



THE SAFETY OF REB A EXECUTIVE SUMMARY

Rebaudioside A (Reb A) is an all natural zero calorie sweetener extracted from the *Stevia rebaudiana* (Bertoni) plant, which belongs to the chrysanthemum family and is native to Brazil and Paraguay. Reb A is the second most abundant glycoside in stevia and is structurally similar to other steviol glycosides, including stevioside. Two hundred times sweeter than sugar, Reb A is suitable for use to sweeten foods and beverages because of its solubility in water and its excellent taste profile.

In April of 2008 a panel of internationally recognized experts confirmed that Reb A meets the Generally Recognized as Safe (GRAS) criteria established by the Food and Drug Administration (FDA). The panel's report was submitted to the US FDA in May 2008 for their review. The following provides a short summary of current safety information on Reb A.

HISTORY OF SAFE USE IN OTHER COUNTRIES

Grown in its native South America, stevia has been consumed by the Guarani people of Paraguay and Brazil for hundreds of years as a natural sweetener. Today, stevia glycosides are used to sweeten foods and beverages in several countries including Japan, South Korea, Malaysia, Taiwan, Russia, Israel, Mexico, Paraguay, Uruguay, Venezuela, Columbia, Brazil and Argentina. More than 100 foods and beverages throughout the world include one or more of the steviosides.

NUMEROUS PEER-REVIEWED STUDIES CONFIRM THE SAFETY OF REB A AND STEVIOL GLYCOSIDES

An extensive database exists for Reb A, steviol glycosides and steviol which supports the safety of Reb A. The data cover the standard range of safety studies for determination of the safety of food ingredients, such as:

- Absorption, distribution, metabolism and excretion (ADME)
- Acute toxicity
- Subchronic toxicity
- Chronic toxicity
- Genotoxicity
- Reproductive/developmental toxicity
- Carcinogenicity

In addition, there have been a number of special studies in animals and humans that address issues related to the safety of steviol glycosides including potential effects on blood pressure and blood glucose control.

Absorption, Distribution, Metabolism and Elimination

The absorption, distribution, metabolism and elimination (ADME) of Reb A and other steviosides have been extensively studied. No absorption or structural modification of steviol glycosides in the stomach was found in animals or human volunteers. The principal steviol glycosides, Reb A and stevioside are metabolized in experimental animals and humans by intestinal bacteria by successive hydrolysis of glucose moieties. Based on the results of all of the metabolism studies, ingested steviol glycosides are eliminated in the feces or hydrolyzed to steviol prior to absorption from the gut. Because of the common hydrolysis pathways of steviol glycosides, any study in which the test material was a steviol glycoside is relevant in evaluating the safety of Reb A. Human fecal microflora were found to completely hydrolyze Reb A to steviol.

Carcinogenicity, Mutagenicity and Reproductive Toxicity

There is no evidence of carcinogenicity, mutagenicity or reproductive/developmental effects based on the results of more than 50 studies in animals. The only consistent findings in any of the studies were decreases in food consumption and decreases in weight in animals who received the highest doses of steviol glycosides. These doses were significantly above levels that would be consumed by humans.

Effects on Blood Glucose and Blood Pressure in Human Volunteers

The effects of the oral administration of stevioside in humans have been evaluated in several studies for durations of one day to two years. These studies confirm that Reb A will not have an effect on blood glucose levels or on blood pressure in normal healthy humans. Reb A and other steviol glycosides may decrease blood pressure slightly in hypertensive individuals who are not taking antihypertensive medications; however, this effect is not considered to be adverse.

Acceptable Daily Intake (ADI)

The totality-of-evidence related to the safety evaluation of Reb A supports an acceptable daily intake (ADI) of 12 mg/kg bw/day (expressed as Reb A). In fact, in June 2008 Joint Food and Agriculture Organization (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) reviewed all of the data on steviol, including recently released data, and raised its ADI recommendation to 0-4 mg/kg bw/day which correlates to 12 mg/kg bw/day of Reb A. This equates to 818 mg of Reb A or 30 packets of PureVia™ for a person weighing 150-lb (68 kg).

The estimated daily intake (EDI) of Reb A from the proposed uses including tabletop sweeteners, sweetened ready-to-drink iced teas, diet carbonated soft drinks, fruit juice drinks, energy drinks, flavored waters, cereal bars, oatmeal, and sweetened cold cereals, was estimated using the maximum proposed use rates and data from the most recent National Health and Nutrition Examination Survey (2003-2004). The EDI on a “per user” basis is approximately 2 mg/kg bw/day at the mean and 5 mg/kg bw/day for individuals who consume large amounts, (e.g. the upper 90th percentile consumer). The

assumptions that were used in estimating consumer intakes from all proposed uses are conservative and, therefore, the estimates most certainly overestimate potential consumer intakes of Reb A. Even with these conservative assumptions, all calculated EDIs for the food categories of interest are well below the ADI (12 mg/kg bw/day). For example, one packet of PureVia™ contains 27 mg of Reb A. The ADI of Reb A for a 150-lb (68 kg) person would be equivalent to the amount found in 30 packets of PureVia™ sweetener.