APPLICATION TO AMEND SCHEDULE 15 OF THE AUSTRALIA NEW ZEALAND FOOD STANDARDS CODE TO ALLOW THE ADDITION OF STEVIOL GLYCOSIDES IN FRUIT DRINKS

Submitted to:

Food Standards Australia New Zealand
PO Box 7186
Canberra BC ACT 2610
Australia

Submitted by:

Australian Beverages Council Ltd
2/2 Allen Street,
Waterloo NSW 2017
Australia

&

New Zealand Beverage Council
PO Box 47
Auckland 1140
New Zealand

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GENERAL REQUIREMENTS

A APPLICANT DETAILS

(a) Applicant

Australian Beverages Council Ltd (ABCL)

(c) Name of contact person

(b) Address

(d) Nature of applicant's business

Peak industry association of Australian non-alcoholic beverage manufacturers

(e) Details of other individuals, companies or organisations associated with the application

New Zealand Beverage Council
PO Box 47
Auckland 1140
New Zealand
T: +64 9 302 9932
E: info@nzbeveragecouncil.org.nz

Peak industry association of New Zealand non-alcoholic beverage manufacturers.

B PURPOSE OF THE APPLICATION

The Australian Beverages Council and the New Zealand Beverages Council are seeking to amend Schedule 15 relating to Standard 1.3.1 of the Australian New Zealand Food Standards Code (FSC), to include:

- The addition of steviol glycosides in Fruit Drinks at a level of 200 mg/kg steviol equivalents.

C JUSTIFICATION FOR THE APPLICATION

(a) The need for the proposed change

Schedule 15 of the Australia New Zealand FSC currently allows the following permissions for steviol glycosides in Non-Alcoholic Beverages and Brewed Soft Drinks:

Table 1. Schedule 15 – Permission for Steviol Glycosides in Non-Alcoholic Beverages and Brewed Soft Drinks.

S15-5 Permissions for food additives	Maximum Permitted Level
14.1.2.1 Fruit and Vegetable Juices	50mg/kg
14.1.2.2.1 Fruit Drink	Not permitted
14.1.2.2.2 Low Joule Fruit and Vegetable Juice Products	125mg/kg
14.1.3 Water Based Flavoured Drinks	200mg/kg
14.1.4 Formulated Beverages	200mg/kg

FSANZ (2016b)

In line with overseas trends, demand for reduced and low kilojoule drinks in the broader water based beverage category has expanded significantly in the past decade in Australia and New Zealand. This trend continues as shown in data from Nielsen spanning the period 1997-2011 (Levy & Shrapnel, 2014). Between 2007 and 2011 a 46% drop in sugar consumption per capita from beverages was reported, showing consumers preference for reduced sugar beverages.

At present intense sweeteners including aspartame (951), acesulphame potassium (950), alitame (956), and aspartame-acesulphame salt (962) are permitted in fruit drinks. However, trend data shows Australian and New Zealand consumers would prefer options containing steviol glycosides (960) to other intense sweeteners. As unlike other intense sweeteners steviol glycosides are plant-based.

Low joule fruit and vegetable juice products that are currently permitted to contain steviol glycosides at just 125mg/kg are often less palatable due to low level of juice required to formulate these products as low joule. The resulting beverages do not meet consumer expectations, leading to poor sales and hence a relatively short product lifespan. Water based beverages containing 200mg/kg steviol glycosides and higher levels of sugar are performing successfully overseas. These products typically allow a 30 - 50% reduction in sugar. Consumers are seeking midway products, not labelled diet while providing lower kilojoules. These beverages are not currently accommodated for by the fruit drink category under the FSC. The ABCL feels the appropriate level for consideration is 200mg/kg, as this level will meet Australian and New Zealand consumer palatability requirements. Currently several diluted juice products in Australia and New Zealand are achieving a 50% sugar reduction using steviol glycosides. These are not eligible to be to be labelled as fruit drinks as the FSC does not permit the addition of steviol glycosides to fruit drinks. They are currently categorised as “fruit flavoured drinks”, whereas fundamentally these are fruit drinks.

(b) The advantages of the proposed change over the status quo

The proposed change would allow beverage manufacturers to create more innovative products with reduced sugar and comparable palatability to fruit juice. It would also allow for more accurate naming of reduced sugar beverages that contain fruit juice.

The food industry has seen considerable improvements in flavour technology which has allowed for better use of steviol glycosides in beverages. The industry has also seen substantial refinement in the quality of steviol glycosides available, including tailoring to drink applications and manufacturing conditions.

C.1 Regulatory Impact Information

C.1.1 Costs and benefits of the application

Manufacturers and importers of steviol glycosides and foods containing steviol glycosides, would benefit from the market opportunities for sale both domestically and internationally, as well as continuing product innovation and reformulation. Since steviol glycosides are already approved for many food uses within Australia and New Zealand, there is no added cost to the Government however, this allows the opportunity to provide consumers with education around choice. Costs and benefits for industry, consumers and government are summarised in tables below.

Table 2. Cost of Application.

Costs	
Industry	• Reformulation costs • Labelling compliance
Consumers	• Cost of steviol glycosides is more than sugar
Government	• Regulatory change

Table 3. Benefits of Application.

Benefits	
Industry	• Increased product offering
Consumers	• More choices in fruit drink category • Reduced energy option for fruit based beverage
Government	• Opportunity for public education

a) Cost and benefits to the consumer

It is not envisioned that fruit drinks sweetened with steviol glycosides would be any more expensive to the consumer than current fruit drink type products. The main benefit is that it gives consumers a greater choice of lower kilojoule beverages with acceptable sweet taste profiles.

b) Cost and benefits to the industry and business in general

While there will be product formulation costs associated for industry in developing new fruit drinks sweetened with steviol glycosides, it is not expected that these would be greater than current product formulation costs.

The benefit to industry would be their ability to offer a wider choice of beverages to consumer, in particular reduced sugar products. It would allow industry to continue to innovate and provide alternatives to current full sugar products.

Approval of the use of steviol glycosides in fruit drinks would also provide clarity and consistency in product labelling. Currently the exclusion of fruit drinks permits confusion.

c) Costs and benefits to government

It is not expected that this change would have any cost impact on Government.

C.1.2 Impact on international trade

Overseas markets currently permit steviol glycosides in fruit drinks. This change would allow manufacturers who also operate in these markets to have one formulation of the same product for either importation into Australia and New Zealand, or export from Australia and New Zealand to other countries.

D INFORMATION TO SUPPORT THE APPLICATION

This application is supported by manufacturer and supplier members of the ABCL and the NZBC.

E ASSESSMENT PROCEDURE

Consistent with current policy, the request for change to use steviol glycosides in fruit drinks would be considered a General Procedure (Level 1) endeavour. This would require an amendment to Schedule 15 of Standard 1.3.1 – Food Additives of the Australia New Zealand FSC. Allowing steviol glycosides in 14.1.2.2.1 Fruit Drink, changing the value from Not Permitted to 200mg/kg.

F CONFIDENTIAL COMMERCIAL INFORMATION (CCI)

The application contains no confidential commercial information.

G EXCLUSIVE CAPTURABLE COMMERCIAL BENEFIT (ECCB)

Neither the ABCL, the NZBC or their Members, have any exclusive capturable commercial benefit. The permission to add steviol glycosides to fruit drinks would apply to all manufacturers.

Although the manufacturers of steviol glycosides will derive some economic benefit from approval of the application, other food manufacturers who use steviol glycosides will also derive some economic benefit. In addition, there are several different manufacturers of steviol glycosides and therefore the economic benefit would be spread and not be exclusive.

H INTERNATIONAL AND OTHER NATIONAL STANDARDS

H.1 International Standards

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) first assessed the safety of steviol glycosides during its 51st meeting in 1998 (JECFA, 1999). Additional safety data on steviol glycosides was reviewed at the 63rd, 68th, 69th and 73rd JECFA meetings (JECFA 2005, 2007, 2008, 2010). At the 63rd Committee meeting a temporary acceptable daily intake (ADI) of 2 mg/kg body weight/day was set. In 2008, the temporary status of the ADI was removed, raising the ADI to 4 mg/kg body weight for steviol glycosides. In addition to this, specifications requiring purity levels of greater than 95% for steviol glycosides were established. In 2010, JECFA revised the specifications for steviol glycosides to include two additional steviol glycosides, rebaudioside D and rebaudioside F, within the purity criteria (JECFA, 2010). In March 2011, at the 43rd Session of the Codex Committee on Food Additives (CCFA)

recommended steviol glycosides provisions in the General Standards of Food Additives (GSFA) to be considered (CCFA, 2011).

H.2 Other national standards or regulations

H.2.1 European Union

Following a request from the European Commission, the European Food Safety Authority (EFSA) carried out an exposure assessment of steviol glycosides from their use as a food additive, taking into account the proposed extension of its use. In 2010, the EFSA Panel on Food Additives and Nutrient Sources added to Food adopted a scientific opinion on the safety of steviol glycosides and established an ADI of 4 mg/kg body weight per day. Conservative estimates of exposure, in both adults and children, suggested that it is likely that the ADI would be exceeded at the maximum proposed use level (EFSA, 2010). In 2011, EFSA carried out a revised exposure assessment of steviol glycosides based on reviewed proposed uses and concluded that, even if the estimates were reduced, the high-level dietary exposure in children may still exceed the ADI.

EFSA published their scientific opinion in 2014 which extended the use of steviol glycosides to the following beverage categories at levels that are higher than the previous 10 mg/kg level:

- 29 mg/kg in tea beverages and instant coffee, and instant cappuccino products;
- 29 mg/kg in coffee and herbal infusion beverages; and
- 20 mg/kg in malt-based and chocolate/cappuccino flavoured drinks (EFSA, 2014).

The current scientific opinion included an exposure assessment of steviol glycosides considering the proposed extension of use, and the panel concluded that the *"dietary exposure to steviol glycosides is similar to the exposure estimated in 2014 and therefore does not change the outcome of the safety assessment."* (EFSA, 2015).

H.2.2 United States

In December 2008, the United Stated Food and Drug Administration (FDA) raised no objections to the use of stevia rebaudiana outlined in GRAS Notice No. GRN 000252 for use in several foods, including fruit juice drinks at a level 150 – 500 mg/kg (GRN Nos. 000252). Since this time 43 GRAS notices (GRN Nos 000253, 000275, 000278, 000282, 000287, 000303, 000304, 000318, 000323, 000329, 000337, 000348, 000349, 000354, 000365, 000367, 000369, 000375, 000380, 000388, 000389, 000393, 000395, 000418, 000448, 000452, 000456, 000461, 000467, 000473, 000493, 000512, 000516, 000536, 000548, 000555, 000607, 000619, 000626, 000632, 000638, 000662, and 000667) for highly-purified steviol glycosides or glycosylated steviol glycosides have been submitted to the FDA for review. No objections have been raised by the FDA regarding the use of the steviol glycoside products for use as general-purpose sweeteners in foods (U.S. FDA, 2008a,b, 2009a-d, 2010a-e, 2011a-i, 2012a-e, 2013a-f, 2014a-c, 2015a-d, 2016a-f).

H.2.3 Canada

Health Canada published its final clearance for use of steviol glycosides as a sweetener in foods in July 2012 (Health Canada, 2012a). The use of steviol glycosides as a sweetening agent in a variety of food and beverage categories was approved at levels of up to 0.35%, calculated as steviol equivalents (Health Canada, 2012b). In the beginning of 2016, Health Canada approved the use of rebaudioside M for use as a high-intensity sweetener under the same conditions as the previously approved steviol glycosides (Health Canada, 2016).

H.2.4 Asia

Steviol glycosides are permitted as a food additive (sweetening agent) in several Asian countries including, Japan, South Korea, China, Malaysia, Indonesia, Singapore, and Taiwan.

The Ministry of Health and Welfare in Japan has approved stevia extracts, α-glucosyltransferase-treated stevia, powdered stevia, and stevia extract (Japan Food Chemical Research Foundation, 2014). Purified stevioside and stevia rebaudiana leaf extracts are permitted for general use in a variety of foods and beverages including pickling gum, pickles, dried seafood, meat, fish, soy sauce, bean pastes, sugarless chewing gums, juices, cola, table-top sweeteners, and ice cream in Japan (Marie, 1991; Das *et al.*, 1992; Ferlow, 2005).

The Food Safety and Standards Authority of India approved the use steviol glycosides as a sweetener in eleven food and beverage categories on 20 August 2014 (FSSAI, 2014). This included dairy based flavoured drinks, fruit nectars, non-carbonated water-based non-alcoholic beverages, carbonated water and soft drink concentrates at a maximum level of 200mg/kg steviol equivalents.

H.2.5 Central/South America

In Brazil, Argentina, Paraguay, Uruguay, Mexico, Peru, and Colombia stevioside, *S. rebaudiana* leaves, and highly refined extracts are permitted for use as low-calorie sweeteners.

H.2.6 Other Jurisdictions

Steviol glycosides are also permitted in the following countries Nigeria, Israel, Russia, Switzerland, Turkey and Ukraine.

I STATUTORY DECLARATION

Statutory Declaration can be found in Appendix A.

K CHECKLIST

Checklist can be found in Appendix B.

APPLICATIONS FOR FOOD ADDITIVES

A TECHNICAL INFORMATION ON STEVIOL GLYCOSIDES

A.1 Nature and technological function of steviol glycosides

Steviol glycosides are purified extracts of *Stevia rebaudiana.* The function of steviol glycosides use in fruit drinks is as an intense sweetener, which would enable the reduction of sugar in fruit drinks.

Steviol glycosides, are currently permitted in fruit juice (50mg/kg), low joule fruit and vegetable juice drinks (125mg/kg) and water based flavoured beverages (200mg/kg) (FSANZ, 2016c).

In order to produce a fruit drink with 30 – 50% substitution of sugar with equivalent sweetness to other water based beverages and fruit juice, a level of 200mg/kg steviol glycosides is required.

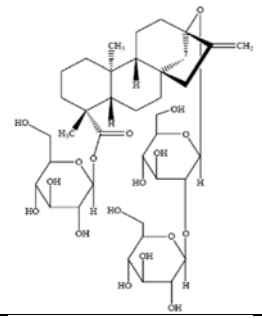
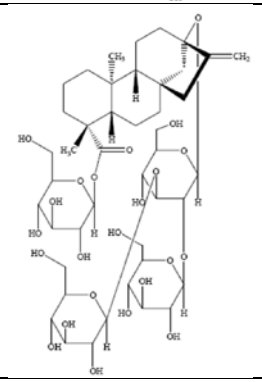
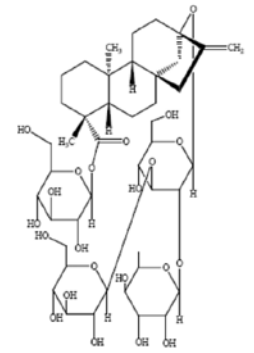
Steviol glycosides have been determined as stable under various conditions of use in foods and beverages. The stability of steviol glycosides was last reviewed by FSANZ in A1132 (FSANZ, 2016d).

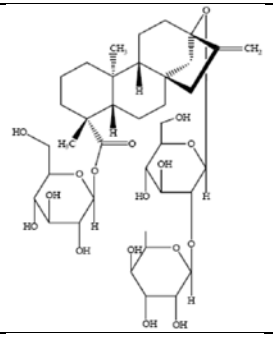
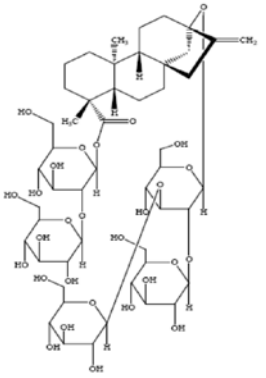
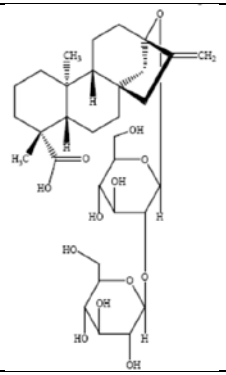
A.2 Information to enable identification of steviol glycosides

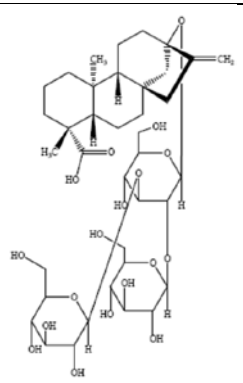
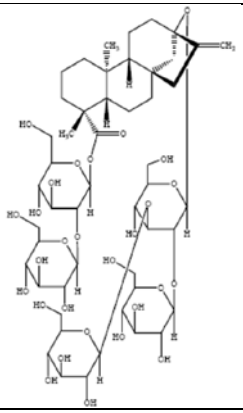
JECFA has defined steviol glycosides as product obtained from the leaves of *Stevia rebaudiana* Bertoni. Steviol glycosides have the food additive number INS 960 (JECFA, 2005). Table 4. identifies steviol glycosides that are currently approved for used by FSANZ.

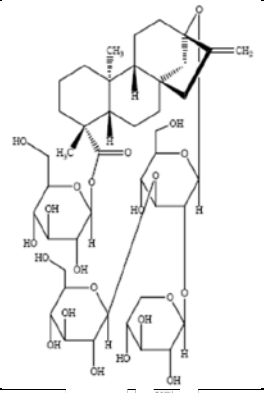
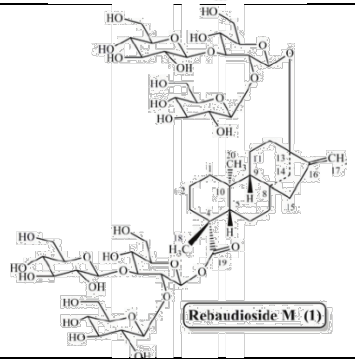
Synonyms, Trade Names, and Abbreviations
steviol glycosides, rebiana, rebaudioside A, Truvia™

Table 4. Identification of Steviol Glycosides.

Chemical Name	Structure Formula	Common Name	CAS Number	Formula	Molecular Weight (g/mol)
13-[(2-O-β-D-glucopyranosyl-β-D-glucopyranosyl)oxy] kaur-16-en-18oic acid β-D-glucopyranosyl ester		Stevioside	57817-89-7	$C_{38}H_{60}O_{18}$	804.87
13-[(2-O-β-D-glucopyranosyl-3-O-β-D-glucopyranosyl-βDglucopyranosyl) oxy] kaur-16-en-18-oic acid β-D-glucopyranosyl ester		Rebaudioside A	58543-16-1	$C_{44}H_{70}O_{23}$	967.01
13-[(2-O-6-deoxy-β-L-mannopyransoyl-3-O-β-D-glucopyranosyl-βDglucopyranosyl) oxy] kaur-16-en-18-oic acid β-D-glucopyranosyl ester		Rebaudioside C	63550-99-2	$C_{44}H_{70}O_{22}$	951.01

Chemical Name	Structure Formula	Common Name	CAS Number	Formula	Molecular Weight (g/mol)
13-[(2-O-6-deoxy-β-L-mannopyransoyl-β-D-glucopyranosyl)oxy] kaur16-en-18-oic acid β-D-glucopyranosyl ester		Dulcoside A	64432-06-0	$C_{38}H_{60}O_{17}$	788.87
13-[β-D-glucopyranosyl)oxy] kaur-16-en-18-oic acid β-Dglucopyranosyl ester		Rubusoside	63849-39-4	$C_{32}H_{50}O_{13}$	642.73
13-[(2-O-β-D-glucopyranosyl-β-D-glucopyranosyl)oxy] kaur-16-en-18oic acid		Steviolbioside	41093-60-1	$C_{32}H_{50}O_{13}$	642.73

Chemical Name	Structure Formula	Common Name	CAS Number	Formula	Molecular Weight (g/mol)
13-[(2-O-β-D-glucopyranosyl-3-O-β-D-glucopyranosyl-βDglucopyranosyl) oxy] kaur-16-en-18-oic acid		Rebaudioside B	58543-17-2	$C_{38}H_{60}O_{18}$	804.87
13-[(2-O-β-D-glucopyranosyl-3-O-β-D-glucopyranosyl-βDglucopyranosyl) oxy] kaur-16-en-18-oic acid-2-O-β-Dglucopyranosyl-β-Dglucopyranosyl este		Rebaudioside D	63279-13-0	$C_{50}H_{80}O_{28}$	1129.15

Chemical Name	Structure Formula	Common Name	CAS Number	Formula	Molecular Weight (g/mol)
13-[(2-O-β-D-xylopyranosyl-3-O-β-D-glucopyranosyl-βDglucopyranosyl) oxy] kaur-16-en-18-oic acid β-D-glucopyranosyl ester		Rebaudioside F	438045-89-7	$C_{43}H_{68}O_{22}$	936.99
2-O-β-D-glucopyranosyl-3-O-β-Dglucopyranosyl-β-D-glucopyranosyl)oxy]kaur-16-en-18-oic acid, 2-O-β-Dglucopyranosyl-3-O-β-D-glucopyranosyl-β-D-glucopyranosyl ester		Rebaudioside M	1220616-44-3	$C_{56}H_{90}O_{33}$	1291.3

A.3 Information on the chemical and physical properties of steviol glycosides

Food grade specifications for steviol glycosides, finalised by JECFA, require not less than 95% of the total preparation to be comprised of ten named steviol glycosides, on a dried weight basis (JECFA, 2010). Preparations of steviol glycosides are white or light yellow powders that are either odourless or have a slight odour. Steviol glycoside powder preparations are freely soluble in water and ethanol. Steviol glycoside solutions have a pH between 4.5 – 7.0 (1 in 100 solution), and have sweetness profiles that range between 200-300-fold (compared to sucrose) depending on the particular steviol glycosides present in a JECFA-defined 95% pure preparation and the testing methodology details.

A.4 Information on impurity profile

The major component of high purity steviol glycoside preparations that adhere to JECFA specifications (>95% purity) are one or a mixture of steviol glycosides. As a general matter, the composition of the steviol glycoside mixtures can vary depending to the *S. rebaudiana* cultivar from which the steviol glycosides are extracted, as well as differences in the manufacturing process (EFSA, 2010). According to JECFA specifications, the impurities representing the other 5% of the material should not include more the 1% total ash, nor should residual methanol or ethanol be present at greater than 200ppm and 5000 ppm, respectively. In addition, the specifications state that arsenic and lead levels should not exceed 1 ppm in the high purity steviol glycoside preparations (JECFA, 2010).

A.5 Manufacturing process

Manufacturers use the same basic steps to extract steviol glycosides from the leaves of the stevia plant, although there is some variation in the later stages of purification and separation of glycosides. The process generally involves:

- Extraction from the leaves by dissolving the steviol glycosides in warm/hot water in a batch system, 3 – 5 times, or by a continuous reverse flow system;
- Flocculation and precipitation of suspended matter;
- Filtration;
- Concentration by vacuum assisted evaporation;
- Adsorption (and release by alcohol) in a resin exchange process;
- Ion-exchange purification;
- Further filtration and concentration; and
- Spray drying or crystallisation.

Further processing to concentrate and separate a high rebaudioside A product is often undertaken and may involve patented procedures, such as some enzymatic modification.

A.6 Specification for identity and purity

Specification for steviol glycoside mixture, including rebaudioside M, is outlined in Schedule 3 of the FSC (FSANZ, 2016e).

A.7 Information for food labelling

Steviol glycosides are considered to be intense sweeteners and flavour enhancers when added to various food products. Steviol glycosides have been assigned the INS number of 960.

A.8 Analytical method for detection

Reverse-phase high-performance liquid chromatography (RP-HPLC) coupled with tandem mass spectrometry is used for detection of steviol glycosides, due to its high selectivity and multianalyte capability since different sweeteners are frequently used in mixtures to achieve the desired taste, flavour or mouthfeel. This methodology is outlined in "*The Determination of eight artificial sweeteners and common Stevia rebaudiana glycosides in non-alcoholic and alcoholic beverages by reversed phase liquid chromatography coupled with tandem mass spectrometry*" by Kubica *et al*., 2015.

A.9 Potential additional purposes of the steviol glycosides when added to food

Steviol glycosides are added to food either as an intense sweetener, or to replace the sweetness normally provided by sugars (FSANZ, 2016a).

Steviol glycosides differ from other permitted intense sweeteners as these are sourced from plant material rather than chemical synthesis. They are recognised by manufacturers as an opportunity to provide consumers with access to an alternative reduced energy option, and to increase beverage choices. Consumer demand for more natural ingredients and lower kilojoule products globally has seen steviol glycosides experience significant growth in recent years as the trend for low and reduced sugar products continues to grow within the non-alcoholic beverage market as it provides a natural alternative.

B INFORMATION RELATED TO THE SAFETY OF STEVIOL GLYCOSIDE

The safety of steviol glycosides has been reviewed by FSANZ several times. FSANZ first approved the use of steviol glycosides as an intense sweetener in a wide variety of foods in 2008 (FSANZ, 2008). FSANZ allowed an increase in the maximum permitted level of steviol glycosides in ice cream, water based beverages, brewed soft drinks, formulated beverages and flavoured soy beverages, of up to 200 mg/kg and in plain soy beverages, of up to 100 mg/kg, following the assessment of A1037 (FSANZ, 2011). A new steviol glycoside, rebaudioside M, was approved for use in the same food categories and at the same use levels are previously permitted steviol glycoside products by FSANZ in 2015 (FSANZ, 2015).

During the creation of this submission, FSANZ approved A1132 to broadening the definition of steviol glycosides (FSANZ, 2016d). This safety assessment includes summaries of toxicology studies that have been published or made available since these safety evaluations. Some of the studies outlined below are also included in A1132, as this was written prior to the applications approval.

B.1 Information on the toxicokinetics and metabolism of steviol glycoside

As summarised in previous FSANZ safety evaluations, much of the toxicology literature has focused on the potential mutagenicity and genotoxicity of steviol glycosides. Overall, *in vitro* and *in vivo* studies have consistently demonstrated that stevioside and rebaudioside A, are not mutagenic or genotoxic (Brusick, 2008, and Urban et al., 2013). The single exception, an *in vivo* study by Nunes *et al.* (2007), had significant methodological limitations that led experts and regulators to conclude that the study is irrelevant to the health and safety of high purity steviol glycosides in animals or humans (Brusick, 2008; JECFA, 2008; EFSA, 2010; Urban *et al.*, 2013).

The only relevant genotoxicity study not accounted for in the prior FSANZ safety evaluations (note that A1132 does review this study) was published in 2009 by Williams and Burdock. This study reported on a battery of *in vitro* and *in vivo* genotoxicity tests of 95.6% pure rebaudioside A, and was designed according to the International Conference on Harmonization recommendations (Williams and Burdock, 2009). The *in vitro* assays included the Ames test (OECD #471), the mammalian chromosome aberration test (OECD #473), and the mouse lymphoma test (OECD #476). Rebaudioside A produced no positive mutagenic effects in any of the assays at concentrations as high as 5 mg/plate.

The two *in vivo* assays conducted were the mouse micronucleus test (OECD #474), and the unscheduled DNA synthesis (UDS) test in rats (OECD #486). For the micronucleus test, a single intraperitoneal injection was administered to mice in three dose groups. Animals in the highest dose group (750 mg rebaudioside A/kg bw) exhibited some signs of toxicity (e.g. spontaneous activity reduction, rough fur, prone position, and cramping), though no cytotoxicity was evident. No statistically significant genotoxic effects were observed in any rebaudioside A dose group relative to vehicle control (e.g. no increase in polychromatic immature erythrocytes or micronucleated immature erythrocytes), while positive control animals (administered cyclophosphamide) demonstrated an increase in the incidence of micronucleated immature erythrocytes. In the UDS test, rats were administered a single oral gavage dose of 2 g/kg bw.

Per OECD guidelines, hepatocytes were collected after 2-h and 16-h. No toxicity or genotoxicity was reported for any of the rebaudioside A-treated animals, while both positive control animals (administered dimethylnitrosamine and 2-acetylaminofluorene) elicited a significant increase in hepatocyte UDS at their respective sampling times. Overall, these genotoxicity study results add to the large database for steviol glycosides and steviol, and support the interpretation of previous studies reviewed in the previous FSANZ safety evaluations.

B.2 Information on the toxicity of steviol glycoside

No additional studies on steviol glycoside acute toxicity in animals have been published since the previous FSANZ safety evaluations. However, four unpublished acute toxicology studies on rebaudioside A (98% purity) conducted by Eurofins/Product Safety Laboratories were included in a 2012 FDA GRAS notification (Mini Star Intl. GRN418, 2012). Oral (0.233 – 5 g/kg) and dermal (2 g/kg) rebaudioside A exposures in rats produced no acute toxicity effects. In addition, rebaudioside A did not elicit primary skin irritation (0.5 g) or primary eye irritation (0.04 g) in rabbits upon dermal or ocular exposures. These

results support the prior findings in the published literature that steviol glycosides are not acutely toxic in laboratory animals.

Application A1132 also discusses the following study. A single subacute animal assay was conducted as a bridging toxicity study to investigate whether previous toxicity studies on rebaudioside A would be appropriate to support the safety evaluation of rebaudioside D. The study by Nikiforov *et al.* (2013) was performed in accordance with US FDA testing guidelines. The study design included the oral administration of 0, 500, 1000, or 2000 mg/kg/day rebaudioside D (purity = 93.5%, with the remaining 6.5% comprised mostly of other steviol glycosides), or 2000 mg/kg/day rebaudioside A (purity = 98.9%), to five groups of 20 Crl:CD(SD) rats (10 male, 10 female) respectively, for 28 consecutive days. Doses normalised to consumption rates and body weights for the males and females in each test group were 506 and 495, 1027 and 1012, 2042 and 2016, and 2043 and 1965 mg/kg/day, respectively. There were no adverse changes observed in clinical observations, terminal body weights, organ weights, or food consumption, or any remarkable differences in hematological, serum chemistry or urinalysis endpoints between control animals and those administered either rebaudiosides A or D. With one exception, functional observational battery and motor activity endpoints were not impacted by either steviol glycoside at tested doses relative to control animals. The females in all rebaudioside D dose groups had significantly lower ambulatory activity relative to control, though the authors hypothesised that this was the result of quicker habituation of these animals, and not related to treatment. In fact, no differences in ambulation were observed in the highest dose rebaudiosides A and D treatment group females, and no differences were reported in any of the treatment group males relative to control group males. Nikiforov *et al.* (2013) concluded that the study was appropriate as a bridging study for rebaudioside D, and that it verified the safety of rebaudioside D for human consumption.

As summarised in the FSANZ safety evaluations of high purity steviol glycoside preparations, clinical studies have demonstrated that steviol glycosides are well tolerated in humans and are not associated with adverse effects in healthy humans as well as individuals with type-2 diabetes or who are hypotensive. In addition to the clinical research summarised in the previous safety evaluations, it should be noted that a recent study was published that compared the impact of pre-meal ingestion of stevia (Whole Foods 365 brand; steviol glycoside purity not reported) with that of other sweeteners (i.e. aspartame or sucrose) on food intake, satiety, and postprandial glucose and insulin levels in healthy lean and obese individuals between the ages of 18-50 (Anton *et al.*, 2010). The study reported that stevia significantly lowered post-meal glucose levels relative to sucrose preloads, and significantly lowered post-meal insulin levels compared to both aspartame and sucrose preloads. Effects on hunger and satiety were not different between the three sweeteners. However, critical study limitations (e.g. no reported steviol glycoside composition, purity, or even relevant dose metric) suggest that the results of this study are not likely to influence the current regulatory position regarding the safety of steviol glycoside in humans.

Overall, the results of these most recent additions to the toxicology and clinical literature of high purity steviol glycosides support the safety of high purity preparations.

B.3 Safety assessment reports prepared by international agencies or other national government agencies

The safety of steviol glycosides has assessed by several scientific and regulatory bodies, including FSANZ, JECFA, FDA, EFSA, and Health Canada. Due to the significant interest in the use of steviol glycosides extensive testing has been carried out.

JECFA has reviewed the safety of steviol glycosides in four separate meetings and has established an ADI for steviol glycosides of 0 to 4 mg/kg body weight expressed as steviol equivalents (JECFA, 1999, 2005, 2007, 2008, 2010).

C INFORMATION RELATED TO THE DIETARY EXPOSURE TO STEVIOL GLYCOSIDES

C.1 List of food groups or foods proposed to contain steviol glycosides

Fruit Drink, category 14.1.2.2.1 in Schedule 15.

C.2 The maximum proposed level of steviol glycosides for fruit drinks

This application seeks to amend Schedule 15 relating to Standard 1.3.3 to allow steviol glycosides in Fruit Drinks to a maximum level of 200mg/kg.

C.3 The likely level of consumption of fruit drinks

Disclosure: The Beverage Councils undertook to commission the attached Interlek Report: *Dietary Exposure Assessment to Support Extension Use of Steviol Glycosides to Fruit Drinks in Australia/New Zealand* (12 July 2016) (For full report refer APPENDIX C).

The Australian Health Survey does not state the consumption of fruit drinks. They are included in fruit and vegetable juices and drinks (ABS, 2015). This is the same for the New Zealand Nutrition Survey (University of Otago & Ministry of Health, 2011).

Based on the general nature of cordial and fruit drinks, a beverage based on water, fruit and sugar. It could reasonably be assumed that the pattern of consumption (and thereby the exposure to any ingredients contained therein) of these beverage types would be similar, whereby an individual would select one or the other, not both at the same time, over a prolonged period of time. In a comparable manner, 'cordials' are beverages typically based on concentrated fruit juices, water and sugar (or sweeteners; although this category is not defined in the FSC); the same principle is likely to apply to consumption patterns. In addition, in several of tables within the FSANZ Consumption of Intense Sweeteners in Australia and New Zealand: Benchmark Survey 2003, intakes of 'cordials' and 'fruit drinks' were presented together, likely due to the similar pattern of consumption (FSANZ, 2004). There was no definition provided in the report for this food category, and it is noted that the questionnaire provided to participants included examples such as 'Ocean Spray Litestyle', 'Cranberry Classic' and 'Sunraysia Diet

Lemon Squash' to represent 'fruit drinks'. As such, intakes of fruit juice-based beverages have been adequately represented in the estimated intakes of intense sweeteners as reported in the study results.

The methodology utilised as part of the two-assessment approach undertaken in the risk evaluation for application A1037 (assessment models by FSANZ and sweetener substitution method) considers exposure by consumers to *all* sweetened beverages consumed as part of the typical diet. This includes those originating from 'fruit drinks', as well as considering identical food use level for other beverages. The assumptions included in both assessment approaches were sufficiently conservative to consider brand loyal consumers, who may select sweetened beverages containing steviol glycosides all the time. As such, it is not appropriate to conduct an additional assessment to consider the present extension for use (FSANZ, 2011).

C.4 The percentage of fruit drinks in which steviol glycosides is proposed to be used

During FSANZ risk assessments of Applications A540 and A1037, a dietary exposure assessment (DEA) had been conducted to evaluate the anticipated intake by the Australia and New Zealand populations to this sweetener based on the proposed food use applications. In addition, as part of the latter submission, the applicant included an assessment of potential exposure to rebaudioside A, using a sweetener substitution method published by Renwick (2008) to demonstrate that the anticipated exposure would not pose a concern for consumers (FSANZ 2008, 2011). Applications A1108 and A1132 did not conduct an intake assessment as approval of addition steviol glycosides was to be used under the same conditions as previously permitted steviol glycosides (FSANZ 2015, 2016d).

The FSANZ approach considered a default value for market share penetration and brand loyalty to the top contributing food categories, e.g. water-based beverages and flavoured milk, in the three scenarios conducted as shown in Table 5. There are clear similarities in the definition of the sub-categories included as part of the water-based beverages (soft drinks, cordials and formulated beverages) brand-loyalty scenario with that of 'fruit drinks'. The exposure levels determined using the 3 scenarios (20 to 110% ADI) would be representative of a range of consumption patterns, including those of individuals who are brand loyal to steviol glycoside-sweetened beverages, albeit at the upper end. However, based on the assumptions included in this model, these results are considered protective for the population.

Considering that the proposed use level for fruit drinks is the same as both beverages types presented in the table, 200 mg/kg, it can reasonably be assumed that exposure from fruit drinks would be considered in the calculated exposure levels for this scenario. It is noted that this scenario resulted in the highest estimated exposure levels, with a range of 50 to 110% of the ADI, however it was concluded that the assumptions included in the assessment, were sufficiently conservative that this would not present a safety issue for consumers.

Table 5. DEA Conducted by FSANZ to Determine Exposure to Steviol Glycosides (FSANZ, 2011).

Assessment Description	Range of 90th Percentile Results, % ADI
No Brand Loyalty Assumption that steviol glycosides are added to all food and beverage categories, considering a 30% market share	20 to 60

Brand Loyalty – Water-Based Beverages Assumption that steviol glycosides are added to water-based beverages at 100% MPL, and all other categories considering 30% market share	50 to 110
Brand Loyalty – Flavoured Milk Assumption that steviol glycosides are added to flavoured milk at 100% MPL, and all other categories considering 30% market share	55 to 100

ADI = acceptable daily intake; bw = body weight; DEA = dietary exposure assessment; FSANZ = Food Standards Australia New Zealand; MPL = maximum permitted level.

The sweetener substitution method included a series of exclusion criteria and conservative assumptions in order to provide protective, yet realistic (considering actual consumer patterns for approved sweeteners) average and high level exposure estimates to a novel intense sweetener. Sweetened beverages are a well-recognised source of intense sweeteners, as such, many of the studies placed additional focus on this food category. The predicted exposure levels (28 to 40% ADI) may therefore be representative of all sweetened beverages, including fruit drinks.

It is concluded that the above-mentioned exposure estimates are sufficiently conservative to support the proposed extension of use of steviol glycosides to fruit drinks at 200 mg/kg without resulting in an expected change in the pattern of consumption. As opposed to an increase in the total estimated dietary exposure levels by the total Australian and New Zealand populations.

C.5 Information relating to the use of the steviol glycosides in other countries

Table A-1 in Appendix C provides a summary of the food groups included in the individual studies that were conducted to determine the exposure level by the population cohort. These studies included populations in the US, Canada, UK, Germany, Denmark, the Netherlands, France and Brazil. Sweetener-containing beverages were typically the highest contributor to intakes, and was therefore the primary focus by researchers. However, rebaudioside A, was found in a wide arrange of food categories as shown below:

- carbonated beverages,
- powdered drinks,
- dilutable drinks,
- frozen drinks,
- iced teas,
- hot chocolate,
- hot tea,
- coffee,
- milk-based flavoured drinks and shakes.
- desserts including puddings, topping, frozen novelties
- yoghurt,
- cereals,
- soups,
- canned meals,
- spreads

- table-top sweeteners,
- chewing gum,
- confectionary,
- diabetic products.

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APPENDIX A

Statutory Declaration

Statutory Declaration – New Zealand

STATUTORY DECLARATION

Oaths and Declarations Act 1957[1]

I, solemnly and sincerely declare that:

1. The information provided in this Application to amend schedule 15 of the Australia New Zealand Food Standards Code to include the addition of Steviol Glycosides in Fruit Drinks fully sets out the matters required; and
2. The information is true to the best of my knowledge and belief; and

3. No information has been withheld which might prejudice this application to the best of my knowledge and belief.

And I make this solemn declaration conscientiously believing the same to be true and by virtue of the Oaths and Declarations Act 1957.

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[1] http://www.legislation.govt.nz/act/public/1957/0088/latest/DLM314553.html.

[2] A statutory declaration must be made before a person authorised to take a statutory declaration under section 9 of the Oaths and Declarations Act 1957.

APPENDIX B

Checklists

General requirements (3.1.1)		
Check	**Page No.**	**Mandatory requirements**
☑	NA	A Form of application ☑ *Application in English* ☑ *Executive Summary (separated from main application electronically)* ☑ *Relevant sections of Part 3 clearly identified* ☑ *Pages sequentially numbered* ☑ *Electronic copy (searchable)* ☑ *All references provided*
☑	5	B Applicant details
☑	5	C Purpose of the application
☑	5	D Justification for the application ☑ *Regulatory impact information* ☑ *Impact on international trade*
☑	8	E Information to support the application ☑ *Data requirements*
☑	8	F Assessment procedure ☑ *General* ☐ *Major* ☐ *Minor* ☐ *High level health claim variation*
☑	8	G Confidential commercial information ☐ *CCI material separated from other application material* ☐ *Formal request including reasons* ☐ *Non-confidential summary provided*
☑	NA	H Other confidential information ☐ *Confidential material separated from other application material* ☐ *Formal request including reasons*
☑	8	I Exclusive Capturable Commercial Benefit ☑ *Justification provided*
☑	8	J International and other national standards ☑ *International standards* ☑ *Other national standards*
☑	10	K Statutory Declaration
☑	10	L Checklist/s provided with application ☑ *3.1.1 Checklist* ☑ *All page number references from application included* ☐ *Any other relevant checklists for Chapters 3.2–3.7*

Food additives (3.3.1)		
Check	**Page No.**	**Mandatory requirements**
☑	11	A.1 Nature and technological purpose information
☑	11	A.2 Identification information
☑	16	A.3 Chemical and physical properties
☑	16	A.4 Impurity profile
☑	16	A.5 Manufacturing process
☑	16	A.6 Specifications
☑	17	A.7 Food labelling
☑	17	A.8 Analytical detection method
☑	17	A.9 Additional functions
☑	18	B.1 Toxicokinetics and metabolism information
☑	18	B.2 Toxicity information
☑	20	B.3 Safety assessments from international agencies
☑	20	C.1 List of foods likely to contain the food additive
☑	20	C.2 Proposed levels in foods
☑	20	C.3 Likely level of consumption
☑	21	C.4 Percentage of food group to contain the food additive
☑	22	C.5 Use in other countries (if applicable)
☐	NA	C.6 Where consumption has changed, information on likely consumption

APPENDIX C

Dietary Exposure Assessment to Support Extension of Use of Steviol Glycosides to Fruit Drinks in Australia/New Zealand

Prepared by: Intertek Scientific & Regulatory Consultancy
Room 1036, Building A8
Code Technology Park
Ively Road, Farnborough
www.intertek.com

July 12, 2016

Dietary Exposure Assessment to Support Extension of Use of Steviol Glycosides to Fruit Drinks in Australia/New Zealand

1.0 BACKGROUND

1.1 Regulatory Status

Steviol glycosides (INS 960) are currently permitted for use in a range of food and beverage applications, as laid out under Standard 1.3.1. Schedule 15 of the Australian New Zealand Food Standards Code ("the Code" hereafter) (FSANZ, 2016a,b). The specific permitted applications and use levels were subject to pre-market risk assessment by the Food Standards Australia and New Zealand (FSANZ). The initial assessment was conducted in 2008, which was in response to an application (A540) for addition of this sweetener to a range of food and beverage categories; this was followed by a subsequent submission (application A1037) in which a request for an increase in the permitted use levels in specific categories was made (FSANZ, 2008, 2010).

The Australasian beverage sector, wishes to extend the permitted use of this sweetener to one additional beverage category, Category 14.1.2.2.1 Fruit Drinks, as defined under Standard 2.6.2 of the Code as (FSANZ, 2016c):

"a product that is prepared from:

- *(a) One or more of the following:*
  - *(i) fruit juice;*
  - *(ii) fruit purée*
  - *(iii) concentrated fruit juice;*
  - *(iv) concentrated fruit purée;*
  - *(v) comminuted fruit;*
  - *(vi) orange peel extract; and*
- *(b) one or more of the follow:*
  - *(i) water;*
  - *(ii) mineralized water; and*
  - *(iii) sugars"*

Table 1.1-1 includes a summary of the currently approved applications under Category 14.1 (non-alcoholic beverages), along with the additional proposed food use category. The proposed use level for Category 14.1.2.2.1 is consistent with the already-permitted use levels in Categories 14.1.3 Water-Based Flavoured Drinks, and 14.1.4 Formulated Beverages, *i.e.,* 200 mg/kg.

Table 1.1-1 Approved and Proposed Applications of Steviol Glycosides (INS 960) in Non-Alcoholic Beverages (Category 14.1)

Food Category	Maximum Permitted Level (mg/kg)
Approved	
14.1.2.1 Fruit and Vegetable Juices	50
14.1.2.2.2 Low Joule Fruit and Vegetable Juice Products	125
14.1.2.2.3 Soy Bean Beverage (Plain or Flavoured)	100 (plain); 200 (flavoured)
14.1.3 Water-based Flavoured Drinks	200
14.1.4 Formulated Beverages	200
14.1.5 Coffee, coffee substitutes, tea, herbal infusions and similar products	100
Proposed	
14.1.2.2.1 Fruit Drinks	200

1.2 Dietary Exposure Assessments

As part of both of the above-mentioned FSANZ risk assessments (applications A540 and A1037), a dietary exposure assessment (DEA) had been conducted to evaluate the anticipated intake by the Australia/New Zealand population to this sweetener based on the proposed food use applications. For both of the risk assessments, FSANZ conducted a DEA using national nutrition data combined with proposed use levels. In addition, as part of the latter submission, the applicant included an assessment of potential exposure to rebaudioside A using a sweetener substitution method as published by Renwick (2008) to demonstrate that the anticipated exposure would not pose a concern for consumers.

The resulting exposure levels from both of these assessment approaches are described in the sections that follow.

1.2.1 FSANZ DEA Method

Results of the DEA for the most recent application (A1037) are most pertinent as this assessment included all currently approved food uses and use levels. FSANZ conducted 3 separate assessments which considered market share and brand loyalty to the sweetener, the details of which as summarized in Table 1.2-1; additional information on the assumptions are provided in Section 2.1. This table also identifies the range of 90th percentile estimates of exposure, presented as a proportion of the acceptable daily intake (ADI; 0 to 4 mg/kg body weight/day) determined for each individual population group. In all instances, the highest estimated results were obtained for young children aged 2 to 6 years of age, which is expected due to their comparatively higher intake of foods on a body weight basis and higher energy needs during development when compared with the rest of the population (FSANZ, 2009).

Under the first scenario, 30% market uptake was assumed for steviol glycosides (*i.e*., assuming that a consumer selects steviol glycoside-sweetened foods 30% of the time), the 90th percentile estimates of intake were determined to range between 20 and 60% of the ADI. Although this model accounted for the market penetration of the ingredient, there was no specific consideration for 'brand loyalty', whereby a consumer always chooses the same product within a food category, which may contain steviol glycosides at the maximum permitted level. Two 'brand loyalty' scenarios were conducted based on the categories contributing most highly to total dietary intakes – 'water-based beverages' and 'flavoured milk'. When brand loyalty to water-based beverages were examined (*i.e.* 100% market uptake for these products, with 30% market uptake to all other food categories), 90th percentile intakes ranged from 50 to 110% of the ADI. When brand loyalty to the food group 'flavoured milk' was examined, high level intakes range between 55 and 100% of the ADI. It should be noted in the latter assessment, estimates were not determined for adult population groups, as flavored milk products were not a major contributor to total dietary intakes by adults.

Table 1.2-1 DEA Conducted by FSANZ to Determine Exposure to Steviol Glycosides

Assessment Description	Range of 90th Percentile Results, % ADI
1. No Brand Loyalty Assumption that steviol glycosides are added to all food and beverage categories, considering a 30% market share	20 to 60
2. Brand Loyalty – Water-Based Beverages Assumption that steviol glycosides are added to water-based beverages at 100% MPL, and all other categories considering 30% market share	50 to 110
3. Brand Loyalty – Flavoured Milk Assumption that steviol glycosides are added to flavoured milk at 100% MPL, and all other categories considering 30% market share	55 to 100

ADI = acceptable daily intake; bw = body weight; DEA = dietary exposure assessment; FSANZ = Food Standards Australia New Zealand; MPL = maximum permitted level.

1.2.2 Sweetener Substitution Method

The results for the sweetener substitution method are presented in Table 1.2-2, based on the published data in the Renwick (2008) assessment. More details on the method are provided in Section 2.2. In summary, the estimated 'high' consumer exposure level for the general adult population (*i.e.*, non-diabetic adults) reached 28% of the ADI; whereas among population groups of particular interest, *i.e.* children and diabetic individuals (children and adults), the resulting exposure level ranged between 38 and 40% of the ADI.

Table 1.2-2 Dietary Exposure to Steviol Glycosides, as Steviol Equivalents, Based on Sweetener Substitution Method (Renwick, 2008)

Population Group	Exposure Level, mg/kg bw/day (% ADI)	
	Average Consumer	High Consumer
Non-diabetic adults	0.4 (10)	1.1 (28)
Diabetic adults	0.5 (13)	1.5 (28)

Table 1.2-2 Dietary Exposure to Steviol Glycosides, as Steviol Equivalents, Based on Sweetener Substitution Method (Renwick, 2008)		
Non-diabetic children	0.7 (18)	1.6 (40)
Diabetic children	1.1 (28)	1.5 (38)

ADI = acceptable daily intake; bw = body weight.

2.0 CRITICAL REVIEW OF DEA METHODOLOGY

In the following sections, details are provided on the key assumptions of both the FSANZ and sweetener substitution methods, along with the food groups investigated, and specific considerations for the proposed extension of steviol glycosides to 'fruit drinks'.

2.1 FSANZ DEA Method

FSANZ conducted three DEAs using food consumption data available from the most recent Australian and New Zealand national nutrition surveys, combined with the approved and proposed use levels[1] for steviol glycosides in the dietary modelling computer program, DIAMOND.

2.1.1 Assumptions

A number of conservative assumptions were incorporated into the exposure assessment models, including:

- In the absence of specific data on actual use levels or concentrations of steviol glycosides in food, maximum permitted levels (MPLs) were used;
- Every food code within a specific food group were assumed to contain the intense sweetener[2]; the assessment report specifically noted that for 'fruit and vegetable juices', all food codes complying with this category description were assumed to contain steviol glycosides, however in reality only sweetened (and not pure) versions are likely to contain any intense sweetener;
- It was assumed that steviol glycosides were the only sweeteners on the market and/or consumed; this overestimates the market penetration for this sweetener as the market for this type of ingredient is shared by a number of intense sweeteners;
- Recipe fractions were included for foods used in mixed dishes;
- It was assumed that there are no reductions in the levels of steviol glycosides from food preparation or processing;

[1] Ice cream and edible ices 200 mg/kg; water based flavoured drinks 200 mg/kg; formulated beverages 200 mg/kg, soy beverage, unflavoured 100 mg/kg; soy beverage, flavoured 200 mg/kg

[2] Exceptions were coffee or tea and non-flavoured milks as these were assumed not to contain steviol glycosides

- Intakes by consumers-only were investigated;
- Brand loyalty scenarios were conducted for water-based beverages (total population) and flavored milks (children only).

FSANZ noted that these assumptions would result in a considerable overestimate of steviol glycosides exposure.

2.2.2 Food Groups Investigated

Table 2.2.2-1 summarizes the permitted and proposed applications of steviol glycosides used in FSANZ's DEA.

Table 2.2.2-1 Summary of Permitted and Proposed Food Categories, Corresponding DIAMOND Food Classification and Steviol Glycosides Concentration Used for Dietary Exposure Assessment

DIAMOND Food Code	Food Name	Steviol glycosides[#] concentration (mg/kg)*
1.1.2	Liquid milk products and flavoured liquid milk	115
1.2.2	Fermented milk products and rennetted milk products	176
3	Ice cream & edible ices	**200**~
3.1	Ice confection sold in liquid form	115
	Ice cream & ice confection reduced & low fat	208
4.3.2	Fruits & vegetables in vinegar/oil/brine/alcohol	160
4.3.4.2	Low joule chutneys, jams & spreads	450
4.3.6	Fruit & vegetable preparations including pulp	208
5.1	Chocolate & cocoa products	550
5.2	Sugar confectionery	1100
6.3	Processed cereal & meal products	250
7.1.4	Fancy breads	160
7.2	Biscuits, crackers, cakes, pastries & scones	160
11.4	Table-top sweeteners	400000^
13.3	Formula meal replacements & formulated supplementary foods	175
13.4	Formulated supplementary sports foods	175
14.1.2.1	Fruit & vegetable juices	50
14.1.2.2.2	Low joule fruit & vegetable juice products	125
14.1.3	Water based flavoured drinks	**200**~
14.1.4	Formulated beverages	**200**~
14.1.5	Coffee (or substitute), tea, herbal infusion & similar products	100
14.1.7.1	Soy beverage, unflavoured	**100**~
14.1.7.2	Soy beverage, flavoured	**200**~
20.2.1.1	Desserts, dairy [except ice cream]	150

Table 2.2.2-1 Summary of Permitted and Proposed Food Categories, Corresponding DIAMOND Food Classification and Steviol Glycosides Concentration Used for Dietary Exposure Assessment		
20.2.1.1.1.2	Custard mix, custard powder & blancmange mix/powder	80
20.2.1.2	Desserts, no-dairy	150
20.2.1.2.3.1	Jelly	260
20.2.4.1	Snack foods, dairy or fat based	150
20.2.6.1	Sauces & syrups, sweet	320
20.2.6.2	Gravy, sauces & condiments	320
20.2.6.3.1	Dips, dairy or fat based	150
20.2.6.3.3	Spreads, dairy or fat based	320
20.2.7	Mayonnaise & salad dressings	320

DIAMOND = DIetAry Modelling Of Nutritional Data.
[#] Expressed as steviol equivalents.
* Steviol glycosides concentration data as listed in Schedule 1 of Standard 1.3.1 and the amendments proposed by the Applicant.
[~] Changes proposed in this Application - A1037. Existing permissions for these foods are as follows: ice cream and edible ices 64 mg/kg; water based flavoured drinks 160 mg/kg; formulated beverages 160 mg/kg, soy beverage, unflavoured 65 mg/kg; soy beverage, flavoured 175 mg/kg.
[^] Concentration value used as a proxy for GMP (Good Manufacturing Practice) permission.

2.1.3 Considerations for Fruit Drinks

As mentioned in Section 1.1, 'water-based beverages' were determined to be one of the primary contributor to intake for all population groups. As such, a brand loyalty scenario was conducted considering this category, which was identified to include 'soft drinks, cordials and formulated beverages'. Notably, the latter beverage type is a separate food category (14.1.3) and is defined under Section 2.6.2 of the Code (FSANZ, 2016c) as:

"a non-carbonated, ready-to-drink, flavoured beverage that:

- *(a) is water-based; and*
- *(b) contains added vitamins or minerals or both vitamins and minerals; and*
- *(c) contains no more than 240 mL/L of fruit from one or more of the following sources:*
  - *(i) fruit juice;*
  - *(ii) fruit purée;*
  - *(iii) concentrated fruit juice;*
  - *(iv) concentrated fruit purée;*
  - *(v) comminuted fruit;*
  - *(vi) orange peel extract; and*
- *(d) contains no more than 75 g/L of sugars; and*
- *(e) does not contain:*
  - *(i) carbon dioxide; or*
  - *(ii) caffeine; and*

(f) is not mixed with any other beverage."

There are clear similarities between this definition and that provided for a fruit drink (see Section 1.0), *i.e.,* a beverage based on water, fruit and sugar. As such, it could reasonably be assumed that the pattern of consumption (and thereby the exposure to any ingredients contained therein) of these beverage types would be similar, whereby an individual would select one or the other, not both at the same time, over a prolonged period of time. In a similar manner, 'cordials' are beverages typically based on concentrated fruit juices, water and sugar (or sweeteners; although this category is not defined in the Code); the same principle is likely to apply to consumption patterns. Considering that the proposed use level for 'fruit drinks' is the same as both of these beverages types, *i.e.,* 200 mg/kg, it can reasonably be assumed that exposure from fruit drinks would be considered in the calculated exposure levels for this scenario. It is noted that this scenario resulted in the highest estimated exposure levels, with a range of 50 to 110% of the ADI, however it was concluded that the assumptions included in the assessment (as described in Section 2.1.1), were sufficiently conservative that this would not present a safety issue for consumers.

2.2 Sweetener Substitution Method

2.2.1 Assumptions

The calculation of predicted exposure to rebaudioside A by Renwick (2008) utilized published global post-market surveillance data on the dietary exposure estimates for approved intense sweeteners. The results for dietary surveys from various jurisdictions were utilized to determine the 'average' and 'high' consumer intakes of intense sweeteners, which were expressed as sucrose equivalents, *i.e.,* relative sweetness intensity compared with sucrose. Individual study results were split according to the population cohort in order to predict exposure levels for 4 population groups:

- non-diabetic adults
- diabetic adults
- non-diabetic children
- diabetic children.

A number of conservative assumptions were applied in the selection of exposure values to be incorporated into the exposure prediction model, namely:

- Reported exposure levels for 'consumers only' were selected;

- Unusually low reported intakes of intense sweeteners by a specific population group were excluded to avoid diluting the final exposure values used for the prediction model (examples included Leclercq *et al.*, 1999; Arcella *et al.*, 2004; van Rooij-van den Bos *et al.*, 2004);

- Sweeteners for which the reported intakes were generally lower than those of others were excluded, *i.e.,* intakes of acesulfame-k, alitame, sucralose, cyclamate were lower than those of aspartame and saccharin, and as such were not included;

- Calculations for intakes by 'high' consumers were typically based on the 90th percentile intake value reported, however higher percentiles were included if the 90th percentile was not reported in the study documentation;

- Among children, given the differences in age groupings in published studies, the overall values used to predict average and high level intakes were based on the age group within each study that showed the highest exposure level;

- A default body weight value of 65 kg was utilized to convert absolute intakes to per kilogram body weight intakes - this is lower than the default values utilized in many jurisdictions for the purposes of risk assessment (U.S. EPA, 2011; EFSA, 2012), and also are noted to be lower than actual mean body weights reported in national health surveys Australian Bureau of Statistics, 2012; CDC, 2015; UKDA, 2015);

- The overall prediction model assumes that novel compounds will achieve the same market penetration of those currently available on the market.

After applying the above-mentioned exclusion criteria, a total of 17 dietary surveys were included in the final calculations for predicted exposure to intense sweeteners. Each of the exposure levels were converted to 'sucrose equivalents' based on the relative sweetness to sucrose; which acted as a 'common currency' for all sweeteners investigated. The estimated values from each study were pooled; these values were not weighted to the number of subjects in order to avoid providing a disproportion weight being given to studies unnecessarily - it was noted each individual study is representative of a particular population cohort at a particular time, and the values should be equally represented in the final calculations.

Other considerations associated with the final selected estimates of exposure related to the individual studies are listed in Table A-1 of Appendix A. The key assumptions which ensure that the resulting predicted exposure values may be considered sufficiently conservative include the following:

- Some of the earlier studies were conducted at a time when only a limited number of intense sweeteners were approved, *e.g.*, Heybach and Ross (1989) was conducted at a time when only aspartame was approved as a sweetener in Canada. These estimates may be considered to represent the intakes by brand loyal consumers (*i.e.,* consumers who always choose the same product within a food category, which may contain the intense sweetener).

- Several studies utilized the maximum reported/permitted level for the sweetener of interest rather than analytical data (Renwick, 1999[3]; Garnier-Sagne *et al.*, 2001; Magnuson *et al.*, 2007).

- Some studies utilized food categories as opposed to individual foods (Heybach and Ross, 1989; Magnuson *et al.*, 2007), thereby not considering the actual usage patterns of the individual sweeteners.

- Numerous studies which were categorized as part of the 'general population' (and thereby used to calculated the predicted exposure for 'non-diabetic adults') by Renwick (2008) included individuals with expected higher intakes *e.g.* diabetics, individuals on sugar/weight-restrictive diets (Heybach and Ross, 1989, MAFF, 1990; Hinson and Nicol, 1992; Toedo and Ioshi, 1995; Renwick, 1999; Butchko *et al.*, 2002; FSANZ, 2004).

- Toledo and Ioshi (1995) only included individuals who were intense sweetener consumers; the average values for intakes of aspartame and saccharin from this study were utilized to calculate the predicted average intakes for 'non-diabetic adults'.

Overall, this was a robust approach to assessing exposure to intense sweeteners, and was noted by FSANZ to hold advantages over other methods as it is based on actual (post-market) consumption of foods sweetened with intense sweeteners, thereby considering actual consumer patterns (FSANZ, 2010).

2.2.2 Food Groups Investigated

Table A-1 also provides a summary of the food groups included in the individual studies when calculating the exposure level by the population cohort. Most notably, every study examined intakes from sweetener-containing beverages. This category was typically the highest contributor to intakes, and was therefore the primary focus by researchers. In fact, several studies investigated only exposure from beverages (FSA, 2003; Leth et *al.*, 2007). The level of detail used to describe this category varied significantly, with some simply reporting levels for 'non-alcoholic beverages' (MAFF, 1990[4]; Bär and Biermann, 1992; Hinson and Nicol, 1992; Toledo and Ioshi, 1995; Renwick, 1999; Wilson *et al.*, 1999; Garnier-Sagne *et al.*, 2001), whereas other studies presented results for arbitrary beverage categories, notably the categorization of beverages differed according to the individual study, as listed below:

- Carbonated, non-carbonated (Morgan *et al.*, 1982);

- Carbonated soft drinks, powdered soft drinks, frozen juices/drinks (Heybach and Ross, 1989);

- Cocoa, fizzy drinks, squashes or cordials (MAFF, 1990 – diabetics);

[3] Where analytical data was unavailable
[4] General population only; additional descriptor included for diabetic individuals

- Sodas, cordials, lemonade syrups (Hulshof *et al.*, 1995);
- Aerated soft drinks, cordials (NFA, 1995);
- Carbonated soft drinks, cordials, fruit drinks (FSANZ, 2004);
- Carbonated, non-carbonated (Leth *et al.*, 2007);
- Carbonated, dilutable (e.g., fruit squashes, cordials), powdered, tea or coffee, natural still, commercial still, infant formula [Food Standards Agency UK (FSA), 2003].

2.2.3 Considerations for Fruit Drinks

Based on the general recognition of a high level of contribution of beverage categories to total intake of intense sweeteners and a deliberate focus on exposures to intense sweeteners from these categories, it is expected that *all* sweetened beverages consumed as part of the usual diet have been considered in the predicted intense sweetener exposure levels presented in Table 1.2-1 above. As such, it is likely that the proposed use of steviol glycosides in 'fruit drinks' may result in a *change* in the pattern of consumption (*i.e.,* change in the contributing beverage categories), as opposed to an increase in the total exposure level.

Of note, the intake of intense sweeteners from 'fruit drinks' was reported in a study report published by FSANZ (2004), which was inherently built to be conservative, as participants were selected on the basis of their high consumption of sweetener-containing foods. Although, there was no definition provided in the report for this food category, it is noted that the questionnaire provided to participants included examples such as 'Ocean Spray Litestyle', 'Cranberry Classic' and 'Sunraysia Diet Lemon Squash' to represent 'fruit drinks'. As such, intakes of fruit juice-based beverages have been adequately represented in the estimated intakes of intense sweeteners as reported in the FSANZ (2004) study results.

As mentioned in Section 2.1.3, there is no specific definition of a 'cordial' under the Code; however, based on the general nature of these products, it may be reasonably assumed that the pattern of consumption of cordials and fruit drinks would be similar, whereby one would be consumed in place of another. Cordials have specifically been included as a category investigated in a number of the above-mentioned studies (MAFF, 1990; NFA, 1995; FSA, 2003; FSANZ, 2004). In addition, in several of tables within the FSANZ (2004) report, intakes of 'cordials' and 'fruit drinks' were presented together, likely due to the similar pattern of consumption.

In summary, based on a critical and comprehensive review of the assumptions, methodologies, and specific food groups included in the studies used to predict exposure to intense sweeteners by Renwick (2008), it is concluded that potential exposure of steviol glycosides from proposed uses in 'fruit drinks' would not result in a meaningful increase in the total exposure to this food additive in the consuming population.

3.0 SUMMARY AND CONCLUSIONS

Based on the information presented in Section 2.0, it is the applicants' view that the methodology utilized as part of the two assessment approaches which were undertaken as part of the risk assessment for application A1037 (*i.e.,* assessment models by FSANZ and sweetener substitution method) would consider exposure by consumers to *all* sweetened beverages consumed as part of the typical diet, including those originating from 'fruit drinks', particularly considering the identical food use level for other beverages. In addition, the assumptions included in both of the assessment approaches were sufficiently conservative to consider brand loyal consumers, who may select sweetened beverages containing steviol glycosides all of the time. As such, it is not appropriate/necessary to conduct an additional assessment to consider the present extension for use.

The FSANZ approach considered a default value for market share penetration and also brand loyalty to the top contributing food categories, *i.e.,* 'water-based beverages' and 'flavoured milk', in the three scenarios conducted. As mentioned above, there are clear similarities in the definition of the sub-categories included as part of the water-based beverages (*i.e.* soft drinks, cordials and formulated beverages) brand-loyalty scenario with that of 'fruit drinks'. The exposure levels determined using the 3 scenarios (*i.e.,* 20 to 110% ADI) would be representative of a range of consumption patterns, including those of individuals who are brand loyal to steviol glycoside-sweetened beverages, albeit at the upper end. However, based on the assumptions included in this model, these results are considered protective for the population.

The sweetener substitution method included a series of exclusion criteria and conservative assumptions in order to provide protective, yet realistic (*i.e.,* considering actual consumer patterns for approved sweeteners) average and high level exposure estimates to a novel intense sweetener. Sweetened beverages are a well-recognized source of intense sweeteners, as such, many of the studies placed additional focus on this food category. The predicted exposure levels (*i.e.,* 28 to 40% ADI) may therefore be considered to be representative of all sweetened beverages, including fruit drinks.

Taken together, following a critical review of the available estimates of intense sweetener intake, it was concluded that the above-mentioned exposure estimates may be considered sufficiently conservative to support that the proposed extension of use of steviol glycosides to 'fruit drinks' at a use level which is equivalent to other beverages of a similar nature (*i.e.*, 200 mg/kg) would be expected to result in a *change* in the pattern of consumption (*i.e.,* change in the contributing beverage categories), as opposed to an increase in the total estimated dietary exposure levels by the total Australian/New Zealand population.

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DISCLAIMER

Appendix
Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
General U.S. population (n = 1,135; aged 5 to 18 years; Fall 1977) - Total consumer population	600 (saccharin)	NA	All foods and beverages recorded by participants; results analyzed according to the following categories: • Artificially sweetened carbonated beverages • Artificially sweetened non-carbonated beverages • All other artificially sweetened beverages and food	• 7-day food diary • Artificially sweetened carbonated beverages contributed most significantly to saccharin intake (88%) • Value utilized in predictive Reb A calculation is the highest reported value of all sub-populations	Morgan *et al*. (1982)
General Canadian population (n=5,555 wave I; n=4,872 wave II; aged 2 years and over; February/April1987 and July/September 1987) - Total consumer population - Children (<2 years)	234 (aspartame) 369 (aspartame)	1,026 (aspartame) NA	All foods and beverages recorded by participants in the coded food diary according to the following categories: • Carbonated soft drinks • Powdered soft drinks	• 7-day coded food diary • Foods and beverages were recorded according to food categories which were marketed in Canada and contained aspartame • Product-specific concentration data were used	Heybach and Ross (1989)

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
- Children 2-5 years	NA	1,568 (aspartame)	• Puddings/ gelatins/ topping mixes • Table-top sweeteners • Chewing gum • Children's multi-vitamin supplements • Frozen juices/ drinks • Frozen novelties/ freeze pops • Iced tea mixes • Hard candies/ breath mints • Hot chocolate/ cocoa • Hot flavoured tea mixes • Milk-based flavoured drinks and shakes • Pie • Ready-to-eat cereals • Wine cooler	• Diabetics, individuals on 'sugar-avoiding diets' and 'weight loss diets' included in population cohort	
- Diabetic adults	427 (aspartame)	1,485 (aspartame)			

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
			• Yoghurt		
UK population *2 surveys conducted - September 1987 amongst the general population aged 2 to 64 years (n=681); September 1988 – supplementary survey targeted towards diabetic adults (n=89)* - General UK population (1987 cohort; aged 2-64 years) - Diabetic adults (1988 cohort)	180 (aspartame) 270 (saccharin) 354 (aspartame) 258 (saccharin)	306[b] (aspartame) 780[b] (saccharin) 1,656[b] (aspartame) 2,100[b] (saccharin)	Food diary requested information on the following foods and beverages categories: • Non-alcoholic drinks (*e.g.* fizzy/still/squashes, instant soups) • Powdered drinks (*e.g.* hot chocolate) • Instant dessert (*e.g.* instant whip) • Tea and coffee • Table-top sweeteners • Yogurt • Diabetic products Questionnaire administered requested information on the following products: • Tea • Instant coffee • Fresh coffee • Drinking chocolate • Cocoa	• 7-day food diary plus questionnaire on habitual usage of sweeteners • 2 separate surveys conducted, both conducted in September, as this month was deemed to be most representative of average intakes across the year • Targeted approach to enrolling diabetic individuals in the second survey (1988), food consumption recorded via 4-day food diary • Product-specific concentration data utilized (provided by product manufacturers) • Sources of sweeteners omitted from the study included natural sources, pharmaceutical products, and	Ministry of Agriculture Fisheries and Food (MAFF, 1990)

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
			• Fizzy drinks which are 'diet' or 'low calorie' • Ordinary fizzy drinks • Squash or cordials which are 'diet' or 'low calorie' • Other squashes or cordials • Table-top sweeteners Food diary administered to diabetic individuals also requested information on the foods targeted towards diabetics (*e.g.* baked beans) Questionnaire administered to diabetics also requested information on the following products made specially for diabetics or 'diet/low calorie' products	alcoholic or low-alcoholic beverages • Diet soft drinks contributed the highest intake of aspartame to the general population and saccharin for ages 10 to 34 years • Conventional soft drinks contributed the highest intake of saccharin in children aged 2 to 9 years	
General UK population (n=647; aged 1 to 75 years			All foods and beverages recorded by participants;	• 7-day food consumption survey	

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
of age; November/ December 1988) - Total consumer population - Children 1-5 years Diabetic adults	 72 (aspartame) 120 (saccharin) NA NA	 288 (aspartame) 390 (saccharin) 666 (acesulfame) 504 (aspartame) 735 (saccharin) 432 (aspartame) 525 (saccharin)	results analyzed according to the following categories: • Beverages • Table-top sweeteners • Food	• Recorded food consumption for 9 days, but disregarded the first 2 days to reduce initial inconsistencies • Study conducted in November/December based on analysis which demonstrated that this was a period which approximated the average beverage consumption levels • Diabetic adults and pregnant women were included within the study cohort • Product-specific concentration data used (provided by product manufacturers or analytical data) • Beverages were the primary source of all three sweeteners (60-98%)	Hinson and Nicol (1992)
General German population (2 phases: September			All foods and beverages recorded by participant; results	• 24 hour- food recall	

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
1988 and May 1989; n=2,291) - Total consumer population	216 (aspartame) 90 (saccharin)	504 (aspartame) 180 (saccharin)	analyzed according to the following categories: • Foods • Beverages • Table-top sweeteners	• Second phase of study utilized 7-day food recorded for subjects (n=40) whose aspartame or cyclamate consumption exceeded the ADI by 75% in the initial study • Brand-specific concentration data used (provided by product manufacturer or by chemical analysis) • Sample included individuals adhering to a diet (diabetic or weight control) • Table-top sweeteners and beverages were the most important sources of sweeteners (>80% of total intake) • Intake data for diabetics (n=58) were excluded from final predictive Reb A calculations in Renwick (2008) assessment because	Bär and Biermann, (1992)

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
				values were abnormally low	
Brazilian consumers of intense sweeteners (n=673; July-September 1990 and December to March 1991) -Total consumer population	216 (aspartame) 240 (saccharin)	NA	Only sweetener-containing food and drinks recorded by participants. Results were analyzed according to the following categories: • Table-top sweeteners • Diet soft drinks • Others (desserts, jellies, yogurt, chocolate)	• Only intense sweetener consumers were included in the assessment • Food frequency questionnaire utilized to record intake (daily, weekly, or monthly basis) • Product-specific concentration data (analytical measurement for soft drinks and table-top sweeteners ; alternatively from product label) • Table-top sweeteners were the major source of sweeteners, followed by soft drinks • Diabetics were included in the study cohort	Toledo and Ioshi (1995)
Denmark general population (n=1,233 from 473			All foods and beverages were recorded. Results	• 7-day food consumption survey	Renwick (1999)

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	**Heavy Level (sweetener name)[a]**			
households; April-June 1991)			analyzed according to the following categories: • All products • Beverages • Foods • Table-top sweeteners	• Diabetic individuals (n=76) and pregnant women (n=79) were included in the population • All individuals within a household were included in the survey – can influence overall estimate patterns • Product-specific concentration data was used for table-top and weight reduction products (determined from the label) and beverages (obtained from producer and measured analytically); maximum permitted concentration for foodstuffs was assumed when concentration was unavailable from the label or producer – slight overestimation • Food categories that contributed the most to the intake of each sweetener:	
- Total consumer population	126 (aspartame) 90 (saccharin)	270 (aspartame) 300 (saccharin)			
- Children (1-5 years)	262 (acesulfame) 155 (aspartame)	1,022 (acesulfame)			
- Children (10-14 years)	NA	623 (aspartame)			
- Diabetic adults	216 (aspartame) 132 (saccharin)	792 (aspartame) 399 (saccharin)			

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
				- *Acesulfame K*: beverages - *Aspartame*: beverages and foods - *Cyclamate*: beverages and table-top sweeteners - *Saccharin*: table-top sweeteners	
Netherlands, 1992 (n=6,218; aged 1 to 92 years) - Total consumer population	270 (aspartame) 60 (saccharin)	936 (aspartame) 300 (saccharin)	• Diet soft drinks (sodas, cordials, lemonade syrups) • Table-top sweeteners (coffee tea, other drinks) • Diet yoghurt, desserts	• 7-day FFQ of sub-population completed by subset of population (n=6,060)	Hulshof et al. (1995)
Australian population (n=128; aged 12 to 39 years), 1994 - Total consumer population	504 (aspartame) 150 (saccharin)	1,656 (aspartame) 840 (saccharin)	• Aerated soft drinks • Cordials • Table-top sweeteners • Flavoured milk • Flavoured yoghurt • Jam • Jelly • Chewing gum	• 7-day food record • Product-specific concentration data	NFA (1995)
Subjects from the UK with no dietary restrictions (n=188; aged 3 to 74 years)			Selected food categories likely to contain sweeteners:	• 48 –hour FFQ based on survey of MAFF (1990) survey (above)	Wilson *et al.* (1999)

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
- Total consumer population	150 (saccharin)	NA	• Soft and powdered drinks • Desserts • Soups • Caned meals • Spreads • Snacks • Sugar-free confectionary • Chewing gum • Table-top sweeteners • Diabetic foods	• Product-specific concentration data utilized (from product manufacturers) • Authors suggest that discrepancies between intake results from questionnaires versus urine samples are likely due to limited food groups included in the questionnaires (may not capture all products that contain the sweeteners)	
U.S. population cohort participating in National Health and Nutrition Examination Survey (NHANES) 2001-2002 (n=9,701)			• All foods in which aspartame is likely utilized • Approach: food codes searched using the keywords 'aspartame', 'diet' and 'sweetener' • Products were excluded following confirmation that aspartame is not	• Two 24-hour recalls • Assessment was based on categories of foods consumed, as opposed to brand – specific consumption data • Maximum reported concentration of aspartame applied to all food codes – likely overestimation	Magnuson et al. (2007)
- Total consumer population	882 (aspartame)	1,872 (aspartame)			
- Children (3-5 years)	1,019 (aspartame)	NA			

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
			used (*e.g.* baked goods)	• No correction for the use of other artificial sweeteners or blends of sweeteners – likely overestimation	
Australia and New Zealand general population (aged 12 years and over; August- September 2002 and January-February 2003) - Total consumer population - Diabetic adults	436 (aspartame) 138 (saccharin) 312 (sucralose) 416 (aspartame) 159 (saccharin) 276 (sucralose)	904 (aspartame) 384 (saccharin) 792 (sucralose) 958 (aspartame) 387 (saccharin) 624 (sucralose)	Intake recorded of 12 selected food groups: • Carbonated soft drinks • Cordials • Fruit drinks • Table-top sweeteners • Confectionaries • Flavoured yogurts and mousses • Jellies and milk based puddings • Jam or conserves • Flavoured milks • Canned fruits • Toppings • Ice creams	• 7-day recall food diary (n=400) completed by potential high consumers of intense sweeteners • Additional 187 diabetics or individuals with impaired glucose tolerance were recruited to supplement this cohort (total n=298) • Product-specific concentration data used • Subjects identified in a preliminary screen as likely to have higher than average intakes – as such 90th percentile of consumers would have overestimate 90th percentile of the original consumer population	Food Standards Australia New Zealand (FSANZ, 2004)

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
				• Carbonated soft drinks contributed the most to intakes of all 3 sweeteners (52-66%); cordials/ fruit drinks contributed the most to cyclamate (51%) intake; table-top sweetener contributed the most to saccharin intake (49%)	
General U.S. population (n~ 12,000; 1984-1992) - Total consumer population - Children (2-5 years) - Diabetic adults	 NA NA NA	 414 (aspartame) 666 (aspartame) 509 (aspartame)	All foods and beverages	• 14-day food consumption survey • Intake of aspartame is calculated from the number of occasions an individuals consumed a product containing the ingredient, the average portion size of the food for that individuals age and sex, and the amount of aspartame in that particular food • Children, diabetics, individuals on weight-reduction programs and pregnant women were all included in the study cohort	Butchko *et al.*, 2002 (results adapted from Butchko and Kotsonis, 1991, 1994

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
Denmark general population (n=3,098; aged 1 to 80 years;1995)			Beverages only. Calculations conducted for the following four categories (based on categories of analytical data available): • With carbon dioxide, light • With carbon dioxide, with sugar • No carbon dioxide, light • No carbon dioxide sugar	• 7-day pre-coded record method with closed answering categories supplemented with a possibility for open answers • Data based on Danish Dietary Survey • Concentration data based on analytical measurements for non-alcoholic beverages (n=116)	Leth *et al.* (2007)
- Children (1-3 years)	200 (acesulfame)	460 (acesulfame) 1,584 (aspartame)			
- Boys (7-10 years)	684 (aspartame)	NA			
Young children from the UK who consumed soft drinks (n=1,110; aged 1½ to 4½ years; January-March and July-September 2001)			Beverages only: • Carbonated drinks • Still drinks (natural or commercial) • Dilutable drinks • Powdered drinks • Tea and coffee • Infant formula	• 7-day food consumption survey which recorded all drinks • Participants were limited to children who consumed soft drinks • Product-specific concentration data (provided by product manufacturer) • Dilutable drinks were the main source of intake	Food Standards Agency UK (FSA, 2003)
- Total consumer population	184 (acesulfame) 608 (aspartame)	744[b] (acesulfame) 2,162[b] (aspartame)			

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
	348 (saccharin)	1,149[b] (saccharin)			
French, insulin-dependent children (n=227; aged 2 to 20 years; June-October 1997) - Diabetic children (2-20 years) - Diabetic children (2-6 years)	NA 550 (acesulfame) 1,071 (aspartame) 330 (saccharin)	800[b] (acesulfame) 1,404[b] (aspartame) 390[b] (saccharin) NR	All foods and beverages were recorded. Analysis was conducted according to EU legislative categories: • Non-alcoholic beverages • Desserts • Confectionary • Chewing gum • Fruits and fruit preparations • Sauces • Table-top sweeteners	• Prospective 5-day diary record • Non-alcoholic beverages contributed the most significantly to sweetener intakes (56 to 75%) • Product-specific concentration data used for table-top sweeteners (product label); maximum permitted level utilized for sweetener concentrations in sugar-free products in accordance with EU law (European Directive 94/35/EC – EC, 1994) • All sugar-free products were assumed to be sweetened at the maximum authorized level for each sweetener	Garnier-Sagne *et al.* (2001)
Canada children with type I diabetes				• 24-hour dietary recall	

Table A-1 Summary of Studies Utilized in the Calculation of Rebaudioside A Intakes (Renwick, 2008)

Population Group, Characteristics, and Time of Data Collection	Estimated Intake of Intense Sweeteners, as Sucrose Equivalents (mg/kg body weight/day)		Food Groups Included in Assessment	Key Attributes/Assumptions	Reference
	Mean (sweetener name)	Heavy Level (sweetener name)[a]			
mellitus (n=56; aged 2 to 6 years) - Total consumer population	738 (aspartame)	1,404 (aspartame) 540 (sucralose)	• All foods and beverages, as well as multivitamins and minerals	• Brand-specific concentration data (provided by product manufacturers) • Food groups that contributed most to sweetener intake were diet soft-drinks and other sugar-free beverages; sugar-free yogurts with added sweeteners; sugar-free syrup; sugar-free gum and multi-vitamins	Devitt *et al.* (2004)

ADI = acceptable daily intake; EU = European Union; FFQ = food frequency questionnaire; MAFF = Ministry of Agriculture, Fisheries and Food; NA = Not applicable - value not utilized in final prediction calculations; NDNS = National Diet and Nutrition Survey; NHANES = United States National Health and Nutrition Examination Survey; NR = Not Reported; Reb A = Rebaudioside A; UK = United Kingdom

[a] 90th percentile, unless otherwise specified

[b] 97.5th percentile value utilized