, 2014), *available at* https://www.regulations.gov/document?D=FDA-2008-P-0638-0018; Denial Letter from CDRH to Codonics, Inc., FDA-2008-P-0444 (April 19, 2011), *available at* https://www.regulations.gov/document?D=FDA-2008-P-0444-0005; Denial Letter from CDER to Foley & Lardner LLP, FDA-2006-P-0020 (November 5, 2010), *available at* https://www.regulations.gov/document?D=FDA-2006-P-0020-0009; and Denial Letter from David Horowitz, Assistant Commissioner of Policy, to Ralph D. Childs, FDA-2007-P-0385 (September 8, 2009), *available at* https://www.regulations.gov/document?D=FDA-2007-P-0464-0003.

For this reason, FDA must deny ChromaDex's petition.

Sincerely,

Arcta Kupferberg

Partner

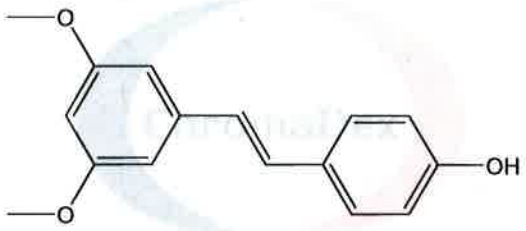
ChromaDex®

pTeroPure

Certificate of Analysis

PRODUCT NAME	Pterostilbene
PART NUMBER	00016996
STANDARD TYPE	Food Grade Bulk Material
LOT NUMBER	00016996-0807
REPORT NUMBER	CDXA-RSS-5706-00
DATE OF SAMPLE	07/17/2013
DATE OF REPORT	08/09/2013

Structure



CHEMICAL NAMES	4-(2-(3,5-Dimethoxyphenyl)ethenyl)phenol; 3,5-Dimethoxy-4'-hydroxy-trans-stilbene; 3',5'-Dimethoxy-4-stilbenol
CHEMICAL FORMULA	$C_{16}H_{16}O_3$
MOLECULAR WEIGHT (MW)	256.30
PUBLISHED MELTING POINT	NA
CHEMICAL FAMILY	Stilbenoids
CAS NUMBER	[537-42-8]

ASSAY RESULTS

TEST	METHOD	ANALYTE	SPECIFICATION	RESULT
HPLC (wt %)	NA	Pterostilbene	99.0 ± 2.0%	99.9 %
Residual Solvents	NA	Dichloromethane Methyl tert-butyl ether Hexane Ethyl acetate Cyclohexane Toluene	NMT 600 ppm NMT 5000ppm NMT 290 ppm NMT 5000 ppm NMT 3880 ppm NMT 890 ppm	82 ppm 9 ppm 29 ppm 21 ppm 2 ppm 74 ppm
Heavy Metals	ICP-MS	Lead Arsenic Cadmium Mercury	NMT 0.5 ppm NMT 1 ppm NMT 1 ppm NMT 1 ppm	< 0.05 ppm < 0.5 ppm < 0.25 ppm < 0.1 ppm
Microbial	99.1-CD-2.0-000244 99.1-CD-2.0-000245 99.1-CD-2.0-000236 99.1-CD-2.0-000237 99.1-CD-2.0-000243 99.1-CD-1.0-000373 99.1-CD-3.0-000235	Total Plate Count Yeast and Mold Coliform E. coli Staphylococcus Enterobacteriaceae Salmonella	NMT 1000 CFU/g NMT 100 CFU/g NMT 10 CFU/g NMT 10 CFU/g NMT 10 CFU/g NMT 10 CFU/g Not Detected	≤ 1000 CFU/g ≤ 100 CFU/g < 10 CFU/g < 10 CFU/g < 10 CFU/g < 10 CFU/g Not Detected
Appearance	NA	Color, Form	Off-white to light brown powder	Off-white solid

STORAGE CONDITIONS

STORAGE	Room Temperature in a dry place.
EXPIRATION DATE	07/2016under the above conditions.

Gamini Jayatilake

Digitally signed by Gamini Jayatilake
DN: cn=Gamini Jayatilake, c=US, o=ChromaDex Analytics, ou=CDXA, email=GaminiJ@chromadex.com
Date: 2013.08.09 10:33:14 -06'00'

REVISION HISTORY

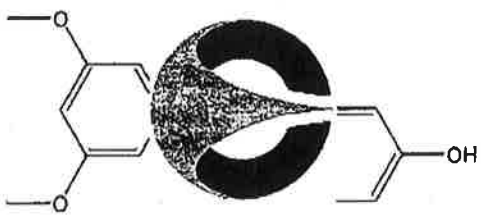
Revision History	Date of Revision	Document/Changes
00	08/09/2013	New report

ChromaDex. CONNECTION | pTeroPure | analytics | consulting | ingredients | standards

Certificate of Analysis

PRODUCT NAME	Pterostilbene
PART NUMBER	00016996
STANDARD TYPE	Food Grade Bulk Material
LOT NUMBER	ADPEPVSP10020315
REPORT NUMBER	CDXA-RSS-6599-00
DATE OF SAMPLE	04/30/2015
DATE OF REPORT	05/04/2015

Structure



CHEMICAL NAMES	4-(2-(3,5-Dimethoxyphenyl)ethenyl)phenol; 3,5-Dimethoxy-4'-hydroxy-trans-stilbene; 3',5'-Dimethoxy-4-stilbenol
CHEMICAL FORMULA	$C_{16}H_{16}O_3$
MOLECULAR WEIGHT (MW)	256.30
PUBLISHED MELTING POINT	NA
CHEMICAL FAMILY	Stilbenoids
CAS NUMBER	[537-42-8]

MANUFACTURER ASSAY

TEST	METHOD	ANALYTE	SPECIFICATION	RESULT
Identity	HPLC (retention time)	Pterostilbene	Conforms	Conforms
Purity	HPLC (area%)	Pterostilbene	NLT 98%	99.5 %
Residual Solvents	GC/FID-Headspace	THF Methanol Toluene Ethyl acetate Acetone Dichloromethane Hexane	NMT 720 ppm* NMT 3000 ppm* NMT 890 ppm* NMT 5000 ppm* NMT 5000 ppm* NMT 600 ppm* NMT 290 ppm*	ND 8 ppm 93 ppm ND ND ND 1 ppm
Heavy Metals	ICP-OES	Lead Arsenic Cadmium Mercury	NMT 0.5 ppm NMT 1 ppm NMT 1 ppm NMT 1 ppm	< 0.50 ppm < 0.50 ppm < 0.50 ppm < 0.50 ppm
Microbial	USP†	Total Plate Count Yeast and Mold E. coli	NMT 1000 CFU/g NMT 100 CFU/g Absent/10g	30 CFU/g < 10 CFU/g Absent/10g
Appearance	NA	Color, Form	Off-white to light brown powder	Off-white powder

*ICH Harmonized Tripartite Guideline: Impurities: Guideline for Residual Solvents, Q3C(R5), Version 4, 04 February 2011 Option 1 Limits. Option 2 limits would need to be calculated if Option 1 limits are not met.

**Result not as precise as specification in instances where ICP-OES data from qualified supplier is used. pTeroPure® pterostilbene is synthetic and no heavy metals have historically been detected by ICP-MS.

Re CS155114 07/19/17

ELY50002

ChromaDex. CONNECTION | pTeroPure | analytics | consulting | ingredients | standards

Certificate of Analysis

STORAGE CONDITIONS

STORAGE	Room Temperature in a dry place.
RE-TEST DATE	02/2018 under the above conditions.

Matthew Moreno

Digitally signed by Matthew Moreno
DN: cn=Matthew Moreno, o=ChromaDex, Inc., ou=Quality Assurance, email=MMoreno@chromadex.com, c=US
Date: 2015.05.13 16:07:06 -07'00'

REVISION HISTORY

Revision History	Date of Revision	Document/Changes
00	05/04/2015	New report

CS15114