Summary of the application: Nicotinamide riboside (NR) (NIAGEN®)

Applicant: ChromaDex, Inc., 11821 Parklawn Drive Suite 310 Rockville, MD 20852 USA

The novel food application concerns request for authorisation to place on the market a synthetic form of nicotinamide riboside (NR) (NIAGEN®). Nicotinamide riboside is found in small quantities in milk and exhibits the biologic activity of nicotinamide and niacin. In accordance with Annex I of Directive 2002/46/EC niacin may be used in the manufacture of food supplements. The applicant also requests that nicotinamide riboside (NR) be added to the list of niacin forms specified in Annex II of Directive 2002/46/EC.

Nicotinamide riboside (NR) (NIAGEN®) is proposed for use in food supplements as a source of NR, delivering not more than 300 mg NIAGEN®/day. NIAGEN® is intended for use in healthy adults and is not formulated for use in small children.

The information provided on the identity, composition, specifications, and lack of batch-to-batch variability of NIAGEN® demonstrates control of the production process and does not raise safety concerns. Moreover, the results of extensive preclinical and clinical studies show that NIAGEN® is safe at the proposed use levels and that NR is metabolized similarly to nicotinamide. An Ames assay, in vitro chromosome aberration assay, and an in vivo micronucleus assay show that NIAGEN® is not genotoxic. A 90-day toxicology study in rats administered NIAGEN® establishes a NOAEL of 300 mg/kg/day. A rat developmental toxicity and a one-generation rat reproductive toxicity demonstrate that NIAGEN® is not a developmental or reproductive toxicant. Safety pharmacology and 28-day toxicity studies in juvenile dogs demonstrate that NIAGEN does not adversely affect cardiovascular, respiratory, or neurological function. Additionally, comparison of the NOAELs determined in the 28-day juvenile dog study compared to the 90-day rat toxicology study demonstrates a lack of differential species sensitivity to toxicity. A single dose clinical pharmacokinetic study conducted in healthy adults shows that the ingestion of up to 1000 mg NIAGEN®/day is safe and NR is metabolized similarly to nicotinamide in healthy humans, producing nicotinamide-related metabolites. Four long-term clinical trials conducted in healthy adults show that the ingestion of up to 2 grams of NIAGEN® per day and for up to 12 weeks is safe and well tolerated (i.e., no clinically adverse effects on haematology, clinical chemistry, urinalysis or liver or kidney function) and NR is metabolized to nicotinamide-related metabolites, including the coenzyme nicotinamide adenine dinucleotide NAD+. Together these results demonstrate that NR is another form of niacin. Additionally, application of uncertainty factors to the highest doses tested in the long-term human trials provides an adequate margin to support the safety of NIAGEN® intake from supplements at 300 mg/day.

The applicant has applied for data protection in accordance with Article 26 of the novel food regulation.