

29 November 2019
[103–19]

Call for submissions – Application A1183

Enzymatic production of rebaudioside E from stevia leaf extract

FSANZ has assessed an application made by Blue California to seek approval for a new specification for the steviol glycoside rebaudioside E, produced by an enzymatic conversion method using an enzyme processing aid derived from a genetically modified strain of *Pichia pastoris*. FSANZ has prepared a draft food regulatory measure. Pursuant to section 31 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act), FSANZ now calls for submissions to assist consideration of the draft food regulatory measure.

For information about making a submission, visit the FSANZ website at [information for submitters](#).

All submissions on applications and proposals will be published on our website. We will not publish material that that we accept as confidential, but will record that such information is held. In-confidence submissions may be subject to release under the provisions of the *Freedom of Information Act 1991*. Submissions will be published as soon as possible after the end of the public comment period. Where large numbers of documents are involved, FSANZ will make these available on CD, rather than on the website.

Under section 114 of the FSANZ Act, some information provided to FSANZ cannot be disclosed. More information about the disclosure of confidential commercial information is available on the FSANZ website at [information for submitters](#).

Submissions should be made in writing; be marked clearly with the word ‘Submission’ and quote the correct project number and name. While FSANZ accepts submissions in hard copy to our offices, it is more convenient to receive submissions electronically through the FSANZ website via the link on [documents for public comment](#). You can also email your submission directly to submissions@foodstandards.gov.au.

There is no need to send a hard copy of your submission if you have submitted it by email or via the FSANZ website. FSANZ endeavours to formally acknowledge receipt of submissions within 3 business days.

DEADLINE FOR SUBMISSIONS: 6pm (Canberra time) 23 January 2020

Submissions received after this date will not be considered unless an extension had been given before the closing date. Extensions will only be granted due to extraordinary circumstances during the submission period. Any agreed extension will be notified on the FSANZ website and will apply to all submitters.

Questions about making submissions or the application process can be sent to standards.management@foodstandards.gov.au.

Hard copy submissions may be sent to one of the following addresses:

Food Standards Australia New Zealand
PO Box 5423
KINGSTON ACT 2604
AUSTRALIA
Tel +61 2 6271 2222

Food Standards Australia New Zealand
PO Box 10559
The Terrace WELLINGTON 6143
NEW ZEALAND
Tel +64 4 978 5630

Table of contents

EXECUTIVE SUMMARY	2
1 INTRODUCTION.....	4
1.1 THE APPLICANT	4
1.2 THE APPLICATION.....	4
1.3 THE CURRENT STANDARD	4
1.3.1 <i>Australia and New Zealand standards</i>	4
1.3.2 <i>International standards</i>	6
1.4 REASONS FOR ACCEPTING APPLICATION	7
1.5 PROCEDURE FOR ASSESSMENT	7
2 SUMMARY OF THE ASSESSMENT.....	7
2.1 RISK ASSESSMENT	7
2.2 RISK MANAGEMENT	8
2.2.1 <i>Specification for steviol glycosides</i>	8
2.2.2 <i>Enzyme processing aids</i>	8
2.2.3 <i>Labelling considerations</i>	9
2.2.4 <i>Risk management conclusion</i>	10
2.3 RISK COMMUNICATION.....	10
2.3.1 <i>Consultation</i>	10
2.3.2 <i>World Trade Organization (WTO)</i>	10
2.4 FSANZ ACT ASSESSMENT REQUIREMENTS	11
2.4.1 <i>Section 29</i>	11
2.4.2 <i>Subsection 18(1)</i>	12
2.4.3 <i>Subsection 18(2) considerations</i>	13
3 DRAFT VARIATION	14
4 REFERENCES.....	14
ATTACHMENT A – DRAFT VARIATIONS TO THE <i>AUSTRALIA NEW ZEALAND FOOD STANDARDS CODE</i>	16
ATTACHMENT B – DRAFT EXPLANATORY STATEMENT.....	18

Supporting document

The [following document](#) which informed the assessment of this Application is available on the FSANZ website:

SD1 Risk and technical assessment – Application A1183 – Enzymatic production of rebaudioside E from stevia leaf extract

Executive summary

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. Rebaudioside E is known as a 'minor' steviol glycoside as it is present in the stevia leaf at low levels compared to 'major' steviol glycosides.

Substances used as food additives must comply with any relevant identity and purity specifications listed in Schedule 3 – Identity and Purity. Section S3—35 of Schedule 3 currently includes a specification for steviol glycosides prepared from the leaves of *Stevia rebaudiana* Bertoni, which includes rebaudioside M and rebaudioside D produced by enzymatic conversion.

Blue California has applied to amend the Australia New Zealand Food Standards Code (the Code) to include a new production method in Schedule 3 of the Code for rebaudioside E, a steviol glycoside. The enzyme processing aid used in Blue California's enzymatic conversion method is already permitted by the Code to be used in the manufacture of rebaudioside M and rebaudioside D.

The new production method is based on an enzymatic conversion process using an enzyme processing aid derived from a genetically modified (GM) strain of *Pichia pastoris* (*P. pastoris*). The starting material is purified stevia leaf extract, produced from *Stevia rebaudiana* Bertoni (stevia) leaves using the traditional hot water extraction process. Blue California's product contains no less than 85% rebaudioside E and no less than 95% total steviol glycosides. This preparation is designated as high purity rebaudioside E (≥85% rebaudioside E; ≥95% total steviol glycosides).

The enzymatic conversion method used by Blue California is technologically justified in that it yields a higher amount of rebaudioside E, compared to the low levels in the stevia leaf. Blue California claims that its high purity rebaudioside E preparation has preferential taste characteristics compared to preparations containing major individual steviol glycosides alone.

A risk assessment did not identify any health or safety concerns associated with Blue California's rebaudioside E preparation produced using the specified enzyme processing aid.

Based on the information above and on other relevant considerations, it was deemed appropriate to prepare a draft variation to the specification for steviol glycosides from *Stevia rebaudiana* Bertoni in section S3—35 to include the steviol glycoside rebaudioside E produced from enzymatic conversion, using a specific protein engineered enzyme derived from a GM strain of *P. pastoris*.

The sweetness potency of Blue California's rebaudioside E preparation was determined by Blue California to be approximately 179 times sweeter than sucrose. This is less than that currently in the specification in section S3—35, which is 'approximately 200 to 300 times sweeter than sucrose'. FSANZ proposes to amend the description of steviol glycosides from *Stevia rebaudiana* Bertoni in paragraph S3—35(4)(a) to refer to 'approximately 150 to 300 times sweeter than sucrose'.

It was also considered appropriate to prepare a draft variation to Schedule 18 – Processing aids, to permit the use of a protein engineered enzyme containing a UDP-glucosyltransferase and sucrose synthase (EC 2.4.1.13) component, sourced from *P. pastoris* as a processing aid - for the production of rebaudioside E.

These amendments would allow the use of Blue California's high purity rebaudioside E preparation (≥85% rebaudioside E; ≥95% total steviol glycosides) in accordance with the

Code's existing permissions and limits for steviol glycosides.

1 Introduction

1.1 The Applicant

Blue California is a developer, producer and distributor of intense sweeteners, including steviol glycosides for the global food and beverage industry.

1.2 The Application

Blue California (the applicant) applied to amend the Australia New Zealand Food Standards Code (the Code) to permit an enzymatic conversion process to produce rebaudioside E. The production process results in a highly purified preparation containing no less than 85% rebaudioside E and no less than 95% total steviol glycosides. This preparation is designated as high purity rebaudioside E ($\geq 85\%$ rebaudioside E; $\geq 95\%$ total steviol glycosides). The enzymatic conversion process is enabled by a processing aid, designated as UGT-A¹. UGT-A is a protein engineered enzyme that contains two plant enzymes expressed as a fusion protein, derived from a genetically modified (GM) strain of *Pichia pastoris* (*P. pastoris*). The plant enzymes include an uridine diphosphate (UDP)-glucosyltransferase and a sucrose synthase.

The current permission for rebaudioside E in the Code is for rebaudioside E extracted from *Stevia rebaudiana* Bertoni leaves by hot water extraction. Conversely, the applicant uses an enzymatic conversion method to produce a high purity rebaudioside E preparation, using purified stevia leaf extract as the starting material. Whilst the rebaudioside E produced using enzymatic conversion is identical to that produced from the plant, this production method for rebaudioside E has not previously been assessed by FSANZ. The production method has however been assessed for two other rebaudiosides, rebaudioside M and rebaudioside D, under applications A1157 and A1172 (FSANZ 2018, FSANZ 2019a, respectively).

The applicant has not asked to change the purity specification ($\geq 95\%$ steviol glycosides on a dried basis, under section S3—35 of Schedule 3) or proposed extending the use of rebaudioside E in additional food products. Nor has it proposed to increase or alter the quantities of rebaudioside E in permitted food products.

1.3 The current standard

1.3.1 Australia and New Zealand standards

Australian and New Zealand food laws require food for sale to comply with the following requirements of the Code, as relevant to this application.

1.3.1.1 Food additives

Subsection 1.1.1—10(6) provides that, unless expressly permitted by the Code, a food for sale cannot contain, as an ingredient or component: a substance ‘used as a food additive’.

Section 1.3.1—3 details which substances are permitted to be used as a food additive for the purposes of the Code.

Permission to use ‘steviol glycosides’ is contained in schedule 15. Schedule 15 lists the specific food additive permissions for different categories of foods in the table to section

¹ UGT is an abbreviation of UDP-glucosyltransferase

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 Good Manufacturing Practice (GMP) levels. As 'steviol glycosides' is not a GMP food additive, it is not listed in schedule 16.

Section 1.1.2—11 also provides that a substance is 'used as a food additive' if it is added to a food to perform one or more technological functions listed in Schedule 14 and is one of a number of substances listed in that section. These include a substance identified in the table to section S15—5 as a permitted food additive.

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.

1.3.1.2 Processing aids

Enzymes used in food processing and manufacturing are considered processing aids as although they may be present in the final food, they no longer provide a technological purpose in the final food.

Paragraph 1.1.1—10(6)(c) provides that a food for sale must not have, as an ingredient or a component, a substance that is used as a processing aid, unless expressly permitted.

Section 1.1.2—13 defines the expression 'used as a processing aid'. That definition imposes certain conditions on substances permitted by Standard 1.3.3 and Schedule 18 to be used as a processing aid, such that it does not perform a technological function in the final food for sale.

Standard 1.3.3 and Schedule 18 list the permitted processing aids. Enzymes of microbial origin permitted to be used as processing aids are listed in the table to subsection S18—4(5) or in the table to subsection S18—9(3) of Schedule 18, depending on whether a technological purpose has been specified.

1.3.1.3 Food produced using gene technology

Paragraph 1.1.1—10(6)(g) requires that the presence of a food produced using gene technology as an ingredient or component in a food for sale must be expressly permitted by the Code. Section 1.5.2—3 of the Code provides that permission for use as a food additive or processing aid also constitutes the permission required by paragraph 1.1.1—10(6)(g).

1.3.1.4 Identity and purity requirements

Paragraphs 1.1.1—15(1)(a) and (b) require substances used as food additives and processing aids respectively, to comply with any relevant identity and purity specifications listed in Schedule 3.

Section S3—35 of Schedule 3 provides a specification for steviol glycosides prepared from the leaves of *Stevia rebaudiana* Bertoni.

1.3.1.5 Labelling requirements

Paragraph 1.1.1—10(8) of the Code provides that the labelling of a 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 of Standard 1.5.2 outlines requirements for labelling of certain foods for sale that consist of or have as an ingredient, food that is a genetically modified food. For the purposes of the Code, *genetically modified food* is defined in subsection 1.5.2—4(5) as a *food produced using gene technology* that contains novel DNA or novel protein or is listed in section S26—3.

1.3.2 International standards

Steviol glycosides are approved for use in a number of other jurisdictions, including the European Union, Canada, United States of America (USA), South America, Asia, the Middle East and Africa (PureCircle Stevia Institute, 2019). The applicant's rebaudioside E preparation is considered Generally Recognised as Safe (GRAS) in the USA for use as a table top sweetener and as a general purpose non-nutritive sweetener in foods (USFDA 2019). Information regarding the USA, Canada and European Union regulations, and standards developed by the international bodies Joint FAO/WHO Expert Committee on Food Additives (JECFA) and Codex Alimentarius is provided below.

1.3.2.1 Codex Alimentarius

Codex Alimentarius is an international body, incorporating the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO), that sets international food standards. Codex Alimentarius has a General Standard for Food Additives (GSFA, CODEX STAN 192-1995) that contains provisions for food additives in various food categories (Codex 2019a). The GSFA contains permissions for the addition of steviol glycosides (as steviol equivalents) to a wide variety of food categories up to maximum permitted levels.

1.3.2.2 Joint FAO/WHO Expert Committee on Food Additives (JECFA)

FAO JECFA Monograph 20 includes a specification for steviol glycosides obtained from a hot water extraction from the leaves of *S. rebaudiana* Bertoni ('Steviol glycosides from *Stevia rebaudiana* Bertoni') (JECFA 2017). This specification does not apply to steviol glycosides produced by enzymatic conversion. The specification includes a mixture of any of the steviol glycosides extracted from the stevia leaf rather than an earlier defined list of steviol glycosides. The purity of steviol glycosides from *S. rebaudiana* Bertoni must be no less than 95% total steviol glycosides on the dried basis.

JECFA considered specifications for steviol glycosides at their 87th meeting in June 2019. A framework was adopted for developing specifications for steviol glycosides produced by four different methods, including enzyme modified steviol glycosides. This new specification is yet to be published (FAO/WHO 2019).

1.3.2.3 United States of America (USA)

In the USA there have been over 50 GRAS notifications relating to steviol glycosides

submitted to the USA Food and Drug Administration (FDA) for review. GRN No. 823 relates to the same production method and preparation as this application. GRN No. 823 was submitted by the applicant in 2018 and the US FDA responded with 'no questions' to the GRAS status². Therefore, the applicant's rebaudioside E is considered GRAS for use as a table top sweetener and as a general purpose non-nutritive sweetener in foods (USFDA 2019).

1.3.2.4 Canada

In Canada 'Steviol glycosides from *Stevia rebaudiana* Bertoni' are permitted in a variety of foods, provided they comply with the relevant international specifications for steviol glycosides (either JECFA or Food Chemicals Codex) and relevant conditions for use and requirements of the Food and Drug Act (Health Canada 2019).

1.3.2.5 European Union

Steviol glycosides preparations are permitted as food additives in a variety of different food categories (European Commission 2011) provided they comply with the European Commission specifications for steviol glycosides (European Commission 2016). The specification applies only to steviol glycosides preparations extracted from the leaves of the *S. rebaudiana* Bertoni plant using traditional methods.

1.4 Reasons for accepting Application

The Application was accepted for assessment because:

- it complied with the procedural requirements under subsection 22(2) of the FSANZ Act
- it related to a matter that warranted the variation of a food regulatory measure.

1.5 Procedure for assessment

The Application is being assessed under the General Procedure.

2 Summary of the assessment

2.1 Risk assessment

FSANZ has carried out an assessment to determine whether there are any potential public health and safety concerns associated with the applicant's high purity rebaudioside E preparation ($\geq 85\%$ rebaudioside E; $\geq 95\%$ total steviol glycosides), produced using the specified enzyme processing aid (see SD1).

The enzyme processing aid UGT-A has previously been assessed and approved under application A1157 (FSANZ 2018).

An acceptable daily intake (ADI) of 0-4 mg/kg bodyweight for steviol glycosides, expressed as steviol, was established by FSANZ in 2008 and JECFA in 2009, and confirmed at their 82nd meeting in 2016. This ADI is appropriate for rebaudioside E produced using enzymes from *GM P. pastoris* as it is chemically the same as rebaudioside E extracted traditionally from *Stevia rebaudiana* Bertoni and would therefore follow the same metabolic pathway in humans. Toxicological and other relevant data published subsequent to FSANZ's previous assessments of steviol glycosides raised no concerns regarding the safety of steviol

² 'No questions' response means the FDA does not question the basis for the notifier's GRAS conclusion (USFDA 2016).

glycosides and did not indicate a need to amend the ADI.

FSANZ is aware that a number of research papers have reported on possible links between consumption of intense sweeteners and unwanted metabolic effects resulting in weight gain, but considers that the current weight of evidence does not support a causal relationship. FSANZ will continue to monitor the emerging scientific literature in this area.

The applicant is not requesting a change to the foods permitted to contain steviol glycosides as a food additive nor do they propose to increase the maximum permitted levels of steviol glycosides in foods. FSANZ has previously conducted a dietary exposure assessment using the current permissions to use steviol glycosides as a food additive and therefore no dietary exposure assessment was necessary for this application.

In conclusion, FSANZ's risk assessment has not identified any safety concerns associated with the applicant's high purity rebaudioside E preparation ($\geq 85\%$ rebaudioside E; $\geq 95\%$ total steviol glycosides), produced using the enzyme processing aid UGT-A.

2.2 Risk management

2.2.1 Specification for steviol glycosides

Based on the conclusion that there are no public health and safety concerns, and on other considerations detailed in section 2.4 below, it was considered appropriate to prepare an amendment to the specification for steviol glycosides from *Stevia rebaudiana* Bertoni (section S3—35 of the Code) to include rebaudioside E produced by an enzymatic conversion method using specific processing aids derived from a GM strain of *P. pastoris*.

Amending the steviol glycoside specification ensures rebaudioside E produced by enzymatic conversion has the same permissions for use as a food additive as other steviol glycosides already included in specifications in the Code. The new specification refers to the production of rebaudioside E via enzymatic conversion. It is not necessary to add a new specification for the approximately 10% of other steviol glycosides contained in the applicant's rebaudioside E preparation, as they already comply with section S3—35 of the Code.

The sweetness equivalency to sucrose of the applicant's high purity rebaudioside E product ($\geq 85\%$ rebaudioside E; $\geq 95\%$ steviol glycosides) was reported in the application to be 137 times sweeter than sucrose upon evaluation by a sensory panel. The applicant has subsequently provided additional information, which shows that the sweetness is approximately 179 times sweeter than sucrose. Paragraph S3—35(4)(a) of the Code describes the sweetness level for steviol glycosides as 'approximately 200 to 300 times sweeter than sucrose'. FSANZ therefore proposes to amend paragraph S3—35(4)(a), for the purposes of A1183, to refer to the sweetness level for steviol glycosides as 'approximately 150 to 300 times sweeter than sucrose'.

However, FSANZ notes that under the Call for Submissions for A1176, it was also proposed that the sweetness potency be amended to 'approximately 150 to 300 times as sweet as sucrose' (FSANZ 2019b). The amendment to paragraph S3—35(4)(a) of the Code proposed for the purposes of A1183 will not be required if the proposed change under A1176 is approved before the completion of A1183.

2.2.2 Enzyme processing aids

It was also considered appropriate to propose an amendment to Schedule 18 to extend the use of the protein engineered enzyme UGT-A sourced from a GM strain of *P. pastoris* to include production of rebaudioside E. This will ensure compliance with the Code in regards to the use of the processing aid, and the very low possibility of the processing aid being present

in the final rebaudioside E preparation.

This express permission for the enzyme's use as a processing aid will also provide the permission for the potential presence in the rebaudioside E steviol glycoside preparation as a food produced using gene technology. FSANZ considers the processing aid is a food produced using gene technology for Code purposes as it is derived from 'an organism that has been modified using gene technology' (i.e. GM microorganisms).

2.2.3 Labelling considerations

2.2.3.1 Ingredient labelling

Under existing labelling requirements in the Code (unless the food is exempt from the requirement for a statement of ingredients) the applicant's rebaudioside E preparation would require declaration as a food additive in the statement of ingredients on the label of foods. These ingredient labelling requirements currently 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 the proposed change to the Code is to the specification rather than approval of the rebaudioside E itself as a food additive, the existing labelling requirements relating to steviol glycosides would apply.

The Codex Committee on Food Additives (CCFA) at its 50th Session (March 2018) updated the INS numbers for steviol glycosides, which were subsequently adopted into the Class Names and International Numbering System for Food Additives (CXG 36-1989) by the Codex Alimentarius Commission (Codex 2019b). 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). As CCFA has not completed its work on the production method described in this application, a new INS number is not assigned at the present time.

When considering A1170, A1172 and A1176, FSANZ decided not to include 960a and 960b in the Code at that stage for various reasons (FSANZ 2019c, FSANZ 2019a, FSANZ 2019b). These reasons included the desire to provide a more coordinated approach and efficient transition for the labelling of steviol glycosides produced by all new novel methods of production compared to an unsystematic or ad-hoc approach for individual methods of production through various applications. This also maintains a level playing field for suppliers of steviol glycosides or for manufacturers of foods containing steviol glycosides produced using novel production methods, given INS numbers are not available for all methods.

For these reasons, FSANZ considers that the most appropriate INS number for labelling purposes, for all steviol glycosides at this stage, is 960. FSANZ will consider changes to this INS number in the future, if further changes are made to the INS list.

The FSANZ website has been updated to provide information on the new production methods. This advises consumers wanting to know the source of any particular steviol glycosides in foods that they can ask the manufacturer who should advise them accordingly.

In terms of the enzymes used as processing aids, paragraphs 1.2.4—3(2)(d) and (e) of the Code exempts processing aids from the requirement to be declared in the statement of ingredients. This exemption will apply to the processing aids approved in this application.

2.2.3.2 Labelling as 'genetically modified'

Section 1.5.2—4 of the Code requires certain foods for sale that consist of or have as an ingredient, food that is genetically modified to be labelled with the statement 'genetically

modified'. The Code's labelling requirements imposed by section 1.5.2—4 apply to foods for retail sale and to foods sold to a caterer under subsection 1.2.1—8(1) and section 1.2.1—15 respectively.

FSANZ's assessment is that Blue California's rebaudioside E ($\geq 85\%$ rebaudioside E; $\geq 95\%$ total steviol glycosides) is not a food produced using gene technology as it is not derived from an organism that has been modified using gene technology. This is in contrast to the enzyme processing aid used for its manufacture, which is a food produced using gene technology for Code purposes. As such, Blue California's rebaudioside E preparation does not require labelling as 'genetically modified'.

The enzyme used as a processing aid to manufacture Blue California's high purity rebaudioside E preparation is highly unlikely to be present as an ingredient in food for sale which contains this preparation. Furthermore, it is understood that the rebaudioside E preparation itself would not be sold for retail sale or to a caterer because it is a highly concentrated intense sweetener. As such, it is highly likely that the requirement to label the processing aid as 'genetically modified' would not apply to a food for sale that contains the rebaudioside E preparation because the labelling requirements only apply to food that consists of, or has as an ingredient, a genetically modified food under section 1.5.2—4.

2.2.4 Risk management conclusion

Taking account of the risk assessment conclusions in section 2.1 and other considerations outlined in section 2.4 below, the risk management conclusion is to permit the applicant's method of producing high purity rebaudioside E preparation ($\geq 85\%$ rebaudioside E; $\geq 95\%$ total steviol glycosides), i.e. rebaudioside E produced by an enzymatic conversion method using a specific enzymatic processing aid derived from a GM strain of *P. pastoris*.

The protein engineered processing aid (containing a UDP-glucosyltransferase and a sucrose synthase (EC 2.4.1.13)) used to produce rebaudioside E will also be listed as an enzymatic processing aid in subsection S18—9(3). The permission is already in place for the enzymatic production of rebaudioside D and is one of the processing aids required for the enzymatic production of rebaudioside M. The A1183 draft variation was drafted subject to proposed amendments by A1176 to section S3—35.

2.3 Risk communication

2.3.1 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 are notified via the Food Standards Notification Circular, media release, FSANZ's social media tools and Food Standards News.

The process by which FSANZ considers standard development matters is open, accountable, consultative and transparent. Public submissions are 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.

The draft variation will be considered for approval by the FSANZ Board taking into account public comments received from this call for submissions.

2.3.2 World Trade Organization (WTO)

As members of the World Trade Organization (WTO), Australia and New Zealand are obliged

to notify WTO members where proposed mandatory regulatory measures are inconsistent with any existing or imminent international standards and the proposed measure may have a significant effect on trade.

There are relevant international standards for steviol glycosides. Amending the Code to include a new identity and purity specification for rebaudioside E produced by an enzymatic conversion method is unlikely to have a significant effect on international trade as the specification is not substantially different to the international specification for other steviol glycosides produced by the traditional hot water extraction method. Therefore, a notification to the WTO under Australia's and New Zealand's obligations under the WTO Technical Barriers to Trade or Application of Sanitary and Phytosanitary Measures Agreement was not considered necessary.

2.4 FSANZ Act assessment requirements

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

2.4.1 Section 29

2.4.1.1 Consideration of costs and benefits

The Office of Best Practice Regulation (OBPR) granted FSANZ a standing exemption from the requirement to develop a Regulation Impact Statement for the approval of additional processing aids or food additives (OBPR correspondence dated 24 November 2010, reference 12065). This standing exemption was provided as permitting additional processing aids or 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, has given consideration to the costs and benefits that may arise from the proposed measure for the purposes of meeting FSANZ Act requirements. 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 is 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 considers to either approve or reject the application (retain the status quo). This analysis considers amending the Code to include the food additive, i.e. a new specification for rebaudioside E produced by an enzymatic conversion method using a specific processing aid.

The consideration of the costs and benefits in this section is not intended to be an exhaustive, quantitative economic analysis of the proposed measure and, in fact, most of the effects that were considered cannot easily be assigned a dollar value. Rather, the assessment seeks to highlight the likely positives and negatives of moving away from the status quo by amending the Code as requested.

FSANZ's conclusions regarding costs and benefits of the proposed measure is set out below. However, information received from the call for submissions may result in FSANZ arriving at different conclusions.

Costs and benefits of including a new specification for rebaudioside E produced by an enzymatic conversion method using a specific processing aid

Steviol glycosides, in general, can be used as intense sweeteners in reduced energy and no-added sugar products.

The applicant may have an advantage over other intense sweetener manufacturing businesses from this voluntary permission. The applicant agreed with FSANZ and acknowledged in correspondence after submitting its application that there is an exclusive capturable commercial benefit. The impact on other competing Australia-New Zealand manufacturers is unknown.

The applicant and down-stream retailers may reduce prices for the consumer in some existing products containing the food additive in this application, where there are cost savings from using it. Due to the voluntary nature of the permission, the applicant will only produce and downstream retailers will only use the food additive (prepared using the specific enzyme processing aid) where they believe a net benefit exists. There are other methods available to produce steviol glycosides and steviol glycosides of other sweetness profiles are available.

There may also be greater substitution from products containing sugar or other sweeteners that have a less attractive taste, to products containing the steviol glycosides in this application. That may increase the quality and choice of food products available to consumers.

The greater choice for consumers (highlighted above) may allow them to further maximise their utility by choosing a food or drink they may prefer, including more choice of food or drink with reduced energy content. It may also result in some products becoming cheaper.

Permitting the food additive and associated enzyme processing aid may result in a small cost to government in terms of adding these to the current range of food additives and processing aids that are monitored for compliance.

Conclusions from cost benefit considerations

FSANZ's assessment is that the direct and indirect benefits that would arise from permitting the use of the food additive and enzyme processing aid in question most likely outweigh the associated costs.

2.4.1.2 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.

2.4.1.3 Any relevant New Zealand standards

The Standards and Schedules relevant to the draft variation apply in both Australia and New Zealand. There are no relevant New Zealand Standards.

2.4.1.4 Any other relevant matters

Other relevant matters are considered below.

2.4.2 Subsection 18(1)

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

2.4.2.1 Protection of public health and safety

FSANZ concluded that there are no public health and safety concerns associated with the use of the high purity rebaudioside E preparation ($\geq 85\%$ rebaudioside E; $\geq 95\%$ steviol glycosides) produced by an enzymatic conversion method using a processing aid (a protein engineered enzyme that contains both uridine diphosphate (UDP) glucosyltransferase, and sucrose synthase (EC 2.4.1.13)); derived from a genetically modified strain of *P. pastoris*. For further detail refer to section 2.1 above and SD1.

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

The generic labelling requirements will apply when these steviol glycoside preparations are added to food as an ingredient (see section 2.2.3 above).

2.4.2.3 The prevention of misleading or deceptive conduct

No issues have been identified with this application relevant to this objective.

2.4.3 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 the application. Other technical information including scientific literature was also identified and used by FSANZ 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, the majority of which relate to steviol glycosides extracted directly from stevia leaves rather than by enzymatic conversion. As outlined in section 1.3.2.2, JECFA recently adopted a framework for developing specifications for steviol glycosides by four different methods of production, including enzyme modified steviol glycosides (FAO/WHO 2019).

The applicant's rebaudioside E is permitted for use in the USA.

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

Permission to use this particular rebaudioside E preparation as a food additive will provide additional choice to Australian and New Zealand food manufacturers, enabling access to an intense sweetener with preferential taste characteristics compared to preparations containing major individual steviol glycosides alone.

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

No issues were identified for this application relevant to this objective

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

The Policy Guideline ‘Addition to Food of Substances other than Vitamins and Minerals’³ 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 has determined that the addition to food of the applicant’s rebaudioside E preparation would be consistent with these specific order policy principles.

3 Draft variation

The draft variation to the Code is at Attachment A and is intended to take effect on gazettal.

A draft 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.

4 References

Codex 2019a, General Standard for Food Additives,
<http://www.fao.org/gsaonline/index.html;jsessionid=64CA5BB29D301405C4DD6FA3239EA22D>
Accessed 7 October 2019

Codex 2019b, CXG 36-1989, Class Names and the International Numbering System for Food Additives <http://www.fao.org/fao-who-codexalimentarius/codex-texts/guidelines/en/> Accessed 7 October 2019

European Commission 2011, Commission Regulation (EU) No 1131/2011 of 11 November 2011 amending Annex II to Regulation (EC) No 1333/2008 of the European Parliament and of the Council with regard to steviol glycosides. Available at <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32011R1131&from=EN> Accessed 7 October 2019

European Commission 2016, Commission Regulation (EU) 2016/1814 of 13 October 2016 amending the Annex to Regulation (EU) No 231/2012 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 as regards specifications for steviol glycosides (E 960). Off J Eur Union 59(L278):37-41. Available at: <https://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1570415600099&uri=CELEX:32016R1814> Accessed 7 October 2019

FAO/WHO (2019) Joint FAO/WHO Expert Committee on Food Additives, Eighty-seventh meeting, Rom, 4-13 June 201. Summary and Conclusions. Available at https://www.who.int/foodsafety/areas_work/chemical-risks/JECFA87_Summary_Report.pdf?ua=1 Accessed 7 October 2019

FSANZ (2018) Application A1157 [Enzymatic production of rebaudioside M](#). Food Standards Australia New Zealand, Canberra.

FSANZ (2019a) Application A1172 [Enzymatic production of rebaudioside D](#). Food Standards Australia

³ <http://foodregulation.gov.au/internet/fr/publishing.nsf/Content/publication-Policy-Guideline-on-the-Addition-of-Substances-other-than-Vitamins-and-Minerals>

New Zealand, Canberra.

FSANZ (2019b) Application A1176 [Enzymatic production of steviol glycosides](#). Food Standards Australia New Zealand, Canberra.

FSANZ (2019c) Application A1170 [Rebaudioside MD as a steviol glycoside from *Saccharomyces cerevisiae*](#). Food Standards Australia New Zealand, Canberra.

Health Canada 2019, 9. List of Permitted Sweeteners (Lists of Permitted Food Additives). Available at <https://www.canada.ca/en/health-canada/services/food-nutrition/food-safety/food-additives/lists-permitted/9-sweeteners.html> Accessed 7 October 2019

JECFA (2017). Steviol glycosides from *Stevia rebaudiana Bertoni* [New specifications prepared at the 84th JECFA, 2017), Superseding tentative specifications prepared at the 82nd JECFA (2016)]. In: *Compendium of Food Additive Specifications*. 84th Meeting, Rome, 6-15 June 2017 (FAO JECFA Monographs 20). Rome, Italy: Food and Agriculture Organization of the United Nations (FAO) /Geneva, Switz.: World Health Organization (WHO), pp. 50-69. Available at: <http://www.fao.org/documents/card/en/c/4b06cdda-3e70-4c80-b7e5-56034601836b/> Accessed 7 October 2019

PureCircle Stevia Institute 2019, Map Infographic Where in the World is Stevia Approved? <https://www.purecirclestevia.com/resources/infographics/map-infographic> Accessed 7 October 2019

USFDA (2016) [About the GRAS Notification Program](#), October 2016. Accessed 7 October 2019.

USFDA (2019). GRAS Notices Inventory. Washington (DC): U.S. Food and Drug Administration (U.S. FDA). Available at: <https://www.accessdata.fda.gov/scripts/fdcc/index.cfm?set=GRASNotices> Accessed 7 October 2019

Attachments

- A. Draft variations to the *Australia New Zealand Food Standards Code*
- B. Draft Explanatory Statement

Attachment A – Draft variations to the *Australia New Zealand Food Standards Code*



Food Standards (Application A1183 – Enzymatic production of Rebaudioside E) Variation

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 Delegate]

[Insert name and title 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.

Schedule

1 Name

This instrument is the *Food Standards (Application A1183 – Enzymatic production of Rebaudioside E) Variation*.

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

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

3 Commencement

The variation commences on the date of gazettal.

Schedule

[1] Schedule 3 is varied by

[1.1] omitting subparagraph S3—35(2)(d)(iii), substituting

- (iii) a sucrose synthase (EC 2.4.1.13) sourced from *Escherichia coli*;
- (e) by enzymatic conversion of purified stevia leaf extract to produce rebaudioside E using a protein engineered enzyme that:
 - (i) contains both of the following components:
 - (A) UDP-glucosyltransferase; and
 - (B) sucrose synthase (EC 2.4.1.13); and
 - (ii) is sourced from *Pichia pastoris* strain UGT-A.

[1.2] omitting paragraph S3—35(4)(a), substituting

- (a) Description—white to light yellow powder, approximately 150 to 300 times sweeter than sucrose;

[2] Schedule 18 is varied by inserting in the table to subsection S18—9(3), in alphabetical order

Protein engineered enzyme that:	For the conversion of purified stevia leaf	GMP
(a) contains both of the following components -	extract to produce rebaudioside E.	
(i) UDP-glucosyltransferase;		
and		
(ii) sucrose synthase (EC		
2.4.1.13); and		
(b) is sourced from <i>Pichia pastoris</i>		
strain UGT-A.		

Attachment B – Draft 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 A1183 which seeks approval for a new specification for the steviol glycoside rebaudioside E produced by an enzymatic conversion method using a processing aid derived from a genetically modified strain of *Pichia pastoris*. The Authority considered the Application in accordance with Division 1 of Part 3 and has prepared a draft Standard.

2. Purpose

The Authority has prepared a draft variation for the following purposes:

- a. Amend the specification of steviol glycosides from *Stevia rebaudiana* Bertoni in subsection S3—35(2) of the Code to:
 - i. include, in that specification, a reference to the enzymatic conversion method used to produce the A1183 applicant's rebaudioside E (this would permit steviol glycoside preparations containing rebaudioside E produced by that method to be used as a food additive in accordance with the existing permissions and limits for steviol glycosides in the Code); and
 - ii. increase the sweetness range in the description for steviol glycosides from *Stevia rebaudiana* Bertoni from 'approximately 200 to 300 times sweeter' to 'approximately 150 to 300 times sweeter' than sucrose.
- b. Amend Schedule 18 of the Code to permit a particular substance to be used as a processing aid in the manufacture of the A1183 applicant's rebaudioside E preparation in accordance with Standard 1.3.3 of the Code

3. Documents incorporated by reference

The variations to food regulatory measures do not incorporate any documents by reference.

4. Consultation

In accordance with the procedure in Division 1 of Part 3 of the FSANZ Act, the Authority's consideration of Application A1183 will include one round of public consultation following an assessment and the preparation of a draft variation and associated assessment summary.

A Regulation Impact Statement was not required because the proposed variations to Schedules 3 and 18 are likely to have a minor impact on business and individuals (OBPR reference 12065).

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

6.1 Item [1]

Item [1] amends section S3—35 of the Code which sets out the specification for steviol glycosides from *Stevia rebaudiana* Bertoni.

Item [1.1] amends subsection S3—35(2) by omitting subparagraph S3—35(2)(d)(iii) and inserting in its place subparagraph S3—35(2)(d)(iii) and new paragraph S3—35(2)(e).

Paragraph S3—35(2)(d) will be inserted into the Code by the draft variation for Application A1176, subject to approval. The amendment made by item [1.1] changes the punctuation at the end of that paragraph to reflect the addition of new paragraph S3—35(2)(e).

New paragraph S3—35(2)(e) specifies the following process by which a steviol glycosides preparation can be obtained from the leaves of the *Stevia rebaudiana* Bertoni plant—the enzymatic conversion of purified stevia leaf extract to produce rebaudioside E using a protein engineered enzyme that contains both uridine diphosphate (UDP) glucosyltransferase, and sucrose synthase (EC 2.4.1.13); and is sourced from *Pichia pastoris* (strain UGT-A).

The effect of inserting new paragraph S3—35(2)(e) is to permit a steviol glycoside preparation to contain rebaudioside E produced using the above enzymatic conversion process to be used as a food additive, in accordance with the existing food additive permissions in the Code for steviol glycosides.

Item [1.2] increases the sweetness range in the description for steviol glycoside preparations obtained from the leaves of the *Stevia rebaudiana* Bertoni plant from ‘approximately 200 to 300 times sweeter than sucrose’ to ‘approximately 150 to 300 times sweeter than sucrose’.

6.2 Item [2]

Item [2] amends Schedule 18 by inserting a new entry into the table to subsection S18—9(3). This table lists permitted substances that may be used as processing aids for specific technological purposes.

The new entry lists a protein engineered enzyme containing both of the following components: UDP-glucosyltransferase, and sucrose synthase (EC 2.4.1.13); and which is sourced from *Pichia pastoris* strain UGT-A.

The specified technological purpose for this enzyme is the conversion of purified stevia leaf extract to produce rebaudioside E.

The maximum permitted level at which the enzyme may be present in food must be consistent with Good Manufacturing Practice (as defined by section 1.1.2—2(3) of the Code).