Summary of the dossier: *beta*-Nicotinamide mononucleotide (*beta*-NMN)

Applicant: Effepharm (Shanghai) Co., Ltd., Bld 4, No.1, Mid Wangdong Rd, Shanghai 201601, China

Effepharm (Shanghai) Co., Ltd. intends to introduce *beta*-NMN as a novel food ingredient in the European Union (EU). *beta*-NMN is produced by chemical synthesis in a multi-step process under controlled conditions with a Hazard Analysis and Critical Control Points (HACCP) plan in place. It is intended for use in food supplements at up to 300 mg/day for adults.

Specification parameters for identity and compositional characteristics of the ingredient, as well as appropriate limits for residual solvents, microbiological, and heavy metal contaminants, have been established. Analytical data for several independent representative batches of *beta*-NMN demonstrate that the production process results in a final ingredient that consistently meets the proposed specifications and is absent of potential contaminants. Data has also been provided to demonstrate *beta*-NMN is stable for its intended shelf-life of 24 months.

The absorption, distribution, metabolism, and excretion (ADME) of *beta*-NMN has been discussed in-depth and demonstrates *beta*-NMN to be absorbed intact from the gastrointestinal tract. As confirmed by pre-clinical and clinical studies in the literature and studies conducted by Effepharm, in which *beta*-NMN was associated with increases in blood nicotinamide and nicotinamide adenine dinucleotide, *beta*-NMN is bioavailable in the context of Directive 2002/46/EC.

beta-NMN is considered not to be nutritionally disadvantageous for consumers under the proposed conditions of use.

Pivotal toxicology studies conducted with *beta*-NMN include multiple genotoxicity studies including a bacterial reverse mutation test, in vitro micronucleus assay, *in vitro* and *in vivo* chromosomal aberration assays, and a 90-day gavage toxicity study in rats. *beta*-NMN was confirmed as non-genotoxic, and the highest dose tested was the no-observed-adverse-effect level (NOAEL) in the 90-day study. This NOAEL provides a sufficient margin of safety compared with the highest exposure from its intended use in food supplements for adults. Additionally, *beta*-NMN was also well tolerated in several controlled clinical trials, including a clinical trial conducted by the applicant.

As *beta*-NMN is 99% pure, produced under HACCP by chemical synthesis, and none of the raw materials or processing aids used in its production contain any of the allergens specified under Regulation (EU) No 1169/2011, it can be concluded that the allergenic potential of *beta*-NMN is very low. This is further substantiated by the endogenous nature of *beta*-NMN.