

**27 August 2019**  
**[92–19]**

## **Call for submissions – Application A1176**

### **Enzymatic production of Steviol Glycosides**

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FSANZ has assessed an Application made by PureCircle Limited to seek approval for a new specification for steviol glycosides produced by an enzymatic conversion method using enzymes derived from genetically modified strains of *Escherichia coli*. 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 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](mailto: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) 8 October 2019**

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](mailto:standards.management@foodstandards.gov.au).

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

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## Supporting document

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

SD1           Risk assessment – Application A1176 – Enzymatic production of Steviol Glycosides

## Executive summary

PureCircle Limited (PureCircle) has applied to amend the Australia New Zealand Food Standards Code (the Code) to permit an enzymatic conversion method to produce steviol glycoside preparations. The method uses three enzymes derived from genetically modified (GM) strains of *Escherichia coli* K-12, namely two UDP-glucosyltransferases and sucrose synthase. The resulting three different steviol glycoside preparations have a high content of Rebaudiosides M and/or D, or Rebaudioside (Reb) AM, subject to the starting material (Reb A or stevioside respectively). The starting material is extracted from the *Stevia rebaudiana* Bertoni (stevia) leaves. Reb M, D and AM are known as 'minor' steviol glycosides as they are present in the stevia leaf at low levels compared to other 'major' steviol glycosides.

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.

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 Reb M and Reb D produced by enzymatic conversion. The source of the enzymes used by PureCircle and one of the resulting steviol glycoside preparations (high in Reb AM) are however, different to those already included in the specification.

The processing aids used in PureCircle's enzymatic conversion method are not currently permitted to be used by the Code.

FSANZ has therefore carried out an assessment to determine whether there are any potential public health and safety concerns associated with PureCircle's steviol glycoside preparations produced using the specified enzyme processing aids. This risk assessment did not identify any health or safety concerns.

The enzymatic conversion method used by PureCircle is technologically justified in that it yields higher amounts of steviol glycosides that are present in stevia leaves in 'minor' amounts. PureCircle claims preparations containing these steviol glycosides have preferential taste characteristics compared to preparations containing major individual steviol glycosides alone.

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 (S3—35) to include steviol glycosides (Reb D, Reb M and Reb AM) produced from enzymatic conversion using specific enzymes derived from GM strains of *E. coli*.

Additionally, the sweetness potency of preparations of steviol glycosides with a high Reb AM content was determined by PureCircle to be approximately 150 times sweeter than sucrose. This is less than that currently in the specification in S3—35, which is approximately 200-300 times sweeter than sucrose. FSANZ therefore proposes to also amend the specification to refer to approximately 150-300 times sweeter than sucrose.

It was also considered appropriate to prepare a draft variation to Schedule 18 – Processing aids permitting the use of the protein engineered enzymes UDP-glucosyltransferase and sucrose synthase, sourced from (GM) *E. coli* as processing aids for the production of Reb D, Reb M or Reb AM.

The express permission for the enzymes' use as processing aids will also provide the required permission for their potential presence in the steviol glycoside preparations as a food produced using gene technology. The enzymes are food produced using gene technology for Code purposes as they are derived from 'an organism that has been modified using gene technology'.

These amendments would allow the use of PureCircle's steviol glycoside preparations in accordance with the Code's existing permissions and limits for steviol glycosides.

# 1 Introduction

## 1.1 The Applicant

PureCircle Limited (PureCircle) is a producer of high purity steviol glycoside ingredients for the global food and beverage industry. PureCircle has offices in the United States of America and in Malaysia.

## 1.2 The Application

PureCircle has applied to amend the Australia New Zealand Food Standards Code (the Code) to permit an enzymatic conversion process using specified enzymes to produce steviol glycoside preparations. The enzymes used are derived from GM strains of *Escherichia coli* K 12, namely UDP-glucosyltransferases and sucrose synthase.

The resulting steviol glycoside preparations have a high content of the minor rebaudiosides, Rebaudiosides (Reb) M and/or Reb D, or Reb AM, subject to the starting material (Reb A or stevioside respectively). The starting material is extracted from the *Stevia rebaudiana* Bertoni (stevia) leaves. Reb M, D and AM are known as ‘minor’ steviol glycosides as they are present in the stevia leaf at low levels compared to other ‘major’ steviol glycosides.

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

## 1.3 The current standards

### 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. The permitted food additives for different food categories are listed in the table to section S15—5.

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 of that schedule provides that use as an intense sweetener is a permitted purpose.

Schedules 15 and 16 list the specific food additive permissions for different categories of foods.

#### 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 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 of the Code provides that permission for use as a 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) requires 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.

## **1.3.2 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, 2018). FSANZ understands that the three steviol glycoside preparations produced using the specific enzymatic conversion method in this application are not approved in Canada or Europe, and in the USA there is a Generally Recognized as Safe (GRAS) notice for the steviol glycosides preparation with a high Reb M content. Further detail for these countries, as well as standards developed by the international bodies JECFA and Codex Alimentarius is provided below.

### **1.3.2.1 Codex Alimentarius**

Codex Alimentarius is an international body, incorporating the Food and Agriculture Organisation 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 2018a). 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)**

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.

Although not directly related to this Application, it is of relevance to note that in the next Code Maintenance Proposal FSANZ will consider the need to omit the existing specifications S3—31 – Specification for rebaudioside M and S3—32 – Specification for steviol glycoside mixture including rebaudioside M as these are now covered by JECFA Monograph 20 which is referenced in S3—2. Additionally, FSANZ will consider the need to amend S3—35 to remove reference to steviol glycoside preparations obtained from the leaves of the *Stevia rebaudiana* Bertoni plant for the same reason.

The Joint FAO/WHO Expert Committee on Food Additives considered specifications for steviol glycosides at their 87<sup>th</sup> meeting in June 2019. A framework was adopted for developing specifications for steviol glycosides by four different methods of production, 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 Generally Recognised as Safe (GRAS) notices relating to steviol glycosides submitted to the USA Food and Drug Administration (FDA) for review. In particular the FDA issued a ‘no questions’<sup>1</sup> response to PureCircle’s GRAS notice for steviol glycosides with a high Reb M content produced by enzymatic conversion of Reb A from stevia leaf extract (GRN 745). To date, excluding pending notifications, the US FDA has not raised any objections to the GRAS status of these steviol glycoside products for use as a 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 2018).

### **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.

## **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.

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<sup>1</sup> ‘No questions’ response means the FDA does not question the basis for the notifier’s GRAS conclusion (USFDA 2016).

## 1.5 Procedure for assessment

The Application is being assessed under the General Procedure of the FSANZ Act.

# 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 PureCircle's steviol glycoside preparations prepared using the specified enzyme processing aids.

The host strain for the enzyme processing aids, *E. coli* K-12, is not pathogenic or toxigenic and has a history of use for the production of food enzymes. Genes for three enzymes were introduced into *E. coli* K-12, generating three distinct production strains. Molecular characterisation of the production strains has confirmed the enzyme coding sequence is as expected and has not undergone any rearrangement, and the introduced DNA is stably inherited. The production strains have also been shown to be genetically stable.

Previous assessments of steviol glycosides by FSANZ and JECFA have confirmed that steviol glycosides share a metabolic pathway to steviol, which is then glucuronidated and excreted in the urine. The unpublished data presented in the current application confirm that Reb AM, an isomer of Reb D, is also metabolised to steviol.

Individual steviol glycosides produced using enzymes from GM *E. coli* are chemically the same as the equivalent individual steviol glycoside extracted directly from leaves of *Stevia rebaudiana* Bertoni. Evidence has been provided that proteins used in production have been effectively removed and do not pose an allergenic hazard.

No new evidence of adverse effects of steviol glycosides has been identified that would justify changing the ADI of 0 to 4 mg/kg body weight, expressed as steviol, for steviol glycosides previously established by FSANZ. This is therefore appropriate for steviol glycosides produced by enzymatic conversion using enzymes produced by GM *E. coli* that are the subject of this application.

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.

In conclusion, FSANZ's risk assessment has not identified any health or safety concerns associated with PureCircle's steviol glycosides preparations.

## 2.2 Risk management

### 2.2.1 Specification for steviol glycosides

Based on the conclusion above, that there are no public health and safety risks, and on other considerations detailed in section 2.4, it was considered appropriate to propose an amendment to the specification for steviol glycosides from *Stevia rebaudiana* Bertoni (S3—35) to include steviol glycosides (Reb D, Reb M and Reb AM) produced by an enzymatic conversion method using specific enzymes derived from GM strains of *E. coli*. Amending the steviol glycosides specification ensures the steviol glycosides preparations that are the subject of this application have the same permissions for use as a food additive as other steviol glycosides preparations already included in specifications in the Code.



As the primary specification, the FAO JECFA Monographs 20 (2017) does not include the chemical name for Reb AM, this has been included in the specification in S3—35.

According to the application, the sweetness potency of preparations of steviol glycosides with a high Reb AM content was determined to be approximately 150 times sweeter than sucrose. This is less than that currently in the specification in S3—35, which is approximately 200-300 times sweeter than sucrose. FSANZ therefore proposes to amend the specification to refer to approximately 150-300 times sweeter than sucrose. As this allows for a reduction in sweetness, FSANZ does not anticipate any impact on steviol glycoside preparations currently required to comply with this specification.

## **2.2.2 Enzyme processing aids**

It was also considered appropriate to propose an amendment to Schedule 18 permitting the use of the protein engineered enzymes UDP-glucosyltransferase and sucrose synthase sourced from GM *E. coli* as processing aids. This is because it is possible (although highly unlikely) that the steviol glycoside preparations may contain traces of these enzyme processing aids and unless expressly permitted by the Code, a food for sale must not contain, as an ingredient or a component, a substance that was used as a processing aid. The draft variation lists the specific enzymes as processing aids in subsection S18—9(3) for the specific technological purpose of the conversion of purified stevia leaf extract to produce one or more of the following: Reb D, Reb M; and Reb AM.

The express permission for the enzymes' use as processing aids will also provide the permission for their presence in the steviol glycosides preparations as a food produced using gene technology. The enzymes are a food produced using gene technology for Code purposes as they are derived from 'an organism that has been modified using gene technology' (i.e. GM microorganisms).

FSANZ's assessment is that the use of the enzymes as processing aids to manufacture the steviol glycoside preparations does not itself, make those preparations GM foods. As the preparations are not derived from an organism that has been modified using gene technology, FSANZ's determination is that these preparations are not of themselves a food produced using gene technology.

## **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 steviol glycosides 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 code number 960 (as listed in Schedule 8). As the proposed change to the Code is to the specification rather than approval of the steviol glycosides themselves 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 International Numbering System (INS) numbers for steviol glycosides, which were subsequently adopted into the Class Names and International Number System for Food Additives (CXG 36-1989) by the Codex Alimentarius Commission at its meeting in July 2018 (Codex 2018b). 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). The CCFA has not completed its work; for example, the production

method used under this application does not have a new INS number assigned at the present time. For this reason, the most appropriate INS number is 960. FSANZ will consider changes to the INS number for steviol glycosides in the future, if further changes are made to the INS list.

In terms of the enzymes used as processing aids, the Code exempts processing aids from the requirement to be declared in the statement of ingredients.

### **2.2.3.2 Labelling as ‘genetically modified’**

Section 1.5.2—4 requires certain foods for sale that consist of or have as an ingredient, food that is genetically modified to be labelled as ‘genetically modified’. The Code’s labelling requirements, including those imposed by section 1.5.2—4, generally apply only 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 PureCircle’s steviol glycoside preparations are not food produced using gene technology as they are not derived from an organism that has been modified using gene technology, in contrast to the enzyme processing aids used for their manufacture, which are food produced using gene technology for Code purposes. As such, PureCircle’s steviol glycoside preparations that are the subject of this application do not require labelling as ‘genetically modified’.

The enzymes used as processing aids to manufacture PureCircle’s steviol glycoside preparations are highly unlikely to be present as an ingredient in food for sale which contains these preparations. Furthermore, it is understood that the steviol glycoside preparations themselves would not be sold for retail sale or to a caterer because they are highly concentrated intense sweeteners. As such, it is highly likely that the requirement to label the processing aids as ‘genetically modified’ would not apply to a food for sale that contains the steviol glycoside preparation(s) because the labelling requirements only apply to food that consists of, or has as an ingredient, a GM food under section 1.5.2—4(1).

### **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 PureCircle’s steviol glycosides preparations (Reb D, Reb M and Reb AM) produced by an enzymatic conversion method using specific enzymes derived from GM strains of *E. coli*. It was also considered appropriate to permit the use of the protein engineered enzymes UDP-glucosyltransferase and sucrose synthase, sourced from GM *E. coli* as processing aids for the production of steviol glycoside preparations with a high content of Reb D, Reb M or Reb AM.

## **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 steviol glycosides 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 steviol glycosides produced by an enzymatic conversion method using specific enzymes. FSANZ is of the view that no other realistic food regulatory measures exist, however information received may result in FSANZ arriving at a different outcome.

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.

*Costs and benefits of including a new specification for steviol glycosides produced by an enzymatic conversion method using specific enzymes*

Steviol glycosides are used as intense sweeteners in reduced energy and no-added sugar products. The benefits provided are the ability to potentially more efficiently and effectively produce minor steviol glycosides, where minor steviol glycosides can have better taste attributes compared to other steviol glycosides (the results of taste tests).

Due to the voluntary nature of the permission, industry will only use the food additive (prepared using the specific enzyme processing aids) where they believe a net benefit exists. There are other methods available to industry to produce minor steviol glycosides. It is of benefit to industry to have additional choice available to them, especially where the food additive has preferential taste characteristics compared to preparations containing major individual steviol glycosides alone or is cheaper.

PureCircle may have an advantage over other intense sweetener manufacturing businesses from this voluntary permission. PureCircle acknowledges in its application that there is an exclusive capturable commercial benefit. The impact on other competing Australia-New Zealand manufacturers is unknown.

PureCircle and down-stream retailers may reduce prices for the consumer in some existing products containing the food additive, where there are cost savings from using it.

There may also be greater substitution from products containing sugar or other sweeteners that have a less attractive taste, to generally better tasting minor steviol glycosides. 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. It may also result in some products becoming cheaper.

Permitting the food additive and associated enzyme processing aids 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 aids 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 risks associated with the use of the steviol glycosides preparations produced by an enzymatic conversion method using enzymes derived from genetically modified strains of *E. coli*. 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. PureCircle 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 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.

FSANZ understands that the three steviol glycoside preparations produced using the specific enzymatic conversion method in this application are not approved in Canada or Europe, and in the USA there is a GRAS notice for the steviol glycosides preparation with a high Reb M content.

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

Permission to use these particular steviol glycoside preparations as food additives will provide additional choice to Australian and New Zealand food manufacturers, enabling to 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'<sup>2</sup> 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 steviol glycosides preparations that are the subject of this application 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 2018a, General Standard for Food Additives,  
<http://www.fao.org/gsfonline/index.html;jsessionid=64CA5BB29D301405C4DD6FA3239EA22D>  
Accessed 19 July 2019

Codex 2018b, 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 22 July 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 22 July 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://publications.europa.eu/en/publication-detail/-/publication/ebcc38ed-91d5-11e6-8e27-01aa75ed71a1/language-en> Accessed 22 July 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](https://www.who.int/foodsafety/areas_work/chemical-risks/JECFA87_Summary_Report.pdf?ua=1)

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<sup>2</sup> <http://foodregulation.gov.au/internet/fr/publishing.nsf/Content/publication-Policy-Guideline-on-the-Addition-of-Substances-other-than-Vitamins-and-Minerals>

Health Canada 2018, 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 9 July 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 23 January 2019

PureCircle Stevia Institute 2018, Map Infographic Where in the World is Stevia Approved? <https://www.purecirclestevia.institute.com/resources/infographics/map-infographic> Accessed 19 July 2019

USFDA (2016) [About the GRAS Notification Program](#), October 2016. Accessed 1 August 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 22 July 2019

## Attachments

- A. Draft variation 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 A1176 – Enzymatic production of Steviol Glycosides) 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]

[Insert name 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 A1176 – Enzymatic Production of Steviol Glycosides) 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 subsection S3—35(1), substituting

###### (1) In this section:

**prescribed rebaudiosides** are:

- (a) rebaudioside D;
- (b) rebaudioside M; and
- (c) rebaudioside AM.

**rebaudioside AM** means the steviol glycoside with the chemical name: 13-[(2-O-β-D-glucopyranosyl-β-D-glucopyranosyl)oxy]kaur-16-en-18-oic acid, 2-O-β-D-glucopyranosyl-3-O-β-D-glucopyranosyl-β-D-glucopyranosyl ester.

###### (1A) This specification relates to a steviol glycosides preparation obtained from the leaves of the *Stevia rebaudiana* Bertoni plant.

##### [1.2] omitting paragraph S3—35(2)(c), substituting

- (c) by enzymatic conversion of purified stevia leaf extract to produce rebaudioside D using a protein engineered enzyme that:
  - (i) contains both UDP-glucosyltransferase (EC 2.4.1.17) and sucrose synthase (EC 2.4.1.13) components; and
  - (ii) is sourced from *Pichia pastoris* strain UGT-A;
- (d) by enzymatic conversion of purified stevia leaf extract to produce one or more prescribed rebaudiosides using a combination of enzymes that contains:
  - (i) a UDP-glucosyltransferase from *Stevia rebaudiana* sourced from *Escherichia coli*; and
  - (ii) a UDP-glucosyltransferase from *Solanum lycopersicum* sourced from *Escherichia coli*; and
  - (iii) a sucrose synthase (EC 2.4.1.13) sourced from *Escherichia coli*.

##### [1.3] 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

##### [2.1] inserting in the table to subsection S18—9(3), in alphabetical order

Sucrose synthase (EC 2.4.1.13) sourced from *Escherichia coli* K-12 containing the gene for sucrose synthase from *Arabidopsis thaliana*

For the conversion of purified stevia leaf extract to produce one or more of the following: rebaudioside D, rebaudioside M; and rebaudioside AM

GMP

[2.2] inserting in the table to subsection S18—9(3), in alphabetical order

Uridine diphosphate (UDP) glucosyltransferase sourced from <i>Escherichia coli</i> K-12 containing the UDP glucosyltransferase gene from <i>Solanum lycopersicum</i>	For the conversion of purified stevia leaf extract to produce one or more of the following: rebaudioside D, rebaudioside M; and rebaudioside AM	GMP
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[2.3] inserting in the table to subsection S18—9(3), in alphabetical order

Uridine diphosphate (UDP) glucosyltransferase sourced from <i>Escherichia coli</i> K-12 containing the UDP glucosyltransferase gene from <i>Stevia rebaudiana</i>	For the conversion of purified stevia leaf extract to produce one or more of the following: rebaudioside D, rebaudioside M; and rebaudioside AM.	GMP
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## **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.

FSANZ accepted Application A1176 which seeks approval for a new specification for steviol glycosides produced by an enzymatic conversion method using enzymes derived from genetically modified strains of *Escherichia coli* (*E. coli*). The Authority considered the Application in accordance with Division 1 of Part 3 and has prepared a draft variation to amend the Code.

### **2. Purpose**

The Authority has prepared a draft variation to amend subsection S3—35 of Schedule 3 of the Code. The amendment will include in the specification provided by subsection S3—35(2) a reference to the enzymatic conversion method used to produce the A1176 applicant's Rebaudioside D, M and AM. The amendment's effect would be to permit steviol glycoside preparations containing Rebaudioside D, M and/or AM produced by that production method to be used as a food additive in accordance with the existing permissions and limits for steviol glycosides in the Code.

The Authority has also prepared a draft variation to amend Schedule 18 of the Code to permit the use of the specific enzymes as processing aids in the processing of the A1176 applicant's Rebaudiosides D, M and AM 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 A1176 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.

### **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 [1.1]*

Item [1.1] amends Schedule 3 of the Code by omitting subsection S3—35(1) and inserting in its place new subsections S3—35(1) and S3—35(1A). New subsection S3—35(1) will provide a definition of the terms 'prescribed rebaudiosides' and 'rebaudioside AM' for the purposes of section S3—35, *particularly* paragraph S3—35(2)(d) as provided by Item 1.2 below. New subsection S3—35(1A) will restate the current section S3—35(1).

#### 6.2 Item [1.2]

Item [1.2] adds a new paragraph (d) to subsection S3—35(2) of Schedule 3 of the Code.

The item does this by omitting paragraph S3—35(2)(c) and inserting in its place new paragraphs S3—35(2)(c) and (d).

Paragraph S3—35(2)(c) will be inserted into the Code by the draft variation approved by FSANZ for Application A1172, which will take effect prior to this proposed variation prepared following the assessment of Application A1176.

Item [1.2] will restate and not amend paragraph S3—35(2)(c).

The new paragraph S3—35(2)(d) includes a reference to the enzymatic conversion of purified stevia leaf extract to produce Rebaudiosides D, M and/or AM. The enzymatic conversion processes uses the following combination of enzymes:

- a uridine diphosphate (UDP) glucosyltransferase from *Stevia rebaudiana* sourced from *Escherichia coli*
- a UDP-glucosyltransferase from *Solanum lycopersicum* sourced from *Escherichia coli*
- a sucrose synthase (EC 2.4.1.13) sourced from *Escherichia coli*.

The effect of this amendment is to permit steviol glycoside preparations containing Rebaudioside D, M and/or AM produced using this method to be used as food additives in accordance with the existing food additive permissions in the Code for steviol glycosides.

#### 6.3 Item [1.3]

Item [1.3] amends the requirement for steviol glycoside preparations obtained from the leaves of the *Stevia rebaudiana* Bertoni plant from 200 to 300 times sweeter than sucrose to 150 to 300 times sweeter than sucrose.

#### 6.4 Item [2]

Item [2] amends Schedule 18. The item inserts new entries into the table to subsection S18—9(3). The effect of the new entries is to permit the use of specific enzymes as processing aids for the following technological purpose - the conversion of purified stevia leaf extract to produce one or more of the following: rebaudioside D, rebaudioside M; and rebaudioside AM. The permitted enzymes are:

- Sucrose synthase (EC 2.4.1.13) sourced from *Escherichia coli* K-12 containing the gene for sucrose synthase from *Arabidopsis thaliana*
- Uridine diphosphate (UDP) glucosyltransferase sourced from *Escherichia coli* K-12 containing the UDP glucosyltransferase gene from *Solanum lycopersicum*
- UDP glucosyltransferase sourced from *Escherichia coli* K-12 containing the UDP glucosyltransferase gene from *Stevia rebaudiana*.

The permissions include the condition that the maximum permitted amount used as a processing aid must be consistent with Good Manufacturing Practice (GMP) (as defined by section 1.1.2—2(3) of the Code).

