

Safety Assessment of Orthosilicic acid-vanillin complex (OSA-VC)

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Introduction

An application for the authorisation of Orthosilicic Acid-Vanillin Complex (OSA-VC) was submitted to the Food Safety Authority of Ireland (FSAI) by Dexsil Labs of Belgium in accordance with *Article 4* of the novel food Regulation (EC) No. 258/97. The application was accepted by the FSAI on July 31st of 2014.

The novel ingredient is a vanillin-stabilised form of orthosilicic acid intended for use as a source of silicon in food supplements in line with Directive 2002/46/EC. Silicon (Si) is ubiquitous in the environment, found mainly as insoluble silicates, but small amounts of soluble silicon are naturally present in water, chiefly as orthosilicic acid, $\text{Si}(\text{OH})_4$ which is the most bioavailable source of silicon. Silicon, in its different forms, has widespread industrial applications including use as a food additive (anti-caking agent), a means to clarify beverages and control viscosity, an anti-foaming agent, a dough modifier and an excipient in drugs and vitamins pills. As a result, humans encounter silicon through both environmental exposure and as a dietary/medicinal component.

Vanillin (4-hydroxy-3-methoxybenzaldehyde) in contrast is not a mineral but an organic phenolic aldehyde used as a flavouring agent in a variety of foods and beverages. It is the primary natural component of the extract of the vanilla bean with significant amounts also made from lignin, a by-product from the wood-pulp industry. Vanillin (4-hydroxy-3-methoxybenzaldehyde) is not covalently bound into the OSA-VC complex and is therefore available for absorption and subsequent metabolism upon ingestion. The vanillin used to produce this novel ingredient (OSA-VC) is produced via a synthetic process using the ex-catechol route.

The ingredient is classed as novel in accordance with *Article 1.2(c)* of the novel food Regulation (EC) No 259/97: “foods and food ingredients with a new or intentionally modified primary molecular structure”. The application dossier was prepared pursuant to Class 2 of Commission Recommendation 97/618/EC “Complex novel food from a non-GM source”, and sub-class (2) “the source of the novel food has no history of food use in the Community”.

I. Specification of the novel food

OSA-VC is water soluble and produced as a transparent liquid with an acidic pH of approximately 2.4. Product specifications are provided which focus on silicon and vanillin content, while heavy metal and microbial levels are also provided and supported by batch analysis results. Analysis for pesticide or food allergen content is

not required due to the production process, while the presence of mycotoxins is not expected or detected. The stability of OSA-VC at room temperature has been established at 24 months.

II. Effect of the production process applied to the novel food

Details of the chemical process are provided with quality systems in place (certified to ISO 9001:2008 standards) that underlie the production of OSA-VC. Vanillin is synthesised utilising the ex-catechol route, while silicon is derived from potassium orthosilicate ($\text{SiO}_2 \cdot \text{K}_2\text{O}$, CAS N° 1312-76-1). Compositional analysis confirms the identity of residual impurities (ethanol, phosphoric acid) that are present at low levels (<0.5% in total) in the final product while benzene is not detected.

III. History of the source organism

This is not applicable.

IX. Anticipated intake/extent of use of the novel food

The applicant intends to market OSA-VC in two different dosages. The standard dose will be as a 15ml/day dietary supplement (99.8% OSA-VC complex) equivalent to 14.8 ml OSA-VC which would provide 10.1 - 18.2 mg silicon per day. An alternative dose will be as a single dietary supplement (45 ml/day, 99.8% OSA-VC complex equivalent to 44.5 ml OSA-VC) to be taken for 1 week only. This would provide 30.3 - 54.9 mg silicon per day and the consumer would revert to normal dosage after this period. The proposed supplemental intake of OSA-VC when added to normal silicon intake (estimated at 20 - 40 mg/day) would not exceed the safety intake ranges of silicon dioxide of up to 1,500 mg /d (equivalent to 700 mg silicon per day) as determined by EFSA.

X. Nutritional information on the novel food

Silicon is estimated to be the third most abundant trace element in the human body in which it is thought to have a structural role. It is ubiquitous in the environment and is present in a number of plant based foods, though the main source of the most bioavailable form (orthosilicic acid- $\text{Si}(\text{OH})_4$) is water. In 2009, EFSA recognised the bioavailability of silicon from choline-stabilised orthosilicic acid which is authorised in Europe as a source of silicon in food supplements. A bioavailability study carried out by the applicant indicated that the supplement is well tolerated, with no evidence to indicate that it interferes with the bioavailability of other nutrients in the diet. However, there is some evidence that silicon can reduce the exposure to and therefore potential toxicity of aluminium by interfering with its bioavailability.

Vanillin (4-hydroxy-3-methoxybenzaldehyde) is not covalently bound in the OSA-VC complex and is therefore available for absorption and subsequent metabolism. Vanillin is a flavouring substance authorised for use in food in the EU and is a member of chemical group 23 (benzyl alcohols/aldehydes/acids/esters/acetal) as defined in Annex I of the Commission Regulation (EC) No 1565/20001. EFSA have

published three opinions on chemically defined flavouring substances used in or on foodstuffs for human consumption or used as feed additives for all animal species, all of which belong to chemical group 23. In all three reports the consulted panels concluded that the substances do not give rise to safety concerns at their levels of dietary intake.

XI. Microbiological information on the novel food

The microbiological status of the novel ingredient is controlled by product specifications and supported by batch test results.

XII. Toxicological information on the novel food

The toxicology studies presented were a mix of applicant sponsored studies involving OSA-VC, EFSA opinions and studies on silicon/silicates and vanillin from the scientific literature. Most studies cited were either not conducted to, or were of unknown GLP status. Where OSA-VC was investigated, it was done so according to GLP and OECD guidelines where appropriate.

Absorption, distribution, metabolism and excretion (ADME)

Orthosilicic acid [Si(OH)₄] is soluble in water and other fluids and is the most bioavailable form of silicon for humans. Once silicon has been absorbed and reaches general circulation it is distributed throughout the body, with significant levels found in organs such as the liver, spleen, lungs and kidneys. Absorbed silicon is filtered by the kidneys and excreted in urine within hours of absorption, with very little reabsorbed by the tubules. An applicant-sponsored human volunteer study on OSA-VC confirmed the bioavailability and urinary excretion of silicon from dietary OSA-VC with no adverse effects reported. Silicon (1-2g) is widely distributed in the human body and is found in body fluids and various tissues (connective tissues, including aorta, bone, skin, tendon and trachea. Silicon is considered to be integrally bound to connective tissues and their components and to play an important structural role.

Vanillin (4-hydroxy-3-methoxybenzaldehyde) is not covalently bound into the OSA-VC complex and is therefore available for absorption once ingested. The absorption, distribution, metabolism and elimination of vanillin were not investigated by the applicant. However, EFSA has previously addressed the metabolism of vanillin which appears to be readily absorbed, extensively metabolised and rapidly eliminated. Vanillin is subject to metabolic pathways and kinetics comparable to those followed by benzoates, benzyl derivatives and salicylates. Consequently, its presence in food is not expected to generate residues of safety concern.

General toxicity

Very few studies on the toxic effects of soluble silicon exist. There are a number of studies available on the ingestion of silicates and polysilicic acid (colloid silica) which are relatively insoluble forms of silicon and therefore have poor bioavailability. There

are no studies available for OSA-VC that address skin and eye irritation, sensitisation, photo-toxicity, mutagenicity or carcinogenicity, and reproductive toxicity.

Acute toxicity of OSA-VC

Oral toxicity from elemental or organic silicon has not been identified in humans or other animals, even in rats and mice fed up to 1,000 times the normal dietary intake. Silicon can accumulate at up to ten times normal levels without obvious adverse effects in patients on dialysis that experience renal failure.

An applicant sponsored acute oral toxicity study of OSA-VC in rats was carried out according to the principles of OECD guideline 423. There were no deaths observed and no signs of toxicity. In addition, treatment-related post-mortem macroscopic findings were normal and an LD₅₀ of greater than 37.9 mg/kg body weight was recorded.

The use of vanillin as a food additive is approved in the EU and in other countries. A recent EFSA opinion concerning flavouring substances concluded the acute toxicity of vanillin to be in the range 1,000 – 4,370 mg/kg for a variety of animal species.

Repeated dose toxicity

Though silica intake by inhalation has known carcinogenic potential, silicates are not significantly toxic in oral acute or short-term oral or parenteral toxicity studies in animals. An applicant sponsored repeat dose 90-day rat oral toxicity study on OSA-VC did not result in mortalities or any other significant treatment-associated physiological or clinical effects. A NOAEL of approximately 212 mg OSA/kg bw/day was deduced.

The "Screening Information Data Set" (SIDS) program operated under the auspices of the Organization for Economic Cooperation and Development (OECD) produced a monograph of vanillin in 1996 which concluded that it poses no particular risk to human health. This report described several repeated dose toxicity studies with vanillin in rats which suggested that the NOAEL could be as high as 2,500 mg/kg/day. A more recent 90 day oral rat study (2003) of vanillin found no significant effects on body weight, food consumption, haematological and clinical chemistry parameters, organ weights, or histopathology and established a NOAEL of 400 mg/kg bw/day.

Genotoxicity and Carcinogenicity

A recent review of the toxicology of synthetic amorphous silica (SAS) described a number of *in vitro* and *in vivo* mutagenicity tests and concluded there was no evidence of mutagenic potential. Genotoxicity was observed *in vitro*, usually at dose levels and concentrations that also induced cytotoxicity, but no genotoxicity was found after *in vivo* exposure of experimental animals.

The applicant has not provided studies on the mutagenicity or carcinogenicity profile of OSA-VC due to technical limitations (solubility) of the test material. In addition,

specific data on the genotoxicity of orthosilicic acid is not evident in the scientific literature.

There is sufficient evidence to conclude that vanillin poses very little risk with respect to carcinogenicity or mutagenicity. As far back as 1968, JECFA in their monograph for vanillin established an ADI of 0–10 mg/kg of body weight for vanillin based on a NOAEL of 1,000 mg/kg of body weight per day in a 2-year feeding study in rats.

Reproductive toxicity

While reproductive/developmental studies on OSA-VC are not available, such studies on related silicon materials (including choline-stabilised OSA) have not identified any cause for concern.

Interactions of OSA-VC with other dietary components

There is evidence that silicon binds aluminium, thereby reducing its bioavailability and by doing so its potential toxicity.

Allergenicity

Due to the production method and lack of protein or use of excipients in the final product, there is no cause for concern with regard to allergenicity.

Conclusions

The consumption of silicon, in its various forms, and vanillin is not considered a significant safety risk in the EU. The novel ingredient is an orthosilicic acid-vanillin complex (OSA-VC) which is intended for use in the EU as a food supplement in two dosage forms. The nutritional and toxicological information provided by the applicant does not identify any safety concerns with respect to the consumption of OSA-VC at the intended dosage levels.

Recommendation

On the basis of the information provided by the applicant, along with subsequent clarifications, the Food Safety Authority of Ireland has not identified any safety concerns with the consumption of food supplements containing OSA-VC at the proposed use levels. Therefore, the FSAI considers that this novel ingredient, produced by Dexsil Labs meets the criteria for novel food set out in *Article 3.1.* of the novel food Regulation (EC) No 258/97.