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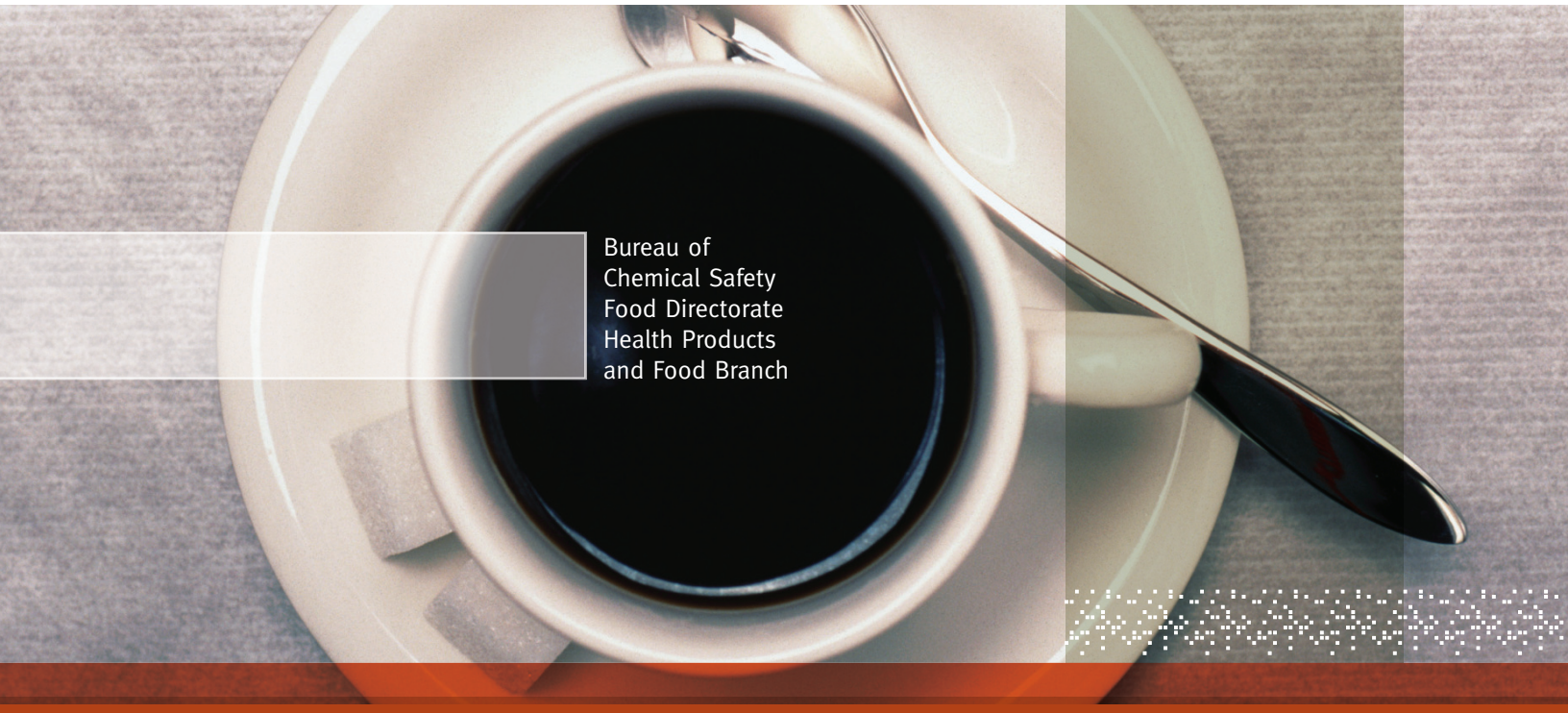
Information Document on the Proposal to

Reinstate Saccharin for Use as a Sweetener in Foods in Canada



Bureau of
Chemical Safety
Food Directorate
Health Products
and Food Branch

Canada

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Document d'information sur la proposition de réinscription de la saccharine à titre d'additif alimentaire au Canada

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Abstract:

In the 1970's, studies suggested that sodium saccharin was carcinogenic in laboratory rats. On this basis, saccharin was de-listed as a food additive in Canada, although restricted access as a table top sweetener was maintained. Since that time, further studies have suggested that the carcinogenic effect of sodium saccharin in rats is not relevant to humans. Both the Joint Food and Agriculture Organization of the United Nations/World Health Organization (FAO/WHO) Expert Committee on Food Additives (JECFA), and the European Commission's Scientific Committee on Foods has established an acceptable daily intake (ADI) for sodium saccharin. Health Canada scietists have concluded to a similar ADI. The International Agency for Research on Cancer (IARC) has conducted a complete evaluation of saccharin's carcinogenic potential in humans and has concluded that sodium saccharin can no longer be considered a "possible carcinogen in humans". In May 2000, the U.S. National Toxicology Program (NTP) dropped saccharin from its list of suspected cancer-causing chemicals, indicating that the rodent carcinogenicity data are not sufficient to list this chemical as a "reasonably anticipated human carcinogen."

Health Canada's Food Directorate has received a food additive submission to re-list saccharin for use in a variety of foods in Canada.

Purpose and Scope of the Information document

The purpose of this document is to provide background information and to provide a summary of the evidence used by Health Canada's scientists in support of the proposal to re-list saccharin as a sweetener in foods in Canada. It has been widely shared with concerned groups, including public health associations, federal departments, consumer associations, food sectoral associations, medical associations, trade associations, and food manufacturers, prior to proceeding to the pre-publication (in Canada Gazette Part I) of a schedule of amendments containing the re-listing of saccharin and its salts as food additives for certain food categories.

Background

Saccharin was de-listed from the Food and Drug Regulations for use as a sweetening agent in the late 1970's because, on the basis of animal studies, it was believed to have the potential to cause cancer in humans. As a result, saccharin was not permitted to be used as an additive in foods or beverages in Canada, nor could products containing saccharin be sold. In the absence of alternative sweeteners at the time of this prohibition, and for the benefit of individuals who have to reduce their calorie intake for medical or other reasons, saccharin continued to be available as a table top sweetener, subject to strict requirements for labelling and place of sale. The Departmental position established at that time is still in effect today. Internationally, saccharin's use in foods and beverages is permitted in the United States, Great Britain, Europe, Australia, New Zealand and many Asian countries, including Japan.

Current Situation

Health Canada's Food Directorate has received a submission from the Calorie Control Council of Atlanta, Georgia, to reinstate saccharin as a food additive in Canada. The requested products and levels of use are based on the current use patterns in the United States.

Table 1: Maximum Requested Levels (mg/kg) for Saccharin

Breath mints	1500	Liqueurs	1200
Canned fruits	100	Soft drinks	300
Chewing gum	2500	Table-top Sweeteners	GMP*
Frozen Desserts	25	Whipped Toppings	900
Fruit Toppings	900	Jams and Jellies	200

**GMP refers to "Good Manufacturing Practice." The content of packages of table-top sweeteners would contain approximately 40–50 mg saccharin which is the equivalent sweetening power of 2 teaspoons of sugar.*

Safety of Sodium Saccharin for humans

An assessment in which lifetime exposure in rats was extended to include the gestation and lactation periods through the mother's milk demonstrated that exposure to 5% and 7.5% saccharin in the diet could produce benign and malignant tumours in the bladder of the male and female rat. The male rat was more sensitive than the female rat to the development of tumours.

A subsequent study in rats showed that the critical period of exposure to sodium saccharin for development of tumours started at birth through exposure from mother's milk. This study also showed that no significant increase in the incidence of tumours occurred at concentrations of less than 3% in the diet.

Scientists who interpret the human health implications of cancer caused by sodium saccharin in rats are assisted in this effort by additional studies in the areas of pharmacokinetics (the study of the absorption, distribution, metabolism and excretion of a substance); genotoxicity (the study of adverse effects on DNA); initiation-promotion modelling (the study and prediction of whether a substance causes cancer itself or creates conditions conducive to cancer formation); and epidemiology (the study of populations for specific health-related cause and effect relationships).

The following observations have been made:

- An important consideration in predicting the potential carcinogenicity of a substance is whether or not it binds to DNA. In this regard, studies have shown that saccharin does not bind to DNA and, therefore, this available evidence supports the safety of saccharin.
- Extremely high doses of sodium saccharin starting at birth or at least in the first 5 or 6 weeks of life, were required to induce bladder tumours in rats. High doses of some other organic acids that are part of a normal diet or that occur naturally in the body have also been shown to induce the same changes as sodium saccharin in the bladder lining of the rat. For example, high doses of sodium ascorbate (vitamin C) were found to induce bladder tumours in rats in the same type of study.
- Recent work has shown that the formation of a crystal deposit in rat urine is associated with the later development of bladder cancer in rats. The formation of this urinary deposit, leading to changes in the bladder lining and the formation of tumours, is dependent upon properties of urine found in rats and/or brought on in rats by the high doses of sodium saccharin used experimentally. In humans or other species (mouse, monkey), all of the necessary conditions leading to formation of the urinary deposit in rats do not occur. Studies in rats also indicate that when the experimental conditions are changed to prevent a deposit from forming, no changes of the bladder are observed in response to consumption of saccharin.

These facts suggest that the cancer-causing effect of sodium saccharin in rats is not relevant to humans, providing confidence that sodium saccharin can be safely consumed by humans.

Therefore, it is possible to establish an Acceptable Daily Intake (ADI) for saccharin in humans based on the non-carcinogenic, reversible changes (increased diurises and reduced feed efficiency) observed in the rat at high dietary concentrations. An ADI is the estimated amount of a substance that can be ingested daily, over a lifetime, without any appreciable risk. The ADI for sodium saccharin, at 5 mg/kg body weight, is 100 times less than the highest dose in the rat at which no effects relevant to human health would be seen. This incorporates a safety assessment for children, since in the study used to derive the ADI, rats were exposed to sodium saccharin in the diet for their entire lifetime.

Concerns were raised in several public fora that a number of issues in the risk assessment of sodium saccharin had not been satisfactorily addressed. These included concerns that saccharin produced tumours in sites other than the urinary bladder in rats, produced bladder tumours in animal species other than rats, and that epidemiological studies indicated a higher risk for bladder cancer in certain sub-groups of the population consuming saccharin. These concerns have been carefully investigated and it was concluded that the only consistent and reproducible effect in valid experimentation was the development of bladder tumours in rats fed at least 3% sodium saccharin in the diet, starting from birth, an effect which has been shown not to be relevant to humans. Due to inadequacies in the available data no overall conclusion could be drawn from the epidemiological studies with regard to increased risk in sub-groups of the adult human population from consuming saccharin.

International comparison

Since the de-listing of saccharin in Canada, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) has reviewed the toxicological data on saccharin several times. JECFA concluded in 1993 that "on the basis of data reviewed to date, it would be inappropriate to consider the bladder tumours induced in male rats by sodium saccharin to be relevant to the assessment of a toxicological hazard to humans" and at the 41st meeting in 1993, an ADI of 0-5 mg/kg body weight was established for the consumption of saccharin and its salts.

In June, 1995, the European Commission's Scientific Committee on Foods reviewed the data available at the time on saccharin and approved an ADI of 0-5.0 mg/kg body weight for sodium saccharin (0-3.8 mg/kg body weight as acid saccharin).

In October, 1998, the International Agency for Research on Cancer (IARC) downgraded saccharin from a Category IIB Carcinogen (possibly carcinogenic to humans) to a Category III Carcinogen (not classifiable as to its carcinogenicity in humans) based on a re-evaluation of the animal data. This category is used for agents for which there is strong, consistent evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans or does not predict carcinogenic risk to humans.

In May 2000, the U.S. National Toxicology Program (NTP) dropped saccharin from its list of suspected cancer-causing chemicals, indicating that new studies show no clear association between saccharin and human cancer.

Dietary Exposure

Health Canada scientists have calculated the potential daily intake of saccharin based on consumption data for the relevant foods and the proposed levels of use. These calculations indicate that intakes of saccharin from the proposed uses would not be expected to exceed the widely adopted ADI of 5 mg/kg body weight.

This conclusion is supported by results of consumption studies from countries such as Australia, Denmark, Germany, the United Kingdom and the United States, where saccharin is permitted for use in foods. If the proposal to re-list saccharin is approved, and after a suitable time passes to allow for full market penetration of the products listed in Table 1, the Calorie Control Council

has agreed to conduct a consumption monitoring study to identify actual intakes of saccharin in the Canadian population.

Labelling

A Labelling regime for several high intensity sweeteners has already been established in Division 1 of the Food and Drug Regulations. The Labelling regime requires that the presence of the sweetener be clearly stated on the food package and provides consumers with the information needed to make an informed choice with respect to consuming sweeteners. A similar Labelling regime for saccharin would also be developed in Division 1 of the Regulations.

Recommendation

The weight of toxicological evidence and the lack of a consistent association in epidemiological studies suggests that carcinogenic effects of saccharin noted in rats are not relevant to humans. As a result, it is considered that saccharin could be re-listed in the Canadian *Food and Drug Regulations* for use as a sweetener in the proposed food categories. It is recommended that Table IX, Division 16 of Part B of the Food and Drug Regulations be modified as shown in Table 2 below to permit the use of saccharin and its calcium, potassium and sodium salts in the following areas of use at the levels indicated.

Table 2: Proposed Addition to Table IX, Section B.16.100

Item No.	***Column I*** ***Additive***	***Column II*** ***Permitted in or Upon***	***Column III*** ***Maximum Level of Use***
S.1	Saccharin and its calcium, potassium and sodium salts	(1) Breath freshener products	(1) 1500 ppm, calculated as saccharin
		(2) Canned fruits, except those for standardized in this Part	(2) 100 ppm, calculated as saccharin
		(3) Chewing gum	(3) 2500 ppm, calculated as saccharin
		(4) Frozen desserts	(4) 25 ppm, calculated as saccharin
		(5) Fruit, whipped or dessert toppings	(5) 900 ppm, calculated as saccharin
		(6) Liqueurs, except those standardized in this Part	(6) 1200 ppm, calculated as saccharin
		(7) Soft drinks	(7) 300 ppm, calculated as saccharin
		(8) Jams, jellies and marmalades, except those standardized in this Part	(8) 200 ppm, calculated as saccharin
		(9) Table-top sweeteners	(9) Good Manufacturing Practice

The content of packages of table-top sweeteners would contain approximately 40–50 mg of saccharin which has the equivalent sweetening power of 2 teaspoons of sugar.

Finally, it is recommended that saccharin be brought into the labeling regime established for high intensity sweeteners in Division 1 of the Regulations.

ADDITIONAL INFORMATION

Additional information on this proposal could be obtained by submitting a request to the Food Directorate in the Health Products and Food Branch (HPFB) via e-mail: bcs-bipc@hc-sc.gc.ca (please use the words "Saccharin Notification" in the e-mail subject box) or by mail to:

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