Exhibit 4

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

Food and Drug Administration
College Park, MD 20740-3835

Claire Kruger, Ph.D., D.A.B.T.
Spherix Consulting, Inc.
11900 Parklawn Drive
Suite 200
Rockville, MD 20852

Re: GRAS Notice No. GRN 000635

Dear Dr. Kruger:

The Food and Drug Administration (FDA) is responding to the notice, dated March 8, 2016, that you submitted on behalf of ChromaDex, Inc. (ChromaDex) in accordance with the agency's proposed regulation, proposed 21 Code of Federal Regulations (CFR) 170.36 (62 FR 18938; April 17, 1997; Substances Generally Recognized as Safe (GRAS); the GRAS proposal). FDA received the notice on March 9, 2016, filed it on March 29, 2016, and designated it as GRAS Notice No. GRN 000635.

The subject of the notice is nicotinamide riboside chloride (NR). The notice informs FDA of ChromaDex's view that NR is GRAS, through scientific procedures, for use as a source of vitamin B_3 in vitamin waters, protein shakes, nutrition bars, gum, chews, and powdered beverages at a maximum level of 0.0057% by weight as consumed. ChromaDex states that NR is not intended for use in products under USDA jurisdiction or in foods intended for infants and toddlers.

As part of its notice, ChromaDex includes the statement of a panel of individuals (ChromaDex's GRAS panel) that evaluated the data and information that are the basis for ChromaDex's GRAS determination. ChromaDex considers the members of its GRAS panel to be qualified by scientific training and experience to evaluate the safety of substances added to food. ChromaDex's GRAS panel evaluated estimates of dietary exposure, method of production, and product specifications, as well as published studies supporting the safety of NR. Based on this review, ChromaDex's GRAS panel concluded that NR produced in accordance with current good manufacturing practices (cGMP) that meets its established food grade specifications is GRAS under the conditions of its intended use.

ChromaDex provides information on the identity and composition of NR. NR is a precursor of the coenzyme nicotinamide adenine dinucleotide and is a source of vitamin B_3. ChromaDex describes NR as a water-soluble, off-white powder. ChromaDex's product contains ≥95% NR and water.

ChromaDex describes the manufacture method of NR, which occurs through a two-step chemical synthesis. In the first step, D-ribofuranose tetra-acetate reacts with gaseous hydrogen chloride to yield nicotinamide-D-riboside triacetate chloride. In the second step, nicotinamide-D-riboside triacetate is deacetylated in the presence of ammonium hydroxide to yield nicotinamide riboside chloride. The product is vacuum dried to remove the residual solvents before milling and sieving. ChromaDex states that all raw materials and processing aids used in the manufacture of NR are food-grade and are used in accordance with cGMP.

ChromaDex provides specifications for NR. These specifications include purity (95-102%); residual solvents, including acetone (≤3000 milligrams (mg)/kilogram (kg)) and methanol (≤740 mg/kg); reaction by-products; microbial contaminants; and heavy metals, including arsenic (≤1 mg/kg), mercury (≤1 mg/kg), and lead (≤0.5 mg/kg). ChromaDex also provides the results of three non-consecutive lot analyses showing that each lot meets the specifications. The results of stability studies show that powdered NR is stable for up to 11 months under ambient conditions (25°C and 60% relative humidity). In solution at 4ºC, NR is stable for up to 83 days.

ChromaDex estimates the dietary exposure to NR from its intended uses in foods using data from the 2009-2010 National Health and Nutrition Examination Surveys (NHANES). The estimated users-only dietary exposure to NR from its intended uses in foods by consumers aged 2 and older is 51 mg/person/day (0.8 mg/kg body weight (bw)/day) at the mean and 145 mg/person/day (2.2 mg/kg bw/day) at the 90th percentile.

ChromaDex summarizes pivotal published safety studies on NR. In a 90-day subchronic toxicity study, oral administration of NR at up to 300 mg/kg bw/day in rats did not result in treatment-related adverse effects. Additionally, ChromaDex discusses several studies that evaluated the physiological effects of prolonged NR supplementation in mice for up to 48 weeks. The highest oral dose in these studies was 500 mg/kg bw/day. No adverse effects were reported in any of these studies. NR was evaluated in an Ames assay, *in vitro* chromosome aberration assay, and *in vivo* rat micronucleus assay demonstrating that NR is non-genotoxic and non-clastogenic under the conditions of these assays.

ChromaDex estimates an upper tolerable intake level (UL) of 3 mg/kg bw/day, or 180 mg/day assuming a body weight of 60 kg, which was derived by applying a conservative 100-fold safety factor to the no-observed adverse-effect level determined from the 90-day study. The mean estimated daily intake of NR from the intended uses is below this UL.

Based on the totality of the available data and information, ChromaDex concludes that NR is GRAS under the conditions of its intended use.

Potential Labeling Issues

In describing the intended use of NR and in describing the information that ChromaDex relies on to conclude that NR is GRAS under the conditions of its intended use, ChromaDex raises a potential issue under the labeling provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act). This issue consists of the potential health benefits described for NR in the notice. Under section 403(a) of the FD&C Act, a food is misbranded if its labeling is false or misleading in any particular. Section 403(r) of the FD&C Act lays out the statutory framework for the use of labeling claims that characterize the level of a nutrient in a food or that characterize the relationship of a nutrient to a disease or health-related condition. If products that contain NR bear any claims on the label or in labeling, such claims are the purview of the Office of Nutrition and Food Labeling (ONFL) in the Center for Food Safety and Applied Nutrition. The Office of Food Additive Safety neither consulted with ONFL on this labeling issue nor evaluated the information in your notice to determine whether it would support any claims made about NR on the label or in labeling.

Section 301(ll) of the FD&C Act

Section 301(ll) of the FD&C Act prohibits the introduction or delivery for introduction into interstate commerce of any food that contains a drug approved under section 505 of the FD&C Act, a biological product licensed under section 351 of the Public Health Service Act, or a drug or a biological product for which substantial clinical investigations have been instituted and their existence made public, unless one of the exemptions in section 301(ll)(1)-(4) applies. In its review of ChromaDex's notice that NR is GRAS

for the intended uses, FDA did not consider whether section 301(ll) or any of its exemptions apply to foods containing NR. Accordingly, this response should not be construed to be a statement that foods that contain NR, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information provided by ChromaDex, as well as other information available to FDA, the agency has no questions at this time regarding ChromaDex's conclusion that NR is GRAS under the intended conditions of use. The agency has not, however, made its own determination regarding the GRAS status of the subject use of NR. As always, it is the continuing responsibility of ChromaDex to ensure that food ingredients that the firm markets are safe, and are otherwise in compliance with all applicable legal and regulatory requirements.

In accordance with proposed 21 CFR 170.36(f), a copy of the text of this letter responding to GRN 000635, as well as a copy of the information in this notice that conforms to the information in the GRAS exemption claim (proposed 21 CFR 170.36(c)(1)), is available for public review and copying at www.fda.gov/grasnoticeinventory.

Sincerely,

Dennis M. Keefe -S

Digitally signed by Dennis M. Keefe -S
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Dennis M. Keefe, Ph.D.
Director
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

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