Summary of the application: 2'-Fucosyllactose (2'-FL)

Applicant: Amyris, Inc., 5885 Hollis Street, Suite 100, Emeryville, California, 94608 United States of America.

Amyris, Inc. (Amyris) submits the present novel food application for 2'-fucosyllactose (2'-FL), which is a naturally occurring oligosaccharide consisting of lactose (galactose and glucose) and fucose that is found in human breast milk. 2'-FL is currently authorised as a novel food ingredient under Commission Implementing Regulation (EU) 2017/2470 of 20 December 2017 establishing the Union list of novel foods in accordance with Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods for use in a variety of food products, including infant formula and follow-on formula and food supplements.

Currently authorised 2'-FL ingredients are produced by chemical synthesis or with the authorised microbial sources of genetically modified strains of *Escherichia coli* K-12 or BL21. Amyris seeks to amend the specification of 2'-FL in the European Union (EU) Union list of novel foods to include another microbial source for 2'-FL, namely a genetically modified strain of *Saccharomyces cerevisiae* (*S. cerevisiae*) CEN.PK113-7D. This strain is used to manufacture Amyris's 2'-FL ingredient via fermentation. Amyris has demonstrated their 2'-FL produced by a genetically modified strain of *S. cerevisiae* CEN.PK113-7D to be chemically and structurally identical to 2'-FL naturally occurring in breast milk and by extension, to other 2'-FL ingredients currently on the EU marketplace. *S. cerevisiae* has been granted Qualified Presumption of Safety (QPS) status in the EU by the European Food Safety Authority (EFSA) and the genetic modifications introduced into *S. cerevisiae* do not indicate a concern.

Amyris's 2'-FL is manufactured and purified using food-grade raw materials and processing aids in accordance with a detailed Hazard Analysis and Critical Control Points (HACCP) plan. Amyris's 2'-FL ingredient is a powder with area % of ≥86% 2'-FL. The purity of Amyris's 2'-FL ingredient is within the range of purity limits for the currently authorised 2'-FL ingredients (≥86% versus ≥83 to ≥90%). Other minor carbohydrate components in Amyris's 2'-FL ingredient are mostly similar to those for authorised 2'-FL ingredients on the Union list. The levels of other specified carbohydrates within Amyris's 2'-FL ingredient are not expected to pose a concern for safety. Batch analyses data confirm that the final ingredient meets specifications, including limits for heavy metal and microbiological contaminants. Additional analytical data confirm that there are no concerns from potential contaminants, including mycotoxins, endotoxins, polychlorinated biphenyls (PCBs), dioxins, pesticides, and residual minerals, amino acids, and biogenic amines. The final 2'-FL ingredient contains no residual production organism or production organism-derived deoxyribonucleic acid (DNA). Amyris's 2'-FL is expected to have a shelf-life of 3 years when stored under ambient temperatures in the sealed original packaging. Data from an accelerated stability study demonstrate that Amyris's 2'-FL is stable for a duration equivalent to the product shelf-life.

Amyris is not requesting any changes to the conditions of use currently authorised for 2'-FL in Table 1 of the Union list under Commission Implementing Regulation (EU) 2017/2470 of 20 December 2017 (as amended). Amyris's 2'-FL ingredient is intended to serve as an alternative source of 2'-FL. Thus, there will be no changes in the target population or exposure to 2'-FL as a result of the current application. The absorption, distribution, metabolism, and excretion of Amyris's 2'-FL is expected to be identical to that of 2'-FL which occurs naturally in human breast milk as they are chemically and structurally identical. Furthermore, there will be no significant effects on the nutritional profile of 2'-FL resulting from Amyris's proposed amendments to the specifications for 2'-FL on the Union list. Tier 1 genotoxicity studies on Amyris's 2'-FL ingredient were conducted in accordance with relevant Organisation for Economic Co-operation and Development (OECD) Test Guidelines (TG) (471 and 487) and in compliance with Good Laboratory Practice (GLP). The results demonstrate that Amyris's 2'-FL is

non-mutagenic at concentrations up to 5,000 µg/plate under the conditions of the study (the OECD TG 471 maximum recommended concentration) and does not have potential for induction of chromosomal aberrations in human lymphocytes at concentrations up to 2,200 µg/mL. These studies support the safety of the microbial source of Amyris's 2'-FL ingredient (a genetically modified strain of *S. cerevisiae* CEN.PK113-7D).

On the basis that Amyris's 2'-FL ingredient is chemically and compositionally similar to other 2'-FL ingredients currently authorised on the Union list, EFSA's existing safety conclusions on other 2'-FL ingredients may be extended to support the safety of Amyris's 2'-FL produced by microbial fermentation of a genetically modified strain of *S. cerevisiae* CEN.PK113-7D.

The results of recently published studies on other 2'-FL ingredients continue to support the safety of 2'-FL and are in agreement with the results of the existing risk assessment as conducted in 2015 by EFSA. The amendments proposed by Amyris to the specifications and microbial source of 2'-FL do not negatively impact its nutritional value, metabolism, or level of undesirable substances compared to 2'-FL ingredients that are currently approved. Furthermore, the amendments proposed by Amyris to the specifications and microbial source of 2'-FL do not affect the results of the existing risk assessment for 2'-FL as currently included in the Union list.

The safety of 2'-FL from a genetically modified strain of *S. cerevisiae* CEN.PK113-7D under the authorised conditions of use for 2'-FL as detailed in Table 1 of the Union list is supported by the totality of evidence.