



**27 June 2019**  
**[85-19]**

Approval report – Application A1172

Enzymatic production of rebaudioside D

---

Food Standards Australia New Zealand (FSANZ) has assessed an application made by SweeGen, Inc. to amend the Australia New Zealand Food Standards Code (the Code) to include a new specification for rebaudioside D (Reb D) produced by an enzymatic conversion method.

On 12 February 2019, FSANZ sought submissions on a draft variation and published an associated report. FSANZ received seven submissions.

FSANZ approved the draft variation on 12 June 2019. The Australia and New Zealand Ministerial Forum on Food Regulation was notified of FSANZ's decision on 20 June 2019.

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

## Table of contents

|                                                                                                |           |
|------------------------------------------------------------------------------------------------|-----------|
| <b>EXECUTIVE SUMMARY .....</b>                                                                 | <b>3</b>  |
| <b>1 INTRODUCTION .....</b>                                                                    | <b>4</b>  |
| 1.1 THE APPLICANT .....                                                                        | 4         |
| 1.2 THE APPLICATION .....                                                                      | 4         |
| 1.3 THE CURRENT STANDARDS .....                                                                | 4         |
| 1.3.1 <i>International standards</i> .....                                                     | 5         |
| 1.4 REASONS FOR ACCEPTING APPLICATION .....                                                    | 7         |
| 1.5 PROCEDURE FOR ASSESSMENT .....                                                             | 7         |
| 1.6 DECISION .....                                                                             | 7         |
| <b>2 SUMMARY OF THE FINDINGS .....</b>                                                         | <b>7</b>  |
| 2.1 SUMMARY OF ISSUES RAISED IN SUBMISSIONS .....                                              | 7         |
| 2.2 RISK ASSESSMENT .....                                                                      | 10        |
| 2.3 RISK MANAGEMENT .....                                                                      | 10        |
| 2.3.1 <i>Labelling considerations</i> .....                                                    | 11        |
| 2.3.2 <i>Risk management conclusion</i> .....                                                  | 12        |
| 2.4 RISK COMMUNICATION .....                                                                   | 12        |
| 2.4.1 <i>Consultation</i> .....                                                                | 12        |
| 2.5 FSANZ ACT ASSESSMENT REQUIREMENTS .....                                                    | 12        |
| 2.5.1 <i>Section 29</i> .....                                                                  | 12        |
| 2.5.2 <i>Subsection 18(1)</i> .....                                                            | 14        |
| 2.5.3 <i>Subsection 18(2) considerations</i> .....                                             | 14        |
| <b>3 REFERENCES .....</b>                                                                      | <b>15</b> |
| ATTACHMENT A – APPROVED DRAFT VARIATION TO THE AUSTRALIA NEW ZEALAND FOOD STANDARDS CODE ..... | 17        |
| ATTACHMENT B – EXPLANATORY STATEMENT .....                                                     | 19        |

### Supporting document

The [following document](#)<sup>1</sup> which informed the assessment of this application is available on the FSANZ website:

SD1 Risk and technical assessment report (minor change from Call for Submissions)

---

<sup>1</sup>

<http://www.foodstandards.gov.au/code/applications/Pages/A1172EnzymaticproductionofRebaudiosideD.aspx>

## Executive summary

The SweeGen, Inc. application sought to add permission in the Australia New Zealand Food Standards Code (the Code) for a steviol glycoside, rebaudioside D (Reb D), produced by a novel production method. The method was based on an enzymatic conversion process using an enzyme processing aid (UGT-A) sourced from a genetically modified (GM) strain of *Pichia pastoris*.

The Code permits the use of Reb D and other steviol glycosides as food additives (with technological purpose of intense sweetener) in various food categories subject to prescribed limits, and also imposes identity and purity specifications (Schedule 3 – Identity and Purity) with which Reb D and other steviol glycosides must comply. Specifications currently listed in Schedule 3 did not allow for SweeGen’s production method.

The application sought to amend Schedule 3 to include a reference to this new production method. This would allow the use of SweeGen’s Reb D in line with the Code’s existing permissions and limits for currently permitted steviol glycosides.

FSANZ’s risk assessment—based on the best available scientific evidence—confirmed that neither SweeGen’s Reb D nor the enzyme used to manufacture that Reb D posed a public health and safety risk. The risk assessment also found that the use of the enzyme to manufacture the Reb D in the way proposed by SweeGen (i.e. as a processing aid) was technologically justified.

A total of seven submissions were received on FSANZ’s assessment report; all of which were supportive. Issues raised in submissions have been addressed. A submission from the New Zealand Ministry for Primary Industries identified the need for amendments to the draft variation, to address additional changes needed to Schedule 3 of the Code, as a result of recent updates to one of the primary sources of specifications listed in Schedule S3—2. These suggestions were assessed and some of the suggested changes will be made via the 2019 Code Maintenance Proposal, as it was considered a more appropriate vehicle to make these changes since they are not directly related to the application. No changes to the draft variations for this application were made.

FSANZ has approved a draft variation to amend Schedule 3 to include a reference to the production method for SweeGen’s Reb D in the specifications for steviol glycosides. The draft variation also amended Schedule 18 to permit the use of the enzyme as a processing aid in the manufacture of that Reb D, ensuring compliance with the Code.

The express permission for the enzyme’s use as a processing aid also provided the required permission for the enzyme’s potential presence in the Reb D as a food produced using gene technology. The enzyme is a food produced using gene technology for Code purposes as it was derived from ‘an organism that has been modified using gene technology’.

# 1 Introduction

## 1.1 The applicant

SweeGen, Inc. is a science-based developer, producer, and distributor of non-caloric sweeteners for the food, flavour and beverage industries. The applicant has indicated that all rights of Blue California (the applicant for A1157, being a comparable application) have been granted to SweeGen, Inc. in relation to steviol glycosides.

## 1.2 The application

This application was similar to Application A1157 which sought a new method to produce rebaudioside M<sup>2</sup> (Reb M) While the current application shares a common enzyme, a UGT-A and sucrose synthase fusion protein, A1157 assessed two additional enzymes, UGT-B1 and UGT-B2, in order to produce a different steviol glycoside.

The application sought to change the Code to permit an alternative production method for the food additive, Reb D, a type of steviol glycoside with the technological purpose of an intense sweetener. Steviol glycosides are traditionally produced using hot water extraction of the *Stevia rebaudiana* Bertoni (stevia) leaf, followed by purification and recrystallisation using methanol or ethanol. In this application, SweeGen used the enzyme processing aid uridine'5 diphospho-glucuronosyl transferase (UGT-A), previously assessed and approved in A1157, to convert stevia extract into Reb D.

The Code currently permits the use of steviol glycosides as food additives with the INS number 960. They are permitted in a wide range of food classes listed in the table to section S15—5 at maximum permitted levels (MPLs), and at Good Manufacturing Practice (GMP) for tabletop sweeteners only. Therefore no amendments to Schedule 15 of the Code would be required to permit use of this particular steviol glycoside.

However, the current specifications for identity and purity did not allow for SweeGen's production method. SweeGen had not asked to change the purity specification or proposed extending the use of Reb D in additional food products. Nor did it propose increasing or altering the permitted quantities of Reb D in permitted food products.

Current permissions for steviol glycosides in the Code and international permissions for SweeGen's Reb D are provided below.

## 1.3 The current 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.

### *Permitted use*

Subsection 1.1.1—10(6) of the Code 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'; a substance that was 'used as a processing aid'; or a food produced using gene technology'.

---

<sup>2</sup> <http://www.foodstandards.gov.au/code/applications/Pages/A1157-EnzymaticproductionofRebaudiosideM.aspx>

### *Food additives*

Section 1.3.1—3 of the Code 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 of the Code.

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 purposes listed in schedule 14 of the Code 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 food products.

### *Processing aids*

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.

Standard 1.3.3 and Schedule 18 list the permitted processing aids. The table to subsection S18—9(3) lists those substances, including enzymes, that are permitted to be used as processing aids for specific technological purposes.

Section 1.1.2—13 defines the expression ‘used as a processing aid.’ That definition imposes requirements 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 purpose in the final food for sale.

Enzymes used in food manufacturing and/or processing 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.

### *Identity and purity requirements*

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

Section S3—35 of Schedule 3 provides a specification for steviol glycosides prepared from the leaves of *Stevia rebaudiana* Bertoni. The specification permits only one method of production, namely extraction using the traditional hot water extraction method. The SweeGen Reb D does not comply with this specification due to its different method of production.

#### **1.3.1 International standards**

Steviol glycosides, which includes Reb D, are approved for use as food additives with the technological purpose of sweetener around the world including in Europe, Central/South America, Asia, Africa and the Middle East (PureCircle Stevia Institute, 2018). Permissions for some of these countries are described in the following sections. Safety assessments have also been performed on steviol glycosides by international expert committees such as the Joint FAO/WHO Expert Committee on Food Additives (JECFA).

### 1.3.1.1 Codex Alimentarius

Codex Alimentarius is the international food standards setting body established by the United Nation's Food and Agriculture Organization and the World Health Organization. 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 2018). The GSFA contains provisions for steviol glycosides in a wide variety of food categories.

### 1.3.1.2 JECFA

JECFA has assessed the safety and specifications of steviol glycosides a number of times, most recently at the 82<sup>nd</sup> meeting in 2016 (JECFA 2017b). That meeting re-evaluated the safety, dietary exposure and specifications of steviol glycosides, as well as updated its Chemical and Technical Assessment. The safety and Acceptable Daily Intake (ADI) of steviol glycosides were confirmed. New, amended tentative specifications for "steviol glycosides from *Stevia rebaudiana* Bertoni" were produced at the 82<sup>nd</sup> meeting and finalised at its 84<sup>th</sup> meeting (JECFA 2017a). The definition in this specification includes a production method that the steviol glycosides are obtained from a hot water extraction from the leaves of *S. rebaudiana* Bertoni. The specification has expanded the definition to include a mixture of any of the steviol glycosides extracted from the stevia leaf rather than the 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 specifications for steviol glycosides finalised at the 84<sup>th</sup> meeting (JECFA 2017a) are included in the Compendium of Food Additive Specifications, which is a primary source of specifications listed in Schedule S3—2 of the Code i.e.:

(1)(b)(xii) FAO JECFA Monographs 20 (2017)

As such, the current specifications in section S3—31 for rebaudioside M (Reb M) and section S3—32 for steviol glycoside mixture including rebaudioside M are no longer required since they are now captured by the updated JECFA specification. As such they are obsolete and so can be removed from Schedule 3. Making these changes is not appropriate as part of the assessment of this application as they are outside the issues considered. However, FSANZ has agreed that they can be removed as part of the 2019 Code Revision Proposal (P1051) since their removal tidies up the Code and does not have any unintended consequences.

### 1.3.1.3 United States

In the United States there have been over 50 Generally Recognised as Safe (GRAS) notices relating to steviol glycosides submitted to the US Food and Drug Administration (FDA) for review. To date, excluding pending notifications, the US FDA has not raised any objections to the GRAS status of these steviol glycosides products for use as a sweetener in foods. GRN No. 715 relates to the same production method and product as this application. GRN No. 715 was submitted by Blue California (all rights have now been granted to SweeGen, Inc., the applicant for this application) in 2017 and the US FDA responded with no questions to the GRAS status. Therefore, SweeGen's Reb D is considered GRAS for use as a table top sweetener and as a general purpose non-nutritive sweetener in foods (US FDA 2017).

### 1.3.1.4 Canada

Health Canada expanded the definition of steviol glycosides as permitted food additive sweeteners to include all steviol glycosides in the *S. rebaudiana* Bertoni plant in 2017 (Health Canada 2017). The applicant has Health Canada correspondence provided in the application confirming that this includes SweeGen's Reb D. Item S.1.2 of the *List of Permitted*

*Sweeteners* in the Canadian *Food and Drugs Act* permits the use of this Reb D as a sweetener food additive in a variety of food categories provided it complies with the relevant international specifications for steviol glycosides (either JECFA or Food Chemicals Codex) and relevant conditions for its use and requirements of the Food and Drug Act (Health Canada 2018).

### **1.3.1.5 European Union**

Steviol glycosides 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). This European specification applies to preparations of steviol glycosides that contain eleven named steviol glycosides which include Reb D at levels not less than 95% on the dried basis. The specification applies only to steviol glycosides extracted from the leaves of the *S. rebaudiana* Bertoni plant, similar to the JECFA and Food Chemicals Codex specifications.

## **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 was assessed under the General Procedure.

## **1.6 Decision**

The draft variation as proposed following assessment was approved without change. The variation takes effect on gazettal. The approved draft variation is at Attachment A.

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

# **2 Summary of the findings**

## **2.1 Summary of issues raised in submissions**

FSANZ sought public comments on the draft variation included in the call for submissions report between 12 February 2019 and 26 March 2019.

FSANZ received seven submissions from government agencies and industry groups. Issues raised in two submissions have been addressed in Table 1 below. Supportive submissions that did not include any issues for consideration were received from one government agency and four industry associations.

**Table 1: Summary of issues raised in submissions**

| Issue                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Raised by                                          | FSANZ response (including any amendments to drafting)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>The NZBC indicated its strong support, with the following comments:</p> <p>(i) The inclusion of this Reb D within the category of currently permitted foods was supported, as well as foods that will be permitted in the future.</p> <p>(ii) Omissions of permissions in any one non-alcoholic beverage class (as per A1149) would need to be avoided.</p> <p>(iii) It was noted that although the Reb D would not require labelling as ‘genetically modified’, ‘GMO free’ claims or claims of similar meaning on products using Reb D produced by this method would be inappropriate.</p>                                                                                                                          | <p>New Zealand Beverage Council</p>                | <p>In response to the NZBC comments, FSANZ noted that:</p> <p>(i) Permission for Reb D in any food categories in the future would be subject to the standard pre-market assessment and approval process undertaken by FSANZ..</p> <p>(ii) All of the existing permissions for use of steviol glycosides in Schedule 15 of the Code also cover the Reb D that is the subject of this application.</p> <p>(iii) The Code does not regulate ‘GMO free’ claims or claims of similar meaning. These types of representations are voluntary and are subject to fair trading laws and food acts in Australia and New Zealand, which prohibit representations about food that are, or are likely to be, false, misleading or deceptive.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>NZ MPI supported the amendment to the Code, with the following comments:</p> <p>(i) The Codex Committee on Food Additives (CCFA) updated the International Numbering System (INS) numbers to distinguish steviol glycosides from different sources (e.g. plant sources (960(a)) versus alternative technologies (960(b))). As such, NZ MPI suggested that this report explain that changes to the INS numbers in the Code, in line with CCFA, will be needed in the future, enabling consumers to be informed about the source of the steviol glycosides.</p> <p>(ii) Recently adopted JECFA specifications for steviol glycosides from <i>Stevia rebaudiana</i> Bertoni (JECFA 2017a) are included in the JECFA</p> | <p>New Zealand Ministry for Primary Industries</p> | <p>With regards to NZ MPI’s comments:</p> <p>(i) FSANZ is aware of updates made to the INS numbers for steviol glycosides, but notes that the CCFA and also JECFA has not yet completed this work. It is understood that JECFA will be considering the different production methods for producing steviol glycosides at it June 2019 meeting, which will be communicated to CCFA. Therefore, until this issue has been finalised by CCFA the most appropriate INS number is 960. FSANZ will consider changes to the INS names and numbers in the Code for different production methods of steviol glycosides in the future, in line with any changes made to the INS list. This issue has been explained in section 2.3.1.1 of this report.</p> <p>(ii) FSANZ noted NZ MPI’s comments regarding the continued requirement for a specification in Schedule 3 of the Code for specific steviol glycosides from <i>Stevia rebaudiana</i> Bertoni, given that the updated JECFA specification referenced under S3—2 addresses all types of steviol glycosides obtained from the stevia leaf and not a defined list. However this JECFA specification is still only for the aqueous</p> |

| Issue                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Raised by | FSANZ response (including any amendments to drafting)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>Compendium of Food Additive Specifications<sup>3</sup>, which is a primary source of specifications listed in Schedule S3—2 of the Code. As such, NZ MPI suggests that S3—35 (which is a specification for steviol glycosides from <i>Stevia rebaudiana</i> Bertoni) is no longer required. In addition, as the JECFA specification has expanded on the definition to include a mixture of steviol glycoside compounds, rather than being limited to a defined list of nine steviol glycosides, NZ MPI's understanding is that this will affect S3—31 and S3—32. Further, the title of S3—35 may need revising, as it will be relevant to high purity Reb M and Reb D only.</p> |           | <p>extraction of the steviol glycosides and not for the additional production methods which are now being captured by the recently updated S3—35 (23 January 2019 amendment due to application A1157). It is therefore inappropriate to remove S3—35. FSANZ also considered NZ MPI's comments in relation to S3—31 and S3—32. FSANZ determined that the current specifications S3—31 and S3—32 are obsolete since they are appropriately captured by the updated JECFA specification. However, it is not appropriate to make the changes to Schedule 3 as part of the assessment of this current application as they are not directly related to the issues dealt with of the application. FSANZ has determined however that these two specifications can be removed as part of the 2019 Code Revision Proposal (P1051) as it will be removing other obsolete Code provisions. Therefore, no changes to the drafting has been made in this report for this application.</p> |

<sup>3</sup> FAO JECFA Monographs 20 (2017)

## 2.2 Risk assessment

FSANZ conducted an assessment of the public health and safety risks associated with the SweeGen's Reb D as a food additive (see SD1) and concluded:

- Recent assessments by FSANZ, Health Canada and JECFA confirmed that all steviol glycosides undergo the same metabolic pathway to steviol, which is then glucuronidated and excreted in the urine.
- A group ADI, expressed as steviol, was therefore appropriate to cover dietary exposure to all steviol glycosides. Toxicological and other relevant data published subsequent to FSANZ's most recent steviol glycosides assessment (Application A1157, assessment completed in October 2018), raised no concerns requiring a change to the existing ADI of 0-4 mg/kg bodyweight (bw)/day steviol.
- SweeGen's Reb D that is the subject of this application was chemically the same as Reb D extracted directly from *S. rebaudiana* Bertoni and would therefore follow the same metabolic pathway.
- SweeGen's Reb D complies with international purity specifications for steviol glycosides.
- No major allergens were used to culture the yeast or at any other stage of the production process.
- The enzyme processing aid UGT-A had previously been assessed and approved under application A1157.

In conclusion, FSANZ's risk assessment did not identify any safety concerns associated with SweeGen's Reb D produced using the enzyme processing aid UGT-A.

## 2.3 Risk management

The risk management options available to FSANZ, after assessment, were to reject the application or to prepare a draft variation to amend the Code to permit SweeGen's Reb D for use as a food additive at levels and in food classes currently permitted in the Code for steviol glycosides.

Due to the risk assessment conclusion that there are no public health and safety risks, amendments to Schedule 3 of the Code to permit the use of SweeGen's Reb D as a food additive, at the levels and in the foods currently permitted for steviol glycosides in the Code, were considered appropriate. Amending the steviol glycosides specification in Schedule 3 to allow SweeGen's production method for Reb D ensured this steviol glycoside preparation had the same permissions as other steviol glycoside preparations already listed in the Code.

It was also appropriate to include an amendment to Schedule 18 permitting the use of the enzyme UGT-A produced from a GM *P. pastoris* strain as a processing aid used for the production of Reb D to ensure regulatory certainty, in a similar way and for similar reasons to that determined in FSANZ's assessment of A1157.

Paragraph 1.1.1—10(6)(g) of the Code 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).

FSANZ's assessment is that the enzyme's use as a processing aid to manufacture Reb D did

not itself, make the Reb D a GM food. As the Reb D itself was not derived from an organism that had been modified using gene technology, FSANZ's determination was that SweeGen's Reb D was not itself a food produced using gene technology.

### **2.3.1 Labelling considerations**

#### **2.3.1.1 Ingredient labelling**

Under existing labelling requirements in the Code (unless the food is exempt from the requirement for a statement of ingredients) SweeGen's Reb D 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 change to the Code was to the production method and specification for Reb D rather than approval of Reb D itself as a food additive, the existing labelling requirements relating to steviol glycosides apply.

The Codex Committee on Food Additives (CCFA) at its 50<sup>th</sup> 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 (CCFA 2018). 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 in the Code for Reb D in the future, if changes are made to the INS list.

In terms of the enzyme used as a processing aid to manufacture SweeGen's Reb D, the Code exempts processing aids from the requirement to be declared in the statement of ingredients.

#### **2.3.1.2 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 was that SweeGen's Reb D was not a food produced using gene technology as it was not derived from an organism that had been modified using gene technology, in contrast to the enzyme processing aid used for its manufacture, which was a food produced using gene technology for Code purposes. As such, SweeGen's Reb D does not require labelling as 'genetically modified'.

The enzyme used as a processing aid to manufacture SweeGen's Reb D was highly unlikely to be present as an ingredient in a food for sale which contains Reb D. Furthermore, it was understood that SweeGen's Reb D itself would not be sold for retail sale or to a caterer because it is a highly concentrated intense sweetener. As such, the requirement to label the processing aid as 'genetically modified' does not apply to a food for sale that contains Reb D because the labelling requirements only apply to food that consisted of, or had as an ingredient, a GM food under section 1.5.2—4(1).

### **2.3.2 Risk management conclusion**

Taking account of the risk assessment conclusions in (section 2.1), the risk management considerations (section 2.2) along with the benefits to industry and consumers (section 2.4.1.1), the risk management conclusion was to permit the use of SweeGen's Reb D as a food additive manufactured using the novel enzymatic production method.

To provide that permission, section S3—35 of Schedule 3 of the Code had been amended to refer to the specific manufacturing method for SweeGen's Reb D.

The permitted technological purpose of SweeGen's Reb D's use as a food additive was that of an intense sweetener permitted in Schedule 15. These permissions were those currently permitted for steviol glycosides at the current MPLs and specified food classes, and at GMP levels for tabletop sweeteners. It has similarly utilised the current INS number 960.

The protein engineered enzyme used to produce Reb D had also been listed as an enzymatic processing aid in subsection S18—(9)(3). Permission for this enzyme processing aid had been limited to the specific purpose of producing Reb D from purified stevia leaf extract only at the use level of GMP.

## **2.4 Risk communication**

### **2.4.1 Consultation**

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

The process by which FSANZ considers standard development matters is open, accountable, consultative and transparent. Public submissions were called to obtain the views of interested parties on issues raised by the application and the impacts of regulatory options. FSANZ acknowledges the time taken by individuals and organisations to make submissions on this application.

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

## **2.5 FSANZ Act assessment requirements**

### **2.5.1 Section 29**

#### ***2.5.1.1 Consideration of costs and benefits***

The Office of Best Practice Regulation (OBPR) granted FSANZ a standing exemption from the requirement to develop a Regulatory Impact Statement for the approval of additional 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, had given consideration to the costs and benefits that may arise from the proposed measure for the purposes of meeting FSANZ Act considerations. The FSANZ Act

required 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 (Section 29 (2)(a)).

The purpose of this consideration was to determine if the community, government, and industry as a whole was likely to benefit, on balance, from a move from the status quo. This analysis considered either approving or rejecting the application (retain the status quo). This analysis considered the option of permitting the use of Reb D produced by an enzymatic conversion method as a food additive in certain foods. FSANZ was of the view that no other realistic food regulatory measures existed.

The consideration of the costs and benefits in this section was not intended to be an exhaustive, quantitative economic analysis of the proposed measures and, in fact, most of the effects that were considered could not easily be assigned a dollar value. Rather, the assessment sought to highlight the likely positives and negatives of moving away from the status quo by permitting the use of Reb D produced by an enzymatic conversion method as a food additive in certain foods.

*Costs and benefits of permitting the use of Reb D produced by an enzymatic conversion method as a food additive in certain foods.*

The use of SweeGen's Reb D as a food additive in the manner proposed would not pose a health or safety risk for consumers. The benefits to the consumer would mirror those for other steviol glycosides currently permitted for use in Australia and New Zealand. SweeGen's Reb D, like other steviol glycosides, would be used in foods and beverages to replace sugar, which will benefit consumers seeking products that have reduced sugar and/or energy content.

Consumers may also benefit from the choice of additional food products which have more favourable sensory characteristics, compared to those using other major glycosides (i.e., stevioside, rebaudioside A). They would also be able to access products manufactured with this particular Reb D, which are currently manufactured overseas.

The development of the new technology to produce a steviol glycoside with preferential sensory characteristics for product development can provide a benefit in terms of product and/or competitive advantage to food manufacturers.

In the US, SweeGen's Reb D produced via enzymatic conversion of purified stevia leaf extract has GRAS status for use as a table top sweetener and a general purpose non-nutritive sweetener in foods. Permission to use SweeGen's Reb D as a food additive, enables Australia/New Zealand food manufacturers to access and use a product assessed as safe that is available to their overseas competitors. This will improve their capacity to compete in overseas markets. Use by industry is voluntary, therefore it will only be used where industry believe a net benefit exists above using existing intense sweeteners.

Since SweeGen did not propose an extension for the use of Reb D in additional food products nor did it wish to propose to increase the permitted quantities of Reb D in permitted food products, there was no perceived benefit or added cost to governments.

However, the approval of the enzyme as a processing aid may result in a small cost to government in terms of adding the enzyme to the current range of enzymes that are monitored for compliance.

*Conclusions from cost benefit considerations*

FSANZ's assessment was that the direct and indirect benefits that would arise from permitting the use of Reb D produced by an enzymatic conversion method as a food additive in certain foods most likely outweigh the associated costs.

**2.5.1.2 Other measures**

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

**2.5.1.3 Any relevant New Zealand standards**

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

**2.5.1.4 Any other relevant matters**

Other relevant matters are considered below.

**2.5.2 Subsection 18(1)**

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

**2.5.2.1 Protection of public health and safety**

FSANZ concluded that there are no safety concerns associated with SweeGen's Reb D produced using an enzyme from GM *P. pastoris*. For more detail, see SD1.

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

The generic labelling requirements will apply to the use of Reb D in food (see section 2.3.1).

**2.5.2.3 The prevention of misleading or deceptive conduct**

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

**2.5.3 Subsection 18(2) considerations**

FSANZ has also had regard to:

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

FSANZ used the best available scientific evidence when undertaking the risk analysis, which is provided in SD1 – the risk and technical assessment report. The applicant submitted a dossier of scientific studies and other technical information including scientific literature. This information dossier, together with other technical information including scientific literature, was used in assessing the application.

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

The SweeGen's Reb D specifications (identity and purity, but not production method) are identical to those established by JECFA (JECFA 2017a) and the Food Chemicals Codex (Food Chemicals Codex 2018).

SweeGen's Reb D is permitted for use in the USA and Canada.

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

Permission to use this particular Reb D as a food additive will enable Australian and New Zealand food manufacturers to access and use a product assessed as safe that is available to some overseas competitors. This will improve their capacity to compete in overseas markets. See discussion at section 2.5.1.1 above.

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

SweeGen's Reb D had been assessed as safe and is permitted for use in the USA and Canada. It was therefore appropriate that Australian and New Zealand food manufacturers can also benefit by gaining permission to use this particular Reb D, which was claimed to provide more favourable sensory characteristics.

- **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>4</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 permitting SweeGen's Reb D produced by an enzymatic conversion method, is consistent with these specific order policy principles.

### 3 References

Codex 2018, General Standard for Food Additives,  
<http://www.fao.org/gsfonline/index.html;jsessionid=64CA5BB29D301405C4DD6FA3239EA22D>  
Accessed 25 October 2018

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>

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

---

<sup>4</sup> <http://foodregulation.gov.au/internet/fr/publishing.nsf/Content/publication-Policy-Guideline-on-the-Addition-of-Substances-other-than-Vitamins-and-Minerals>

## OFFICIAL

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: [http://eur-lex.europa.eu/legalcontent/EN/TXT/?uri=uriserv%3AOJ.L\\_.2016.278.01.0037.01.ENG](http://eur-lex.europa.eu/legalcontent/EN/TXT/?uri=uriserv%3AOJ.L_.2016.278.01.0037.01.ENG) .

Food Chemicals Codex 2018, United States Pharmacopeial Convention (2018) 11<sup>th</sup> ed, United States Pharmacopeial Convention, Rockville, MD

Health Canada 2017, *Notice of Modification to the List of Permitted Sweeteners to Enable the Use of Steviol Glycosides from Stevia rebaudiana Bertoni as a Sweetener*. (Reference Number: NOM/ADM-0102). Ottawa (ON): Health Canada, Bureau of Chemical Safety, Food Directorate, Health Products and Food Branch. <https://www.canada.ca/en/health-canada/services/food-nutrition/legislation-guidelines/acts-regulations/modification-list-permitted-sweeteners-steviol-glycosides.html> Accessed 25 October 2018

Health Canada 2018, 9. List of Permitted Sweeteners (Lists of Permitted Food Additives). In: *Lists of Permitted Food Additives*. Ottawa (ON): Health Canada. <https://www.canada.ca/en/health-canada/services/food-nutrition/food-safety/food-additives/lists-permitted/9-sweeteners.html> Accessed 25 October 2018

JECFA 2017a, 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 25 October 2018

JECFA 2017b, Stevia glycosides (addendum). In: *Safety Evaluation of Certain Food Additives*. Eighty-second Meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA), June 7-16, 2016. (WHO Food Additives Series, no 73). Geneva, Switz.: World Health Organization / Rome, Italy: Food and Agriculture Organization of the United Nations (FAO), pp. 181-218, 490-493. <http://apps.who.int/iris/bitstream/10665/258934/1/9789241660730-eng.pdf?ua=1> Accessed 25 October 2018

PureCircle Stevia Institute 2018, Map Infographic Where in the World is Stevia Approved? <https://www.purecirclestevainstitute.com/resources/infographics/map-infographic> Accessed 25 October 2018

## Attachments

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

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



### **Food Standards (Application A1172 – Enzymatic Production of Rebaudioside D) 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 Delegate's details]

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 A1172 – Enzymatic Production of Rebaudioside D) 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 omitting paragraph S3—35(2)(b), substituting

- (b) by enzymatic conversion of purified stevia leaf extract to produce rebaudioside M using protein engineered enzymes that:
  - (i) contain both UDP-glucosyltransferase (EC 2.4.1.17) and sucrose synthase (EC 2.4.1.13) components; and
  - (ii) are sourced from both of the following:
    - (a) a *Pichia pastoris* strain expressing UGT-A;
    - (b) a *Pichia pastoris* strain expressing both UGT-B1 and UGT-B2;
- (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.

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

|                                                                                                                                                                                                               |                                                                                  |     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|-----|
| Protein engineered enzyme that:<br>contains both<br>UDP-glucosyltransferase (EC<br>2.4.1.17) and sucrose synthase (EC<br>2.4.1.13) components; and is<br>sourced from <i>Pichia pastoris</i> strain<br>UGT-A. | For the conversion of purified stevia leaf<br>extract to produce rebaudioside D. | GMP |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|-----|

## Attachment B – Explanatory Statement

### 1. Authority

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

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

The Authority accepted application A1172 which sought an amendment to Schedule 3 of the Code to prescribe a new specification for rebaudioside D (Reb D) produced by a particular enzymatic conversion method. The Authority considered the application in accordance with Division 1 of Part 3 of the FSANZ Act and prepared a draft variation.

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

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

### 2. Purpose

The Authority has approved a draft variation to amend subsection S3—35(2) of Schedule 3 of the Code. The amendment includes in the specification provided by that subsection a reference to the enzymatic conversion method used to produce the A1172 applicant's Reb D. The amendment's effect permits Reb D produced by that production method to be used as a food additive in accordance with the existing permissions and limits for steviol glycosides (including containing Reb D) in the Code.

The Authority also prepared a draft variation to amend Schedule 18 of the Code to permit the use of the specific enzyme as a processing aid in the processing of the A1172 applicant's Reb D 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 A1172 included 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 Schedule 3 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

### *Item [1]*

Item [1] amends Schedule 3 of the Code. The item adds a new paragraph (c) to the subsection S3—35(2).

The new paragraph S3—35(2)(c) includes a reference to the enzymatic conversion of purified stevia leaf extract to produce Reb D using a protein engineered enzyme that: contains both UDP-glucosyltransferase (EC 2.4.1.17) and sucrose synthase (EC 2.4.1.13) components; and is sourced from *Pichia pastoris* strain UGT-A.

The effect of this amendment is to permit Reb D produced using this method to be used as a food additive in accordance with the existing food additive permissions in the Code for steviol glycosides (including steviol glycosides containing Reb D).

### *Item [2]*

Item [2] will amends Schedule 18. The item inserts a new entry into the table to subsection S18—9(3). The effect of the new entry is to permit the use of a specific enzyme as a processing aid in the manufacture of Reb D for the following technological purpose: the conversion of purified stevia leaf extract to produce Reb D. The permitted enzyme is a protein engineered enzyme that: contains both UDP-glucosyltransferase (EC 2.4.1.17) and sucrose synthase (EC 2.4.1.13) components; and is sourced from *Pichia pastoris* strain UGT-A. The permission includes the condition that the maximum permitted amount used as a processing aid must be consistent with Good Manufacturing Practice (as defined by section 1.1.2—2(3) of the Code).