27 September 2021
172–21

Approval Report – Application A1222

Steviol glycosides from *Yarrowia lipolytica*

Food Standards Australia New Zealand (FSANZ) has assessed an application made by Avansya V.O.F. (Avansya) to permit the use of a steviol glycoside mixture as an intense sweetener. The steviol glycoside mixture is produced by fermentation from a genetically modified *Yarrowia lipolytica* production strain, expressing steviol glycoside biosynthesis pathway genes from *Stevia rebaudiana* Bertoni.

On 11 June 2021, FSANZ sought submissions on a draft variation and published an associated report. FSANZ received 7 submissions, plus one late submission.

FSANZ approved the draft variation on 15 September 2021. The Food Ministers' Meeting (formerly the Australia New Zealand Ministerial Forum on Food Regulation) was notified of FSANZ's decision on 27 September 2021.

This Report is provided pursuant to paragraph 33(1)(b) of the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act).

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Supporting document

The following document which informed the assessment of this application is available on the FSANZ website:

SD1 Risk and technical assessment - Application A1222 – Steviol glycosides from *Yarrowia lipolytica.*

Executive summary

Avansya V.O.F (Avansya) applied for a variation to the Australia New Zealand Food Standards Code (the Code) to permit the use of a steviol glycosides mixture (primarily rebaudioside M with lesser amounts of rebaudioside D, that may contain minor amounts of other steviol glycosides). Food Standards Australia New Zealand (FSANZ) assessed the application in accordance with the *Food Standards Australia New Zealand Act 1991* (FSANZ Act).

The steviol glycosides mixture is produced by fermentation of simple sugars using a genetically modified *Yarrowia lipolytica* (*Y. lipolytica*) production strain (VRM0014). This genetically modified yeast contains novel genes involved in steviol glycoside biosynthesis. Most of the novel genes were derived from *Stevia rebaudiana* Bertoni, with additional genes sourced from other plant species. The steviol glycoside mixture, produced for use as a food additive in the form of a steviol glycosides preparation, is denoted rebaudioside MD by Avansya.[1]

Steviol glycosides are currently permitted by the Code to be used in certain foods as food additives up to specified maximum permitted levels. They are used as an intense sweetener or flavour enhancer. However, there is no permission for Avansya's rebaudioside MD preparation. Substances used as food additives must comply with (among other things) any relevant identity and purity specifications listed in Schedule 3 — Identity and Purity. Section S3—39 of the Code sets out specifications for certain steviol glycoside preparations produced using a fermentation process. While Avansya's rebaudioside MD meets the purity parameters of specifications in this section, Avansya's production strain is not listed.

No potential public health and safety concerns were identified with Avansya's rebaudioside MD preparation produced by genetically modified *Y. lipolytica* VRM0014.

The safety assessment did not identify any concerns associated with the host organism *Y. lipolytica,* or the novel proteins expressed by the introduced genes for the biosynthesis of rebaudioside MD*.* The host *Y. lipolytica* production strain is neither pathogenic nor toxigenic and has a long history of safe use in foods. Characterisation of the genetically modified production strain confirmed both the insertion and stable inheritance of steviol glycoside biosynthesis genes. Neither the host organism nor residual DNA or residual protein were detectable in the final rebaudioside MD preparation.

No new evidence of adverse effects of steviol glycosides has been identified that would justify a change in the Acceptable Daily Intake (ADI) established by FSANZ in 2008. The applicant provided an *in vitro* anaerobic metabolism study demonstrating that the metabolic fate of rebaudioside MD is equivalent to other steviol glycosides previously assessed by FSANZ. Therefore the ADI of 0-4 mg/kg bw expressed as steviol is appropriate for the rebaudioside MD preparation produced using genetically modified *Y. lipolytica* VRM0014, the subject of this application.

After assessing the application, FSANZ considered that it was appropriate to prepare a draft variation to amend the Code to permit the use of Avansya's rebaudioside MD preparation as a food additive (intense sweetener) at current levels and in those food classes which currently permit steviol glycosides.

Following assessment and the preparation of the draft variation, FSANZ called for

[1] A steviol glycoside preparation that was the subject of another application - A1170 – was referred to as rebaudioside MD. It is a mixture of rebaudioside M and rebaudioside D. Under this application (A1222) the distribution of steviol glycosides is similar and the preparations are considered chemically equivalent. For consistency, the preparation under this application is also referred to as rebaudioside MD.

submissions regarding the draft variation on 11 June 2021. Seven submissions were received, all of which were fully supportive (see Section 2.1 of this report for details of submissions made). In addition, one late submission was received which supported the application and draft variation.

Based on the information above and on other relevant considerations set out in this report, FSANZ has decided to approve the proposed draft variation without change. The draft variation amends the Code to include Avansya's steviol glycosides preparation in section S3—39 so that the specifications in that section for steviol glycosides obtained from fermentation would also apply to Avansya's steviol glycosides preparation. This amendment will have the effect of permitting the use of Avansya's steviol glycosides preparation as a food additive in accordance with the Code's existing permissions and limits for steviol glycosides, including the requirement that the preparation complies with specifications set out in section S3—39.

1 Introduction

1.1 The Applicant

The applicant is Avansya V.O.F. (Avansya). Avansya, a general partnership under the laws of The Netherlands between Cargill Sweeteners Holding B.V. (Cargill) and DSM Food Specialities Stevia B.V. (DSM), is a manufacturer of fermentation–derived sweeteners used in the global food and beverage industries.

1.2 The application

The application sought an amendment to Schedule 3 of the Australia New Zealand Food Standards Code (the Code) to permit their purified steviol glycoside preparation, produced by fermentation of simple sugars using a genetically modified *Yarrowia lipolytica* (*Y. lipolytica*) production strain (VRM0014). This purified steviol glycoside mixture is primarily comprised of rebaudioside M with lesser amounts of rebaudioside D, and may contain minor amounts of other steviol glycosides. The mixture, produced for use as a food additive in the form of a steviol glycosides preparation, is denoted rebaudioside MD by Avansya.[2]

Steviol glycosides are permitted for use in food as food additives. They are used by the food industry as an intense sweetener.

Substances used as food additives must comply with any relevant identity and purity specifications listed in Schedule 3 — Identity and Purity. The current specifications for steviol glycosides in the Code apply to products extracted from the *Stevia rebaudiana* Bertoni plant either by hot water extraction or by enzymatic conversion of the plant extract, as well as via a fermentation process. The individual steviol glycosides (rebaudiosides M and D and minor other steviol glycosides) produced under Avansya's fermentation method are identical to those produced from the plant. Section S3—39 of the Code contains the specifications for certain steviol glycoside preparations produced using a fermentation process. Avansya's strain of *Y. lipolytica* is not listed in S3—39 and the specifications do not apply to Avansya's rebaudioside MD, therefore Avansya's rebaudioside MD is currently not a permitted steviol glycosides preparation.

1.3 The current Code requirements

Australian and New Zealand food laws require food for sale to comply with the following requirements of the Code.

Paragraph 1.1.1—10(6)(a) provides that, unless expressly permitted by the Code, a food for sale cannot contain, as an ingredient or component, a substance that is used as a food additive. The Code also imposes identity and purity specifications with which rebaudioside MD and other steviol glycosides must comply.

The Code currently permits the use of steviol glycosides as food additives with the INS number 960. They are permitted in a wide range of food categories listed within the table to section S15—5 at maximum permitted levels and at Good Manufacturing Practice (GMP) for tabletop sweeteners only.

However, the current specifications for identity and purity do not apply to Avansya's particular

[2] A steviol glycosides preparation that was the subject of another application - A1170 - is referred to as rebaudioside MD. It is a mixture of rebaudioside M and rebaudioside D. Under this application (A1222) the distribution of steviol glycosides is similar and the preparations are considered chemically equivalent. For consistency, the preparation under this application is also referred to as rebaudioside MD.

Y. lipolytica production strain.

1.3.1 Food additives

Section 1.1.2—11 defines the expression 'used as a food additive'. Subsection 1.1.2—11(1) provides that a substance is 'used as a food additive' in relation to a food if both of the following conditions are met: the substance is added to the food to perform one or more technological functions listed in Schedule 14; and the substance is identified in subsection 1.1.2—11(2) – this includes (among other things) a substance identified in the table to section S15—5 as a permitted food additive.

Section 1.3.1—3 details when substances are permitted to be used as food additives in food.

Schedule 14 lists the permitted technological purposes of food additives. The table in section S14—2 provides that use as an intense sweetener is a permitted purpose.

Schedule 15 lists the specific food additive permissions for different categories of foods in the table to section S15—5. 'Steviol glycosides' is listed in that table as a permitted food additive for various food categories.

Schedule 16 sets out the types of substances that may be used as food additives in any food at GMP levels. As 'steviol glycosides' is not such a food additive, it is not listed in Schedule 16.

Section 1.5.2—3 provides that permission for use as a food additive also constitutes the permission required by paragraph 1.1.1—10(6) for a food produced using gene technology.

1.3.2 Labelling

Paragraph 1.1.1—10(8) of the Code provides that food for sale must comply with all relevant labelling requirements imposed by the Code for that food.

The Code's labelling requirements which apply to foods for retail sale and to foods sold to a caterer are set out in Divisions 2 and 3 of Standard 1.2.1 respectively.

The Code requires the labels of most packaged food to contain a statement of ingredients. Subsection 1.2.4—7(1) requires food additives to be declared in the statement of ingredients by one of the following methods: if the food additive can be classified in accordance with Schedule 7—the relevant class name followed in brackets by the name or code number of the food additive specified in Schedule 8; or else, the name of the food additive specified in Schedule 8.

Schedule 7 lists the food additive class names that can be used in the statement of ingredients. Schedule 8 lists the names and code numbers of food additives that are to be used for labelling purposes.

Section 1.5.2—4 outlines requirements for labelling of certain foods for sale that consist of, or have as an ingredient (including food additives and processing aids), food that is a *genetically modified food*[3].

[3] Subsection 1.5.2—4(5) defines ***genetically modified food*** to mean a *food produced using gene technology that contains novel DNA or novel protein; or is listed in section S26—3 as subject to the condition that its labelling must comply with this section (*that being section 1.5.2—4*).

1.3.3 Identity and purity requirements

Paragraph 1.1.1—15(1)(a) of the Code requires substances used as food additives to comply with any relevant identity and purity specifications listed in Schedule 3 of the Code.

Primary source specifications for steviol glycosides are contained within section S3—2, being either paragraph S3—2(1)(b) [the FAO[4] JECFA[5] Monograph, (JECFA 2017)], S3-2(1)(c) [the Food Chemicals Codex (FCC 2018)] or S3—2(1)(d) [European Commission Regulation No 231/2012 laying down specifications for food additives (EC 2012, EC 2016)].

Section S3—39 sets out specifications for certain steviol glycosides preparations produced via a fermentation process. These specifications apply to the following preparations listed in that section:

- rebaudioside MD, using a genetically modified *Saccharomyces cerevisiae* strain (*S. cerevisiae*); and
- rebaudioside M using a different strain of *S. cerevisiae.*

As Avansya's steviol glycosides preparation is not listed in section S3-39, the specifications in this section do not apply to it.

1.4 International Standards

Steviol glycosides are approved for use in a number of other jurisdictions, including the European Union, Canada, South and North Asia, Asia Pacific, United States of America (USA), Central/South America, the Middle East and Africa (PureCircle Stevia Institute 2021). In the European Union, commercially available steviol glycoside products must comply with the specifications for steviol glycosides (INS number 960) adopted by the European Commission in 2012 and updated in 2016 (EC 2012, EC 2016).

1.4.1 JECFA

The 87th JECFA meeting in June 2019 established a framework for steviol glycosides building on JECFA's assessments and specifications at earlier meetings. The 87th meeting also prepared four steviol glycosides specification annexes, for the different production methods (JECFA 2020). These are:

- hot water extraction from the leaves of *Stevia rebaudiana* Bertoni (stevia) plant (Annex 1)
- fermentation using genetically modified microorganisms (Annex 2)
- enzymatic modification (bioconversion) of the stevia plant extract using enzymes (Annex 3)
- glycosylation of stevia plant extracts using enzymes to add glucose units to steviol glycosides (Annex 4, tentative pending further information to finalise).

The JECFA meeting in 2019 also confirmed that steviol glycosides prepared using any of these production methods, that comply with the specifications for the different production methods and purity requirements, were considered equivalent in terms of safety and the earlier determined Acceptable Daily Intake (ADI) applies (JECFA 2019a, JECFA 2019b). Annex 2 (above) states that steviol glycosides from fermentation are obtained from the non-toxigenic non-pathogenic strains of *Yarrowia lipolytica* and *Saccharomyces cerevisiae* that have been genetically modified with heterologous genes from multiple donor organisms to overexpress steviol glycosides. Under A1222, FSANZ is assessing a *Y. lipolytica* production

[4] The Food and Agriculture Organization of the United Nations.
[5] The Joint FAO/World Health Organization (WHO) Expert Committee on Food Additives.

strain (strain VRM0014).

It is important to note that the steviol glycosides specifications from the 87th JECFA meeting in 2019 have not yet been discussed by the Codex Committee on Food Additives (CCFA) or ultimately ratified by the Codex Alimentarius Committee (CAC). Therefore these specifications are not yet part of the official JECFA Combined Compendium of Food Additive Specifications. The most current JECFA steviol glycosides monograph is monograph 20 from the 84th JECFA meeting in 2017.

1.4.2 United States of America

The applicant's rebaudioside MD has GRAS (Generally Recognized as Safe) status for a variety of food and beverage uses (GRN 882).[6] The US Food and Drug Administration (FDA) reviewed the self-assessed GRAS notification describing the production of Cargill Incorporated's rebaudioside M produced using the same production strain of *Y. lipolytica* being assessed under A1222, and responded on 2 February 2020 with a "no questions" letter regarding the GRAS status of rebaudioside MD.[7] The FDA does not make its own assessment of such GRAS notifications.

1.4.3 Canada

Canada has approved the production of steviol glycosides using the fermentation process, from three strains of *S. cerevisiae* (Health Canada 2021).

1.5 Reasons for accepting application

The Application was accepted for assessment because:

- it complied with the procedural requirements under subsection 22(2) of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act); and
- it related to a matter that warranted the variation of a food regulatory measure.

1.6 Procedure for assessment

The application was assessed under the General Procedure.

1.7 Decision

The draft variation as proposed following assessment was approved without change after FSANZ had regard to all submissions received following the call for submissions. The approved draft variation is at Attachment A. The approved draft variation takes effect on gazettal.

The related explanatory statement is at Attachment B. An explanatory statement is required to accompany an instrument if it is lodged on the Federal Register of Legislation.

[6] The notice was submitted by Cargill Incorporated, for rebaudioside M (denoted rebaudioside MD under A1222). Refer to page 10 of the application. The product is designated as rebaudioside M in GRN No. 882. It is the same product designated as rebaudioside MD under the current application.

[7] No questions' response means the FDA does not question the basis for the notifier's GRAS conclusion (USFDA 2016).

2 Summary of the assessment

2.1 Summary of issues raised in submissions

FSANZ sought submissions on the draft variation from 11 June to 22 July 2021.[8] Seven submissions were received within the submission period - 2 from government agencies and 5 from industry bodies. In addition, one late submission was received from an industry body. All submissions supported the application. No issues were raised that were required to be addressed.

Table 1: Summary of submissions

Submitter	FSANZ response
New Zealand Food Safety, Ministry for Primary Industries	Support was noted
Victorian Department of Health and Human Services and the Victorian Department of Jobs, Precincts and Regions	Support was noted
Australian Food & Grocery Council	Support was noted
New Zealand Food & Grocery Council	Support was noted
Australian Beverages Council	Support was noted
International Stevia Council	Support was noted
International Sweeteners Association	Support was noted
Late comment – New Zealand Beverage Council	Support was noted

2.2 Risk assessment

FSANZ assessed the public health and safety risks associated with Avansya's rebaudioside MD as a food additive (see SD1). The summary of this risk assessment is provided below.

The food technology assessment concluded that the applicant's rebaudioside MD preparation produced by fermentation of simple sugars using the applicant's genetically modified *Y. lipolytica* strain VRM0014, expressing steviol glycoside biosynthesis pathway genes, meets the purity parameters of specifications currently listed in section S3—39 which sets out the specifications for steviol glycosides produced by fermentation, but not the specific method of production. These purity parameters are also consistent with international purity specifications for steviol glycosides. The rebaudioside MD preparation is also thermally and hydrolytically stable for food use. Its technological purpose matches that of permitted steviol glycosides preparations produced by the currently permitted methods and meets the proposed purpose as an intense sweetener food additive.

No potential public health and safety concerns were identified with Avansya's rebaudioside MD preparation produced by genetically modified *Y. lipolytica* VRM0014.

The safety assessment did not identify any concerns associated with the host organism *Y. lipolytica* or the novel proteins expressed by the introduced genes for the production of rebaudioside MD. The host *Y. lipolytica* production strain is neither pathogenic nor toxigenic and has a long history of safe use in foods. Characterisation of the genetically modified production strain confirmed both the insertion and stable inheritance of steviol glycoside biosynthesis genes. Neither the host organism, residual DNA or residual protein was detectable in the final rebaudioside MD preparation.

No new evidence of adverse effects of steviol glycosides has been identified that would justify a change in the ADI established by FSANZ in 2008. The applicant provided an *in vitro* anaerobic metabolism study demonstrating that the metabolic fate of rebaudioside MD is

[8] These submissions are on the FSANZ website: A1222 - Steviol glycosides from Yarrowia lipolytica

equivalent to other steviol glycosides previously assessed by FSANZ. Therefore the ADI of 0-4 mg/kg bw expressed as steviol is appropriate for the rebaudioside MD preparation produced using genetically modified *Y. lipolytica* VRM0014, the subject of this application.

Since the call for submissions, FSANZ has not been provided with any additional information to change its above assessment.

2.3 Risk management

Avansya's microbial fermentation production method is comparable to the already permitted rebaudioside MD from application A1170 and rebaudioside M from application A1207 (FSANZ 2019a, FSANZ 2021), which are listed in section S3—39. Cargill was the applicant for A1170. Avansya's application states that the rebaudioside MD preparation produced from its *Y. lipolytica* production strain is chemically equivalent to the rebaudioside MD preparation assessed under A1170 (using a *S. cerevisiae* production strain).

The risk management options available to FSANZ, after assessment, were to either reject the application or to prepare a draft variation to amend the Code to permit Avansya's rebaudioside MD.

FSANZ's risk assessment concluded that Avansya's rebaudioside MD produced via its fermentation method of production using a genetically modified *Y. lipolytica* strain VRM0014 containing the genes for the production of rebaudiosides is safe. FSANZ considers that it was therefore appropriate to approve the draft variation to amend the Code to permit Avansya's steviol glycosides preparation.

FSANZ considers Avansya's steviol glycosides preparation (rebaudioside MD) is a food additive produced using gene technology i.e. 'derived or developed from an organism that has been modified using gene technology'. Paragraph 1.1.1—10(6)(g) requires that the presence as an ingredient or component in a food for sale of a food produced using gene technology must be expressly permitted by the Code. Section 1.5.2—3 provides that permission for use as a food additive also constitutes the permission required by paragraph 1.1.1—10(6)(g) (as noted in section 1.3.1).

Other risk management considerations relate to labelling requirements which are summarised in the sections below.

2.3.1 Labelling

2.3.1.1 Ingredient labelling

Under existing labelling requirements in the Code (unless the food is exempt from the requirement for a statement of ingredients) the rebaudioside MD preparation will require declaration as a food additive in the statement of ingredients on the label of foods. These ingredient labelling requirements require steviol glycosides to be identified in the statement of ingredients using the food additive name 'steviol glycosides' or the International Numbering System (INS) code number 960 (as listed in Schedule 8).

As noted in previous reports (for applications A1170, A1172, A1176, A1183 and A1207) (FSANZ 2019a, FSANZ 2019b, FSANZ 2019c, FSANZ 2020, FSANZ 2021), the CCFA has updated the INS numbers for steviol glycosides. These were subsequently adopted into the Class Names and International Numbering System for Food Additives (CXG 36-1989) by the Codex Alimentarius Commission (Codex 2019). The new numbers distinguish between steviol glycosides produced from the plant (Steviol glycosides from *Stevia rebaudiana* Bertoni – INS 960a) and those produced by fermentation (INS 960b). Numbers have not been assigned however, for other methods of production such as enzymatic conversion. For

various reasons, in particular because the INS listing has not been finalised for steviol glycosides produced by different methods of production, FSANZ decided not to include 960a and 960b in the Code when assessing earlier applications (A1170 (FSANZ 2019a), A1183 (FSANZ 2020), and A1207 (FSANZ 2021)).

FSANZ still considers that at this stage the most appropriate INS number for labelling purposes, for all steviol glycosides, is 960. FSANZ will consider changes to this number in the Code in the future, but only if and when further finalised changes are made to the Codex INS list. This would provide a more coordinated approach and efficient transition compared to an unsystematic or ad-hoc approach through various applications.

The FSANZ website provides information on the various production methods for steviol glycosides[9]. Consumers wanting to know the source of any particular steviol glycosides in foods are advised that they may ask the manufacturer who should advise them accordingly.

2.3.1.2 Labelling as 'genetically modified'

As noted in section 2.3 above, the rebaudioside MD preparation is a *food produced using gene technology.* Standard 1.5.2 generally requires food produced using gene technology to be labelled as 'genetically modified' if it contains novel DNA or novel protein. As discussed in section 3.1.1.1 of SD1, it is highly unlikely that novel protein or DNA will be present in the rebaudioside MD preparation and therefore a food for sale. However, if rebaudioside MD is used as an ingredient in a food for retail sale or a food sold to a caterer and novel DNA or protein is present in the final food, the requirement to label rebaudioside MD as 'genetically modified' would apply in accordance with section 1.5.2—4 of the Code.

2.3.2 Risk management conclusion

FSANZ's risk management conclusion is to permit the use of Avansya's rebaudioside MD produced using a genetically modified yeast strain as a food additive. FSANZ's decision is based on the risk assessment, risk management and the FSANZ Act considerations, including the cost benefit considerations (detailed in section 2.5.1.1).

2.4 Risk communication

2.4.1 Consultation

Consultation is a key part of FSANZ's standards development process.

FSANZ developed and applied a basic communication strategy to this application. All calls for submissions were notified via the Food Standards Notification Circular, media release, FSANZ's social media tools and Food Standards News.

The process by which FSANZ considers standards' development matters is open, accountable, consultative and transparent. Public submissions were called to obtain the views of interested parties on issues raised by the application and the impacts of regulatory options. FSANZ acknowledges the time taken by individuals and organisations to make submissions on this application. All comments are valued and contribute to the rigour of our assessment.

The draft variation was considered for approval by FSANZ having regard to all submissions made during the call for submissions period.

[9] For more information please see the following FSANZ webpage: information on steviol glycosides (960) intense sweetener

2.5 FSANZ Act assessment requirements

When assessing this application and the subsequent development of a food regulatory measure, FSANZ had regard to the following matters in section 29 of the FSANZ Act.

2.5.1 Section 29

2.5.1.1 Consideration of costs and benefits

The Office of Best Practice Regulation (OBPR) granted FSANZ a standing exemption from the requirement to develop a Regulatory Impact Statement for the approval of additional food additives (OBPR correspondence dated 24 November 2010, reference 12065). This standing exemption was provided as permitting additional food additives is a minor, deregulatory change and their use is voluntary. This standing exemption relates to the introduction of a food to the food supply that has been determined to be safe.

FSANZ, however, gave consideration to the costs and benefits that may arise from the proposed measure for the purposes of meeting FSANZ Act considerations. The FSANZ Act requires FSANZ to have regard to whether costs that would arise from the proposed measure outweigh the direct and indirect benefits to the community, government or industry that would arise from the proposed measure (paragraph 29(2)(a)).

The purpose of this consideration was to determine if the community, government, and industry as a whole is likely to benefit, on balance, from a move from the status quo. This analysis considered the costs and benefits of approving the application as compared to rejecting the application (i.e. retaining the status quo).

The consideration of the costs and benefits in this section were not intended to be an exhaustive, quantitative economic analysis of the proposed measures and, in fact, most of the effects that were considered cannot easily be assigned a dollar value. Rather, the assessment sought to highlight the likely positives and negatives of moving away from the status quo by permitting the use of Avansya's rebaudioside MD as an alternative source of an intense sweetener (food additive).

FSANZ's conclusions regarding costs and benefits of the proposed measure are set out below.

Costs and benefits of permitting the use of Avansya's rebaudioside MD as a food additive

Consumers seeking products that have reduced sugar and/or energy content may benefit if additional food products (for example, with an improved sweetness profile) become available due to the use of Avansya's rebaudioside MD as an intense sweetener (food additive).

Industry will benefit from having an additional intense sweetener (food additive) available to them. Due to the voluntary nature of the permission, industry will only use the food additive where they believe a net benefit exists. Avansya's rebaudioside MD is approved as a food additive in the USA which may be a business opportunity for Australia and/or New Zealand industries, although there may also be competing imports from these countries into the domestic market.

Permitting Avansya's rebaudioside MD may result in a small cost to government in terms of adding to the current range of food additives that are monitored for compliance.

Conclusions from cost benefit considerations

FSANZ's assessment at the call for submissions was that the direct and indirect benefits that

would arise from permitting the use of Avansya's rebaudioside MD as a food additive most likely outweigh the associated costs. No further information was received during the consultation process that changed the findings from the analysis of costs and benefits in the call for submissions.

2.5.1.2 Other measures

There are no other measures (whether available to FSANZ or not) that would be more cost-effective than a food regulatory measure developed or varied as a result of the application.

2.5.1.3 Any relevant New Zealand standards

The Standards in the Code relevant to the permitted use of Avansya's rebaudioside MD apply in both Australia and New Zealand. There are no relevant New Zealand-only Standards.

2.5.1.4 Any other relevant matters

Other relevant matters are considered below.

2.5.2 Subsection 18(1)

FSANZ has also considered the three objectives in subsection 18(1) of the FSANZ Act during the assessment.

2.5.2.1 Protection of public health and safety

No potential public health and safety concerns associated with Avansya's rebaudioside MD were identified. For more detail, see SD1.

2.5.2.2 The provision of adequate information relating to food to enable consumers to make informed choices

The labelling requirements for the provision of information to consumers are discussed in section 2.3.1 above. FSANZ considers that those requirements would enable this objective to be satisfied.

2.5.2.3 The prevention of misleading or deceptive conduct

As explained above, Avansya's rebaudioside MD is not obtained from the stevia plant. FSANZ notes that steviol glycosides are sometimes marketed as stevia, a natural sweetener obtained from the leaves of the stevia plant, sometimes accompanied by leaf graphics. Any such marketing as well as claims such as 'natural' would be subject to consumer protection laws, fair trading laws and food laws in Australia and New Zealand that require that marketing and labels do not misinform consumers through false, misleading or deceptive representations.

2.5.3 Subsection 18(2) considerations

FSANZ has also had regard to:

- **the need for standards to be based on risk analysis using the best available scientific evidence**

FSANZ used the best available scientific evidence to conduct the risk assessment which is provided in SD1. The applicant submitted a dossier of scientific studies as part of its application. FSANZ also had regard to other technical information including scientific

literature in assessing the application.

- **the promotion of consistency between domestic and international food standards**

A number of international jurisdictions and standards permit the use of steviol glycosides in foods. As outlined in section 1.4.1, JECFA has adopted a framework for developing specifications for steviol glycosides by four different methods of production, including fermentation. Avansya's rebaudioside MD complies with the JECFA framework specification for steviol glycosides produced by fermentation.

- **the desirability of an efficient and internationally competitive food industry**

Permission to use Avansya's rebaudioside MD as a food additive will enable Australian and New Zealand food manufacturers to access and use a product assessed as safe that is available to some overseas competitors. This will improve their capacity to compete in overseas markets. See discussion in section 2.5.1.1 above.

- **the promotion of fair trading in food**

FSANZ's assessment based on the best available scientific evidence is that Avansya's rebaudioside MD is safe for use as a food additive. It is therefore appropriate that Australian and New Zealand food industries can also benefit by gaining permission to use Avansya's rebaudioside MD.

- **any written policy guidelines formulated by the Forum on Food Regulation**

The Policy Guideline 'Addition to Food of Substances other than Vitamins and Minerals'[10] includes specific order policy principles for substances added to achieve a solely technological function, such as food additives. These specific order policy principles state that permission should be granted where:

- the purpose for adding the substance can be articulated clearly by the manufacturer as achieving a solely technological function (i.e. the 'stated purpose')
- the addition of the substance to food is safe for human consumption
- the amounts added are consistent with achieving the technological function
- the substance is added in a quantity and a form which is consistent with delivering the stated purpose
- no nutrition, health or related claims are to be made in regard to the substance.

FSANZ determined that permitting Avansya's rebaudioside MD produced by fermentation, is consistent with these specific order policy principles.

3 References

Codex 2019, CXG 36-1989, Class Names and the International Numbering System for Food Additives Accessed 29 April 2021

EC (2012) COMMISSION REGULATION (EU) No 231/2012 of 9 March 2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council. Accessed 29 March 2021

EC (2016) COMMISSION REGULATION (EU) 2016/1814 of 13 October 2016amending the Annex to

[10] Food policy guidelines

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Attachments

A. Approved draft variation to the Australia New Zealand Food Standards Code
B. Explanatory Statement

Attachment A – Approved draft variation to the Australia New Zealand Food Standards Code

Food Standards (Application A1222 – Steviol glycosides from *Yarrowia lipolytica*) Variation

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The Board of Food Standards Australia New Zealand gives notice of the making of this variation under section 92 of the *Food Standards Australia New Zealand Act 1991*. The variation commences on the date specified in clause 3 of this variation.

Dated [To be completed by the Delegate]

[Name and position of Delegate]
Delegate of the Board of Food Standards Australia New Zealand

Note:

This variation will be published in the Commonwealth of Australia Gazette No. FSC XX on XX Month 20XX. This means that this date is the gazettal date for the purposes of clause 3 of the variation.

1 Name

This instrument is the *Food Standards (Application A1222 – Steviol glycosides from* Yarrowia lipolytica*) Variation*.

2 Variation to a Standard in the *Australia New Zealand Food Standards Code*

The Schedule varies a Standard in the *Australia New Zealand Food Standards Code*.

3 Commencement

The variation commences on the date of gazettal.

4 Order in which amendments in the Schedule take effect

Amendments in the Schedule take effect in numerical order.

Schedule

[1] Schedule 3 is varied by

[1.1] omitting subsections S3—39(1) and (2), substituting

(1) This specification relates to a steviol glycosides preparation that:

(a) is obtained from fermentation;

(b) is not obtained from the leaves of the *Stevia rebaudiana* Bertoni plant; and

(c) contains steviol glycosides that are only derived from one of the following:

(i) *Saccharomyces cerevisiae* strain CD15407 containing novel genes for the production of steviol glycosides;

(ii) *Saccharomyces cerevisiae* strain Y63348 containing novel genes for the production of steviol glycosides;

(iii) *Yarrowia lipolytica* strain VRM0014 containing novel genes for the production of steviol glycosides.

[1.2] renumbering subsection S3—39(3) as subsection (2).

Attachment B – Explanatory Statement

1. Authority

Section 13 of the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act) provides that the functions of Food Standards Australia New Zealand (the Authority) include the development of standards and variations of standards for inclusion in the *Australia New Zealand Food Standards Code* (the Code).

Division 1 of Part 3 of the FSANZ Act specifies that the Authority may accept applications for the development or variation of food regulatory measures, including standards. This Division also stipulates the procedure for considering an application for the development or variation of food regulatory measures.

The Authority accepted application A1222 which sought an amendment to the Code to permit the use of a steviol glycosides mixture (primarily consisting of rebaudioside M with lesser amounts of rebaudioside D, that may contain minor amounts of other steviol glycosides), produced by fermentation of simple sugars using a genetically modified *Yarrowia lipolytica* strain, as an intense sweetener (food additive). The steviol glycosides mixture is produced for use as a food additive in the form of a steviol glycosides preparation. The Authority considered the application in accordance with Division 1 of Part 3 of the FSANZ Act and has approved a draft variation.

Following consideration by the Australia and New Zealand Ministerial Forum on Food Regulation, section 92 of the FSANZ Act stipulates that the Authority must publish a notice about the standard or draft variation of a standard.

Section 94 of the FSANZ Act specifies that a standard, or a variation of a standard, in relation to which a notice is published under section 92 is a legislative instrument, but is not subject to parliamentary disallowance or sunsetting under the *Legislation Act 2003*.

2. Purpose

The Authority has approved a draft variation amending section S3—39 to include a new source of steviol glycosides—the applicant's *Yarrowia lipolytica* strain VRM0014 containing novel genes for the production of steviol glycosides, in the list of steviol glycosides sources set out in this section. A steviol glycosides preparation to which section S3—39 applies contains steviol glycosides that are *only* derived from one of the listed sources.

Section S3—39 sets out the identity and purity specifications for steviol glycosides preparations obtained from fermentation, *not* from the leaves of the *Stevia rebaudiana* Bertoni plant.

The effect of these amendments is that the specifications in section S3—39 for steviol glycosides preparations obtained from fermentation apply to the applicant's steviol glycosides preparation.

The above amendments permit the applicant's steviol glycosides preparation to be used as a food additive (intense sweetener) in a food for sale. Use of this steviol glycosides preparation as a food additive must be in accordance with the Code's existing permissions and limits for steviol glycosides, including the requirement that the preparation complies with the specifications set out in section S3—39.

3. Documents incorporated by reference

The variation in this instrument does not incorporate any documents by reference.

However, the instrument will vary Schedule 3 of the Code which does incorporate documents by reference. Section 1.1.1—15 of the Code requires certain substances (such as food additives) to comply with any relevant identity and purity specifications listed in Schedule 3. Schedule 3 incorporates documents by reference to set specifications for various substances in the circumstances specified in that Schedule. The documents incorporated include: the Joint FAO/WHO Expert Committee on Food Additives (JECFA) Compendium of Food Additive Specifications (FAO/WHO 2017); the United States Pharmacopeial Convention (2018) Food Chemicals Codex (11th edition); and the Commission Regulation (EU) No 231/2012.

4. Consultation

In accordance with the procedure in Division 1 of Part 3 of the FSANZ Act, the Authority's consideration of application A1222 included one round of public consultation following an assessment and the preparation of a draft variation and associated assessment summary. Submissions were called for on 11 June 2021 for a six-week consultation period.

The Office of Best Practice Regulation (OBPR) granted the Authority a standing exemption from needing to develop a Regulatory Impact Statement for proposed variations of the Code to permit food additives (OBPR correspondence dated 24 November 2010 - reference 12065). This standing exemption was provided as permitting additional food additives is machinery in nature as it is part of implementing a regulatory framework where the use of the new additive is voluntary once the application has been successfully approved. It is a minor, deregulatory change that allows for the introduction of a new version of a food additive to the food supply that has been determined to be safe.

5. Statement of compatibility with human rights

This instrument is exempt from the requirements for a statement of compatibility with human rights as it is a non-disallowable instrument under section 94 of the FSANZ Act.

6. Variation

Item 1 of the draft variation sets out two amendments to Schedule 3.

Sub-item [1.1] amends Schedule 3 by omitting existing subsections S3—39(1) and (2), and replacing them with a revised subsection (1).

Revised subsection S3—39(1) states that the specification in this section relates to a steviol glycosides preparation that meets all of the following conditions—the preparation:

(a) is obtained from fermentation; and
(b) is not obtained from the leaves of the *Stevia rebaudiana* Bertoni plant; and
(c) contains steviol glycosides that are *only* derived from one of the following:
    (i) *Saccharomyces cerevisiae* strain CD15407 containing novel genes for the production of steviol glycosides;
    (ii) *Saccharomyces cerevisiae* strain Y63348 containing novel genes for the production of steviol glycosides;
    (iii) *Yarrowia lipolytica* strain VRM0014 containing novel genes for the production of steviol glycosides.

Revised subsection S3—39(1) includes a reference to a new source of steviol glycosides i.e. steviol glycosides derived from *Yarrowia lipolytica* strain VRM0014 containing novel genes for the production of steviol glycosides.

Consequently, the specifications set out in section S3—39 also apply to a steviol glycoside preparation containing steviol glycosides (which under A1222 are primarily rebaudioside M,

with lesser amounts of rebaudioside D, and possibly other steviol glycosides) derived from this new source.

Sub-item [1.2] amends Schedule 3 by renumbering subsection S3—39(3) as 'S3—39(2)', as a consequence of the amendment in sub-item [1.1] above.

The consequential effect of these amendments is to permit the following steviol glycoside preparation to be used as a food additive (intense sweetener)–a preparation that:

- is obtained by fermentation (*not* from the leaves of the *Stevia rebaudiana* Bertoni plant); and
- contains the steviol glycosides—rebaudiosides M and D (and possibly other steviol glycosides), derived from *Yarrowia lipolytica* strain VRM0014.

Use of this steviol glycoside preparation as a food additive must be in accordance with the Code's existing permissions and limits for steviol glycosides, including the requirement that the preparation complies with the specifications set out in section S3—39.