



Natural Extracted Ingredients

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Food Standards Australia New Zealand
Boeing House
55 Blackall Street
BARTON ACT 2600
PO Box 7186
Canberra BC ACT 2610
Australia

Food Standards Australia New Zealand
Level 3
154 Featherston Street
WELLINGTON 6011
PO Box 10559
The Terrace, Wellington 6143
New Zealand

RE: Rebaudioside M as a steviol glycoside intense sweetener

Dear Sir or Madame,

On behalf of PureCircle Ltd, I would like to thank the Foods Standards Australia New Zealand (FSANZ) for the opportunity to provide comment on the draft food regulatory consideration of "Rebaudioside M as a steviol glycoside intense sweetener".

I highly commend the FSANZ draft approval of Rebaudioside M as an additional steviol glycoside to the permitted steviol glycosides: Rebaudiosides A, B, C, D, E, F, Dulcoside A, Stevioside, Steviolbioside, and Rubusoside. I also support the specification outlined in section 2.6, Table 1 of the supporting document 1, "*Risk and technical assessment report - Application 1108*", where total steviol glycosides is to include any of the eleven steviol glycosides to make more than or equal to 95% of a Stevia leaf extract (sweetener). The draft notification also supports the JECFA petition submitted by Malaysia to change the JECFA steviol glycosides specification to include both Rebaudiosides E and M.

Since the submission of PureCircle dossier to FSANZ for approval of Rebaudioside M, several studies have been published (or being prepared for publication), which support that all steviol glycosides, irrespective of the type and number of sugar moieties attached to the aglycon steviol, display the same metabolic fate. Therefore, the current safety paradigm with Rebaudioside A is applicable to any combination of these glycosides. For your reference, I would like to submit the following table (next page) that outlines the toxicological studies with steviol glycoside molecules with different combinations of sugar (glucose, rhamnose, and xylose) moieties.

In summary, the in-vitro results of the individual steviol glycosides containing different sugar moieties (glucose, rhamnose and xylose), using a human faecal microbial system and a knowledge of the subsequent metabolism (rapid glucuronidation) following absorption from the gastrointestinal tract, it can be concluded that the results from toxicology studies conducted with stevioside, rebaudioside A and rebaudioside D can be bridged to the other 8 glycosides including rebaudioside B, C, E, F, M, dulcoside A, rubusoside and steviolbioside in support of safety (*i.e.*, each of the rebaudiosides is hydrolysed to steviol in a similar manner and at similar rates. Thus toxicology data on specific glycosides can be "read across" to the others).

PureCircle USA

915 Harger Road, Suite 250
Oakbrook, IL USA 60523-1492
Phone +1 630-631-0374 Fax +1 630-361-0384
Email: info@purecircleusa.com Website: www.purecircle.com

Steviol Glycosides	Molecular Structure	Safety Evaluations	References
Stevioside	SvG3	Toxicology & Metabolism	Nakayama et al., 1986; Hutapea <i>et al.</i> , 1997; Sung, 2002; Geuns <i>et al.</i> , 2003, 2007; Koyama et al., 2003a/b; Roberts and Renwick, 2008, Renwick & Tarka, 2008
Reb A	SvG4	Toxicology & Metabolism	
Reb D	SvG5	Toxicology & Metabolism	
Reb M	SvG6	<i>In-vitro</i> metabolism	Purkayastha et al, 2014
Reb B	SvG3	<i>In-vitro</i> metabolism	Purkayastha et al, 2014
Reb E	SvG4	<i>In-vitro</i> metabolism	Purkayastha et al, 2015
Steviolbioside	SvG2	<i>In-vitro</i> metabolism	Purkayastha et al, 2015
Reb C	SvR1G4	<i>In-vitro</i> metabolism	FDA (2014) GRN 536
Dulcoside A	SvR1G3	<i>In-vitro</i> metabolism	Pre-publication report (in preparation)
Reb F	SvX1G3	<i>In-vitro</i> metabolism	Pre-publication report (in preparation)
All steviol glycosides are hydrolyzed to steviol prior to absorption			Wingard <i>et al.</i> , 1980; Nakayama <i>et al.</i> , 1986; Gardana <i>et al.</i> , 2003; Koyama <i>et al.</i> , 2003b, EFSA (2010)

Since steviol glycosides with different types and number (2-6) of sugar moieties clearly show the same metabolic fate, PureCircle believes that other well characterized steviol glycosides should be considered for approval and included in the estimation of the purity of stevia leaf extract (steviol glycosides). As examples, Ohta et al (2010) presented SvR1 G4 (Reb H, J, K), SvR1G5 (Reb N), and SvR1G6 (Reb O), which would follow the same metabolic fate as displayed by steviol glycosides with 2 to 6 glucose molecules or combination of rhamnose and multiple glucose units (Dulcoside A & Reb C).

In conclusion, I would highly commend FSANZ for approval of stevia leaf extract with larger number of steviol glycoside molecules, which will facilitate formulation of food and beverage products with sugar-like taste and reduced sugar content. Thank you.

Sincerely,



Sidd Purkayastha, Ph.D.
VP, Head of Global Scientific & Regulatory Affairs
PureCircle Limited
915 Harger Road, Suite 250
Oak Brook, Illinois 60523

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PureCircle USA

915 Harger Road, Suite 250

Oakbrook, IL USA 60523-1492

Phone +1 630-631-0374 Fax +1 630-361-0384

Email: info@purecircleusa.com Website: www.purecircle.com

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