Executive summary (FSANZ item 3.1.1)

With this application DSM Food Specialties B.V. (DFS) requests a variation of Standard 1.3.1 "*Food Additives*", Schedule 1 of the *Australia New Zealand Food Standards Code* (the Code) with respect to the extension of use of natamycin as a natural preservative in fermented milk products and rennetted milk products of Food categories 1.2.2 and 20.2. The maximum level of use is 5 mg/kg.

The dossier is written according the FSANZ Application Handbook, edition dated 1 September 2013.

Food spoilage through microbial contamination is a common occurrence resulting in significant losses in manufacturing, in the food supply chain and at home. Spoiled foods will be discarded resulting in significant economic cost to the food industry, retailers and consumers. According to the FAO report from 2011 on "Global food losses and food waste", food security is a major concern. In medium and high-income countries, food is to a significant extent wasted at the consumption stage, meaning that it is discarded even if it is still suitable for human consumption. Food losses in industrialized countries are as high as in developing countries with more than 40% of the food losses occurring at retail and consumer levels. It represents a waste of resources used in the production and food that will not be consumed leads to unnecessary CO_2 emissions in addition to loss of economic value of the food produced.

Yeast and moulds are known microorganisms that could cause spoilage of yogurt. Also in Australia the food spoilage caused by fungi is high, and estimated to be in the range of $10.000.000 value wasted per annum.

Natamycin is a natural yeast and mould inhibitor produced by submerged aerobic fermentation of *Streptomyces natalensis*. It has a broad spectrum activity against all moulds and yeasts known as contaminants of food products and is active at very low concentrations. Natamycin is extensively used worldwide, especially in the cheese and sausage industries. It is active only against yeasts and moulds, therefore will not interact with viable bacteria and will improve the quality and shelf life of (non-pasteurized) fermented milk products

A complete safety evaluation was published in the WHO Food Additives Series No. 48: Safety Evaluation of Certain Food Additives and Contaminants: Natamycin (Pimaricin) in 2002. The European Food Safety Authority (EFSA) confirmed the safety of natamycin in their latest re-evaluation in 2009.

Anti-microbial resistance as a consequence of the use of natamycin was and is extensively evaluated not only by International Safety Authorities e.g. EFSA and JECFA but also by DSM Food Specialties.
The EFSA in 2009 concluded with respect to antimicrobial resistance that *"…, induction of natamycin resistant mutants in yeast is reported to be difficult. The Panel concluded that there was no concern for the induction of antimicrobial resistance."*
This confirmed the conclusions from JECFA at their 20th meeting in 1976 and their 57th meeting in 2002: "*Cross-resistance between antifungal polyenes is relatively infrequent. In particular, resistance to natamycin seldom implies resistance to related polyenes. Although cross-resistance with nystatin and amphotericin has been observed, selection of natamycin-resistant strains in vitro has never been accompanied by such cross-resistance. Transferable resistance between bacterial cells depends on the transfer of DNA and does not occur with yeast and fungi, which have a different cell-wall barrier.".*

To substantiate these conclusions further with the latest scientific information, DSM Food Specialties had an independent literature review on natamycin resistance performed and had challenge tests executed to investigate the possible development of natamycin tolerance.
The independent literature review was performed by TNO, the Netherlands organisation for applied scientific research (www.tno.nl).

Based on this literature review, it is concluded that:
- Natamycin resistance is mainly due to natural resistance;
- No reports have been published claiming acquired natamycin resistance in fungi due to horizontal gene transfer;
- Experimental evidence of fungi acquiring resistance to natamycin is not encountered so far.

The independent challenge tests were performed by the Centraalbureau voor Schimmelcultures (CBS) in the Netherlands (www.cbs.knaw.nl). CBS - Fungal Biodiversity Centre is an institute of the Royal Netherlands Academy of Arts and Sciences (KNAW).

Based on these challenge tests, it is concluded that:
- An intensive program aimed at inducing tolerance towards natamycin has resulted in an increase in tolerance of a few individual strains, but did not alter the range of natural variation of sensitivities;
- Resistance to natamycin was not developed;
- One of the strains showed an increased tolerance for amphotericin B and nystatin after training with natamycin: *Aspergillus ochraceus*. The sensitivity towards all three polyene antifungals decreased approximately 3-fold. In contrast, two *Fusarium* strains trained for natamycin tolerance showed an increased sensitivity for the other two antimycotics.
- The selection regime used was much more severe than would be encountered during the use of natamycin as a food preservative.

The overall conclusion based on efficacy, stability and safety data is that natamycin is a safe, suitable and effective natural yeast and mould inhibitor at a low dosage level (i.e. ≤ 5 ppm).
Natamycin will increase the shelf life of yogurt without influencing the organoleptic characteristics of yogurt and contributes simultaneously to economic sustainability through less wastage of food at the manufacturer, retailer and consumer level.