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## **Risk Assessment of "Other Substances" – L-lysine**

**Sigrun Henjum<sup>1\*</sup>, Livar Frøyland<sup>2</sup>, Margaretha Haugen<sup>3</sup>, Kristin Holvik<sup>3</sup>,  
Martinus Løvik<sup>4</sup>, Bjørn Steen Skålhegg<sup>5</sup>, Tonje Holte Stea<sup>6</sup>, Tor A. Strand<sup>7</sup>,  
Grethe S. Tell<sup>8</sup> and Per Ole Iversen<sup>5</sup>**

<sup>1</sup>Norwegian Scientific Committee for Food Safety (VKM), Oslo and Akershus University College of Applied Sciences (HiOA), Norway.

<sup>2</sup>Norwegian Scientific Committee for Food Safety (VKM), Institute of Marine Research (NIFES), Norway.

<sup>3</sup>Norwegian Scientific Committee for Food Safety (VKM), Norwegian Institute of Public Health (FHI), Norway.

<sup>4</sup>Norwegian Scientific Committee for Food Safety (VKM), Norwegian University of Science and Technology (NTNU), Norway.

<sup>5</sup>Norwegian Scientific Committee for Food Safety (VKM), University of Oslo (UiO), Norway.

<sup>6</sup>Norwegian Scientific Committee for Food Safety (VKM), University of Agder (UiA), Norway.

<sup>7</sup>Norwegian Scientific Committee for Food Safety (VKM), Innlandet Hospital Trust (HF), Norway.

<sup>8</sup>Norwegian Scientific Committee for Food Safety (VKM), University of Bergen (UiB), Norway.

### **Authors' contributions**

*This work was carried out in collaboration among all authors. The opinion has been assessed and approved by the Panel on Nutrition, Dietetic Products, Novel Food and Allergy of VKM. All authors read and approved the final manuscript.*

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### **ABSTRACT**

The Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghet, VKM) has, at the request of the Norwegian Food Safety Authority (Mattilsynet; NFSA), assessed the risk of "other substances" in food supplements and energy drinks sold in Norway. VKM has assessed the risk of doses given by NFSA. These risk assessments will provide NFSA with the scientific basis while regulating "other substances" in food supplements.

"Other substances" are described in the food supplement directive 2002/46/EC as *substances other than vitamins or minerals that have a nutritional and/ or physiological effect*. It is added mainly to food supplements, but also to energy drinks and other foods. In this series of risk assessments of "other substances" the VKM has not evaluated any claimed beneficial effects from these substances, only possible adverse effects.

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\*Corresponding author: Email: tron.gifstad@vkm.no;

The present report is limited to the use of L-lysine in food supplements. Risks related to lysine added to food and drinks, protein hydrolysates or high dietary protein intake are outside the scope of the opinion. The report is based on previous risk assessments of lysine and scientific papers retrieved from a comprehensive literature search.

According to information from the NSFA, L-lysine is an ingredient in food supplements sold in Norway. NSFA has requested a risk assessment of 1000, 2000, 2500, 2750 and 3000 mg/day of L-lysine from food supplements. Foods rich in L-lysine are generally protein rich foods such as meat, dairy products, eggs, legumes, and some fish. Based on NHANES III (1988-1994), the overall mean intake of L-lysine from food and food supplements in the United States was 5.3 g/day (IOM, 2005).

L-Lysine, an indispensable amino acid, is present in all proteins in the human body. Its catabolisation takes place mainly in the liver. The two nitrogen groups are transferred to alpha-ketoglutarate to form glutamate. The remaining carbon skeleton is broken down to acetoacetyl-CoA. Lysine is exclusively ketogenic i.e. does not enter gluconeogenesis for the production of glucose.

In the first phase of the present evaluation of L-lysine, previous reports evaluating the safety of L-lysine supplementation in humans were identified. In the second phase, two systematic literature searches have been performed to retrieve scientific papers published before 11 May 2016 (human studies literature search) and before 28 September 2016 (animal studies literature search). Based on these searches, we identified two human studies and one study in rats that could be used for risk assessment of L-lysine in food supplement.

According to a report from the Institute of Medicine in the USA (IOM, 2005), several clinical trials of lysine with intakes ranging from 0.6 to 3.0 g/day for 3 to 6 months have not reported any adverse effects. The same was the case for the two human randomised controlled trials (RCTs) included in this report providing 6 g/day L-lysine orally for 8 weeks to schizophrenic patients. One 90-days subchronic toxicity study with rats was identified, showing a no observed adverse effect level (NOAEL) of 3357 mg/kg bw per day (the highest dose tested), with no functional, biochemical or histological changes in renal function. In the present report, the value of comparison is set to 86 mg/kg bw per day, corresponding to 6000 mg per day in a 70 kg adult; the daily dose provided in the two human RCTs. The calculated margins of exposures (MOE-values) range from 1.2 to 6.0 for the specified supplement doses with 1000-3000 mg/day of L-lysine. MOE-values below 10 (for interindividual differences in humans) is regarded as acceptable since L-lysine is a nutrient that does not cause any known adverse effects. In addition, the overall mean lysine intake according to NHANES III (5.3 g/day) is close to the doses considered in the present risk assessment. The requirement for lysine, 30 mg/kg bw per day, corresponding to 2.1 g/day in a 70 kg adult, is close to the doses considered in the present risk assessment. The NOAEL suggested in the 90 days subchronic rat study supports the suggestion that these doses are well tolerated in humans even with somewhat low MOE-values.

VKM concludes that:

- In adults ( $\geq 18$  years), the specified doses 1000, 2000, 2500, 2750 and 3000 mg/day L-lysine in food supplements are unlikely to cause adverse health effects.
- In adolescents (14 to  $< 18$  years), the specified doses 1000, 2000, 2500, 2750 and 3000 mg/day L-lysine in food supplements are unlikely to cause adverse health effects.
- In children (10 to  $< 14$  years), the specified doses 1000, 2000, 2500, 2750 and 3000 mg/day L-lysine in food supplements are unlikely to cause adverse health effects.

Children younger than 10 years were not within the scope of the present risk assessment.

**Keywords:** *L-lysine; food supplement; adverse health effect; negative health effect; Norwegian Food Safety Authority; Norwegian Scientific Committee for Food Safety; other substances; risk assessment; VKM.*

Available:<https://vkm.no/download/18.645b840415d03a2fe8f25cb5/1502802645406/Risk%20assessment%20of%20%22other%20substances%22%20%E2%80%93%20L-lysine.pdf>

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**COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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