**Risk Assessment of "Other Substances" – D-Glucurono-γ-lactone**

Trine Husøy¹, Ellen Bruzell², Berit Granum¹, Ragna Bogen Hetland¹, Jens Rohloff³, Trude Wicklund⁴ and Inger-Lise Steffensen¹

¹Norwegian Scientific Committee for Food Safety (VKM), Norwegian Institute of Public Health (FHI), Norway.
²Norwegian Scientific Committee for Food Safety (VKM), Nordic Institute for Dental Materials, Norway.
³Norwegian Scientific Committee for Food Safety (VKM), Norwegian University of Science and Technology, Norway.
⁴Norwegian Scientific Committee for Food Safety (VKM), Norwegian University of Life Sciences, Norway.

**Authors’ contributions**

This work was carried out in collaboration between all authors. The opinion has been assessed and approved by the panel on food additives, flavourings, processing aids, materials in contact with food and cosmetics 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 the addition of "other substances" to food supplements and other foods.

"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. VKM has not in this series of risk assessments of "other substances" evaluated any claimed beneficial effects from these substances, only possible adverse effects.

The present report is a risk assessment of D-glucurono-γ-lactone, and it is based on previous risk assessments. A literature search was performed, however, no articles fulfilled the inclusion criteria.

*Corresponding author: Email: Trine.Husoy@fhi.no;
According to information from NFSA, D-glucurono-γ-lactone is an ingredient in energy drinks sold in Norway. NFSA has requested a risk assessment of 24 mg/100 ml of D-glucurono-γ-lactone in energy drinks. Drinking patterns reflecting a high acute intake, a mean chronic intake and a high chronic intake were assessed.

D-glucurono-γ-lactone (CAS no. 32449-92-6; EINECS no. 251-053-3) and its hydrolysis product glucuronic acid are endogenous metabolites in humans and other mammals, they occur naturally in several dietary sources and are readily metabolized to innocuous products and excreted. The estimated exposure to D-glucurono-γ-lactone from naturally occurring sources in the diet is 1-2 mg/day.

No human toxicity data on D-glucurono-γ-lactone was available in the included literature. A no observed adverse effect level (NOAEL) of 1000 mg/kg bw per day, the highest dose tested, was set in 2009 by the European Food Safety Authority (EFSA) (EFSA, 2009) based on a 13 week rat study of daily oral administration of D-glucurono-γ-lactone performed under good laboratory practice. VKM has used the NOAEL of 1000 mg/kg bw per day for the risk characterisation in the present risk assessment.

The risk characterisation is based on the margin of exposure (MOE) approach; the ratio of the NOAEL to the exposure. An acceptable MOE value for a NOAEL-based assessment of D-glucurono-γ-lactone is ≥100, which includes a factor 10 for extrapolation from animals to humans, and a factor 10 for interindividual human variation.

Due to lack of an acute reference dose or other data on acute toxicity for D-glucurono-γ-lactone, it is not possible to characterise the risk related to a high acute drinking pattern for any of the age groups.

For the mean chronic drinking pattern, the intake was estimated to be 58, 65, 64 and 71 ml/day for 3 to <10 year old children, 10 to <14 year old children, 14 to <18 year old adolescents and adults, respectively. With regard to the mean chronic drinking pattern, the MOE values are 1667 for the age group 3 to <10 years, 2500 for the age group 10 to <14 years, 3333 for the age group 14 to <18 and 5000 for adults ≥18 years. VKM concludes that it is unlikely that a daily mean chronic intake of D-glucurono-γ-lactone from energy drinks (containing 24 mg/100 ml) causes adverse health effects to children (3 years and above), adolescents or adults.

For the high chronic drinking pattern, the intake was estimated to be 163, 180, 211 and 320 ml/day for 3 to <10 year old children, 10 to <14 year old children, 14 to <18 year old adolescents and adults, respectively. With regard to the high chronic drinking pattern, the MOE values are 588 for the age group 3 to <10 years, 1000 for the age group 10 to <14 years, 1250 for the age group 14 to <18 and 909 for adults (≥18 years). VKM concludes that it is unlikely that a daily high chronic intake of D-glucurono-γ-lactone in energy drinks (containing 24 mg/100 ml) causes adverse health effects to children (3 years and above), adolescents or adults.

**Keywords:** Adverse health effect; D-glucurono-γ-lactone; energy drink; negative health effect; Norwegian Food Safety Authority; Norwegian Scientific Committee for Food Safety; other substances; risk assessment; VKM.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.