FOOD STANDARDS Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

**[3-08]**
**6 March 2008**

# PROPOSAL P1002 HYDROCYANIC ACID IN READY-TO-EAT CASSAVA CHIPS ASSESSMENT REPORT

## Executive Summary

### Purpose

FSANZ has prepared Proposal P1002 to assess the public health risks associated with hydrocyanic acid (hydrogen cyanide) in ready-to-eat cassava chips. Following an assessment of the risks to public health and safety, and based on the data available, FSANZ is proposing that regulatory measures in the *Australia New Zealand Food Standards Code* (the Code) are required to reduce levels of hydrocyanic acid in ready-to-eat cassava chips to as low as reasonably achievable.

The proposed food regulatory measure is the inclusion in the Code of a maximum level of 10 mg/kg for hydrocyanic acid in ready-to-eat cassava chips. Compliance with the proposed food regulatory measure would reduce the dietary exposure to hydrocyanic acid from ready-to-eat cassava chips and would address the potential public health implications that have recently been identified with these foods.

While not currently within the scope of this proposal, additional regulatory and non-regulatory measures may be required as investigations continue into hydrocyanic acid in other foods. The proposed inclusion of a maximum level for hydrocyanic acid in ready-to-eat cassava chips is considered an appropriate risk management measure while these investigations continue.

### Assessing the Proposal

The Proposal is being assessed under the General Procedure. In assessing the Proposal and the subsequent development of a food regulatory measure, FSANZ has had regard to the following matters as prescribed in section 59 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act):

- whether costs that would arise from a food regulatory measure developed or varied as a result of the Proposal outweigh the direct and indirect benefits to the community, Government or industry that would arise from the development or variation of the food regulatory measure;

- there are no other measures that would be more cost-effective than a variation to Standard 1.4.1 that could achieve the same end;

- any relevant New Zealand standards;

- any other relevant matters.

**Preferred Approach**

It is proposed to vary Standard 1.4.1 – Contaminants and Natural Toxicants of the Code to include a maximum level of 10 mg/kg for total hydrocyanic acid in 'ready-to-eat cassava chips'.

**Reasons for Preferred Approach**

- with proper preparation or processing, cassava and cassava-based foods are safe for human consumption, even though whole, unprocessed cassava may contain naturally occurring cyanogenic substances[1];

- the nature of the processing of 'ready-to-eat cassava chips' is such that existing food regulatory measures in the Code are not considered sufficient to reduce levels of hydrocyanic acid in ready-to-eat cassava chips to as low as reasonably achievable;

- following a risk assessment, a food regulatory measure in the Code for hydrocyanic acid in ready-to-eat cassava chips is proposed to minimise the dietary exposure to hydrocyanic acid and thereby protect public health and safety;

- a maximum level in Standard 1.4.1 is considered to be an appropriate risk management measure while additional information is gathered about other cassava based foods and other foods containing cyanogenic substances;

- a level specifically for 'ready-to-eat cassava chips' only is proposed. This is because no problems have been identified with other cassava based products in Australia or New Zealand at this time, and there are existing food regulatory measures for managing hydrocyanic acid in some other cassava based products;

[1] 'cyanogenic substances' are those substances that produce hydrocyanic acid (hydrogen cyanide) in specific circumstances.

- a maximum level of 10 mg/kg is considered to be practical and reasonably achievable with proper processing of cassava. It is also consistent with the international standard for edible cassava flour (another processed cassava product for direct human consumption) which is the predominant cassava based ingredient in ready-to-eat cassava chips;

- given the potential public health implications, it is proposed that the level come into effect upon gazettal and with no ‘stock in trade’ transitional arrangements;

- at this time, it is not considered appropriate or necessary to prescribe a method of analysis for hydrocyanic acid in ready-to-eat cassava chips as this will restrict the flexibility of industry and compliance agencies to develop more contemporary methods for monitoring hydrocyanic acid in ready-to-eat cassava chips.

FSANZ invites comment on the preferred approach stated above. Specifically, FSANZ encourages comment on the following and will have regard to these comments in further considering this Proposal:

- the levels of hydrocyanic acid that are achievable in ready-to-eat cassava chips and other ready-to-eat foods that contain cassava;

- the need to extend the proposed level to apply to all ready-to-eat foods containing cassava and the basis for this;

- the costs of instituting measures for reducing hydrocyanic acid in ready-to-eat cassava chips to comply with the proposed level;

- the need for any transitional arrangements for the proposed level and the reason for such transitional arrangements;

- the need to prescribe methods of analysis and if so, full details or references of these methods so they could be considered for prescription in the Code; and

- other measures, regulatory or non-regulatory, that may be appropriate for managing the risks associated with hydrocyanic acid in ready-to-eat cassava chips.

**Consultation**

This Proposal is being assessed under the General Procedure in the *Food Standards Australia New Zealand Act 1991,* with one round of public consultation.

FSANZ acknowledges that this Proposal will be of interest to a broad range of stakeholders and has applied a general communication strategy to this Proposal. This will involve advertising the availability of the Assessment Report for public comment in the national press and making the reports available on the FSANZ website. FSANZ will also consult key stakeholders through targeted consultation mechanisms.

In addition, individuals and organisations that make submissions on this Proposal will be notified at each stage of the Proposal. If the FSANZ Board approves the draft variation to the Code, FSANZ will notify the Ministerial Council of its decision. Stakeholders, including the public, will be notified on the gazettal of changes to the Code in the national press and on the FSANZ website.

**Invitation for Submissions**

FSANZ invites public comment on this Report and the draft variation to the Code based on regulation impact principles for the purpose of preparing an amendment to the Code for approval by the FSANZ Board.

Written submissions are invited from interested individuals and organisations to assist FSANZ in further considering this Application/Proposal. Submissions should, where possible, address the objectives of FSANZ as set out in section 18 of the FSANZ Act. Information providing details of potential costs and benefits of the proposed change to the Code from stakeholders is highly desirable. Claims made in submissions should be supported wherever possible by referencing or including relevant studies, research findings, trials, surveys etc. Technical information should be in sufficient detail to allow independent scientific assessment.

The processes of FSANZ are open to public scrutiny, and any submissions received will ordinarily be placed on the public register of FSANZ and made available for inspection. If you wish any information contained in a submission to remain confidential to FSANZ, you should clearly identify the sensitive information, separate it from your submission and provide justification for treating it as confidential commercial material. Section 114 of the FSANZ Act requires FSANZ to treat in-confidence, trade secrets relating to food and any other information relating to food, the commercial value of which would be, or could reasonably be expected to be, destroyed or diminished by disclosure.

Submissions must be made in writing and should clearly be marked with the word 'Submission' and quote the correct project number and name. While FSANZ accepts submissions in hard copy to our offices, it is more convenient and quicker to receive submissions electronically through the FSANZ website using the Standards Development tab and then through Documents for Public Comment. Alternatively, you may email your submission directly to the Standards Management Officer at submissions@foodstandards.gov.au. There is no need to send a hard copy of your submission if you have submitted it by email or the FSANZ website. FSANZ endeavours to formally acknowledge receipt of submissions within 3 business days.

**DEADLINE FOR PUBLIC SUBMISSIONS: 6pm (Canberra time) 3 April 2008**

**SUBMISSIONS RECEIVED AFTER THIS DEADLINE WILL NOT BE CONSIDERED**

Submissions received after this date will only be considered if agreement for an extension has been given prior to this closing date. Agreement to an extension of time will only be given if extraordinary circumstances warrant an extension to the submission period. Any agreed extension will be notified on the FSANZ website and will apply to all submitters.

Questions relating to making submissions or the application process can be directed to the Standards Management Officer at standards.management@foodstandards.gov.au. If you are unable to submit your submission electronically, hard copy submissions may be sent to one of the following addresses:

**Food Standards Australia New Zealand**
**PO Box 7186**
**Canberra BC ACT 2610**
**AUSTRALIA**
**Tel (02) 6271 2222**

**Food Standards Australia New Zealand**
**PO Box 10559**
**The Terrace WELLINGTON 6036**
**NEW ZEALAND**
**Tel (04) 473 9942**

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# INTRODUCTION

Recently, food regulatory agencies in Australia and New Zealand have found that certain cassava based foods (chips or crackers) contain higher than expected levels of hydrocyanic acid (hydrogen cyanide). While the likelihood of someone becoming ill from eating these products was considered low, as a precaution, consumers, particularly children, were urged not to eat these products. These results prompted the national recall of the implicated products in Australia and further investigation by food regulatory authorities.

As part of these investigations, FSANZ prepared a risk assessment in relation to cyanogenic glycosides[2] in cassava chips **(Attachment 2)**. Based, in part, on this risk assessment and as a result of further investigation, FSANZ has prepared this Proposal to:

- consider the potential public health and safety risks associated with the consumption of ready-to-eat cassava chips; and
- develop appropriate risk management strategies to manage these risks, including the need for a maximum level in the Code for hydrocyanic acid (hydrogen cyanide) in these foods.

## 1. The Issue

Cassava naturally contains compounds called cyanogenic glycosides which release hydrocyanic acid (hydrogen cyanide) as a result of enzymatic hydrolysis during processing of the plant tissue. Safe traditional human consumption of cassava is dependent on adequate processing to minimise the cyanogenic glycoside content. If cassava is eaten either raw or after inadequate processing then toxicity in humans may be observed.

FSANZ has been notified of total hydrocyanic acid levels in ready-to-eat cassava chips manufactured in Australia. These results ranged from less than 10 mg/kg up to 145 mg/kg. These levels are much higher than would be expected in cassava based foods which have been adequately processed. This has prompted an examination of the implications of these findings, including the implications for public health and safety.

Accordingly, this Proposal examines the existing regulatory measures in the Code for managing hydrocyanic acid in ready-to-eat cassava chips and assesses the need for additional risk management measures to ensure the protection of public health and safety. This assessment includes consideration of the need for a maximum level in the Code for hydrocyanic acid in ready-to-eat cassava chips.

[2] 'cyanogenic glycosides' are naturally occurring substances that produce hydrocyanic acid (hydrogen cyanide) in specific circumstances.

## 1.1 Terminology

Throughout this Report there are some terms which have the potential to be used ambiguously. To avoid doubt, these expressions have been further explained below. These terms may vary from those used in the risk assessment at Attachment 2 because the risk assessment was published before this report.

### *1.1.1 Hydrocyanic acid*

Throughout this report the term 'hydrocyanic acid' will be used instead of the term 'hydrogen cyanide'. This is because the term 'hydrocyanic acid' is currently used in Standard 1.4.1 – Contaminants and Natural Toxicants which is the standard in which Maximum Levels for substances are included. It is also the term used in Codex Alimentarius Commission standards for processed cassava products.

FSANZ acknowledges that the term 'hydrogen cyanide' is the term recommended by the International Union of Pure and Applied Chemists. It is also the term used in the definition of 'sweet cassava' in Standard 1.1.2 – Supplementary Definitions For Foods, which is based on the Codex Standard for Sweet Cassava.

In this report the term 'hydrocyanic acid' refers to total hydrocyanic acid which includes the hydrocyanic acid which may be enzymatically released from a cyanogenic glycoside as well as any 'free' or unbound hydrocyanic acid in the food.

### *1.1.2 Ready-to-eat Cassava Chips*

The term 'ready-to-eat' is used in the Code and 'ready-to-eat food' is defined in Standard 3.2.2 of the Code as:

> ***ready-to-eat food*** *means food that is ordinarily consumed in the same state as that in which it is sold and does not include nuts in the shell and whole, raw fruits and vegetables that are intended for hulling, peeling or washing by the consumer*

Throughout this Report the term 'ready-to-eat cassava chips' will be used to describe those foods which contain cassava and are represented as snack foods suitable for consumption in the same state in which they are sold, i.e. with no further preparation and ready for immediate consumption. These foods are often represented as 'chips', 'crisps', 'crackers', 'vege crackers' or with other snack food terms. This term does not include processed cassava foods which would not be considered snack foods such as desserts e.g. tapioca pudding.

The term 'ready-to-eat cassava chips' has been used to differentiate those snack foods for direct consumption from raw cassava 'chips' which is a form of cassava that is used in trade but which is intended to be further processed before human consumption. The term 'ready-to-eat cassava chips' does not apply to raw cassava unless the raw cassava is represented as a ready-to-eat food with no further preparation before consumption.

## 2. Current Standard

Cassava (*Manihot esculanta* Crantz) contains naturally occurring substances called cyanogenic glycosides, primarily linamarin[3]. Safe traditional human consumption of cassava is dependent on adequate processing to minimise the linamarin content. Conventional processing usually involves peeling and grating and then soaking in warm water for several days.

### 2.1 *Australia New Zealand Food Standards Code*

The current and specific food regulatory measures for cassava in the Code were developed primarily as part of Proposal P257 – Advice on the Preparation of Cassava and Bamboo Shoots. The following link provides information on the assessment that was undertaken at that time, as well as background about cassava and cassava production:

http://www.foodstandards.gov.au/standardsdevelopment/proposals/proposalp257preparationofcassava21august2002/index.cfm

As a result of the consideration of Proposal P257, the Code was amended to:

- include a prohibition on the sale of cassava other than 'sweet cassava' (Standard 1.4.4 – Prohibited and Restricted Plants and Fungi);

- 'sweet cassava' was defined in the Code (Standard 1.1.2 – Supplementary Definitions for Foods) as 'those varieties of cassava roots grown from *Manihot esculenta Crantz* of the *Euphoribiacae* family that contain less than 50 mg per kg of hydrogen cyanide (fresh weight basis)'; and

- include a requirement for raw cassava to be labelled or accompanied by a statement indicating that sweet cassava should be peeled and fully cooked before being consumed (Standard 1.2.6 – Directions for Use and Storage).

While not developed as part of P257, the Code also includes the following levels for hydrocyanic acid in the following foods: 25 mg/kg in confectionery; 5 mg/kg in stone fruit juices; 50 mg/kg in marzipan; 1 mg/kg per 1% alcohol in alcoholic beverages. Consistent with the international standard that formed the basis for these levels, these levels only apply to a food to which a flavouring substance has been added. The information on these levels has been included as background to this Proposal.

In respect of ready-to-eat cassava chips, the current regulatory measures in the Code are that:

- only raw cassava containing less than 50 mg/kg hydrocyanic acid can be sold and this must be labelled with certain directions for use; and
- raw cassava containing 50 mg/kg or more hydrocyanic acid and derivatives of this cassava must not be sold.

[3] See Attachment 2 for more detail about linamarin.

Raw cassava is whole cassava root or unprocessed cassava and the current limit applies on a 'fresh weight' basis (i.e. approximately 70% moisture).

The current regulatory measures do not address the potential for raw cassava containing less than 50 mg/kg to be dried, minimally processed and then sold as a ready-to-eat food. This is because, at the time the current measures were developed, it was understood that adequate processing of all raw cassava was occurring. There was no information at that time to indicate that dried, minimally processed cassava was being sold as a ready-to-eat food with elevated levels of hydrocyanic acid.

### 2.2 Codex Standards

The Codex Alimentarius Commission has developed and published standards for Sweet Cassava, Edible Cassava Flour and Gari (a product obtained from processing cassava tubers) (also spelled as 'garri'). Throughout this report these standards are regarded and referred to as 'international standards'. The key aspects of these standards are:

- sweet cassava is defined as a raw product containing less than 50 mg/kg of hydrocyanic acid;

- edible cassava flour is defined as a product suitable for direct human consumption and the level of total hydrocyanic acid in the flour must not exceed 10 mg/kg; and

- for gari, another product for direct human consumption, the total hydrocyanic acid must not exceed 2 mg/kg as 'free' hydrocyanic acid.

### 2.3 Requirements in Other Countries

FSANZ has not identified any specific requirements in other countries for hydrocyanic acid in ready-to-eat cassava chips.

## 3. Objectives

In developing or varying a food standard, FSANZ is required by its legislation to meet three primary objectives which are set out in section 18 of the FSANZ Act. These are:

- the protection of public health and safety;
- the provision of adequate information relating to food to enable consumers to make informed choices; and
- the prevention of misleading or deceptive conduct.

In developing and varying standards, FSANZ must also have regard to:

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

- the promotion of consistency between domestic and international food standards;
- the desirability of an efficient and internationally competitive food industry;
- the promotion of fair trading in food; and
- any written policy guidelines formulated by the Ministerial Council.

In the context of this Proposal, the objective of FSANZ is to assess the need for additional risk management measures to ensure the protection of public health and safety, including the need for a maximum level in the Code for hydrocyanic acid in ready-to-eat cassava chips.

## 4. Questions to be answered

The key questions to be answered are:

- What is the risk to public health and safety of hydrocyanic acid from ready-to-eat cassava chips?

- Are additional risk management measures required to protect public health and safety?

- Is a Maximum Level (ML) in the Code for hydrocyanic acid from ready-to-eat cassava chips an appropriate risk management measure?

- Could industry comply with any additional risk management measures, including an ML?

- Could compliance with any risk management measures be effectively monitored, including any ML?

# RISK ASSESSMENT

## 5. Risk Assessment Summary

Following reports of higher than expected levels of hydrocyanic acid in ready-to-eat cassava chips, FSANZ conducted a risk assessment (See Attachment 2) to determine whether such levels were likely to result in potential public health concerns. While both short- and long-term effects may occur following ingestion of cyanogenic glycosides in cassava based foods the risk assessment specifically focussed on:

- estimating the likelihood of toxicity as a result of consuming 200 g of ready-to-eat cassava chips over a period of 1-2 hours; and
- establishing a guidance level for hydrocyanic acid in ready-to-eat cassava chips.

The potential toxicity in relation to hydrocyanic acid in ready-to-eat cassava chips depends primarily on the concentration of residual cyanogenic glycosides.

Any cyanogenic glycosides present in food will undergo fermentation to release hydrocyanic acid following contact with the microflora usually found in the gastrointestinal tract, though predominantly in the colon.

Assuming that the levels of hydrocyanic acid in ready-to-eat cassava chips do not exceed 80 mg/kg, the risk assessment concluded that the consumption of 200 g of ready-to-eat cassava chips by a 20 kg child was unlikely to result in any short-term toxicity.

However, if the content of hydrocyanic acid in the cassava chips was greater than 80 mg/kg or other sources of hydrocyanic acid (e.g. marzipan or stone fruit juice) were consumed within the same 1-2 hours then it may be possible for children's dietary exposure to exceed an acceptable level. The most recent testing by one food regulatory agency in Australia indicates that some hydrocyanic acid levels in ready-to-eat cassava chips may be as high as 145 mg/kg.

To minimise the likelihood of acute toxicity in children arising from the consumption of ready-to-eat cassava chips, a guidance level of 25 mg/kg of hydrocyanic acid was considered appropriate. This value was based on the existing maximum level of 25 mg/kg for hydrocyanic acid in confectionery. The guidance level was an interim measure developed as part of the initial response to the higher than expected levels in ready-to-eat cassava chips.

# RISK MANAGEMENT

## 6. Issues

### 6.1 Risk to public health and safety

Although raw cassava naturally contains toxic cyanogenic glycosides[2], it has been safely consumed by millions of people around the world for many centuries. It is usually made safe for human consumption following appropriate preparation and processing[4]. However, inadequate processing of raw cassava that results in appreciable residual quantities of cyanogenic glycosides may represent a public health risk.

Based on the range of hydrocyanic acid concentrations (<10 up to 145 mg/kg) in ready-to-eat cassava chips that had been provided by food regulatory agencies, the risk assessment indicates that high levels of hydrocyanic acid in ready-to-eat cassava chips may be of potential concern for public health and safety. While the likelihood of an acute cyanide intoxication event occurring is assessed as low, it is nevertheless of concern given the levels that have been reported.

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[4] Cassava processing, FAO Plant Production and Protection Series No. 3, Food and Agriculture Organization.

Based on the current maximum level for hydrocyanic acid in confectionery in the Code, a guidance level of 25 mg/kg for hydrocyanic acid in ready-to-eat cassava chips was proposed by FSANZ as part of the initial response to the higher than expected levels in certain ready-to-eat cassava chips. However, maximum levels for naturally occurring contaminants in food are established at levels which are 'as low as reasonably achievable' (ALARA). If a lower level of cyanogenic glycosides (i.e. HCN <25 mg/kg) in ready-to-eat cassava chips were achievable then this would further reduce the dietary exposure to hydrocyanic acid from these foods.

### 6.2 Additional risk management measures

The Code currently includes a range of regulatory measures to limit and manage hydrocyanic acid in cassava and cassava based foods. These are based on limiting access to varieties of cassava that may contain levels of hydrocyanic acid of 50 mg/kg or above, and ensuring adequate information about processing is provided to consumers. The level of 50 mg/kg currently only applies to raw cassava, which is whole cassava root or unprocessed cassava and the limit applies on a 'fresh weight' basis (i.e. approximately 70% moisture).

Based on the data published by Cardoso et al5, it is possible for hydrocyanic acid levels to be higher in dried cassava products as a result of the removal of moisture from the raw cassava root. If hydrocyanic acid is not lost during this drying process then the hydrocyanic acid in the dried raw cassava may be two and a half times higher in the dried raw cassava. For example, 40 mg/kg hydrocyanic acid in raw cassava could, in theory, be as high as 100 mg/kg in dried raw cassava.

The drying and minimal preparation of cassava into 'raw chip' or 'raw pellet' form is commonplace as these forms are more stable during transport and reduce the bulk of the product resulting in reduced transport costs. These forms are then further processed before being used in food for human consumption.

The existing regulatory measures do not address the potential for raw cassava containing less than 50 mg/kg to be dried, minimally processed and then sold as a ready-to-eat food. This is because, at the time these measures were developed, it was understood that adequate processing of all raw cassava was occurring. There was no information to indicate that dried, minimally processed cassava was being sold as a ready-to-eat food with elevated levels of cyanogenic substances.

The data recently provided to FSANZ indicates that the processing of certain 'ready-to-eat cassava chips' may be insufficient to reduce the levels of hydrocyanic acid. These data also indicate that these levels are of potential public health and safety concern. On this basis, FSANZ considers that an additional regulatory measure is necessary to ensure that hydrocyanic acid in ready-to-eat cassava chips is reduced to a level that is as low as reasonably achievable.

[5] Processing of cassava roots to remove cyanogens, Cardoso, A.P.; Mirione, E.; Ernesto, M.; Massaza, F.: Cliff, J.; Rezaul Haque, M.; Bradbury, J.H. Journal of Food Composition and Analysis, 18 (2005) 451-460.

The proposed regulatory measure is the inclusion in the Code of a maximum level of 10 mg/kg for hydrocyanic acid in ready-to-eat cassava chips. See Section 6.3 below for more details about the basis for this proposed level. Compliance with the proposed maximum level would reduce the dietary exposure to hydrocyanic acid from ready-to-eat cassava chips and would address the potential public health implications that have recently been identified with these foods.

FSANZ has considered the non-regulatory option of encouraging the industry to amend their practices to reduce hydrocyanic acid in ready-to-eat cassava chips. However, given the potential public health risks, FSANZ is of the view that the proposed maximum level is necessary to ensure that levels of hydrocyanic acid in ready-to-eat cassava chips are adequately managed.

FSANZ invites comment on the proposed regulatory measure and other measures, regulatory or non-regulatory, that may be appropriate for managing the risks associated with hydrocyanic acid in ready-to-eat cassava chips.

### 6.3 Maximum Level (ML) for hydrocyanic acid from ready-to-eat cassava chips

In relation to managing naturally occurring substances in food that may be of public health and safety concern, the usual regulatory measure that is adopted is the incorporation of a Maximum Level (ML) in Standard 1.4.1 – Contaminants and Natural Toxicants. This Standard already includes levels for hydrocyanic acid in certain foods. An ML is established only where it serves an effective risk management function and it is established at a level which is consistent with the protection of public health and safety, and which is reasonably achievable.

#### *6.3.1 Ready-to-eat cassava chips*

MLs are usually applied to a raw food and not normally applied to a processed food. However, MLs can be established for nominated processed foods where the setting of an ML for the primary commodity is judged to be ineffective (e.g. hydrocyanic acid in stone fruit juices), including where the contaminant concentrates in the processed food compared with the raw food. The situation with 'ready-to-eat cassava chips' is unusual and establishing a lower ML for whole unprocessed cassava is not considered to be an effective or practical means of ensuring levels are minimised in ready-to-eat cassava chips. On this basis, an ML is proposed to apply to 'ready-to-eat cassava chips' so that raw cassava intended to be further processed can continue to comply with the existing 50 mg/kg limit.

Dried raw cassava is a legitimate product which, with adequate processing, is a safe ingredient in food. There is no intention to prohibit the sale of raw sweet cassava that has been dried and is intended for further processing. In the unlikely event that raw cassava chips were represented in a ready-to-eat form then the proposed ML for ready-to-eat cassava chips would apply.

A level specifically for 'ready-to-eat cassava chips' is proposed to reflect that no problems have been identified with other cassava based products at this time, and that there are existing food regulatory measures for managing hydrocyanic acid in some other cassava based products. FSANZ is proposing to describe 'ready-to-eat cassava chips' in the Code to provide clarity about the range of foods to which the limit applies.

Ultimately, there may be a need to consider other cassava containing foods and other foods which may contain cyanogenic glycosides. However, at this time, the data available for these other foods are insufficient to consider the need for additional food regulatory measures.

A level for 'total hydrocyanic acid' is proposed as this is consistent with other levels in Standard 1.4.1 and is also consistent with international standards for processed cassava products. FSANZ acknowledges that the term 'hydrogen cyanide' is also an appropriate term.

FSANZ proposes that the ML be included in the Table to clause 5 of Standard 1.4.1, rather than in the Table to clause 4 of this Standard. This is because FSANZ considers that the level should apply to all 'ready-to-eat cassava chips' and not only those 'ready-to-eat cassava chips' to which flavouring preparations have been added. This will ensure that the full range of ready-to-eat cassava chips would need to comply with the proposed ML. See section two of this report for information on the current levels in Standard 1.4.1 and their operation.

In summary, an ML in Standard 1.4.1 for hydrocyanic acid in ready-to-eat cassava chips is considered an appropriate risk management measure:

- to reduce the levels of hydrocyanic acid in ready-to-eat cassava chips to as low as reasonably achievable;
- to minimise dietary exposure to hydrocyanic acid and thereby protect public health and safety; and
- to allow additional information to be gathered about other cassava based foods and other foods containing cyanogenic substances.

*6.3.2 Proposed Level of 10 mg/kg*

An ML is established at a level which is consistent with the protection of public health and safety, and which is considered to be reasonably achievable. In considering an appropriate ML for hydrocyanic acid in ready-to-eat cassava chips, FSANZ has noted the following:

- ready-to-eat cassava chips are composed predominantly of cassava, cassava flour or tapioca flour i.e. cassava products that would expected to be adequately processed;

- the Codex international standard for edible cassava flour includes a limit of 10 mg/kg for hydrocyanic acid in edible cassava flour and this standard has been in existence for over ten years;

- it has long been regarded that proper processing of cassava ensures that hydrocyanic acid is removed or destroyed during cassava processing. On this point, FSANZ has noted that there is some compliance monitoring data available on the levels of hydrocyanic acid in cassava products[6]. These data indicate that 10 mg/kg should be readily achievable;
- there is published information indicating that levels of hydrocyanic acid in cassava based ingredients can be reduced with adequate processing[7,8];

- data have been provided to FSANZ indicating that levels of hydrocyanic acid below 10 mg/kg are achievable by some producers of ready-to-eat cassava chips; and

- the risk assessment which indicates that a lower level (i.e. lower than 25 mg/kg), if reasonably achievable, would further reduce the dietary exposure to hydrocyanic acid from these foods.

Based on the information available, FSANZ is of the view that a level of 10 mg/kg for hydrocyanic acid in ready-to-eat cassava chips is appropriate and achievable. Compliance with this limit would minimise dietary exposure to hydrocyanic acid and address the potential public health implications recently identified with these foods. If the cassava based ingredients (e.g. cassava flour) in these chips have been adequately processed to reduce levels of hydrocyanic acid to a level consistent with the international standard, and taking into account the dilution effect of other ingredients in the chips, FSANZ considers that a level of 10 mg/kg should be achievable by manufacturers.

FSANZ invites comment on:

- the proposed ML, including its focus on ready-to-eat cassava chips;
- whether the proposed ML should also apply to other foods containing cassava, including raw cassava intended for further processing;
- why the proposed ML for hydrocyanic acid in ready-to-eat cassava chips may not be achievable; and
- the forms of cassava that are being used and processed by industry, and any costs of instituting measures for reducing the levels of hydrocyanic acid to comply with the proposed ML.

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[6] Natural Toxins in Food Plants, Report No. 27, Risk Assessment Studies, March 2007, Centre for Food Safety, Food and Environmental Hygiene Department, The Government of the Hong Kong Special Administrative Region.
http://www.cfs.gov.hk/english/programme/programme_rafs/programme_rafs_fc_01_17_report.html

[7] http://www.agnet.org/library/pt/2003017/

[8] Processing of cassava roots to remove cyanogens, Cardoso, A.P.; Mirione, E.; Ernesto, M.; Massaza, F.: Cliff, J.; Rezaul Haque, M.; Bradbury, J.H. Journal of Food Composition and Analysis, 18 (2005) 451-460.

### 6.4 Effective Compliance Monitoring

Levels for hydrocyanic acid in foods have been in the Code for many years and no compliance monitoring problems with these levels have been raised with FSANZ. In addition, the international standards for cassava related products have also been in existence for some time. On this basis, FSANZ is of the view that monitoring compliance with any level should be possible and that it is not considered necessary to prescribe a method of analysis for hydrocyanic acid in ready-to-eat cassava chips.

FSANZ does not ordinarily prescribe methods as this can inhibit method development and require the prescribed method to be used even though better, cheaper or more sophisticated methods may be developed in the future.

Prescribing a method may also prevent the use of equivalent methods for monitoring purposes and restricts the flexibility of industry and compliance agencies. In the absence of a prescribed method, analysts would still need to develop and use methods that are 'fit for purpose' and suitably validated.

Notwithstanding this, FSANZ acknowledges that ready-to-eat cassava chips are a unique product and that there may be specific analysis aspects that may justify the prescription of a method. If a method were to be prescribed then there would need to be agreement on the method that should be prescribed, and full details of the method would be needed so this detail could be included in the Code. FSANZ therefore invites comment on the need to prescribe a method for the analysis of hydrocyanic acid in ready-to-eat cassava chips and the details of the method that should be prescribed.

FSANZ also acknowledges that the establishment of a new ML may mean that compliance agencies need to request appointed analysts to develop new methods for regulatory analysis. FSANZ also appreciates that industry may need to develop quality assurance methods to monitor compliance. This may require the purchase of specific standards, reference materials or analytical equipment, as well as the validation of any analytical methods. For this reason, FSANZ invites comment on any transitional arrangements that compliance agencies or industry consider may be necessary.

FSANZ invites comment on the need to prescribe a method and if considered necessary, the details of the method that should be prescribed.

FSANZ also invites comment on any transitional arrangements that may be necessary for compliance agencies or industry to develop suitable compliance arrangements (if these are not already available).

## 7. Options

FSANZ is required to consider the impact of various regulatory (and non-regulatory) options on all sections of the community, including consumers, food industries and governments. The regulatory options available for this Proposal are:

### 7.1 Option 1 – To not vary the Code to incorporate an ML for hydrocyanic acid in ready-to-eat cassava chips

This option maintains the *status quo* and the existing regulatory measures for managing hydrocyanic acid in ready-to-eat cassava chips continue to apply.

### 7.2 Option 2 – Vary the Code to incorporate an ML of 10 mg/kg for hydrocyanic in ready-to-eat cassava chips

This option would require an amendment to Standard 1.4.1 to incorporate an ML that would require all ready-to-eat cassava chips to contain 10 mg/kg or less of hydrocyanic acid.

### 7.3 Option 3 – Vary the Code to incorporate an ML of 10 mg/kg for hydrocyanic in all ready-to-eat foods containing cassava (except confectionery)

This option would require an amendment to Standard 1.4.1 to incorporate an ML that would require all ready-to-eat foods containing cassava, except confectionery, to contain 10 mg/kg or less of hydrocyanic acid. A ML already exists for hydrocyanic acid in flavoured confectionery.

### 7.4 Option 4 – Vary the Code to incorporate an ML of 25 mg/kg for hydrocyanic in ready-to-eat cassava chips

This option would require an amendment to Standard 1.4.1 to incorporate an ML that would require all ready-to-eat cassava chips to contain 25 mg/kg or less of hydrocyanic acid.

## 8. Impact Analysis

### 8.1 Affected Parties

The affected parties may include the following:

- consumers of food products containing cassava, including raw cassava;
- industry sectors such as
  - cassava producers;
  - processors and manufacturers of cassava products; and
  - food retailers;
- Government agencies.

## 8.2 Benefit Cost Analysis

*8.2.1 Option 1 – The status quo: To not vary the Code to incorporate an ML for hydrocyanic acid in ready-to-eat cassava chips*

8.2.1.1 Benefits

There are no particular benefits, for consumers, industry or government agencies, in this option.

8.2.1.2 Costs

- for consumers, there would be potential public health implications arising out of ongoing exposure to higher levels of hydrocyanic acid than is considered necessary;

- for Government agencies, there may be, and there have already been, costs associated with managing responses to the detection of hydrocyanic acid in ready-to-eat cassava chips.

*8.2.2 Option 2 – Vary the Code to incorporate an ML of 10 mg/kg for hydrocyanic in ready-to-eat cassava chips*

8.2.2.1 Benefits

- for consumers, the major benefit would be a reduction in dietary exposure to hydrocyanic acid from ready-to-eat cassava chips;

- for producers and processors of ready-to-eat cassava chips, this option would provide a specific level to which all ready-to-eat cassava chips should adhere;

- for Government agencies, this option would enhance community confidence that regulatory authorities are maintaining standards that minimise dietary exposure to hydrocyanic acid in food products.

8.2.2.2 Costs

- for producers and processors not adequately processing cassava for use in ready-to-eat cassava chips, this option could result in major costs. In the short term this could be in the form of reduced revenue on account of removing certain products from the market. On an ongoing basis, in order to comply with the new maximum limit, such producers may need to limit themselves to certain suppliers, namely those providing adequately processed sweet cassava. This limitation in supply could result in higher costs for inputs. Alternatively, they may have to adopt the more costly option of changing their production processes, to further process their cassava raw materials to reduce the levels of hydrocyanic acid e.g. further processing with water and subsequent drying before further production;

- for consumers, there may be a short term limitation in the range of products available;

- for Government agencies, this option may require them to develop specific analytical methods for measuring hydrocyanic acid in ready-to-eat cassava chips, and develop strategies for ensuring that businesses comply with the maximum level.

*8.2.3 Option 3 – Vary the Code to incorporate an ML of 10 mg/kg for hydrocyanic in all ready-to-eat foods containing cassava (except confectionery)*

<u>8.2.3.1 Benefits</u>

- for consumers, the major benefit would be a reduction in dietary exposure to hydrocyanic acid from not only ready-to-eat cassava chips, but potentially all food products containing cassava;

- for producers and processors of foods containing cassava, this option would provide a specific level to which all ready-to-eat foods containing cassava should adhere;

- for Government agencies, this option would enhance community confidence that regulatory authorities are advocating standards that minimise dietary exposure to hydrocyanic acid in food products. The broader scope of this regulatory measure could assist compliance agencies since they would not need to differentiate between ‘ready-to-eat cassava chips’ and other food products containing cassava.

<u>8.2.3.2 Costs</u>

- for consumers, there may be a short term reduction in the range of products available;

- for producers and processors that are not adequately processing cassava for use in food products, this option could result in major costs as detailed above (See 8.2.2.2);

- for government agencies, this option may require them to develop specific analytical methods for measuring hydrocyanic acid in food products containing cassava, and develop strategies for ensuring that businesses comply with the maximum level.

*8.2.4 Option 4 – Vary the Code to incorporate an ML of 25 mg/kg for hydrocyanic in ready-to-eat cassava chips*

<u>8.2.4.1 Benefits</u>

- for consumers, the major benefit would be a reduction in dietary exposure to hydrocyanic acid from ready-to-eat cassava chips;

- for producers and processors of ready-to-eat cassava chips, this option would provide a specific level to which all ready-to-eat foods containing cassava should adhere;

- for Government agencies, this option would enhance community confidence that regulatory authorities are advocating standards that minimise dietary exposure to hydrocyanic acid in ready-to-eat cassava chips.

8.2.4.2 Costs

- for consumers, there may be a short term reduction in the range of products available;

- for producers and processors of ready-to-eat cassava chips that are not adequately processing cassava for use in food products, this option could result in major costs. These costs are unlikely to be different from Option 2 as the costs of adequate processing are expected to be the same, even though the proposed level for Option 4 is higher;

- for government agencies, this option may require them to develop specific analytical methods for measuring hydrocyanic acid in ready-to-eat cassava chips, and develop strategies for ensuring that businesses comply with the maximum level.

### 8.3 Comparison of Options

In assessing Proposals, FSANZ considers the impact of various regulatory (and non-regulatory) options on all sectors of the community, including consumers, food industries and governments in Australia.

For this Proposal, Option 1 is considered unacceptable because of the potential and unmanaged risks to public health and safety. Options 2, 3 and 4 are all viable options in that they all apply measures that would minimise the dietary exposure to hydrocyanic acid from ready-to-eat cassava chips.

Option 3 of applying an ML of 10 mg/kg to all ready-to-eat cassava containing foods is unlikely to have a major impact if processors are adequately processing the cassava they use. However, extending the ML to all cassava containing foods is not consistent with minimal effective regulation. This is because at this time, only ready-to-eat cassava chips have been identified as containing higher than expected levels of hydrocyanic acid. For this reason, Option 3 is not preferred.

Option 4 is similar to Option 2 but is for a higher maximum level. The costs of implementing Option 2 and Option 4 are not considered to be different, as proper processing of the cassava ingredients for ready-to-eat cassava chips should be able to comply with either level. Option 4 has higher costs for consumers in that consumers would be exposed to what may be considered to be unnecessarily high levels of hydrocyanic acid from ready-to-eat cassava chips. For this reason, Option 4 is not preferred.

Option 2 is the preferred option because:

- it minimises dietary exposure to hydrocyanic acid from ready-to-eat cassava chips and therefore protects public health and safety;
- it is specific to the products for which the issues have been raised and does not extend the impacts to non-implicated businesses and products. For example, it does not impact on raw cassava which will be further processed;
- based on the data available, it should be achievable for industry as the proposed level is the same as that in the international standard for another processed cassava product that is for direct human consumption, namely edible cassava flour; and
- it is not considered to unnecessarily impede trade because it aligns with a relevant international standard for edible cassava flour, which is the predominant ingredient of the ready-to-eat cassava chips.

The conclusion of the impact analysis is that the benefits of Option 2 (incorporating the proposed ML of 10 mg/kg for hydrocyanic acid in ready-to-eat cassava chips in the Code) would outweigh the associated costs.

# COMMUNICATION AND CONSULTATION STRATEGY

## 9. Communication

It is proposed that a maximum level of 10 mg/kg for hydrocyanic acid in ready-to-eat cassava chips be included in the Code. FSANZ is applying a basic communication strategy to this Proposal, which includes advertising the availability of the Assessment Report for public comment in the national press and making the reports available on the FSANZ website.

If the FSANZ Board approves the draft variation to the Code, FSANZ will notify the Ministerial Council of its decision. The Applicant and stakeholders, including the public, will be notified on the gazettal of changes to the Code in the national press and on the FSANZ website.

## 10. Consultation

FSANZ acknowledges that this Proposal may have impacts on a specific industry sector (cassava chip producers, importers and processors). On this basis the public consultation will ensure that these specific sectors of industry have the opportunity to comment on the proposed measures.

### 10.1 World Trade Organization (WTO)

As members of the World Trade Organization (WTO), Australia and New Zealand are obligated to notify WTO member nations where proposed mandatory regulatory measures are inconsistent with any existing or imminent international standards and the proposed measure may have a significant effect on trade.

There are not any specific international standards for ready-to-eat cassava chips, although there are relevant international standards for some other cassava products with which ready-to-eat cassava chips should be compliant i.e. edible cassava flour. Amending the Code to include a maximum level for hydrocyanic acid in ready-to-eat cassava chips is unlikely to have a significant effect on international trade as:

- the level would not apply to raw cassava for further processing;
- producers of processed ready-to-eat cassava chips should already be able to comply with the level if they are adequately processing cassava for human consumption; and
- the proposed level is the same as the level in the relevant international standard for edible cassava flour (another processed cassava product).

Given the trade in raw and processed cassava based products and that no specific international standard exists for ready-to-eat cassava chips, notification will be recommended to the agencies responsible in accordance with Australia's and New Zealand's obligations under the WTO Sanitary and Phytosanitary Measures (SPS) Agreements.  This will enable other WTO member countries to comment on proposed changes to standards where they may have a significant impact on them.

# CONCLUSION

## 11. Conclusion and Preferred Option

Following an assessment of the risks to public health and safety, and based on the data available, FSANZ is proposing that additional regulatory measures to minimise hydrocyanic acid in ready-to-eat cassava chips. This is because the current food regulatory measures in the Code are not considered sufficient to reduce levels of hydrocyanic acid in ready-to-eat cassava chips to as low as reasonably achievable.

The proposed food regulatory measure is the inclusion in the Code of a maximum level of 10 mg/kg for hydrocyanic acid in ready-to-eat cassava chips. The purpose of this measure is to minimise hydrocyanic acid to a level that is as low as reasonably achievable in ready-to-eat cassava chips. Compliance with the proposed food regulatory measure would reduce the dietary exposure to hydrocyanic acid from ready-to-eat cassava chips and would address the potential public health implications that have recently been identified with these foods.

While not currently within the scope of this proposal, additional regulatory and non-regulatory measures may be required in the future as investigations continue into hydrocyanic acid in other foods.

### Preferred Approach

It is proposed to vary Standard 1.4.1 – Contaminants and Natural Toxicants of the Code to include a maximum level of 10 mg/kg for total hydrocyanic acid in 'ready-to-eat cassava chips'.

### 11.1 Reasons for Preferred Approach

- with proper preparation or processing, cassava and cassava-based foods are safe for human consumption, even though whole, unprocessed cassava may contain naturally occurring cyanogenic substances;

- the nature of the processing of 'ready-to-eat cassava chips' is such that existing food regulatory measures in the Code are not considered sufficient to reduce levels of hydrocyanic acid in ready-to-eat cassava chips to as low as reasonably achievable;

- following a risk assessment, a food regulatory measure in the Code for hydrocyanic acid in ready-to-eat cassava chips is proposed to minimise the dietary exposure to hydrocyanic acid and thereby protect public health and safety;

- a maximum level in Standard 1.4.1 is considered to be an appropriate risk management measure while additional information is gathered about other cassava based foods and other foods containing cyanogenic substances;

- a level specifically for 'ready-to-eat cassava chips' only is proposed. This is because no problems have been identified with other cassava based products at this time, and there are existing food regulatory measures for managing hydrocyanic acid in some other cassava based products;

- a maximum level of 10 mg/kg is considered to be practical and reasonably achievable with proper processing of cassava. It is also consistent with the international standard for edible cassava flour (another processed cassava product for direct human consumption) which is the predominant cassava based ingredient in ready-to-eat cassava chips;

- given the potential public health implications, it is proposed that the level come into effect upon gazettal and with no 'stock in trade' transitional arrangements;

- at this time, it is not considered appropriate or necessary to prescribe a method of analysis for hydrocyanic acid in ready-to-eat cassava chips as this will restrict the flexibility of industry and compliance agencies to develop more contemporary methods for monitoring hydrocyanic acid in ready-to-eat cassava chips.

### 11.2 Transitional Arrangements

Given the public health concerns, FSANZ is not proposing any transitional arrangements for the proposed level i.e. it is currently proposed that the level would come into effect upon gazettal. It is also proposed that subclause 1(2) of Standard 1.1.1 not apply.

Notwithstanding this, FSANZ invites comment on whether any transitional arrangements would assist industry in complying with the proposed level or would assist compliance agencies in developing or implementing compliance arrangements (e.g. developing suitable confirmatory methods for compliance purposes).

## 12. Implementation and Review

A maximum level of 10 mg/kg for hydrocyanic acid in ready-to-eat cassava chips in Standard 1.4.1 is proposed as an appropriate risk management measure while additional information is gathered about other cassava based foods and other foods containing cyanogenic substances.

## ATTACHMENTS

Attachments to the Assessment Report include:

1. Draft variations to the *Australia New Zealand Food Standards Code*
2. Cyanogenic Glycosides in Cassava Chips – Risk Assessment

**Attachment 1**

## Draft variation to the *Australia New Zealand Food Standards Code*

*Section 94 of the FSANZ Act provides that standards or variations to standards are legislative instruments, but are not subject to disallowance or sunsetting*

**To commence: on gazettal**

**[1]** ***Standard 1.4.1*** *of the Australia New Zealand Food Standards Code is varied by* –

[1.1] *inserting in subclause 5(1)* –

**Ready to eat cassava chips** means the product containing sweet cassava that is represented as ready for immediate consumption with no further preparation required including crisps, crackers or 'vege' crackers.

[1.2] *inserting after subclause 5(3)* –

(4) Subclause 1(2) of Standard 1.1.1 does not apply to ready to eat cassava chips for the purposes of the Table to clause 5.

[1.3] *inserting in the* Table to clause 5

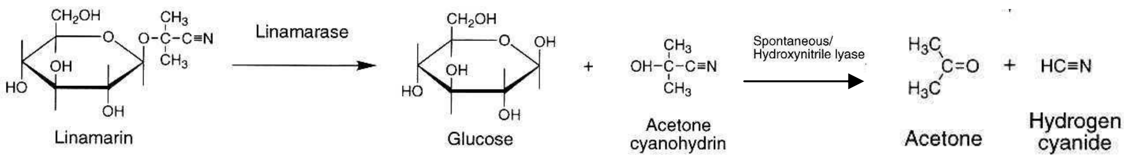
| | |
|---|---|
| **Hydrocyanic acid, total**<br>Ready to eat cassava chips | 10 mg/kg |

## Attachment 2

# Risk Assessment

### Introduction

Cassava (*Manihot esculanta* Crantz) is grown for its enlarged starch-filled roots and is consumed in a number of forms: flour used for cooking; root slices; root chips; grated root (pan fried, baked or steamed), steamed whole root or tapioca pearls made as a pudding. The focus of these risk assessment considerations is cassava chips made from the root. Cassava contains potentially toxic compounds called cyanogenic glycosides, primarily linamarin and a small amount of lotaustralin (ethyl linamarin). Linamarin is chemically similar to glucose but with cyanide (CN ion) attached. Cyanogenic glycosides are toxic because they release hydrogen cyanide (HCN) as a result of enzymatic hydrolysis following maceration of the plant tissue. Safe traditional human consumption of cassava is dependent on adequate processing to minimise the linamarin content. If cassava is eaten either raw or after inadequate processing then toxicity may be observed. Conventional processing usually involves peeling and grating and then soaking in warm water for several days. This allows the cassava's own natural enzymes to convert the linamarin to glucose and hydrogen cyanide gas. The released hydrogen cyanide gas disperses slowly and harmlessly. The chemical reaction for the formation of hydrogen cyanide gas from linamarin in cassava is shown below (Figure 1).




### Cyanogenic glycoside content of cassava

There are a number of varieties of cassava, each of which has a different cyanide level. Values from 15-400 mg/kg fresh weight of hydrogen cyanide in cassava roots have been reported in the literature. Sweet varieties of cassava (low cyanide content) will typically contain approximately 15-50 mg/kg hydrogen cyanide on a fresh weight basis. Sweet varieties of cassava can be processed adequately by peeling and cooking (e.g. roasting, baking or boiling), whereas bitter varieties of cassava (high cyanide content) require more extensive processing, involving techniques such as heap fermentation which take several days. Cassava varieties that have high levels of linamarin in the root are not normally traded as food.

### Cyanogenic glycoside content of processed products

In 2004, FSANZ identified information on the cyanogenic potential of cassava flour commercially processed cassava chips prepared from root slices and flour. Cassava flour samples obtained from various African countries and Indonesia had a total cyanide content varying from 13-131 mg/kg. It is understood that most of the chip samples were available in the United States and all samples had a total cyanide content of less than 10 mg/kg.

In 2008, FSANZ was notified of cassava chips manufactured in Australia from cassava pellets imported from Indonesia having a total cyanide content of 59 mg/kg. Follow-up analysis on more batches has revealed even higher quantities (up to 145 mg/kg)

**Risk assessment considerations**

Both acute and chronic effects occur following exposure to cyanogenic glycoside compounds in cassava based foods. These risk assessment considerations are focussed on:

- estimating the likelihood of acute toxicity as a result of consumption of cassava chips; and
- establishing a guidance level for HCN in cassava chips.

**Review of toxicological data**

The potential toxicity of cassava chips depends on the likelihood that its consumption will produce a concentration of HCN that is toxic to exposed humans. The factors important in this toxicity are that the cassava may not have been sufficiently detoxified during processing or preparation and, therefore, high concentrations of HCN or linamarin are present. If cassava is consumed raw or insufficiently processed, HCN will be released for absorption by the action of β-glucosidase in the gastrointestinal tract.

**Absorption, distribution, metabolism and excretion**

*Cyanides*

Following oral administration, soluble cyanide salts, at the physiological pH of the stomach, form predominantly HCN, which can rapidly penetrate mucous, and cell membranes. Absorbed cyanide is converted in the liver to less toxic metabolites such as thiocyanate. Cyanide has not been shown to accumulate in the blood and tissues following chronic oral exposure.

The metabolism of cyanide in the liver has been studied in animals. The major pathway involves conversion to thiocyanate by rhodanese or 3-mercaptopyruvate sulfur transferase. This major route of detoxification requires sulphur donors, which by different metabolic pathways are provided from dietary sulphur amino acids. Three other minor pathways converting less than 20% of the total cyanide involve conversion to 2-aminothiazoline-4-carboxylic acid, incorporation into a 1-carbon metabolic pool or combining with hydroxocobalamin to form cyanocobalamin (vitamin B12). Detoxification is therefore affected by the presence of nutritional factors, such as sulfur-containing amino acids and vitamin B12.

*Linamarin*

Since release of cyanide from linamarin only occurs in the GI tract through microbial fermentation the concentration of cyanide being available for absorption occurs only slowly. This slow rate of absorption allows for more detoxification relative to an equivalent dose of cyanide.

This difference in release and detoxification is thought to account for the marked difference in acute toxicity between equivalent doses of cyanide in linamarin and a cyanide salt (see under acute toxicity).

In well nourished humans and rodents approximately 25% of linamarin present in ingested cassava flour is excreted unchanged in urine. Thiocyanate excretion in the urine suggests that a further 10-20% of the linamarin is enzymatically converted in the gastrointestinal tract to cyanide. It is not known how much of the HCN will be absorbed from the gut, but is expected to be less than 100% due to localised detoxification mechanisms. Studies in isolated perfused rat liver have shown that cyanoglycosides require gut microbial flora for their metabolism and that they are not metabolized by mammalian cells.

*Biochemical effects*

Hydrogen cyanide inactivates the enzyme cytochrome oxidase in the mitochondria of cells by binding to the $Fe^{3+}/Fe^{2+}$ contained in the enzyme. This causes a decrease in the utilization of oxygen in the tissues. Cyanide causes an increase in blood glucose and lactic acid levels and a decrease in the ATP/ADP ratio indicating a shift from aerobic to anaerobic metabolism. Cyanide activates glycogenolysis and shunts glucose to the pentose phosphate pathway decreasing the rate of glycolysis and inhibiting the tricarboxylic acid cycle. Hydrogen cyanide will reduce the energy availability in all cells, but its effect will be most immediate on the respiratory system and heart.

*Acute toxicity*

*Cyanides*

In humans, the clinical signs of acute cyanide intoxication are constriction of the throat, nausea, vomiting, stomach pains, giddiness, headache, palpitations, hyperpnoea and dyspnoea, bradycardia, unconsciousness and violent convulsions followed by terminal coma. Death due to cyanide poisoning occurs when the quantity of ingested cyanide exceeds the ability to detoxify it.

In humans an average fatal dose of cyanide has been calculated from case report studies of intentional or accidental poisonings to be 1.52 mg/kg bw (range

0.56-3.4 mg/kg bw and corresponding to 1-7 mg/kg bw of KCN). The lowest fatal oral dose reported in humans was estimated in 1938 as being 0.56 mg/kg bw cyanide (form not specified) but the analytical measurements of the time lack the precision of current technology.

Laboratory animals such as mouse, rat, rabbit and dog appear to be similarly sensitive. The median oral lethal doses (50% death) for sodium cyanide was calculated to be 3-4 mg $CN^-$/kg bw in rats and rabbits. In dogs the median lethal dose was 2 mg $CN^-$/kg bw whereas in mice it was 6 mg $CN^-$/kg bw with potassium cyanide.

*Linamarin*

In rats the median lethal dose of linamarin was reported to be 450 mg/kg bw, but clinical signs (ataxia, apnoea and paraparesis) and a death were observed at a dose as low as 250 mg/kg bw. This suggests that like classical cyanide intoxication the dose which will result in clinical signs is not much different from that which also causes death.

In hamsters a single oral dose of 120 or 140 mg/kg bw linamarin (by stomach tube) caused deaths and clinical signs (deep and laboured breathing, uncoordinated movement, tremors and hypothermia) were observed in most animals after one hour. No deaths or clinical signs were observed at either 70 or 100 mg/kg bw.

There are no available data on the acute toxicity of linamarin in humans. However, the likelihood of cyanide intoxication from consumption of linamarin in cassava is dependent on body weight and it is possible that a child or person of smaller body weight would not be able to detoxify the cyanide resultant from a meal of inadequately prepared cassava.

*Long-term toxicity*

There have been no adequately reported long term controlled studies in laboratory animals with HCN or linamarin. However, adverse effects noted in humans from long-term cassava consumption include neurological diseases. Konzo is an upper motor neuron disease characterised by irreversible but non-progressive symmetric spastic paraparesis that has an abrupt onset. It mostly affects children and women of childbearing age.  Severe cases have a spastic toe-scissor gait, or patients will not be able to walk at all, and the arms and speech may also be affected. In all reports of epidemics, konzo has been associated with high and sustained cyanogens intake at sub-lethal concentrations from cassava or cassava flour in combination with a low intake of sulphur amino acids. This situation is not expected to occur in Australia.

Tropical Ataxic Neuropathy is used to describe several neurological syndromes attributed to toxico-nutritional causes. The main clinical features of some of the syndromes have included: sore tongue, angular stomatitis, skin desquamations, optical atrophy, neurosensory deafness and sensory gait ataxia. The cause is attributed to dietary cyanide exposure from the chronic monotonous consumption of foods processed from cassava. As cassava products are not a major component of the diet, this situation is not expected to occur in Australia.

Because of the nature of the toxicity of cyanide compounds, no suitable data on subchronic oral exposure to cyanide in humans is available. Reported cases of survival after oral exposure to cyanide typically involve individuals who ingested cyanide in lethal dose range but who received emergency supportive medical treatment.

## International Risk Assessments

In July 2006, the Agency for Toxic Substances and Disease Registry (ATSDR), US Department of Health and Human Services, published a comprehensive risk assessment for cyanide. It cites a 1993 NTP study in which rats were dosed with cyanide in their drinking water for 3 months. It shows a no effect level of 5 mg/kg bw/day for male fertility. Based on this study, a minimum risk level for an intermediate duration (15-364 days) oral exposure to cyanide is 0.05 mg/kg bw/day which represents an exposure of 3 mg/day cyanide for a 60 kg adult, or 1 mg/kg/day for a 20 kg child.

The US EPA oral reference dose for chronic exposure to cyanide is 0.02 mg/kg bw/day (from drinking water). This is derived from a no observed adverse effect level (NOAEL) of 10.8 mg/kg bw/day of cyanide, applying an uncertainty factor of 100 to account for intra- and inter-species variability along with a modifying factor of 5. The modifying factor is employed because cyanide has a higher tolerance when ingested with food than by drinking water. The NOAEL was based on a 2-year dietary study in rats completed in 1955 where the critical affects associated with the lowest observed adverse effect level (LOAEL) were weight loss, thyroid effects and myelin degeneration. For a 60 kg adult, this equates to 1.2 mg. However, the tolerable daily intake associated with food would not include this modifying factor. The tolerable daily intake associated with food consumption would be 0.108 mg/kg bw/day (10.8 mg/kg bw/day, divided by a 100-fold safety factor).

No safe level of intake of cyanide derived from linamarin in cassava and other plant-based foods has been established. JECFA in 1993 and EFSA in 2004 reviewed the toxicology of cyanogenic glycosides from cassava and other plant based foods and concluded that a safe level of intake could not be estimated because of a lack of quantitative toxicological and reliable epidemiological information. However, JECFA concluded that a level up to 10 mg/kg HCN in the Codex Standard for cassava flour was not associated with acute toxicity.

The Australian and WHO Drinking Water Guideline levels are based on an effect level (LOAEL) of 1.2 mg/kg bw/day from a 6-month feeding study in pigs. The effects observed at 1.2 mg/kg bw/day were on behavioural patterns and serum biochemistry. Using the LOAEL from this study and applying a safety factor of 100 to reflect inter- and intra-species variation (no additional factor for a LOAEL was considered necessary because of doubts over the biological significance of the observed changes); a tolerable daily intake (TDI) of 0.012 mg/kg bw/day was calculated. An allocation of 20% of the TDI to drinking-water is made because exposure to cyanide from other sources is normally small and because exposure from water is only intermittent. This results in a guideline value of 0.08 mg/L (rounded figure but 0.07 mg/L for WHO) which is considered to be protective for both acute and long-term exposure.

**Regulatory limits on HCN in food or water**

*Food*

In the Code the following limits apply:

- 25 mg/kg in confectionery; 5 mg/kg in stone fruit juices; 50 mg/kg in marzipan; 1 mg/kg per 1% alcohol in alcoholic beverages.

In the EU, the maximum permitted levels of hydrocyanic acid (HCN) are as follows; 1 mg/kg in foodstuffs, 1 mg/kg in beverages, with the exception of 50 mg/kg in nougat, marzipan or its substitutes or similar products, 1 mg per percent of alcohol in alcoholic beverages and 5 mg/kg in canned stone fruit.

*Water*

The Australian Drinking Water Guidelines has a guideline level of cyanide in drinking water of 0.08 mg/L. The WHO drinking water guideline for cyanide is 0.07 mg/L.

**Risk/safety assessment**

**Source (cassava chips) – HCN content measured by NSW**

Based on recent measurements the cassava-derived crackers contain linamarin which when exposed to appropriate enzymes released approximately 80 mg/kg of HCN. Since about 20% of the HCN released from linamarin in cassava in the GI tract is absorbed it follows that 200 g of cassava chips will yield approximately 3 mg HCN as a systemic dose.

Furthermore since one gram of linamarin can release a maximum of 109.3 mg HCN it follows that the chips contain a maximum of approximately 800 mg/kg linamarin. So in 200 g of cassava chips there will be 160 mg of linamarin.

**Acute toxicity**

1. Humans – lethal dose (HCN)

A lethal oral dose of HCN is reported to be about 1.52 mg/kg bw (range 0.56-3.4 mg/kg bw).

These data are not directly comparable because the HCN released from cassava is likely to be slow which, in turn, would permit detoxification in the liver. These data are included for comparative purposes.

2. Rat – median lethal dose ($LD_{50}$)
   Linamarin – 450 mg/kg bw
   HCN – 4-6 mg/kg bw

Hamster – A single oral dose study with 100 mg/kg bw of linamarin (~2 mg/kg bw available HCN) caused no deaths or clinical signs. Death and clinical signs observed at 120 and 140 mg/kg bw.

**Estimated Dietary exposure**

Two hundred grams of chips (2 packets) is considered to be a reasonable and possible dietary intake for a 20 kg child in a two hour eating session. Hence 200 g of chips eaten by 20 kg child equates to 160 mg (8 mg/kg bw) linamarin (or 0.15 mg/kg bw available HCN).

**Margin of Safety**

Exposure 'dose': is 160 mg/kg bw linamarin (or 0.15 mg/kg bw available HCN) in children.

Toxicity: the lethal dose in rats is 450 mg/kg bw linamarin (or 9 mg/kg bw available HCN in humans).

In hamsters the NOAEL was 100 mg/kg bw linamarin (or ~2 mg/kg bw available HCN).

The safety factor applied to the NOAEL in the single dose study in the hamster is 10-fold rather than the usual 100-fold because humans appear to be approximately as sensitive to HCN as laboratory animals as judged from the acute toxicity data. Thus we do not need to account for variability in extrapolation from laboratory animals to humans. The applied 10-fold safety is intended to account for individual variability in sensitivity within the population.

The margin of safety (MOS) is calculated by the comparing the likely exposure of 8 mg/kg bw linamarin (or 0.15 mg/kg bw available HCN) in children to the safety factor corrected value in hamsters of 10 mg/kg bw linamarin (or 0.2 mg/kg bw available HCN). Hence the MOS is around 10-fold. A MOS of 10 is considered to be acceptable to ensure that individuals sensitive to the effects of HCN are adequately protected.

**Conclusion:** The consumption of 200 g of cassava chips in a 20 kg child is without apparent toxic consequence (i.e. the required margin of safety of 10 was achieved. However, if the content of HCN in the cassava chips is greater than 80 mg/kg or other sources of cyanide (e.g. marzipan or stone fruit juice) are consumed within 1-2 hours then it may be possible to take children over a safe level. The most recent testing undertaken by the NSW Food Authority indicates that some HCN levels in cassava chips may be as high as 145 mg/kg.

**Establishing a guidance level for HCN in cassava chips**

*Using existing regulatory limits*

The Code contains regulatory limits for HCN in certain processed foods: 25 mg/kg in confectionery; 5 mg/kg in stone fruit juice; 50 mg/kg in marzipan; and 1 mg/kg in alcoholic beverages per 1% alcohol content.

FSANZ has conducted a dietary exposure assessment to determine the consumption of chip products relative to confectionery. This was conducted to test the assumption that confectionery consumption may be similar to the consumption of chips. It was proposed that if chip consumption was similar to that of confectionery consumption, the ML of 25 mg/kg in the Code for confectionery may also provide an appropriate level of protection when used as a guidance level for cassava chips.

*Comparing reference health standards from long-term safety studies with existing regulatory limits*

If a guidance level for cassava chips of 25 mg/kg HCN was applied, then the safety margin would increase to around 30-fold for a 20 kg child. This level could probably be achieved through appropriate quality control measures during cassava processing.

**References:**

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