



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

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FINAL ASSESSMENT REPORT

APPLICATION A490

EXEMPTION OF ALLERGEN DECLARATION FOR ISINGLASS

For Information on matters relating to this Assessment Report or the assessment process generally, please refer to <http://www.foodstandards.gov.au/standardsdevelopment/>

Executive Summary

Food Standards Australia New Zealand (FSANZ) received an unpaid Application from the Beer, Wine and Spirits Council of New Zealand (BWSCNZ) in 2003 seeking to amend the Table to clause 4 of Standard 1.2.3 – Mandatory Warning and Advisory Statements and Declarations, of the *Australia New Zealand Food Standards Code* (the Code). BWSCNZ ceased operations in December 2006, and the Application was taken over by the Brewers Association of New Zealand (BANZ). In referring to ‘the Applicant’ this Final Assessment Report refers to BWSCNZ for activities prior to December 2006 and BANZ thereafter.

The Applicant sought an exemption from the requirement to declare isinglass (a processing aid commonly derived from dried swim bladders of certain tropical and subtropical fish) on the label, when present in beer and wine as a result of its use as a clarifying agent. The exemption was initially sought on the basis that isinglass has a long history of use as a fining agent in the production of beer and wine and has not been known to cause adverse reactions in susceptible individuals. Subsequently, the Applicant provided evidence that dietary exposure to isinglass through beer and wine consumption was extremely low. Results of oral challenge studies were also provided indicating that isinglass did not cause an allergic reaction to fish sensitised individuals when consumed at levels substantially higher than the potential exposure levels that may be encountered through the consumption of beer and wine. A new Good Manufacturing Code of Practice to minimise the allergen parvalbumin in isinglass has also been established by the isinglass manufacturing industry.

At Draft Assessment, FSANZ undertook a robust and extensive assessment of the public health and safety implications of this Application. At Draft Assessment, two options were proposed; (1) reject the Application thus maintaining the *status quo*; or (2) prepare a draft variation to the Table to clause 4 of Standard 1.2.3 for exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent.

Risk Assessment

At Final Assessment, the key risk assessment findings include:

- the three main components of isinglass (collagen, elastin and gelatin) are not clinically relevant in IgE-mediated allergy to fish;
- parvalbumin, the allergenic fish protein, is present at very low levels in isinglass;
- isinglass added to beer and wine for clarification is removed by sedimentation, filtration or centrifugation, resulting in residual levels of isinglass which, when detectable at all, do not exceed 1 mg/L of bottled beer or wine;
- parvalbumin, although present in trace amounts in commercial isinglass, is not detectable in the clarified final product as it co-sediments with isinglass and is removed in the filtration process; and

- exposure to isinglass through the consumption of clarified beer and wine would be very low and, based on oral challenge studies, would not be expected to provoke reactions in fish-allergic consumers.

Therefore, taking into account all of the above, FSANZ considers that consumption of isinglass-fined beer and wine is not likely to present a risk of allergic reactions in fish-allergic consumers.

The key risk assessment issues, including issues raised by submitters, are discussed in Section 8 of this Report. Additional information is provided at Attachment 3 – Risk Assessment Report and Attachment 4 – Food Technology Report.

Risk Management

At Draft Assessment, submitters raised concerns regarding the maintenance of the quality of isinglass and its usage. FSANZ considers current production methods and market factors adequately address the quality of isinglass; and the usage and amount of isinglass in food products is managed through existing provisions in the Code for the use of processing aids. Information from the wine and beer industries also emphasises that isinglass is sparingly used as it is one of the most expensive fining agents available.

Some submitters raised further concerns regarding the impact of an exemption on the provision of information for informed choices. FSANZ notes, however, the particular issues raised were not in respect of allergenicity or related matters and, therefore, fall beyond the scope of this Application.

Due to the above factors, FSANZ does not consider further regulatory measures are required. Further detail is provided at Section 9 of this report.

Decision

FSANZ approves a draft variation to the Table to clause 4 of Standard 1.2.3 to grant an exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent.

Reasons for Decision

FSANZ approves the draft variation to the Table to clause 4 of Standard 1.2.3 to grant exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent as it:

- does not raise any health and safety concerns for fish-allergic consumers;
- removes an unnecessary declaration on the product label and thereby enhances the information related to the allergenicity of the product.
- provides fish-allergic consumers with increased choice of beer and wine products;

- supports industry with an added choice of clarifying agent that does not require allergen declaration; and
- the impact analysis concludes that exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent, provides a net benefit to affected parties.

The approved draft variation to the Code is at Attachment 1.

Consultation

In response to the release of the Draft Assessment Report, FSANZ received twenty-seven submissions, with sixteen submissions from consumers, eight from industry, two from government and one from a public health organisation. A summary of submissions on the Draft Assessment Report is at Attachment 2.

Overall, seventeen of the submitters (sixteen consumers and one government) objected to providing an exemption, and eight (industry) provided support for the exemption. Of the remaining two submitters, one provided support, in-principle, indicating concern that the evidence did not show that there is no risk. The other indicated support based on a condition that FSANZ consider making it a requirement that only isinglass with substantially reduced levels of parvalbumin be exempt from allergen declaration.

A significant proportion of submitters who objected to the proposed exemption linked their arguments to FSANZ's second order objective (the provision of adequate information relating to food to enable consumers to make informed choices) as a reason for their decision. The requirement to declare isinglass was seen to enable consumers to make informed choices about foods for ethical, religious, environmental, and other personal reasons with a particular focus on vegetarianism/veganism.

There were two submitters who objected to an exemption as they believed they had experienced an allergic fish-related reaction from consuming wine. Further information was sourced from these submitters in relation to their allergic condition and the products that may have caused allergic reactions.

After considering the submissions to the Draft Assessment Report, FSANZ clarified some of the issues raised by submitters through targeted consultations.

Implementation and Review

The FSANZ Board's decision will be notified to the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council).

Subject to any request for review by the Ministerial Council, the approved draft variation to grant exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent, will come into effect upon gazettal.

CONTENTS

INTRODUCTION.....	3
1. NATURE OF THE APPLICATION	3
1.1 <i>Background to the Application</i>	3
1.2 <i>Basis of the Application</i>	4
1.3 <i>Scope of the Application</i>	4
1.4 <i>Additional information provided by the Applicant since Initial Assessment</i>	5
2. THE ISSUE	5
3. OBJECTIVES	6
4. HISTORICAL BACKGROUND	6
5. CURRENT REGULATIONS.....	7
5.1 <i>Current domestic regulations</i>	7
5.2 <i>Overseas and international regulations</i>	8
5.3 <i>Regulatory differences and its impact</i>	11
6. MATTERS OF RELEVANCE	11
6.1 <i>Parvalbumin</i>	11
6.2 <i>Definition of isinglass</i>	11
6.3 <i>Components of isinglass</i>	11
6.4 <i>Commercial production of isinglass</i>	12
6.5 <i>Isinglass as a processing aid/clarifying agent</i>	13
6.6 <i>Toxicological assessment</i>	14
7. KEY RISK ASSESSMENT QUESTIONS	14
RISK ASSESSMENT	14
8. RISK ASSESSMENT ISSUES	14
8.1 <i>Allergenicity of isinglass</i>	15
8.2 <i>Presence of isinglass in beer and wine</i>	15
8.3 <i>Potential of parvalbumin partitioning out into the bulk liquid</i>	16
8.4 <i>Issues raised in submissions to the Draft Assessment Report</i>	16
8.5 <i>Summary of risk assessment</i>	20
RISK MANAGEMENT.....	21
9. RISK MANAGEMENT MEASURES	21
9.1 <i>Maintaining the quality of isinglass</i>	21
9.2 <i>Usage of isinglass</i>	21
9.3 <i>Issues raised in submissions to the Draft Assessment Report</i>	22
10. OPTIONS.....	24
10.1 <i>Option 1 – Reject the Application</i>	24
10.2 <i>Option 2 – Prepare a draft variation to the Table to clause 4 of Standard 1.2.3</i>	24
11. IMPACT ANALYSIS	24
11.1 <i>Affected parties</i>	24
11.2 <i>Benefit Cost Analysis</i>	25
11.3 <i>Comparison of options</i>	26
COMMUNICATION AND CONSULTATION STRATEGY.....	27
12. CONSULTATION	27
12.1 <i>Public consultation</i>	27
12.2 <i>Targeted consultation</i>	28

12.3	<i>World Trade Organization</i>	28
13.	COMMUNICATION STRATEGY.....	28
CONCLUSION AT FINAL ASSESSMENT		29
14.	CONCLUSION AND DECISION.....	29
15.	IMPLEMENTATION AND REVIEW.....	29
ATTACHMENT 1 - DRAFT VARIATION TO THE <i>AUSTRALIAN NEW ZEALAND FOOD STANDARDS</i> <i>CODE</i>		30
ATTACHMENT 2 - SUMMARY OF SUBMISSIONS TO THE DRAFT ASSESSMENT REPORT.....		31
ATTACHMENT 3 - RISK ASSESSMENT REPORT.....		48
ATTACHMENT 4 - FOOD TECHNOLOGY REPORT		58

INTRODUCTION

In 2003, Food Standards Australia New Zealand (FSANZ) received an unpaid Application from the Beer, Wine and Spirits Council of New Zealand (BWSCNZ) seeking to amend the Code to provide an exemption from the allergen labelling requirements for isinglass when used in the production of beer and wine. BWSCNZ ceased operations in December 2006, and the Application was taken over by the Brewers Association of New Zealand (BANZ). In referring to 'the Applicant' this Final Assessment Report refers to BWSCNZ for activities prior to December 2006 and BANZ thereafter.

This Final Assessment Report discusses matters in relation to providing an exemption from the allergen labelling requirements for isinglass and addresses issues raised in submissions to the Draft Assessment Report. The draft variation to the Code is provided at Attachment 1.

1. Nature of the Application

1.1 Background to the Application

On 12 August 2002, the BWSCNZ, on behalf of the Brewing Industry of New Zealand, wrote to FSANZ requesting that an exemption be granted for isinglass from the mandatory declaration requirements in clause 4 of Standard 1.2.3 – Mandatory Warning and Advisory Statements and Declarations. In the accompanying documentation that was provided to FSANZ, the BWSCNZ requested a permanent exemption, or if this was not possible, a temporary exemption, to allow further scientific evidence to be obtained regarding the non-allergenicity of isinglass.

On 20 September 2002, FSANZ responded to this request, advising that, in the absence of substantial scientific evidence on the relationship between residual levels of isinglass in beer and associated allergenicity, it was not in a position to consider exemptions to the requirements in clause 4 of Standard 1.2.3. However, FSANZ advised that it would consider an application to amend the Standard should further research provide persuasive new evidence in this area.

On 6 January 2003, the BWSCNZ resubmitted the document dated 12 August 2002 and requested that it be considered as an application. It was formally accepted and placed on the FSANZ Work Plan on 7 February 2003.

On 15 October 2003, the Applicant requested that wine also be considered within the scope of their Application. Additionally, the Applicant requested a four-year exemption from the requirement to label for isinglass, in line with the European Commission's proposed amendment to Directive 2000/13/EC. Under this amendment, the European Commission proposed to consider temporary exemptions from allergen labelling until November 2007, for derivatives of allergens that are unlikely to cause allergic reactions, while awaiting further scientific evidence for a permanent exemption.

On 19 December 2003, FSANZ agreed to expand the scope of the Application to include wine. However, FSANZ did not agree to the request for a temporary exemption and sought further information from the Applicant under subsection 34(1) of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act) (as was in force prior to 1 July 2007). A response to this request was received on 28 June 2004.

However, further information provided by the Applicant was considered to be insufficient and a subsequent request for information under subsection 34(1) of the FSANZ Act (as was in force prior to 1 July 2007) was sent in December 2004.

Meanwhile in October 2004, the Applicant provided FSANZ with a copy of the dossier that was submitted to the European Commission by the Brewers of Europe, and the Brewing, Food and Beverage Industry Suppliers Association (BE/BFBI) under the requirements of Commission Directive 2003/89/EC. This dossier titled 'Notification for the temporary exemption from labelling for isinglass used as a clarifying agent in brewing' (the BE/BFBI notification), was used by FSANZ in the assessment of this Application.

On 16 May 2005, FSANZ received further information from the Applicant and proceeded to the Initial Assessment of Application A490. The Initial Assessment Report for Application A490 was advertised for public comment from 5 October to 16 November 2005. Following an assessment of submitters' comments, together with the information provided by the Applicant, FSANZ concluded that sufficient information was not available to progress the Application to the Draft Assessment stage.

In March 2006, FSANZ requested the Applicant to provide further information under subsection 34(1) of the FSANZ Act (as was in force prior to 1 July 2007). In February 2008, FSANZ received further information from the Applicant, and proceeded to the Draft Assessment.

The Draft Assessment Report was reviewed by an allergy expert, Dr Rob Loblay, Director, Allergy Unit at the Royal Prince Alfred Hospital in Sydney. Dr Loblay endorsed the FSANZ preferred regulatory approach. The Draft Assessment Report was advertised for public comment from 1 October to 12 November 2008. Following an assessment of the comments received from submitters and the completion of targeted consultations with submitters on specific issues raised by them, FSANZ proceeded to the Final Assessment.

1.2 Basis of the Application

The Applicant is seeking to amend the Table to clause 4 of Standard 1.2.3. Clause 4 of Standard 1.2.3 requires that fish and fish products must be declared when present in food as an ingredient, an ingredient of a compound ingredient, a food additive or component of a food additive, or a processing aid or component of a processing aid.

Specifically, the Applicant is seeking an exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent. Isinglass is a permitted processing aid commonly derived from dried swim bladders of certain tropical and subtropical fish. A statement such as 'Produced with isinglass (fish product)' is used to declare isinglass on the label. The exemption was initially sought on the basis that isinglass has a long history of use as a fining agent in the production of beer and wine and has not been known to cause adverse reactions in fish-allergic individuals.

1.3 Scope of the Application

This Application is specific to the use of isinglass in the production of beer and wine only.

Isinglass, for the purpose of this Application, is defined as a piscine collagen derived exclusively from the dried swim bladder of tropical and subtropical fish species for use as a fining/clarifying agent in beer and wine. Collagen derived from other parts of fish has not been considered in this Application.

1.4 Additional information provided by the Applicant since Initial Assessment

During Initial Assessment in 2005, FSANZ was aware of a number of scientific studies in progress in Europe, USA and Australia aimed at addressing outstanding questions on the allergenic potential of isinglass. Results of these studies were made available to FSANZ as detailed below.

In February 2008, the Applicant provided FSANZ with a copy of the dossier that was submitted to the European Commission in October 2006 jointly by the BE and the BFBi, in support of a request for an extension of the exclusion from Annex IIIa of Commission Directive 2005/26/EC beyond 25 November 2007, and thus, from the requirement to label isinglass used as a clarifying agent in brewing. This dossier contained analytical studies and clinical trials on isinglass coordinated by FARRP (Food Allergy Research and Resource Program), University of Nebraska, USA. Further investigations related to residues of isinglass in beer were carried out by Brewing Research International.

In April 2008, the Australian Wine Research Institute and Wine Federation of Australia provided relevant scientific information in relation to the use of isinglass in wine. In addition, FSANZ requested specific information in relation to the supply and usage of isinglass by Australian and New Zealand beer and wine manufacturers.

These documents answered the outstanding questions on the allergenic potential of isinglass and enabled the completion of the Draft Assessment of this Application.

2. The Issue

Currently, clause 4 of Standard 1.2.3 requires that fish and fish products must be declared when present in food as an ingredient, an ingredient of a compound ingredient, a food additive or component of a food additive, or a processing aid or component of a processing aid. This declaration enables fish-allergic consumers to be aware of the presence of any potential allergenicity in the food and provides for informed choices in the context of health and safety.

The exemption was initially sought on the basis that isinglass has a long history of use as a fining agent in the production of beer and wine and has not been known to cause adverse reactions in susceptible individuals. Subsequently, the Applicant has provided evidence that dietary exposure to isinglass through beer and wine consumption is extremely low. Results of oral challenge studies have also been provided indicating that isinglass does not cause an allergic reaction to fish sensitised individuals when consumed at levels substantially higher than the potential exposure levels that may be encountered through the consumption of beer and wine. Parvalbumin is identified as the food allergen associated with isinglass. A new Good Manufacturing Code of Practice to minimise the allergen parvalbumin in isinglass has also been established by the isinglass manufacturing industry.

The issue is whether granting an exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent, can have an impact on the health and safety of fish-allergic consumers. That is, is consumption of isinglass-fined beer or wine likely to present a risk of allergic reactions in fish-allergic consumers and therefore, is the fish-related declaration meaningful to those consumers?

3. Objectives

The specific objectives for the assessment of this Application are to:

- consider the granting of an exemption from the mandatory requirement to declare isinglass on the label of beer and wine;
- ensure the protection of the public health and safety of consumers who are allergic to fish; and
- ensure adequate label information is provided to fish-allergic consumers.

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.

4. Historical Background

The current mandatory declaration requirements in Standard 1.2.3 were developed during the review of the Code, as part of Proposal P161 – Review of Specific Labelling Statements, and was gazetted in December 2000. The list of substances included in the Table to clause 4 of Standard 1.2.3 is based on the recommendations of an Expert Panel commissioned by the then Australia New Zealand Food Authority.

These substances are: cereals containing gluten and their products, namely, wheat, rye, barley, oats and spelt and their hybridised strains; crustacea and their products; egg and egg products; fish and fish products; milk and milk products; tree nuts and sesame seeds and their products; peanuts and soybeans and their products; and added sulphites in concentrations of 10 mg/kg or more.

To qualify for mandatory declaration, the substance(s) needed to be recognised by medical experts as a frequent cause of severe systemic reactions resulting in significant morbidity or mortality.

The justification for the mandatory declaration requirements in Standard 1.2.3 was based on the requirement to protect the health and safety of those individuals who are susceptible to adverse reactions from certain foods or substances in foods.

Among the substances included in the Table to clause 4 of Standard 1.2.3, the Code grants exemption from mandatory labelling declaration for beer and spirits made using cereals containing gluten.

5. Current Regulations

5.1 Current domestic regulations

5.1.1 Australia New Zealand Food Standards Code

The Standards relevant to this Application are 2.7.2 – Beer, 2.7.4 – Wine and Wine Product, 1.3.3 – Processing Aids and Standard 1.2.3 – Mandatory Warning and Advisory Statements and Declarations.

Alcoholic beverages meet the definition for food in the FSANZ Act and are therefore required to comply with the General Food Standards set out in Part 1 of the Code. In addition, beer and wine are further regulated by Part 2.7 – Alcoholic Beverages and are defined in Standards 2.7.2 and 2.7.4 respectively.

The Table to clause 6 in Standard 1.3.3 permits isinglass to be used as a processing aid in food. This Standard defines a processing aid as a permitted substance used in the processing of raw materials, foods or ingredients, at the lowest level necessary irrespective of any maximum permitted level specified, to fulfil a technological purpose relating to treatment or processing, but does not perform a technological function in the final food. The Table to clause 6 of Standard 1.3.3 specifies the use of Good Manufacturing Practice (GMP) in regulating the maximum amount of isinglass which may be present in the final food. The relevant GMP criteria are:

- (a) the quantity added to food shall be limited to the lowest possible level necessary to accomplish its desired effect;
- (b) the quantity that becomes a component of food as a result of its use in the manufacture, processing or packaging of a food and which is not intended to accomplish any physical, or other technical effect in the finished food itself, is reduced to the extent reasonably possible; and

- (c) the material is prepared and handled in the same way as a food ingredient.

The Standard most relevant to this Application is Standard 1.2.3. Clause 4 of Standard 1.2.3 requires that the presence of fish or fish products in a food must be declared on a label (or declared in connection with the display of the food or provided to the purchaser on request when a food is not required to bear a label). This requirement is irrespective of the fish or fish product being used as an ingredient; a compound ingredient; a food additive; or a processing aid.

5.1.2 Issues raised in submissions to the Draft Assessment Report

Suggestions were raised by some submitters to the Draft Assessment Report with respect to dealing with exemptions for allergens more generically, rather than on the basis of individual applications. These are addressed below.

- Possible exemptions from the allergen declarations in Standard 1.2.3 should be dealt with in a systematic and broader fashion and not through individual applications.

Applications to FSANZ seeking to change the Code are made by individuals, organisations or companies. FSANZ is required to respond to and assess each application received. Applying general criteria to all possible exemptions from allergen declarations may not be practical due to the diversity of products and their applications. The risk assessment process may require case specific scientific information, as is the case in this Application.

- Standard 1.2.3 should be reviewed so that there is no requirement to declare products of allergens where it can be demonstrated that they do not contain the allergenic protein.

FSANZ considers the above issue to be beyond the scope of this Application. At the request of the Ministerial Council, FSANZ has commenced a review of the regulatory management of food allergens. The overall aim of the review is to determine whether regulatory and non-regulatory measures are meeting the needs of allergic consumers in a manner that is practical for industry to implement, and that is effective in achieving the objectives of food regulatory measures outlined in the FSANZ Act. A number of issues relevant to the regulatory management of food allergens are being considered including a framework to identify non-allergenic ingredients derived from allergenic foods.

5.2 Overseas and international regulations

5.2.1 Codex Alimentarius

The *Codex General Standard for the Labelling of Pre-packaged Foods* [Codex Stan 1-1985] requires the mandatory declaration of substances that are known to cause adverse reactions. The list of substances that are required to be declared includes ‘fish and fish products’, in addition to other major food allergens. The use of isinglass as a processing aid is subject to ingredient declaration in accordance with Sections 4.2.1.4 and 4.2.4 of the *General Standard for the Labelling of Pre-packaged Foods*.

The *Codex General Standard for the Labelling of Pre-packaged Foods* has been in place for many years and no revision relevant to the exemption considered here has taken place as yet.

FSANZ's consideration of the labelling exemption for isinglass used in the clarifying process of wine and beer is based on the more recent scientific information available and is in line with other international regulations.

5.2.2 *United States of America*

In the United States, the Food and Drug Administration's (FDA) Food Allergen Labelling and Consumer Protection Act of 2004 (FALCPA) applies to most domestic and imported food and beverage products. However, it is the responsibility of the Alcohol and Tobacco Tax and Trade Bureau (TTB) to issue regulations with respect to the labelling of wine, distilled spirits and malt beverages. In July 2006, the TTB proposed mandatory labelling of major food allergens used in the production of alcohol beverages. The proposition of mandatory allergen labelling parallels amendments to the Federal Food, Drug and Cosmetic Act contained in the FALCPA.

These proposed regulations were published as an interim rule which allows producers, bottlers and importers of alcoholic beverages to voluntarily declare the presence of major allergens (including fish and proteins derived from fish). The interim regulations set forth mandatory requirements for how such labelling must be applied should an industry member choose to do so. The purpose of introducing interim regulations was to allow adequate time for consultation on the proposed final regulations whilst encouraging the alcohol beverage industry to introduce allergen labelling.

The proposed regulations and interim rule establishes a petition process through which a food ingredient may be exempted from the labelling requirements if the ingredient does not cause an allergic response that poses a risk to human health or if the ingredient does not contain allergenic protein. FSANZ is aware that the TTB is currently considering petitions for the exemption of isinglass.

5.2.3 *Canada*

In February 2004, Health Canada proposed amending the Food and Drug Regulations to enhance allergen labelling requirements on pre-packaged foods for specific allergens. This proposal included the requirement for mandatory labelling of fish by species name. In September 2004, Health Canada amended its original proposal such that fining agents derived from fish, milk and egg, used during the manufacture of standardised alcoholic beverages, would be exempt from the allergen labelling requirements.

Health Canada recently published its proposed regulatory amendments for allergen labelling (including the exemption from labelling for isinglass and other fining agents) in *Canada Gazette, Part I* in July 2008. The final regulations are expected to be published in the *Canada Gazette, Part II*, in early 2009. The exemption was based on a history of use of such fining agents and the lack of documented clinical evidence of allergic reactions caused by consumption of these products. Health Canada has expressed that it may reconsider its position on a labelling exemption for fining agents used in the production of standardised alcoholic beverages, should scientific evidence become available suggesting that residues of these substances remaining in the final beverage could cause a health risk to susceptible individuals.

5.2.4 *European Union Member Countries*

The European Commission's Directive 2000/13/EC provides for the possibility of an exclusion from the allergen labelling requirement for substances derived from allergenic ingredients, for which it has been scientifically established that such substances are unlikely to cause an adverse reaction in susceptible individuals. As a result, Commission Directive 2005/26/EC granted a temporary allergen labelling exemption for specific derivatives of allergenic ingredients or substances until 25 November 2007. This provisional list of exemptions included 'fish gelatine or isinglass used as a fining agent in beer, cider and wine'.

During the period of this temporary labelling exemption, industry sectors wishing to make an application for a permanent labelling exemption were responsible for submitting research to the European Food Safety Authority (EFSA). EFSA received and considered applications for a permanent labelling exemption for isinglass used as a fining agent in beer and wine production.

EFSA considered the information on isinglass used in wine and concluded that 'the data submitted do not allow the Panel to assess the likelihood that isinglass used as fining agent will trigger an allergic reaction in susceptible individuals under conditions of use stated by the applicant'.

EFSA also considered, separately, information on isinglass used in beer and concluded that 'it is not very likely that isinglass used as a clarifying agent in beer will trigger a severe allergic reaction in susceptible individuals under the conditions of production and use specified by the applicant'.

The Commission considered EFSA's opinions and concluded that a permanent exemption from allergen labelling should apply to isinglass used in the production of both beer and wine. Annex IIIa of Commission Directive 2000/13/EC was amended by Commission Directive 2007/68/EC as of 27 November 2007. This amendment stipulates a revised regulatory approach to allergen labelling and includes the requirement that fish and products thereof must be declared on a label except fish gelatine and isinglass used as a fining agent in beer and wine.

5.2.5 *Japan*

Japan's current allergen labelling requirements became enforceable in April 2002 and divides allergen labelling into two categories, mandatory and recommended, according to the number of cases and degree of seriousness of allergic reactions.

Fish is not included on the list of allergens requiring mandatory labelling (these are eggs, milk, wheat, buckwheat and peanuts) and only specific species of fish (salmon and mackerel) are recommended for allergen labelling.

Furthermore, alcohol beverages and related products are not subject to the allergen labelling requirements. Hence labelling of isinglass and other fining agents used in the production of alcoholic beverages is not required in Japan.

5.3 Regulatory differences and its impact

As stated above, labelling exemption for isinglass has already been granted in many countries, including all of the European Union member countries. Currently, beverage manufacturers in Australia and New Zealand supplying the market in these countries would have to meet different isinglass declaration requirements for local and export markets. This regulatory difference to labelling may have an impact on trade and increase the costs to manufacturers.

6 Matters of Relevance

Details of technical information and analytical data related to this Application are provided in the Risk Assessment Report in Attachment 3 and the Food Technology Report in Attachment 4. This section provides some key information related to isinglass. This information has been extracted from the documents provided by the Applicant, the Australian Wine Research Institute, and the Wine Federation of Australia.

6.1 Parvalbumin

Parvalbumin is identified as the food allergen associated with isinglass. Parvalbumins have molecular weights of approximately 10-13 kDa, and acidic pI values¹. Parvalbumins are water soluble and resistant to heat treatment and enzymatic degradation (Aas and Elsayed, 1975 [as cited in Chen et al. 2006]).

6.2 Definition of isinglass

6.2.1 Isinglass definition used by the Applicant (submission 16 May 2005)

Isinglass is a pure form of collagen, which is derived from the dried swim bladders of certain tropical and subtropical fish. In brewing, only isinglass from catfish, croakers and threadfins is used.

6.2.2 Isinglass definition from the BE/BFBi notification

Isinglass is the usual term for piscine collagen. Within the BE/BFBi notification, the term is used exclusively to mean the collagen obtained from the dried swim bladders and does not include collagen from fish skins. This notification states that the isinglass used in brewing is a pure form of collagen derived from the dried swim bladders of a restricted range of specific tropical and subtropical fish species. These species are specific catfish, croakers and threadfins.

6.3 Components of isinglass

The major component of isinglass is type 1 collagen and its denaturation product, gelatin. Isinglass also contains small quantities of elastin, a highly hydrophobic, 72 kDa protein. Collagen, gelatin and elastin constitute about 95% of the dry weight of isinglass. Only residual amounts of the fish protein parvalbumin have been detected in isinglass.

¹ The pH at which the protein is least soluble.

6.3.1 Collagen

Collagen is a protein with a molecular weight of approximately 300 kDa and is present in fish muscle, skin and swim bladder. Intact collagen has a triple helical structure stabilised by cross linkages. Soluble collagen exists mainly as trimers and tetramers with a molecular weight of 800-1300 kDa. The large size of collagen contrasts with known allergenic proteins, which are usually small, compact proteins with molecular weights ranging between 10 kDa and 80 kDa.

Collagen is thermally labile and denatures to gelatin, where the triple helix is unwound to form random coils. Collagen from tropical fish species is most suitable for isinglass production because it remains intact in temperatures up to 29°C, while collagen from coldwater fish species denatures at about 5°C.

6.4 Commercial production of isinglass

The swim bladders of tropical and subtropical fish are used to produce isinglass on a commercial scale for use in the alcohol beverage industry. The swim bladder is an air sac, located in the dorsal part of the body cavity quite separate from the fish muscle tissue. The adherence between the bladder and the body cavity is minimal and as such, it can be readily detached without significant contamination with the fish muscle tissue.

6.4.1 Traditional processing method

The traditional basic production process has been reported to vary between manufacturers, which can also depend on the source and species of the fish. However, a number of steps are considered standard practice. Dried swim bladders are blended according to specific quality and other criteria, followed by granulation, washing, sterilisation with dilute hydrogen peroxide and rinsing. A temperature of less than 15°C is maintained throughout the wet steps. The product is then sold as powder, paste or liquid. The paste and liquid forms include a source of sulphur dioxide as a preservative.

As a result of the traditional processing method the final parvalbumin levels in isinglass have shown to be reduced by about a half compared to the starting material.

6.4.2 New manufacturing protocol (Good Manufacturing Code of Practice)

The three major European isinglass manufacturers (AB Vickers, Kerry Bioscience and Murphy & Son Ltd) have developed a Good Manufacturing Code of Practice for the sourcing and manufacturing of isinglass. This new protocol, which minimises the parvalbumin content in isinglass, includes the following additional steps.

- The fish species with high parvalbumin level in the swim bladder have been excluded.
- A granulation stage to ensure that swim bladder wall particle size does not exceed 25 mm has been introduced. This step increases the surface area thus ensuring adequate sterilising during peroxide wash and improving the extent of washing out of the parvalbumin in the subsequent buffer wash.

- Additional washing steps using phosphate buffer and further water washing have been introduced. Phosphate buffer wash has shown to have the greatest effect in reducing parvalbumin levels in samples containing the highest initial parvalbumin levels.

All of the isinglass produced by the major European manufacturers supplying to the Australian and New Zealand markets is now produced in accordance with the Good Manufacturing Code of Practice (new protocol) designed to minimise the levels of parvalbumin.

6.4.3 Products used by the Applicant

Based on the information received from the beer and the wine industry, isinglass commercially available for their use in Australia and New Zealand is manufactured by the European manufacturers AB Vickers, Kerry Bioscience and Murphy & Son Ltd.

FSANZ has also been made aware of the existence of other European companies who are not manufacturers of isinglass but resellers or blenders of fining agents who source the raw material from the above mentioned manufacturers. In Australia and New Zealand, isinglass is predominantly sourced through a local supply network from the European manufacturers, blenders and resellers.

6.5 Isinglass as a processing aid/clarifying agent

6.5.1 History of usage

At Initial Assessment, the Applicant stated that isinglass has been used in the clarification of beer and wine for over a hundred years. The dossier submitted by BE/BFBi in 2004 made a similar statement and, based on a rigorous literature search, concluded that no isinglass-related allergy cases have been reported. A further literature search was completed by BE/BFBi to identify any reports which might have been published since 2004. No reports of allergic responses to beer or isinglass by fish sensitised individuals have been found.

A literature search has also shown no reports of any adverse reactions to wine ingestion that is attributable to the consumption of isinglass.

6.5.2 Usage levels in beer and wine

The rod-like structural integrity of the collagen triple helix was hypothesised to be crucial for efficient clarification (Hickman *et al.*, 2000). However, a more popular hypothesis of the fining activity is based upon charge interactions. The isinglass is assumed to electronically attract yeast cells with negatively charged cell walls and other suspended charged polyphenolic and protein components. These aggregated complexes would then settle to the bottom of the container. In the sediment, further interactions may take place resulting in a firm sediment that is resistant to disturbance when the clear beverage is drawn off.

The Table to clause 6 of Standard 1.3.3 in the Code specifies the use of Good Manufacturing Practice in regulating the maximum amount of isinglass which may be present in the food (i.e. beer and wine in this instance).

In the brewing process, isinglass is typically added after fermentation and cooling of the beer. The typical usage level is 15 mg/L for brewery conditioned beer and 35-60 mg/L for cask-conditioned beer. Isinglass is subsequently removed by sedimentation followed by filtration or centrifugation. Cask-conditioned beer does not undergo filtration or centrifugation and relies on gravity settling.

In the wine production process, isinglass is added prior to fermentation to remove phenolic compounds from white juice or immediately post fermentation to remove yeast, phenolic and tannin compounds from white wine. The typical usage level is 10-25 mg/L for white wines. It is assumed that isinglass is seldom used in red and rosé wines. Isinglass is removed by sedimentation and filtration. The information provided by the Australian Wine Research Institute states that a laboratory trial is undertaken on individual batches of wine prior to the addition of isinglass to accurately determine the amount of isinglass to be added so as not to result in an over-fined wine.

6.5.3 *Residues of isinglass in beer and wine*

Isinglass added to beer and wine for clarification is removed by sedimentation, filtration or centrifugation resulting in very low residual levels in the final product.

6.6 **Toxicological assessment**

Isinglass is a natural product derived from the swim bladders of tropical and subtropical fish. FSANZ is not aware of any toxicity concerns related to the use of isinglass as a clarifying agent. The BE/BFBI notification reports that in addition to being a source of isinglass, the fish swim bladders (also known as fish maws) are consumed as food in many parts of the world. More than 2750 metric tons are accounted for by such consumption.

7. **Key Risk Assessment Questions**

What is the evidence in relation to the allergenicity of isinglass?

What is the level of isinglass residue present in beer and wine? Is there a risk of an adverse reaction occurring in susceptible individuals from residual isinglass in the final product?

What is the potential of parvalbumin partitioning out into the bulk liquid and then being carried into the final product?

RISK ASSESSMENT

8. **Risk Assessment Issues**

This section assesses the allergenicity of isinglass and addresses risk assessment issues raised by submitters in response to the Draft Assessment Report. The full details of the risk assessment are presented in Attachment 3.

8.1 Allergenicity of isinglass

8.1.1 What is the evidence in relation to the allergenicity of isinglass?

- The three main components of isinglass (collagen, elastin and gelatin) are not of clinical importance in IgE-mediated allergy to fish. Parvalbumin, the allergenic fish protein of clinical significance, is only present in trace amounts in commercial isinglass.
- A number of searches of the published literature failed to identify any reports of adverse reaction to wine or beer that can be attributed specifically to isinglass.
- Oral challenge studies have indicated that isinglass manufactured according to either the traditional or the new protocol, do not provoke allergic reactions. Two separate oral challenge tests have been conducted using twenty-one fish-allergic patients in total. None of the patients had positive reactions to the oral challenge tests.

These findings support the conclusion that isinglass is unlikely to pose a risk to fish-allergic consumers.

8.2 Presence of isinglass in beer and wine

8.2.1 What is the level of isinglass residue present in beer and wine? Is there a risk of an adverse reaction occurring in susceptible individuals from residual isinglass in the final product?

- The Table to clause 6 of Standard 1.3.3 specifies the use of Good Manufacturing Practice in regulating the maximum amount of isinglass which may be present in the food (i.e. beer and wine in this instance).
- Isinglass added to beer and wine for clarification is removed by sedimentation, filtration or centrifugation resulting in very low residual levels in the final product.
- Residual amounts of isinglass in bottled and canned beer are below the limit of detection, and where detectable, do not exceed 1 mg/ L. Isinglass residues are 3 mg/L for keg beer and 5 mg/L for cask beer.
- The results for wine indicate no residual isinglass has been detected in a small sample of commercially available wines fined with isinglass (detection limit 1 mg/L) and made following GMP. Therefore, it has been concluded that the concentration of isinglass is likely to be less than 1 mg/L. Results of subsequent analysis of isinglass-fined wines have supported this conclusion.
- The dose of isinglass, regardless of whether isinglass was manufactured according to either the old or new protocol, tolerated by fish-allergic individuals in the oral challenge studies, far exceeds isinglass levels that may be expected in the volume of beer or wine that could be consumed by an individual within a single sitting.

- Parvalbumin would only constitute a minute fraction of isinglass residue in beer or wine. This is supported by the fact that parvalbumin was not detectable in beer samples fined using isinglass prepared according to the old or new protocol.

8.3 Potential of parvalbumin partitioning out into the bulk liquid

8.3.1 What is the potential of parvalbumin partitioning out into the bulk liquid and then being carried into the final product?

The information provided by the Applicant indicates the following.

- Due to the inherent entrapment property of collagen, it can be expected that the parvalbumin residues present in isinglass would remain entrapped to a certain degree.
- Parvalbumin is insoluble in the acidic conditions of beer and wine. Analytical testing of the sediments indicates that parvalbumin indeed precipitates with the isinglass and is removed prior to packaging the final product.

8.4 Issues raised in submissions to the Draft Assessment Report

The following issues were raised in relation to the risk assessment for this Application.

- There is insufficient clinical proof that isinglass does not raise any safety concerns for fish-allergic consumers.

The Applicant provided information on three clinical studies that have been conducted, in Australia and in Europe, to evaluate the effect of isinglass and isinglass-fined wine on fish-allergic consumers. The three clinical studies, which involved thirty-one fish-allergic patients in total, were conducted according to robust protocols. No allergic reactions related to isinglass were reported under the conditions of the oral challenges described in any of the studies. Taking into account all the other information provided by the Applicant, these results support the conclusions that consumption of isinglass-fined beer and wine does not raise any safety concerns for fish-allergic consumers.

Additionally, since 2005 an explicit exemption has been granted from declaration in beer and wine by the European Commission. FSANZ is not aware of any health risks or concerns in the European Union member countries as a result of this exemption.

- The literature review was based on only one search engine and used only two search terms.

The Applicant has provided the outcomes of a total of three literature searches. Information on two of the literature searches have been presented in the Initial Assessment Report and the Draft Assessment Report. Information on all three searches is now presented in the Final Assessment Report. All three searches have failed to identify any publications that may be relevant to isinglass allergy.

- There are uncertainties with regard to the accuracy and appropriateness of the cod parvalbumin-based ELISA for the assessment of parvalbumin in tropical fish-derived isinglass.

Parvalbumin is a fish protein that appears to be highly conserved among a wide range of fish species including cod and tropical fish species.

Analyses comparing available sequences from a range of fish species have demonstrated close sequence similarity across many fish species as a general rule, and there is no reason to suggest this would not be the case for fish species used in isinglass production. The well purified and characterised cod parvalbumin was used to generate polyclonal antibodies to parvalbumin, to provide broader specificity, allowing detection of parvalbumin from various fish species. Western blot data provided by the Applicant indicates that the cod-parvalbumin polyclonal antibodies detected parvalbumin from tropical fish species. The polyclonal antibodies were utilised in the cod-based ELISA. In addition, the Applicant also provided data where a monoclonal carp-based ELISA was used to detect parvalbumin in various test samples. The two methods vary slightly in their sensitivity and specificity, but together they provided mutually supporting information on the level of parvalbumin in isinglass.

- The test numbers used in the clinical studies are small and therefore, have limited statistical power.

The clinical studies provide information on a total of thirty-one fish-allergic patients, and undoubtedly a larger number would have been desirable. However, the fact that the number of fish-allergic patients that could be recruited is relatively small, may reflect the prevalence of fish allergy in the community. The targeted nature of the recruitment of fish-allergic individuals and the strict qualifying criteria applied in the selection of participants, limits the number of subjects available to participate in clinical studies. No statistical analysis was undertaken due to the small number, however, the studies were conducted according to robust protocols and no allergic reactions were reported under the conditions described in the report. In this case, the high quality of the clinical testing data obtained using a panel of consumers clinically diagnosed to be fish allergic minimises concerns over quantity. These studies, which provide an important piece of scientific evidence, were not considered in isolation. Together with other evidence, the clinical studies support the conclusions that consumption of isinglass-fined beer and wine does not raise any safety concerns for fish-allergic consumers.

- One of the double-blind placebo-controlled food challenges used isinglass in mashed potatoes. This trial was performed in a food matrix in which isinglass is not usually consumed. In addition, alcohol is considered to lower the dose that may trigger a food allergic reaction in susceptible individuals.

Fifteen fish-allergic individuals, aged between 21-66 years, participated in a double-blind placebo-controlled food challenge according to an internationally accepted protocol. The oral challenge material was prepared using four doses (0.5 mg, 5 mg, 15 mg and 30 mg) of isinglass in 40 g mashed potato. The use of mashed potato as a matrix made it possible to use such relatively high doses of isinglass. This could not be achieved if the oral challenge was conducted using isinglass-fined beer or wine based on the extremely low level of isinglass (generally below 1 mg/L) in such beverages.

In relation to the role of alcohol in lowering the dose that may trigger an allergic reaction, it would have to significantly lower the dose for it to be relevant to the level of isinglass that could possibly be present in fined beer and wine (generally below 1 mg/L).

Also, the study report indicates that all individuals have reported regularly consuming beer or wine, at least some of which would have been fined with isinglass, without incident.

This study should be considered in the context of two additional oral challenge studies provided by the Applicant. These are briefly outlined:

A second study was conducted on a younger group of fish-allergic individuals, aged between 6-22 years with isinglass in mashed potato. No allergic reactions were reported in any of the six individuals tested up to a dose of 20 mg isinglass.

The third study included ten fish-allergic subjects and each consumed 100 mL of isinglass-fined or control wine over 10-15 minutes. No subjects developed an allergic reaction requiring medical treatment and no abnormalities were noted during follow-up reports.

Collectively, information from all the oral challenge studies presented by the Applicant, including those where mashed potato was used as a matrix, support the conclusion of the risk assessment.

- The high susceptibility of isinglass to pepsin digestion is presented as evidence of non-allergenicity. Whilst most known allergens are resistant to pepsin digestion this is not a necessary condition for allergenicity. Therefore, this method is unsuitable for assessing the allergenicity of isinglass.

Pepsin digestion information was submitted by the Applicant. However, the information was not considered in the risk assessment and had no bearing on the risk assessment conclusion. Reference to pepsin digestion has been deleted in the Final Assessment Report.

- The data on the prevalence of fish allergy in the Australian and New Zealand populations and the threshold dose of the allergen for fish-allergic individuals are unknown.

FSANZ acknowledges the general lack of information on the prevalence of various food allergies in Australia and New Zealand. There is currently no consensus on a threshold dose for fish allergens. Such information would be a valuable resource and would certainly add to the strength of the evidence base for the assessment of isinglass. However, even in the absence of such information it is possible to reach a scientific conclusion based on all the other information that is available. For example, a published report of a clinical study conducted in Australia provides such information. The study, discussed in more detail in the Risk Assessment Report, presents outcomes of an oral challenge of ten adult fish-allergic individuals with isinglass-fined and un-fined wine. No allergic reactions were reported during two hours post challenge and over the following six days.

- There is a possibility of significant under-reporting of allergic reactions due to:
 - a lack of awareness among wine drinkers and health professionals of the possible presence of fish proteins in wine
 - the tendency to blame other substances including alcohol or food if adverse reactions occurred
 - the lack of reporting of food allergic reactions to an authority or a medical practitioner, especially in adult sufferers

- the absence of a requirement in New Zealand for food allergic reactions to be reported by health professionals to a regulatory authority, nor to document the reaction in a public journal.

Clinical studies discussed above indicate that fish-allergic individuals do not react to isinglass or isinglass-fined wine. Also, the extremely low level of isinglass and the even lower level of parvalbumin that may be present in isinglass-fined beer and wine argues against these suggestions.

- The evidence provided by the beer industry which used isinglass manufactured under the new code of GMP was extrapolated for wine, however, this is not made clear in the Draft Assessment Report.

The Draft Assessment Report presents analytical data on bottled beer and wine which indicates that the level of residual isinglass, if it can be detected at all, is around 1 mg/L. This residual level would be expected regardless of whether the isinglass was prepared according to the old or new protocol. Parvalbumin, the protein of concern to fish-allergic consumers, would only constitute a minute fraction of the isinglass residue in beer or wine. This is supported by the fact that parvalbumin was not detectable in beer samples fined using isinglass prepared according to the old or the new protocol. On this basis, information can be extrapolated and will be clarified as such in the Final Assessment Report.

- The allergenic fish proteins are normally found in the flesh of the fish, but in some rare cases, also collagen can cause allergies. Isinglass contains this particular collagen which is found in fish so theoretically it can cause, in select individuals, an anaphylactic reaction.

There is no credible evidence to support the clinical relevance of this statement. Collagen is not considered by allergy clinicians to be a significant fish allergen and FSANZ is not aware of any reports of anaphylactic reactions to fish collagen. The medical literature reports that IgE to fish collagen has been detected in only a few Japanese individuals. However, the clinical relevance of these findings has not been confirmed by oral challenges. In addition, the oral challenge studies presented in the Risk Assessment Report do not support the suggestion that collagen is relevant in fish allergy. In two of these studies, twenty-one fish-allergic individuals of various ages, were challenged with up to 50 mg fish isinglass (collagen from the fish swim bladder) within a period of two hours. No allergic reactions were reported in any of these individuals.

- The assessment that consumption of isinglass-fined beer and wine is not likely to present a risk of allergic reactions in fish-allergic consumers, does not indicate that there is no risk.

Food regulation does not aim to achieve, and can not deliver, zero risk. FSANZ risk analysis indicates the consumption of isinglass-fined beer and wine is not likely to present a risk of allergic reactions in fish-allergic consumers and therefore it does not require a regulatory measure.

- Two submitters objected to providing an exemption as they have experienced allergic reactions to wine containing fish products and/or seaweed.

Further information was sought from these submitters. One indicated a seaweed specific allergy and no allergy to fish or shellfish. Isinglass is derived from the swim bladders of fish and is not a derivative of seaweed.

Additionally, the labelling exemption is specific to isinglass alone, for use as a clarifying agent in the production of beer and wine. Isinglass and seaweed are unrelated and therefore, the issue raised by the submitter is not relevant in the context of this Application.

The other submitter indicated an allergy to fish and shellfish which had been diagnosed by a medical practitioner specialising in allergies. This submitter also indicated the use of a skin prick test as part of the diagnosis. This submitter was unable to provide the details of the wine that caused the allergic reaction except for the information that the product contained a statement 'may contain fish products'. In this case it cannot be categorically concluded that the reaction to wine ingestion experienced by this submitter is attributable to isinglass without further information and testing.

The scientific evidence shows that isinglass does not raise any health and safety concerns for fish-allergic consumers. In addition, as stated previously since 2005 an explicit exemption has been granted from declaration in beer and wine by the European Commission. FSANZ is not aware of any health risks or concerns in the European Union member countries as a result of this exemption. FSANZ is unable to conclude that the allergic reactions mentioned above are related to the use of isinglass in the fining process of the wine.

- One submitter indicated that a family member had experienced a severe reaction to fish containing a ciguatoxin and continues to experience reactions in circumstances such as, when coming into contact with objects such as hand rails which people who have handled fish have touched.

Fish contaminated with ciguatoxin causes food borne illness in humans, which is unrelated to fish allergy. The Primary Production and Processing Standard for Seafood (Standard 4.2.1) regulates the safety of all seafood in Australia, including toxin contamination. In New Zealand these requirements are covered by the New Zealand Fishing Industry Agreed Implementation Standards. Application A490 deals specifically with the exemption of isinglass from the labelling requirements of mandatory allergen declarations in Standard 1.2.3. Isinglass and ciguatoxin are completely unrelated and therefore, the issue raised by the submitter is not relevant in the context of this Application.

8.5 Summary of risk assessment

In summary, the key risk assessment findings include:

- the three main components of isinglass (collagen, elastin and gelatin) are not clinically relevant in IgE-mediated allergy to fish;
- parvalbumin, the allergenic fish protein, is present at very low levels in isinglass;
- isinglass added to beer and wine for clarification is removed by sedimentation, filtration or centrifugation, resulting in residual levels of isinglass which, when detectable at all, do not exceed 1 mg/L of bottled beer or wine;

- parvalbumin, although present in trace amounts in commercial isinglass, is not detectable in the clarified final product as it co-sediments with isinglass and is removed in the filtration process; and
- exposure to isinglass through the consumption of clarified beer and wine would be very low and, based on oral challenge studies, would not be expected to provoke reactions in fish-allergic consumers.

On the basis of the above, FSANZ considers that consumption of isinglass-fined beer and wine is not likely to present a risk of allergic reactions in fish-allergic consumers.

RISK MANAGEMENT

9. Risk Management Measures

At Draft Assessment submitters raised their concerns regarding the maintenance of the quality of isinglass and its usage, and impact on the provision of information for informed choices. These matters are addressed below.

9.1 Maintaining the quality of isinglass

Isinglass is a highly valued clarifying agent and is specifically sought by wine and beer manufacturers for its superior functionality compared to other clarifying agents. There are a number of market factors that underpin maintenance of high quality isinglass including:

- Isinglass commercially available for use by the beer and wine industry in Australia and New Zealand is manufactured by AB Vickers, Kerry Bioscience and Murphy & Son Ltd. These are the three major manufacturers supplying the world market.
- These three manufacturers have come together in developing a Good Manufacturing Code of Practice, for the manufacture of isinglass low in parvalbumin (new manufacturing protocol).
- All of the isinglass produced by these manufacturers is now produced in accordance with the new manufacturing protocol.
- The commercially available isinglass referred to above has an established market advantage and is widely used by the beverage manufacturers who seek a superior functionality. Any quality issues will undermine its status and use in the market place. As such, there would be no obvious advantage or incentive for isinglass manufacturers to compromise the quality of isinglass.

9.2 Usage of isinglass

The usage of isinglass is regulated in the Code. The Table to clause 6 of Standard 1.3.3 – Processing Aids, specifies the use of Good Manufacturing Practice in regulating the maximum amount of isinglass which may be present in the final food. The relevant Good Manufacturing Practice criteria for isinglass include:

- (a) the quantity added to food shall be limited to the lowest possible level necessary to accomplish its desired effect;
- (b) the quantity that becomes a component of food as a result of its use in the manufacture, processing or packaging of a food and which is not intended to accomplish any physical, or other technical effect in the finished food itself, is reduced to the extent reasonably possible; and
- (c) the material is prepared and handled in the same way as a food ingredient.

Additionally, information from the industry indicates that isinglass is sparingly used as it is one of the most expensive fining agents available.

9.3 Issues raised in submissions to the Draft Assessment Report

This section addresses risk management issues raised by submitters in response to the Draft Assessment Report.

9.3.1 Issues related to the quality and use of isinglass

- How will the isinglass manufacturing standard be monitored?
- Isinglass could be sourced from countries with less stringent manufacturing standards.

There are a number of market factors that support the maintenance high quality of isinglass as outlined in Section 9.1.

Due to these factors FSANZ considers market imperatives will serve to maintain the provision of high quality product and it is unlikely that isinglass in commercial quantities would be sourced from countries with less stringent manufacturing standards. This process will inherently be self monitored by industry and its use of product.

- Impose a condition that only isinglass manufactured using the new manufacturing protocol, is sourced and used.

Only trace amounts of parvalbumin have been detected in isinglass (from 1 µg/g for the new protocol to 10 µg/g for the traditional method). For consumers, exposure to isinglass in the fined beverage (bottled beer and wine) is unlikely to be more than 1 mg/L regardless of which protocol was used to prepare the isinglass. This aspect is already regulated in the Code (Standard 1.3.3) for the use of isinglass as a clarifying agent. Accordingly, consumer exposure to parvalbumin would be in nanogram levels regardless of whether the isinglass manufacturing protocol is old or new. In addition, the oral challenge studies discussed in this report indicate that isinglass prepared according to the old or new protocol (up to 20 mg and 50 mg, respectively) did not provoke allergic reactions in any of the fish-allergic participants.

Therefore, imposing a condition that only isinglass manufactured using the new manufacturing protocol is sourced and used is unjustifiable. Including provisions for manufacturing to the new protocol would be unenforceable.

9.3.2 *An alternative approach to declaring isinglass*

- If beer and wine industry's concern is the use of the term 'fish' on their labels, why not permit the use of the term 'isinglass'?

This Application deals specifically with the labelling requirements for mandatory allergen declarations. The available scientific evidence shows that isinglass is not likely to cause an allergic reaction to fish-allergic consumers. Therefore, FSANZ considers the current requirement for the mandatory declaration of isinglass on product labels of beer and wine is not warranted regardless of how it may be worded.

9.3.3 *Review procedures*

- Regular reviews should be undertaken and if reactions do start to occur, amendments to the Code should be made.

FSANZ can prepare a proposal to amend the Code based on emerging evidence, as appropriate. This would apply to any new evidence relevant to the allergenicity of isinglass when used as a clarifying agent in beer and wine.

9.3.4 *Provision of information beyond allergenicity*

- Labelling is required for vegetarians and vegans, and for people with other ethical, religious, environmental or personal reasons to make informed choices.
- Removing the labelling requirement would breach current Australian and international law regarding the human rights of vegetarians and vegans.
- Allowing an exemption for labelling would be misleading and deceptive as it does not provide adequate information for consumers to make informed choices for example vegetarian/vegan consumers.
- Manufacturers should be required to disclose every ingredient used in the production process for all foods.

The purpose of this Application is to seek an exemption from the labelling requirements of mandatory allergen declarations in Standard 1.2.3. The purpose of allergen declarations is to protect the health and safety of those individuals susceptible to adverse reactions from certain foods or substances in foods. Scientific evidence shows that consumption of isinglass-fined beer and wine, is not likely to present a risk of allergic reactions in fish-allergic consumers. Therefore providing an exemption would enhance the accuracy of product allergenicity information, to enable fish-allergic consumers to make an informed choice. Maintaining the *status quo* on the basis of the consequential use of allergen labelling by vegetarian and vegan consumers to make informed choices goes beyond the scope of this Application.

In Australia and New Zealand food manufacturers have the option of providing the food suitability information specific to vegetarians or vegans on the label on a voluntary basis and may do so as a customer service and to meet the consumer needs. Where manufacturers choose to make a voluntary claim of this type, the general provisions in food law and fair trading law as they relate to misleading or deceptive conduct, apply.

Furthermore, if the food suitability information specific to vegetarians or vegans is not provided on the label of packaged foods, the supplier can be contacted to obtain this information. Standard 1.2.2 of the Code requires the name and address of the supplier to be listed on the label, and many suppliers provide a free call telephone number on their labels. Additionally, information from several sources such as websites and advocacy groups are also available to assist vegetarian and vegan consumers.

A requirement to label packaged foods to enable vegetarians to make informed choices is the subject of a separate Application (A545 – Vegetarian labelling), currently being considered by FSANZ.

There is no requirement in the Code to declare non-allergenic processing aids in the label. Specifically, clause 3 of Standard 1.2.4 does not require the declaration of a substance (other than those mentioned in Table to clause 4 of Standard 1.2.3) used as a processing aid in accordance with Standard 1.3.3. As such, other animal-derived clarifying agents are not required to be labelled. This approach is consistent with ingredient labelling requirements internationally.

10. Options

At Final Assessment two options are presented for addressing this Application:

10.1 Option 1 – Reject the Application

Reject the Application, thus maintaining the *status quo* – this would not allow the exemption from the requirement to declare isinglass on the label when present in beer and wine as a result of its use as a clarifying agent.

10.2 Option 2 – Prepare a draft variation to the Table to clause 4 of Standard 1.2.3

Prepare a draft variation to the Table to clause 4 of the Standard 1.2.3 for exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent.

11. Impact Analysis

11.1 Affected parties

The parties likely to be affected by this Application and preferred approach include:

- **Consumers** of beer and wine who are allergic to fish;
- **Industry** – Australian and New Zealand manufacturers and importers of beer and wine and isinglass manufacturers and distributors supplying to the Australian and New Zealand markets ; and
- **Government**, including the enforcement agencies of Australia States/Territories and New Zealand.

11.2 Benefit Cost Analysis

The Benefit Cost Analysis assesses the immediate and potential impacts of each regulatory option on the affected parties.

11.2.1 Option 1 – Reject the Application

Under this Option, the status quo would be maintained and the Code would not be amended to allow the exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent.

11.2.1.1 Benefits and Costs

It is unlikely that maintaining the *status quo* will greatly impact the identified parties. As beer and wine will continue to be produced and consumed in the current environment, there will be no additional benefits or costs to consumers, industry and government.

11.2.2 Option 2 – Prepare a draft variation to the Table to clause 4 of Standard 1.2.3

11.2.2.1 Benefits

Industry

Granting an exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent, provides the following potential benefits:

- provides industry with an additional choice of clarifying agent that does not require an allergen declaration, therefore, providing greater technical flexibility without creating negative consumer perceptions. FSANZ has been made aware that although isinglass is considered a superior clarifying agent, the brewing industry does not currently use isinglass due to the mandatory declaration requirement.
- industry will be able to use isinglass without incurring allergen labelling costs.
- beer and wine manufacturers in Australia and New Zealand currently supplying the local as well as labelling exempted export markets will not be required to provide separate labelling. Similarly wine and beer imported from the labelling exempted countries would not require additional labelling. This reduces costs and enables manufacturers to compete more effectively in the global environment.

Consumers

- Removing the requirement to declare isinglass should minimise the confusion between perceived and actual risk and contribute positively to a more accurate assessment of products among fish-allergic consumers.
- Generally, fish-allergic consumers will benefit in terms of increased choice of beer and wine products.

Government

- Enforcement agencies would no longer be required to enforce the mandatory allergen declaration for isinglass.
- Since this amendment is not likely to present a health and safety risk to fish-allergic consumers the health care expenditure of government will not be impacted.
- There may be further enhancement in consumer confidence in the regulatory system as a consequence of the improved accuracy in product allergenicity information due to the proposed changes. Enforcement agencies may benefit from this increase in consumer confidence.

11.2.2.2 Costs

Industry

- As the use of isinglass in beer and wine would be a voluntary choice and does not incur additional labelling, no additional costs would be imposed on industry.
- Submissions from industry did not identify any added costs.

Consumers

- Consumers will continue to have a broad choice in terms of quality and price points across the range of beer and wine in the market place.
- Consumers are not expected to incur additional costs.

Government

- There are no expected costs to government as a result of this amendment to the Code.

11.3 Comparison of options

Options 1 and 2 would continue to protect the health and safety of fish-allergic consumers of beer and wine clarified using isinglass. Scientific evidence shows that consumption of isinglass-fined beer and wine is not likely to present a risk of allergic reactions in fish-allergic consumers.

Option 2 will provide fish-allergic consumers with an increased choice of beer and wine products, and enhance the accuracy of product allergenicity information, to enable fish-allergic consumers to make an informed choice. This option will also provide the industry with greater technical flexibility and ease the presence of international trade obstacles due to different labelling requirements.

Overall, a comparison of the options at Final Assessment suggests Option 2 provides greater net benefit to the affected parties.

COMMUNICATION AND CONSULTATION STRATEGY

12. Consultation

12.1 Public consultation

12.1.1 Initial Assessment

The Initial Assessment Report for Application A490 was advertised for public comment from 5 October to 16 November 2005. In response, FSANZ received twenty submissions, with eleven submissions from industry, six from government, and three from consumers.

Overall, eleven of the submitters provided support for the exemption, six objected to providing an exemption and one did not provide a preferred option. Of the remaining two submitters, one indicated cautious support awaiting results of the safety assessment. The other indicated support based on a condition that only isinglass derived from the swim bladders of (tropical and subtropical) fish should be exempt.

12.1.2 Draft Assessment

At Draft Assessment, FSANZ undertook a robust and extensive assessment of the public health and safety implications of this Application. The Draft Assessment Report was advertised for public comment from 1 October to 12 November 2008. In response, FSANZ received twenty-seven submissions, with sixteen submissions from consumers, eight from industry, two from government and one from a public health organisation.

Overall, seventeen of the submitters (sixteen consumers and one government) objected to providing an exemption, and eight (industry) provided support for the exemption. Of the remaining two submitters, one indicated support, in principle, for granting exemptions from mandatory labelling of ingredients derived from allergenic sources. However, with regard to isinglass this submitter expressed concern that the evidence did not indicate that there is no risk. This submitter was also concerned as to how the manufacturing standard that minimises the level of parvalbumin in isinglass will be monitored, and the possible supply of isinglass in the marketplace from a manufacturer with less stringent manufacturing standards.

The other indicated support based on a condition that FSANZ consider making it a requirement that only isinglass with substantially reduced levels of parvalbumin be exempt from allergen declaration for isinglass.

A significant proportion of submitters that objected to providing an exemption linked their arguments to FSANZ's second order objective (the provision of adequate information relating to food to enable consumers to make informed choices) as a reason for their decision. The requirement to declare isinglass was considered as enabling consumers to make informed choices about foods for ethical, religious, environmental, and other personal reasons. In addition, the majority of submitters from this group indicated that they were either a vegetarian or vegan or support the provision of information on this basis.

There were two submitters who objected to providing an exemption since they believe they had experienced an allergic reaction from consuming wine.

A summary of submissions to the Draft Assessment Report is at Attachment 2.

12.2 Targeted consultation

The Draft Assessment Report was reviewed by an allergy expert, Dr Rob Loblay, Director of the Allergy Unit at the Royal Prince Alfred Hospital in Sydney. Dr Rob Loblay endorsed the FSANZ preferred regulatory approach.

Following an assessment of the comments received to the Draft Assessment Report, targeted consultations with submitters on specific issues were conducted. These targeted consultations included contacting submitters who indicated that they have experienced an allergic reaction in response to consuming wine.

12.3 World Trade Organization

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.

The proposed permission has already been granted in some international markets and products with similar allergen labelling exemptions are marketed internationally. FSANZ considers providing an exemption will further reduce variations between countries and facilitate international trade. This position is supported by domestic and international submitters from the industry.

Therefore at Draft Assessment, FSANZ considered it was not necessary to notify WTO member nations of the proposed amendment under either the Technical Barriers to Trade or the Sanitary and Phytosanitary Agreements.

13. Communication Strategy

Submissions indicated support from industry for the proposed labelling exemption. However a significant proportion of other submitters objected to the proposed exemption. The objection was based on the provision of information with a particular focus on vegetarianism/veganism which is beyond the scope of this Application.

After considering the submissions to the Draft Assessment Report, FSANZ completed targeted consultations to clarify some of the issues raised by submitters. These targeted consultations included contacting submitters who indicated that they have experienced an allergic reaction in response to consuming wine.

Issues raised by submitters have been considered and addressed as part of the Final Assessment. Should this standard be amended, FSANZ will work closely with Anaphylaxis Australia and Allergy New Zealand on messages to inform their members that this measure is safe and supported by themselves and allergy specialists. A fact sheet will be placed on the FSANZ website.

CONCLUSION

14. Conclusion and Decision

Decision

FSANZ approves the draft variation to the Table to clause 4 of Standard 1.2.3 to grant an exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent.

FSANZ approves the draft variation to the Table to clause 4 of Standard 1.2.3 to grant exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent as it:

- does not raise any safety concerns for fish-allergic consumers
- removes an unnecessary declaration on the product label and thereby enhances the information related to the allergenicity of the product.
- provides fish-allergic consumers with increased choice of beer and wine products
- supports industry with an added choice of clarifying agent that does not require allergen declaration
- the impact analysis concludes that exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent, provides a net benefit to affected parties.

The draft variation to the Code is at Attachment 1.

15. Implementation and Review

The FSANZ Board's decision will be notified to the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council).

Subject to any request for review by the Ministerial Council, the approved draft variation to grant exemption from the requirement to declare isinglass on the label, when present in beer and wine as a result of its use as a clarifying agent, will come into effect upon gazettal.

ATTACHMENTS

1. Draft variation to the *Australia New Zealand Food Standards Code*
2. Summary of Submissions to the Draft Assessment Report
3. Risk Assessment Report
4. Food Technology Report

Draft Variation to the *Australian New Zealand Food Standards Code*

Standards or variations to standards are considered to be legislative instruments for the purposes of the Legislative Instruments Act (2003) and are not subject to disallowance or sunseting.

To commence: on gazettal

[1] *Standard 1.2.3 of the Australia New Zealand Food Standards Code is varied by omitting from the Table to clause 4, the entry for Fish and fish products, substituting –*

Fish and fish products, except for isinglass derived from swim bladders and used as a clarifying agent in beer and wine.
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APPLICATION A490 – EXEMPTION OF ALLERGEN DECLARATION FOR ISINGLASS
Summary of Submissions on the Draft Assessment Report

Submitter	Sector	Comments
AB Vickers	Industry	<ul style="list-style-type: none"> • Supports the Application. • The robust and comprehensive risk assessment conducted by FSANZ has taken into consideration the best scientific evidence that is now available concerning the allergenic potential of isinglass. • Until quite recently, a lack of scientific evidence had made it difficult to substantiate any claims regarding the likely risk to fish-allergic consumers consuming beverages in which isinglass had been used. Previously, the strongest argument in favour on non-labelling was that isinglass had a long history of safe use without a single recorded incident of allergic reaction. • The scientific studies in the Draft Assessment Report have now confirmed that any residual levels of isinglass that may be present are extremely low, if present at all. • Clinical trials have further demonstrated that isinglass does not elicit an allergic response in fish sensitive individuals at far higher exposure rates than would be encountered in beers and wines. • The isinglass exemption will allow fish sensitive consumers to make informed choices concerning beverage consumption and will allow consumers a wider choice of beverages though the removal of a precautionary-based label approach. • The brewing and winemaking industries will also benefit from this exemption through increased flexibility of choice in processing (clarifying) aids and isinglass producers will benefit through the increased opportunity to trade with Australian and New Zealand beer and wine producers. • The Draft Assessment Report acknowledges the regulatory approach to allergen labelling of isinglass in several countries where labelling exemption has already been granted. An exemption for isinglass in Australia and New Zealand will contribute to increased confidence in allergen labelling statements for those consumers who travel globally. • A consistency in allergen labelling declarations will benefit beverage manufacturers through simplification of labelling strategies and will also benefit isinglass manufacturers who will be able to trade freely with beverage companies.

Submitter	Sector	Comments
Australian Food and Grocery Council (AFGC)	Industry	<ul style="list-style-type: none"> • Supports the Application. • Where there is little clinical evidence of allergic reaction and there is a low risk that the substances are capable of inducing an allergic response at the concentrations present in the final product, then the product should be exempt from mandatory allergen labelling requirements. • The AFGC supports the requirement for allergen labelling and the need to inform consumers, and supports the FSANZ assessment that isinglass-fined beer and wine, are not likely to present a risk of allergic reactions in fish-allergic consumers. • However, the AFGC notes the work being undertaken by FSANZ to review the entire standard, and that the principles and assumptions on which the standard is based need to be reassessed, in line with this recommendation. Such an assessment would provide a comprehensive reassessment of exemptions to allergen labelling, rather than dealing with exemptions in a piece-meal approach.
Brewers Association of Australia & New Zealand	Industry	<ul style="list-style-type: none"> • Supports the Application for the following reasons: • The long and safe use of isinglass in the brewing industry with no evidence that it constitutes a threat to consumers. • The recognition in the Report of the trace amounts of isinglass, and therefore parvalbumins, remaining in the beer, and that threshold doses for allergens would appear to be finite, measurable and detectable. • The absence of clinical evidence to show that isinglass is likely to trigger a dangerous reaction. • The restricted choice for some consumers in the event that labelling is required for the presence of a material which is not likely to cause an allergic reaction. • Where isinglass is not used because of such labelling requirements, the increased unnecessary costs to the consumer and the environment resulting from increased filter powder usage. • Exemptions granted in the EU and the absence of international consensus on the need to label. • The new and standardised process for isinglass production. • In this case, the requirement to label for the presence of isinglass results in misleading information being provided to the consumer.

Submitter	Sector	Comments
Food Technology Association of Australia	Industry	<ul style="list-style-type: none"> • The Technical Sub-Committee agreed with option 2 for the exemption of allergen declaration for isinglass, however, after much debate also considered the following: <ul style="list-style-type: none"> - Beer and wine had been again exempt from another labelling requirement required on all other foods, the rationale for which is still unclear to other food manufacturers as alcohol is no less a nutrient than any other of the specified nutrients and alcoholic beverages are part of the average diet of many consumers. - Is this application the beginning of similar requests for allergen exempt labelling from other manufacturers? - It is understood that egg white (albumen) is also used as a clarifying/fining agent in some sectors of the wine industry and the labelling of this possible allergen has not yet been discussed.
Foster's Group	Industry	<ul style="list-style-type: none"> • Supports the Application for the following reasons: • The long and safe use of isinglass in the brewing industry with no evidence that it constitutes a threat to consumers. • The recognition in the Report of the trace amounts of isinglass, and therefore parvalbumins, remaining in the beer, and that threshold doses for allergens would appear to be finite, measurable and detectable. • The absence of clinical evidence to show that isinglass is likely to trigger a dangerous reaction. • The restricted choice for some consumers in the event that labelling is required for the presence of a material which is not likely to cause an allergic reaction. • Exemptions granted in the EU and the absence of international consensus on the need to label. • The new and standardised process for isinglass production.

Submitter	Sector	Comments
<p>Inter-Industry Coalition:</p> <ul style="list-style-type: none"> - Brewers Association - Distilled Spirits Council of the United States - National Association of Beverage Importers - Presidents' Forum - WineAmerica - Wine Institute 	<p>Industry</p>	<ul style="list-style-type: none"> • Fully supports the Application. • Any labelling for food allergens must take into account whether or not that food will produce an allergic reaction and that labelling for all allergen levels may lead to further restricted diets, increased frustration and risk-taking and undermining the integrity of labelling statements. • Consumers need to trust that allergen labelling information is reliable and not be subjected to misleading, precautionary statements that may be ignored based upon, for example, prior experience consuming the food product in question without an adverse reaction. • A robust, scientifically based labelling allergen schema, which properly identifies those products containing allergenic protein likely to cause adverse reaction, will provide consumers with beneficial, non-misleading information. The exemption of isinglass meets and serves these interests. • With a global economy and free travel among consumers, determinations made by respective government bodies about allergen labelling should not impede trade without serving a public interest. The applicability of an allergen labelling requirement for a particular product should be the same from one country to another. Consumers will benefit from meaningful allergen labelling statements they can rely upon to make food choices whether they are a resident or visiting a particular country. The exemption of isinglass meets these goals.

Submitter	Sector	Comments
New Zealand Winegrowers (NZW)	Industry	<ul style="list-style-type: none"> • Supports the Application, based on the information presented in their submission of 16 November 2005 and the additional findings of the Report (submission lists Draft Assessment Report findings). <p>History of Non-Allergenicity</p> <ul style="list-style-type: none"> • To date, not aware of any incident of a consumer ever having suffered an allergic reaction due to the use of isinglass in wine. Nor has any such incident been relayed to NZW from relevant New Zealand health authorities. The absence of any reported allergic reactions was also noted in the EFSA report. <p>Usage in New Zealand</p> <ul style="list-style-type: none"> • The average level of isinglass addition in New Zealand is approximately 0.05-0.25 g/L. Isinglass is used sparingly as it is one of the most expensive fining agents available. Both the Draft Assessment Report and the Australian Wine Institute submission note that isinglass is not intended to be in the final product and any residue is likely to be negligible due to the filtering and racking processes. <p>Benefits to New Zealand Producers if Exemption is Granted</p> <ul style="list-style-type: none"> • New Zealand and Australia are the only major wine producing countries in the world that require an allergen declaration if isinglass is used in the production of wine. In addition to the concerns of the potential for the requirement to create a trade barrier, it is also relevant to consider the unfairness which arises as a result of importer non-compliance. Mandatory label statements on all New Zealand wine are verified by the producer's compliance with the Wine Act 2003. No such system applies to imported wine, many of which bear no allergy statement and due to difficulty detecting isinglass residues in wine, it is very likely that a proportion of these will have been made using undeclared isinglass. If the exemption is granted, the negative consumer perceptions associated with the declaration of fish products will be removed and compliant producers can compete on a level playing field with non-compliant users of isinglass. • The exemption of isinglass labelling will also: <ul style="list-style-type: none"> - give wine producers the option to choose the best quality clarification option without losing consumer confidence; - increase consumer choice for consumers who suffer from fish allergies, and - reduce costs by removing the need to produce different labels for different vintages and batches or for export markets which do not require the declaration of isinglass. • A considerable body of evidence and international research supports the key findings of the Draft Assessment Report that isinglass raises no safety concerns for fish-allergic consumers when present in wine and beer.

Submitter	Sector	Comments
The Allergen Bureau	Industry	<ul style="list-style-type: none"> • Supports the Application. • Considers that the risk to allergic consumers from the consumption of wine and beer treated with isinglass is very low, that advisory allergen labelling for the presence of fish does not constitute an effective risk management strategy and that the proposed exemption from labelling is justified. • Labelling of allergens represents a risk management strategy intended to inform potentially allergic consumers to the presence of a hazard in food and thereby enable them to make appropriate food choices. In order for this strategy to be effective, the information provided must be understood by, and relevant to, the consumer. Where labelling accurately advises of the presence of an identified allergen, the use of such labelling provides useful information to the consumer. However, the use of allergen advisory labelling in relation to a food component that does not contain the allergen moiety devalues the benefit of allergen labelling. This unnecessarily limits consumer choice and is likely to confuse consumers and can potentially be misunderstood or ignored. • This recommendation is consistent with the recent conclusion of the Scientific Panel on Dietetic Products, Nutrition and Allergies of the European Food Safety Authority (EFSA) that ‘it is not very likely that isinglass used as clarifying agent in beer will trigger a severe allergic reactions in susceptible individuals’ (reference provided). • As identified by FSANZ, the major components of isinglass are type 1 collagen, gelatin and small quantities of elastin. The Bureau is not aware of evidence to suggest that these components are clinically relevant to fish allergies. • The level of parvalbumins in isinglass is reported in the EFSA evaluation and the FSANZ Draft Assessment Report to be very low, in the range 1-34 ppm. The introduction of a modified preparation procedure for isinglass has the potential to yield concentrations up to 10-fold lower and consistently below 1 ppm. • During the development of the Voluntary Incidental Trace Allergen Labelling (VITAL) procedure for labelling of the presence of cross-contact allergens in food, the Lowest Observed Adverse Effect Levels (LOAEL) for total fish protein of 1-100 mg were identified (reference provided). The lower end of this range was used in establishing the first action levels. At this level, subjective responses such as numbness or pruritis at the site of contact or general uneasiness may be reported by sensitive individuals, although these cannot be verified by observers in clinical studies. The first VITAL action level separates Action Level 1 at which it is considered a precautionary advisory statement is not required and Action Level 2 at which a precautionary advisory statement is required. In another comparison of clinical studies, the lowest reported provoking dose was identified as 5 mg (reference provided). Based on parvalbumin concentration in fish muscle of 4000 g/g or 0.4% (reference provided), a consumer would need to drink unrealistic amounts of beer (80 L of cask beer or 200L of packaged beer) to consume an amount of parvalbumin consistent with exposure to 1 mg total protein, that at which only mild subjective reactions are observed in clinical trials.

Submitter	Sector	Comments
New Zealand Food Safety Authority (NZFSA)	Government	<ul style="list-style-type: none"> • Supports option 2 for the exemption of isinglass subject to the following condition: • FSANZ should consider making it a requirement that only isinglass with substantially reduced levels of parvalbumin be exempt from allergen declaration for isinglass. This could be achieved, for example, through an industry guideline or Code of Practice, requiring wine and beer manufacturers to comply with the ‘new code of GMP’ (Good Manufacturing Practice) for the sourcing and use of isinglass as outlined in the Report. <p>Reasons for suggesting a condition</p> <ul style="list-style-type: none"> • The Report states that the three major European manufacturers of isinglass have developed a common code of GMP for the sourcing and manufacturing of isinglass (‘new code of GMP’) to reduce the parvalbumin content in isinglass. The Report also states that the Application claims that nearly 100% of the isinglass used in New Zealand and Australia is sourced from these three manufacturers. NZFSA is concerned that ‘nearly all’ is not ALL, therefore, some isinglass used in the production of wine and beer in New Zealand and Australia is not sourced from the three European manufacturers using the ‘new code of GMP’. There is also no guarantee that imported wines use isinglass manufactured to this new Code. Isinglass not manufactured under the ‘new code of GMP’ is considered to contain higher levels of parvalbumin and therefore, puts fish-allergic consumers at a higher risk of having an allergic reaction. <p>Additional Comments on the Draft Assessment Report</p> <p><i>Correct use of the term GMP</i></p> <ul style="list-style-type: none"> • Throughout the report the term GMP has been incorrectly referred to as Good Management Practice. The term GMP applies to Good Manufacturing Practice which is a different practice to Good Management Practice. <p><i>Risk Assessment</i></p> <ul style="list-style-type: none"> • Agrees with the conclusion in the FSANZ risk assessment that if industry uses isinglass prepared under the industry agreed GMP, then the risk of exposure to fish allergens is expected to be extremely low. • Some concerns in relation to the evidence supplied by the applicant on which this risk assessment was based and asks that these be addressed in the Final Assessment Report. These same concerns were raised in the Opinions of the Scientific Panel on Dietetic Products, Nutrition and Allergies of the European Food Safety Authority (the Panel): <ul style="list-style-type: none"> - While there have been few if any documented reports of adverse events that can be attributed to fish allergy from consuming wine or beer fined with isinglass, it should be noted that there could be a significant underreporting of reactions because it is uncertain whether wine drinkers and health professionals have been aware of the possible presence of fish proteins in wine. - The literature review was based on one search engine and used only two search terms. The Panel noted certain limitations associated with the restricted search strategy used. This would not support the statement in the Report that a comprehensive literature search was undertaken.

Submitter	Sector	Comments
		<ul style="list-style-type: none"> - The Panel noted that there were ‘uncertainties with regard to the accuracy and appropriateness of the cod parvalbumin-based ELISA for the assessment of parvalbumin in tropical fish-derived isinglass’. Therefore, testing for residual isinglass should be treated with caution. - The results of the clinical studies need to be treated with caution as the test numbers are small and therefore, have limited statistical power. - One of the double-blind placebo-controlled food challenges used isinglass in mashed potatoes. The Panel noted that this trial was performed in a food matrix in which isinglass is not usually consumed. In addition it noted that alcohol is considered to lower the dose that may trigger a food allergic reaction in susceptible individuals. - The high susceptibility of isinglass to pepsin digestion is presented as evidence of non-allergenicity. The Panel noted that this method is ‘unsuitable for assessing the allergenicity of isinglass’. Whilst most known allergens are resistant to pepsin digestion this is not a necessary condition for allergenicity. <p>Summary</p> <ul style="list-style-type: none"> • Notes that the Panel took a cautious approach when presenting its opinions on the isinglass exemption, particularly where there was insufficient information available on which to base an opinion. Despite this a permanent exemption for isinglass used as a fining agent in both beer and wine was granted in 2007. • Assume that the evidence provided by the beer industry which used isinglass manufactured under the new code of GMP was extrapolated for wine, however, this is not made clear in the Report. Asks that FSANZ provide the scientific evidence in the Final Assessment Report that would support this extrapolation. Without this evidence believes there is a sound basis to impose the condition with regulatory option 2 as proposed by NZFSA. • Essential that regular reviews are undertaken and if necessary, amendments are made, especially if reactions do start to occur.
Queensland Health	Government	<ul style="list-style-type: none"> • Does not support the Application. • Response made by Queensland Health representing whole of Queensland Government. • Need to err on the side of caution particularly where in relation to the following key assessment findings: <ul style="list-style-type: none"> - ‘parvalbumin is...<u>possibly</u> the sole allergen for most individuals with IgE-mediated allergy to fish’ - ‘the levels of parvalbumin in isinglass manufactured using the new protocol has been shown to be <u>extremely low</u>...’ - ‘a significant amount of isinglass introduced in beer and wine is removed <u>allowing only a residual amount of isinglass to remain</u>...’ - ‘parvalbumin...is <u>unlikely</u> to be present in the bulk of beer or wine....’

Submitter	Sector	Comments
		<ul style="list-style-type: none"> - <u>‘the residual amounts of isinglass that are shown to remain in beer and wine are well below the isinglass dosage used in oral challenge tests...’</u> • Notes the Codex general standard for the labelling of pre-packaged foods. The list of food allergens that are required to be declared includes ‘fish and fish products’. There are no exemptions to these labelling requirements. In addition, there are variations in approaches between countries. • In addition, ‘the data on the prevalence of fish allergy in the Australian and New Zealand populations and the threshold dose of the allergen for fish-allergic individuals are unknown’ (Report, p22). • There would be a significant under-reporting of reactions (if any) against the substances in wine, as most wine drinkers and health professionals are probably unaware of the possible presence of isinglass. They would most likely blame other substances including alcohol or food if adverse reactions occurred. • Dr Andreas Lopata from the Allergy Research Group at RMIT University stated in an ABC radio interview on Thursday, 2 October 2008 that, ‘It is not really known if isinglass itself actually can cause an anaphylactic reaction in fish-allergic people. The major allergens in fish are normally found in the flesh of the fish but in some rare cases also collagen can cause allergies. And isinglass contains this particular collagen which is found in fish so theoretically it can cause in select individuals...an anaphylactic reaction.’ • The first of the reasons for preferred approach by FSANZ to grant an exemption is that it ‘does not raise any <u>safety</u> concerns for fish-allergic consumers.’ However, the second objective for the assessment of the application is to ‘ensure the protection of the <u>public health and safety</u> of consumers who are allergenic to fish.’ Is there any reason why only safety is referred to in the reasons for preferred approach? • Allowing an exemption will undermine the provision of adequate information on the product label to make an informed choice by vegetarians and vegans who will find the ‘extremely low’ levels of isinglass present in beer and wine as unsuitable for vegetarian diets. • Research commissioned by the Sanitarium Health Food Company in 2000 found 2% of Australians reported being vegetarian. • It is of little use in addressing the vegetarian/vegan issue by stating ‘FSANZ is considering Application A545 on vegetarian labelling.’ The Work Plan on FSANZ website notes that it was received on 23 August 2004, starting in 4th quarter of 2006 and initial assessment to the Board in February 2009. Accordingly, clarification is requested. • It is disappointing that FSANZ chose not to show this cost in the benefit cost analysis since the issue of vegetarian labelling was identified following the release of the Initial Assessment Report. • Resources across government, industry and other stakeholders could be better utilised if the issue of allergen declaration generally was addressed at one time rather than by a ‘case-by-case’ type basis.

Submitter	Sector	Comments
Allergy New Zealand	Public Health	<ul style="list-style-type: none"> • Supports, in-principle, the granting of exemptions of mandatory labelling, as long as there is undisputed evidence that the ingredient: <ul style="list-style-type: none"> - is proven to be clinically safe for all individuals allergic to that allergen, and - has been manufactured to strict standards that are monitored and assured by the regulatory authority who has granted the exemption. • Concerned that there is insufficient clinical proof that isinglass ‘does not raise any safety concerns for fish-allergic consumers’ as stated in FSANZ’s reasons for preferred approach. • Accepts that evidence to date indicates that isinglass-fined beer and wine are <u>not likely</u> to present a risk of allergic reactions in fish-allergic consumers, however, this does not indicate that there is <u>no risk</u>. • The FSANZ report states that there are no documented reports of allergic reactions to beer or wine fined isinglass in fish-allergic consumers. However, many food-allergic reactions are never reported to an authority or medical practitioner. Furthermore, there is no requirement in New Zealand for food-allergic reactions to be reported by health professionals to a regulatory authority, nor to document the reaction in a published journal. Therefore, questions the safety of this being used as evidence of no risk. • Two areas of concern regarding the manufacturers of isinglass and use in the wine and beer industry: <ul style="list-style-type: none"> - how will the manufacturing standard be monitored, and - wine and beer manufacturers may source isinglass from another manufacturer in a country with less stringent manufacturing standards. • Fish-allergic individuals are entitled to make an informed choice. • If beer and wine industry’s concern is borne out of the use of the term ‘fish’ on their labels, why not permit the use of the term ‘isinglass’? This will only be of concern to those consumers who are allergic to fish, who would then be advised to avoid products using isinglass. • With ongoing research internationally, the situation may become a lot clearer in regard to the risks to fish-allergic consumers of isinglass-fined wine and beer. It is therefore recommended that FSANZ, in whatever decision it takes in regard to this Application, undertakes to review it within 5 years, or sooner if clearer evidence becomes available.

Submitter	Sector	Comments
Daniel Beecher	Consumer	<ul style="list-style-type: none"> • Does not support the Application. • FSANZ legally required to act in consistency with Australian and international law, regardless of the limited scope of Application A490. As such, despite being beyond the scope of the application, the following objections are immediately relevant to FSANZ’s review of Application A490, since they are directly relevant to the legality of FSANZ’s proposed outcome. • FSANZ’s reasons are irrelevant to the issues raised in this submission. The relevant facts are: <ol style="list-style-type: none"> 1. that the previous decision was the only legally valid decision that FSANZ could make, and 2. that FSANZ would be breaking the law by overturning the previous decision 3. any past oversights of FSANZ’s legal responsibilities should not be used as an excuse for making further breaches of Australian law • For FSANZ to remove the labelling requirement for isinglass would be a breach of current Australian law regarding the human rights of vegetarians and vegans. Particularly human rights and anti discrimination laws, statutory bills of rights, and UN conventions. • The onus is now upon FSANZ to immediately consider the impact of their actions (such as the proposed approval of Application A490) upon the legally protected human rights of vegetarians and vegans. As such, the submitter formally requests that FSANZ immediately desist from approving the Application, or from making any other decisions that allow food manufacturers to reduce or remove the capacity of vegetarians or vegans to be aware of animal derived ingredients within foodstuffs. • The submission provides references (available upon request) to current law that would be contravened if FSANZ were to remove the labelling requirement for isinglass.
Linda Cuthbertson	Consumer	<ul style="list-style-type: none"> • Does not support the Application as a vegetarian. • In order to select wine, the label is checked for fish products and bottles are excluded that fits that category. • It is becoming increasingly difficult to find wines that do not include fish products but the statement on the label enables wines to be chosen that are suitable for vegetarians. • It would be more useful if the label was more specific; the words ‘may contain’ are somewhat vague. • The warning should be retained for dietary purposes so that vegetarians are able to select wines that have no fish content.

Submitter	Sector	Comments
Emma Delaney	Consumer	<ul style="list-style-type: none"> • Does not support the Application. • As a vegan, relies on labels being truthful to make an informed decision. If not informed of a particular ingredient, such as a fish product, it is not clear if the product is vegan. • The ingredient could cause an allergic response in some individuals, even if reaction may only be mild it should be up to the individual with the allergy to decide if they are going to take the risk, not up to companies who do not want to lose profits. • The consumer deserves to know exactly what it is that they are consuming whether they avoid certain ingredients due to ethical reasons, health reason or other reasons. • If fish products are taken off beer and wine labels, the submitter will no longer try new wines as will not be able to trust that the label is truthful and the only choice will be to assume that fish has been used. Therefore, the submitter will only buy wines that are labelled as vegan. This will affect the consumer and the profits of the companies involved. Consumers with an allergy to fish would make a similar decision.
Lynsey Edgar	Consumer	<ul style="list-style-type: none"> • Does not support the Application as a wine consumer who is very allergic to fish. • Suffered an allergic reaction 6 months ago and another time subsequently whilst drinking white wine. On both occasions, the label indicated that fish products were used in the clarifying process. • If exemption is permitted, it will be impossible for consumers to determine if fish products are present. How are consumers who are allergic to fish, ever to be sure they will not experience a reaction to white wine? Information on the label is the only way to be sure, prior to drinking wine, that the consumer will not experience an allergic reaction. • Consumers are entitled to full disclosure of the food products used in producing wine, to make an informed decision, particularly where the decision can affect their health. • If exemption allowed, the consumer will have to maintain own 'safe' list of wines that they can consume. This will curtail purchasing choices as they will not stray from list of known, non-allergy inducing wines.
Eleanor	Consumer	<ul style="list-style-type: none"> • Does not support the Application. • Sister ate a fish that contained an almost lethal dose of ciguatera toxin. She was hospitalised and semi-conscious for a week and not mentally herself for 6 months following. 10 years later she experienced another reaction from paper handled by another person who had eaten fish and continues to get these types of reactions from other people who have handled fish. The toxin firstly stops her thinking but still functioning and then stops her functioning. Therefore, anything that contains fish derived items should be labelled for the wellbeing of all.

Submitter	Sector	Comments
Diane Francis	Consumer	<ul style="list-style-type: none"> • Does not support the Application. • As a vegetarian, does not consume fish and therefore, relies on correct labelling of food and beverage products. • Why should wine be exempt from responsible labelling?
Ron Hewit	Consumer	<ul style="list-style-type: none"> • Does not support the Application due to vegan interests. • The exemption of isinglass labelling in wines will prevent people not wishing to eat fish products from consuming any wine as they cannot tell from the label. • Labels must state if traces of egg whites are used (as opposed to bentonite or similar clarifiers), so there should not be any exemption for fish products. • Other foodstuffs from soups, biscuits and noodles must state if fish or crustacea are included in the product. This permits a choice for those who do not wish to consume these products whether for allergenic, religious, health, or animal welfare reasons. • Without the isinglass labels, wine that does not include this product will be penalised because some people will not purchase any wine for fear of unlabelled isinglass traces. • It seems a poor reason to request an exemption just because wine makers don't wish to include a fish product label. • All foodstuffs should be labelled with all products, it helps indicate the cleanliness and purity of the manufacturing process; traces of unpleasant products should be declared, people need the choice.
Ruth Jackson	Consumer	<ul style="list-style-type: none"> • Does not support the Application. • Removing isinglass from labelling will not allow consumers to make informed choices about purchasing beer and wine. • Ethics in business is not fundamentally a question of whether it is right or wrong to tell the truth...rather ethics in business is fundamentally a question of implementing and maintaining communication systems which question, discuss and validate ethical claims. • Exempting isinglass from labelling effectively takes away the ability of each individual to judge for themselves whether they want to consume a product that contains fish. It is misleading or deceptive because it does not provide adequate information relating to food to enable consumers to make informed choices. • Submitter does not want to drink beer or wine with fish products, so the only option would be to stop drinking alcoholic products unless know they do not contain isinglass. • It is honest to label what is in a product, no matter how minute it is.

Submitter	Sector	Comments
Lynda Kriflik	Consumer	<ul style="list-style-type: none"> • Does not support the Application for vegetarian/vegan interests. • The removal of notification of isinglass in wines is problematic for another group of consumers other than those that suffer allergies. Consumers who choose not to eat or intake animal products will be severely disadvantaged by the removal of warnings indicating that isinglass was used as the refining agent. • Failure to advise consumers of the refining agent is inadequate 'provision on the product label to make informed choices' by any consumers. • Vegetarians/vegans use label information to avoid products that contain rennet or gelatin, both animal products, and expect that labels would also allow them to avoid fish products, regardless of the quantity, as they choose not to include any 'fellow creatures' in their diet. • Submitter has contacted several viniculturalists to express concern that such advice is an ethical recognition of the right to choose dietary intake.
Lefki Pavlidis	Consumer	<ul style="list-style-type: none"> • Strongly disagrees with the Application. • Wishes to know all the ingredients contained in any product for human consumption. • The small traces of fish in beer & wine may or may not cause allergic reactions in people with fish allergies, but FSANZ must also consider the many people who choose not to consume anything that contains animal ingredients for ethical reasons. • Manufacturers should be up-front and provide a full list of ingredients used in the production of their products, so consumers can make the right purchasing decisions according to ethical beliefs.
Kathryn Puxty	Consumer	<ul style="list-style-type: none"> • Does not support the Application. • Labelling is essential for vegetarians and vegans to be able to make an informed decision about which wines they can and can't drink to follow their chosen diet. Whether or not there are significant traces remaining in the wine is irrelevant. The fact that it has been produced using fish (or milk or eggs) is sufficient to make it unsuitable. If this exemption goes ahead then the range of wines that vegetarians and vegans can drink will be greatly limited as we won't know what is suitable and what is not. • If this exemption is granted then an acceptable, or perhaps preferable, alternative would be to make it mandatory to label all wines, or in fact all alcohol, as being suitable for vegetarians and vegans. This is something that many food brands currently do, though they are not obligated to do so. • The wine industry is overreacting the negative reaction of general consumers to the labelling of fish products, since rarely anyone ever reads the labels, and those that do are people with allergies or special diets that make label and ingredient checking a normal part of life. • If labelling is going to be insufficient then the only other option is to avoid products that we cannot be sure about. This will also have a negative impact on many producers in the wine and alcohol industry.

Submitter	Sector	Comments
Penny Rankin	Consumer	<ul style="list-style-type: none"> • Does not support the Application as an allergy sufferer. • The argument that the amount of fish products in wine is so small they could not be harmful is not true. • Submitter experienced an allergic reaction after only 2 sips of wine containing fish products and seaweed and now checks wine labels very carefully. Submitter is dangerously allergic to seaweed which causes angio oedema and can be fatal. • Need to ensure labels continue to list ingredients such as isinglass, fish products and seaweed, so allergy sufferers can avoid them and stay alive without requiring emergency tracheotomies.
Jessica Robinson	Consumer	<ul style="list-style-type: none"> • Does not support the Application. • In the interests of both consumers who have, for ethical, religious, or personal reasons, an opposition to the use of fish products in their consumables, and also the general public for the basic reason that every consumer has a right to know exactly how a product has been produced. • People who have adopted a vegetarian or vegan diet do not purchase beer or wine that has been brewed using isinglass. If there are no standards, these groups of people will not know which products are appropriate for them, causing unnecessary stress, uncertainty and inconveniences. • Understands that the association has concerns that consumers may be put off purchasing a product if they read that it has been produced using fish products. However, it is essentially the responsibility of the consumer to educate themselves in the process of beer and wine production, and omitting certain information from the labels is insulting to the informed consumer and a tactical cover-up of the truth. It does not change the fact that these products are used. If a consumer takes issue with the production process then they have the right to research and make an informed decision about where they place their purchasing power. • It is quite clear that the driving force behind the application is the prospect of higher sales for the beer and wine industry, and accepting their proposal would mean sacrificing the moral duty of a producer of consumables to be truthful.
John Wakerman	Consumer	<ul style="list-style-type: none"> • Does not support the Application. • Whilst labelling may or may not be important for those with fish allergies, it is important for those who simply wish to be informed about what they consume, in whatever concentration. Accurate labelling is also important for those with religious or other beliefs, be they Muslims or vegans. • Where isinglass is used and residual is to be found in beers or wines, it should be thus labelled, regardless of allergenicity. Only thus will consumers be able to make informed choices and not be misled about the content of common foodstuffs or drinks.

Submitter	Sector	Comments
Tara Ward	Consumer	<ul style="list-style-type: none"> • Does not support the Application. • Submission focuses on the objectives of FSANZ, specifically ‘the provision of adequate information relating to food to enable consumers to make informed choices’. • The focus of the application and Draft Assessment Report was limited to consumers of beer and wine <i>who are allergic to fish</i>. This submission considers the impact on <i>all</i> consumers of beer and wine, rather than merely those who are allergic to fish. • The requirement to declare isinglass on beer and wine labels allows consumers to make informed choices about food based on political, religious and/or ethical preferences, including preferences not to purchase products made using animals or fish. • To date, a major obstacle for consumers wishing to make informed food choices has been improper or insufficient labelling. The preferred regulatory approach of granting the exemption will only exacerbate this trend. In the absence of mandatory labelling systems for products containing, or produced with, animal or fish products, this submission urges that exemption not be granted. • According to the Report, the requirement to declare the use of isinglass does not provide accurate information for fish-allergic consumers to make an informed choice. It is difficult to understand how the declaration on a label of factual information regarding the production system associated with a product does not count as ‘accurate’ information. • The mandatory requirement regarding isinglass is not to make assertions about the possibility of an allergic reaction to it, but merely to declare that it was used in the production of food in question. Removing such factual information would diminish the ability of consumers to make an informed choice, as it would conceal the nature of the process used to produce the food. • Retaining the existing limitations of the requirement avoids the need to alter the information on labels according to the changing nature of research findings regarding isinglass and/or the changing social conscience of consumers. • If there is concern about the general level of awareness regarding the potential (or lack thereof) for allergic reactions to isinglass, it would be better to continue the requirement to declare its use, and as well to provide additional information on relevant websites and other sources. • Should the requirement to declare isinglass be removed, it would reduce choice for consumers who do not wish to buy wine or beer where it is unclear whether its production involved the use of isinglass. If consumers concerned about the use of fish products were to cease purchasing wine or beer that does not declare the presence of isinglass, this may result in a <i>cost</i> to certain sectors of the industry.

Submitter	Sector	Comments
Sharnie Wu	Consumer	<ul style="list-style-type: none"> • Does not support the Application. • Submitter spoke to the allergy clinic at Royal Price Alfred Hospital since original submission, who suggested that isinglass is not a major allergy threat. • Therefore, the main reason to label is the need for transparency for consumers who want to know what the product inputs are. Isinglass uses an animal product and consumers need to know this to make informed choices with their purchase. • Many vegetarians and vegans would not buy these wines if they knew that fish had been killed in the process of making them. It is their right to know what they are buying. People have a fundamental civil right to know the truth of what they are putting into their own bodies and make the appropriate decisions. • It is up to the wine industry to market appropriately to avoid the stigma of using fish products. • Also for consideration is the possible environmental impact of using isinglass. In this world of fish populations being severely depleted by overfishing, climate change and ocean pollution, is it absolutely necessary to use fish for an incremental gain in the taste of wine which the wine producers are too embarrassed to tell the public about? • The ultimate goal of FSANZ is ‘A safe food supply and well-informed customers’. The people of Australia and NZ hold FSANZ to this task.

Risk Assessment Report

Definition: Isinglass is a processing aid derived from the swim bladder of tropical and subtropical fish species for use as a fining/clarifying agent.

Risk Assessment

1. General

1.1 Fish allergy - parvalbumin

Allergy to vertebrate fin fish is well documented in the scientific and clinical literature, including double-blind placebo-controlled food challenge (DBPCFC) studies. Fish muscle, skin and roe have been reported to cause allergic reactions, the latter only rarely (Sicherer et al., 2000; Escudero et al., 2007). Allergic reactions to the consumption of fish/fish products may include life-threatening anaphylaxis. Fish allergy reportedly affects 0.4% of the US adult population (Sampson, 2004); but there are currently no data on the prevalence of fish allergy in the Australian and New Zealand adult population.

Parvalbumins are a class of calcium-binding proteins found at highest concentration in fast contracting/relaxing muscle fibres of vertebrates. In fish, parvalbumins are generally associated with skeletal muscle. Parvalbumins have molecular weights of approximately 10-13 kDa, and acidic pI values². Parvalbumins are water soluble and resistant to heat treatment and enzymatic degradation (Aas and Elsayed, 1975-[as cited in Chen et al. 2006]).

Parvalbumins are the allergenic fish proteins, and possibly the sole allergens for most individuals with IgE-mediated allergy to fish. Parvalbumin is the allergen in several fish species including cod, salmon, carp, mackerel and tuna. Parvalbumin sequences from commonly consumed fish species are highly homologous. This would indicate a high likelihood of IgE cross-reactivity to a range of fish species for at least some fish-allergic individuals (Swoboda et al., 2002; Hilger et al., 2004; Van Do, 2005).

There is limited information on the potential allergenicity of fish collagen. In a double-blind, placebo-controlled food challenge (DBPCFC) study, a mild, subjective reaction was reported by one out of 30 fish-allergic patients given 7.6 g codfish skin gelatine (Hansen et al., 2004).

1.2 Fish swim bladder – anatomical location and tissue composition

The swim bladder is an air sac located in the dorsal part of the body cavity of most fish species. As such, it can be readily detached without significant contamination with the fish muscle tissue. The swim bladders from certain tropical and subtropical fish species are used to prepare commercial isinglass.

The major component of isinglass is type 1 collagen and its denatured product, gelatin. Isinglass also contains small quantities of elastin, a highly hydrophobic, 72 kDa protein. Collagen, gelatin and elastin constitute about 95% of the dry weight of isinglass.

² The pH at which the protein is least soluble.

There is no evidence to suggest that elastin is allergenic and, as mentioned above, the clinical relevance of collagen/gelatin allergenicity has not been shown.

Collagen is a protein with a molecular weight of approximately 300 kDa and is present in fish muscle, skin and swim bladder. The fish swim bladder is the source of collagen, known commercially as isinglass. Intact collagen has a triple helical structure stabilised by cross linkages. Soluble collagen exists mainly as trimers and tetramers with a molecular weight of 800-1300 kDa. The large size of collagen contrasts with known allergenic proteins, which are usually small, compact proteins with molecular weight ranging between 10 kDa and 80 kDa.

Collagen is thermally labile and denatures to gelatin, where the triple helix is unwound to form random coils. Collagen from tropical fish species is most suitable for isinglass production because it remains intact in temperatures up to 29°C, while collagen from coldwater fish species denatures at about 5°C. There is no evidence that gelatin is a clinically important allergen in fish-allergic individuals.

1.3 The hazard and the risk

For fish-allergic consumers, fish parvalbumin is the relevant allergen of significance i.e. the hazard. The FSANZ risk assessment process considers that the hazard is the potential to cause an adverse reaction and the risk is the likelihood of the adverse reaction actually occurring within the conditions of exposure. In the context of this Application, the overall risk to fish-allergic consumers is dependent on the level of exposure to parvalbumin through the consumption of isinglass-fined beer and wine.

2. Beer-related data

Information in this section is mainly extracted from documents provided by the Applicant to FSANZ in 2008 (originally submitted by the Brewers of Europe and the Brewing, Food and Beverage Industry Suppliers Association to EFSA in 2006).

2.1 Analytical methods used in beer studies

2.1.1 Isinglass detection

A method has been developed whereby residual isinglass present in fined beers can be concentrated using rabbit polyclonal antibodies raised to pure isinglass. The separated isinglass can then be hydrolysed to its constituent acids and quantified by measuring the content of hydroxyproline, an imino acid characteristic of animal collagens. The limit of detection (LOD) of this method is 0.17 mg isinglass/L of beer. Information provided by the Applicant indicates this method was used to quantify the concentration of isinglass residues which could be present in beer.

2.1.2 Parvalbumin detection

Enzyme-linked immunosorbent assay (ELISA) for fish parvalbumin was used to measure parvalbumin levels in swim bladders, isinglass and beer. Using monoclonal antibody directed against carp parvalbumin, a competitive ELISA was developed and found to be capable of detecting 0.05 µg/ml of carp parvalbumin (or 1 µg/g).

An improved method was developed based on anti-cod parvalbumin polyclonal antibodies which would have broader specificity to detect parvalbumins from a wider range of fish species. The ELISA is specific for parvalbumin and does not substantially cross-react with common food ingredients. The sensitivity of the anti-cod parvalbumin ELISA was shown to be 0.20 µg/g. However, using the sandwich ELISA to measure parvalbumin levels in isinglass samples suggests the possibility of matrix inhibition of two to four-fold. Therefore, quantitative estimates of parvalbumin levels need to take this into account.

2.2 Parvalbumin in fish swim bladder and in isinglass preparations

Although parvalbumin is not a major component of the swim bladder, it has been identified in the swim bladder tissue of a western Atlantic fish (*Opsanus tau* or the oyster toadfish), a species not used in isinglass production. This information raised the question whether parvalbumin may also be present in the swim bladders of some fish species that are used in the commercial production of isinglass. The Applicant provided analytical data on parvalbumin levels in eight isinglass samples from three commercial manufacturers. Using the anti-cod parvalbumin ELISA, six samples were below 10 µg/g, one sample at 34 µg/g and one below 1 µg/g. Various levels of parvalbumin were detected in the swim bladder of seven fish species. According to this information, it is possible to minimise the level of parvalbumin in isinglass by identifying and eliminating fish species with high levels of parvalbumin.

Parvalbumin is soluble in water and dilute salt solutions, at neutral or slightly alkaline pH, making it possible to further minimise residual levels of parvalbumin in isinglass by incorporating a washing step in the manufacturing process. The Applicant provided analytical data which indicates that significant reduction of residual parvalbumin in isinglass is achieved after washing with a phosphate buffer. The effect of different washing procedures on parvalbumin levels was tested. The most effective washing process appears to reduce parvalbumin level by about four-fold.

To ensure minimum parvalbumin content in isinglass, the Applicant indicated that a new Code of Good Manufacturing Practice (GMP) for the manufacture of isinglass low in parvalbumin has been developed and agreed by the industry. The new GMP Code incorporates an additional washing step using phosphate buffer, the introduction of a sieving step in the granulation stage to ensure that swim bladder wall particle size does not exceed 25 µm, and the exclusion of fish species with high parvalbumin levels in the swim bladder. Data presented by the Applicant shows that parvalbumin residues in eight samples of commercial isinglass, prepared using the new GMP, are below 1 µg/g.

2.3 Residues of isinglass and parvalbumin in fined beer

Information provided by the Applicant states that residual amounts of isinglass in bottle and can beer are below the LOD and where detectable, do not exceed 1 mg/L. For keg and cask beer, isinglass residues are at 3-5 mg/L.

Experiments were conducted using ELISA methods in order to determine whether detectable parvalbumin remained in the fined beer. Samples of beer fined with isinglass, containing various levels of parvalbumin, were freeze-dried and tested. Data provided indicates that no parvalbumin could be detected in the beer samples, which included lager and cask ale.

Theoretical calculations suggest that parvalbumin levels would be below the level of detection of the ELISA method used in these tests.

Since parvalbumin residues in beer are too low to measure, the Applicant provided an estimate of potential parvalbumin based on the following information:

- The dose of isinglass during fining is 50 mg/L. This is around the highest dose which would be used commercially for cask beers and is 2-3 times higher than the dose used for most brewery-conditioned beers.
- Residual levels of isinglass in beer, when detectable, range from 1 mg/L for can and bottle beer to 5 mg/L for cask beer. Even in cloudy beer, the level is not reported to exceed 5 mg/L.
- Residual parvalbumin in commercial isinglass products currently on the market (old protocol) is 10 µg/g (cod equivalent) on a dry weight basis.
- Residual parvalbumin in commercial isinglass products using the new GMP protocol is 1 µg/g.
- Parvalbumin most likely co-sediments with isinglass residue and does not partition into the fluid part of the beer (see section 2.4 below).

Based on this information, parvalbumin levels in beer are calculated to be 0.001 µg/L for bottle and can beer, and 0.005 µg/L for cask-conditioned beer using isinglass prepared according to the new protocol. For traditionally prepared isinglass, the levels are estimated to be ten times higher at 0.01 µg/L and 0.05 µg/L for can and cask beer, respectively. These estimated levels of parvalbumin are considered, together with oral challenge studies, in the exposure assessment.

2.4 Parvalbumin levels in beer sediments

Parvalbumin is soluble in water and dilute salt solutions at neutral and alkaline pH. Data provided by the Applicant indicates that the level of parvalbumin in isinglass can be minimised by washing in buffer solution. For any residual parvalbumin, which is not eliminated from isinglass, there are two potential scenarios. Parvalbumin residues would either end up in the sediment or in the fluid. In the acidic environment of beer brewing, parvalbumin would be expected to precipitate with the isinglass to form the sediment. Analytical data provided by the Applicant suggests this to be the case.

Isinglass commercially prepared using the old protocol (which assumes a typical parvalbumin content of 10 µg/g as determined by cod parvalbumin ELISA) was added to beer at a dose of 36 mg/L (0.36 µg parvalbumin/L) of beer. The sediment was collected and tested for parvalbumin content using the cod parvalbumin ELISA. The results suggest that parvalbumin content in isinglass is concentrated in the sediment and therefore, is unlikely to be present in the clear portion of the beer.

2.5 Clinical testing

2.5.1 Skin prick tests

Skin prick testing (SPT) provides information about the presence of IgE antibody specific to a given allergen. Although SPT for food allergy is valid, interpretation can be complex and positive tests often occur without clinical allergy (ASCIA-SPT Manual 2006).

The Applicant provided information on skin prick tests performed using extracts from a number of the fish species that are used in the manufacture of commercial isinglass. Flesh and swim bladder extracts were prepared from six fish species, and checked for microbial contamination to eliminate false positive due to non-allergic inflammation. SPT was performed on eight fish-allergic individuals according to a protocol developed at the Food Allergy Research and Resource Program (FARRP). Samples of blood were also taken from the individuals and tested for IgE antibodies to fish. All eight patients tested were positive when skin tested with fish flesh extracts. Seven of eight patients were positive with fish swim bladder extracts.

Information was also provided by the Applicant on a separate study conducted in France where six patients with verified fish allergy were challenged with commercial isinglass. Two of the six patients were skin-test positive, but all six patients were negative in the oral challenge test (see below).

These skin prick test results, when considered in conjunction with the oral challenge results conducted on the same patients, do not appear to be clinically relevant. This is because individuals may have allergen-specific IgE which leads to positive skin prick tests, but do not react to oral challenge with the same allergen. This is a well-acknowledged and commonly encountered response in food allergy testing.

2.5.2 Oral challenge tests

Controlled oral food challenges are the gold standard in diagnosing food allergy. However, the targeted nature of the recruitment and the strict qualifying criteria, including convincing clinical history, limits the number of subjects available to participate in such studies.

In the context of this Application, oral challenges are conducted to determine whether or not the test samples (isinglass used as a fining agent) can provoke an allergic reaction in fish-allergic individuals.

A protocol for DBPCFC tests were developed by FARRP using isinglass prepared according to the new protocol. Fish-allergic patients were dosed every half an hour with isinglass starting from a low dose and gradually increasing over a period of two hours. The doses used were 0.5, 5, 15 and 30 mg of isinglass in mashed potatoes. In this study, 15 fish-allergic patients were tested but none reacted to the oral challenge with isinglass, even at the very highest dose used. Based on parvalbumin content of 1 µg/g isinglass, the total of the challenge doses is equivalent to over 50 L of beer (or 10 L of cask beer) exceeding the volume that is possible to consume in a single sitting.

Another study was conducted separately in France using isinglass containing 10 µg/g parvalbumin.

According to information provided by the Applicant, this is a typical sample of commercially available isinglass. Six patients with allergy to fish, as determined by oral food challenge or by a convincing clinical history at the time of the study, were included. Each patient received a total of 20 mg of isinglass, mixed with cooked potato, over two hours. None of the patients had positive reactions to the oral challenge (while two of the six patients showed positive reactions in the skin prick test using the same material).

These two studies, conducted by experts in the field using rigorous protocols, provide supporting evidence that isinglass does not pose a safety concern for fish-allergic consumers.

2.6 Exposure assessment

The data suggest that levels of isinglass that may remain in beer do not exceed 1 mg/L for bottle or can beer, and 5 mg/L for cask beer. The level of parvalbumin in isinglass is likely to vary according to the manufacturing protocol (from 1 µg/g for the new protocol to 10 µg/g for the old protocol). No data are available on the level of parvalbumin in beer because it is below the LOD for current methodologies. As parvalbumin is known to be insoluble in the acidic environment of fermentation, it is expected to co-sediment with isinglass which is removed during the beverage production and is not consumed.

FSANZ notes that currently there are no agreed thresholds for any food allergen including parvalbumin. A threshold is the lowest dose of the allergen (parvalbumin) that can trigger an allergic reaction in fish-allergic individuals. However, the levels of parvalbumin that may be consumed in isinglass-fined beer are likely to be very low (estimated to be 0.001-0.005 µg/L for new protocol isinglass and ten fold higher at 0.01-0.05 µg/L for old protocol isinglass).

The oral challenge studies indicate that isinglass prepared according to either the old or the new protocol did not provoke allergic reactions in any of the 21 fish-allergic individuals. The isinglass doses used in these studies and corresponding volumes of beer are as follows:

Isinglass prepared according to:	The cumulative oral challenge dose (no reactions observed):	Equivalent volume of beer
New manufacturing protocol	50.5 mg isinglass (isinglass was given in increasing dose of 0.5 mg, 5 mg, 15 mg and 30 mg in about 40 grams in mashed potato over 2 hours)	50 L of bottle/can beer 10 L of cask beer
Old manufacturing protocol	20 mg isinglass	20 L of bottle/can beer 4 L of cask beer

An average drinker of beer may consume about 1.5 L of beer within a single sitting, while a heavy drinker of beer may consume up to 3 L of beer within a single sitting. Clearly the dose of isinglass tolerated by fish-allergic individuals in the oral challenge studies, as reported by the Applicant, far exceeds isinglass levels that may be expected in the volume of beer that could be consumed by an individual within a single sitting.

In light of the normal constraints on the volume that can be consumed by an individual within a few hours, FSANZ considers that potential exposure to parvalbumin through the consumption of beer fined with isinglass is likely to be extremely low.

2.7 Literature search

Two literature searches were provided by the Applicant to demonstrate the rarity of reports on beer allergy. The searches, conducted in 2004 and in 2006, had numerous search words and covered 33 databases³. These extensive searches have failed to identify any publications that may be relevant to fish allergy due to consumption of beer.

3. Wine-related data

Information in this section is derived from documents provided to FSANZ by the Australian Wine Research Institute (AWRI) in April 2008; and from EFSA opinion (Request N° EFSA-Q-2006-154 – published in the EFSA Journal 2007, 533:1-8).

3.1 Usage of isinglass in wine

Information provided to FSANZ by the AWRI indicates that isinglass is used under GMP (as required in the Code under Standard 1.3.3) as a fining agent mainly in the production of white wine.

The amount of isinglass used is determined for individual batches to avoid overuse, but typically falls between 10-25 mg isinglass/L of wine. Isinglass is removed by sedimentation followed by racking, which may include high performance centrifugation or filtration.

3.2 Residual amounts of isinglass in wine

Analytical data, commissioned by the AWRI, is provided for two commercial samples of isinglass-fined wine produced according to GMP (Hofman et al., 2002). The analytical method is based on partial purification of collagen from the test sample followed by analysis using sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE) technique. The wine samples had been fined with 0.42 and 4.4 mg isinglass/L wine, respectively. No collagen bands were detected in the wine samples. Using the same method, collagen residues could be recovered and detected in beer samples spiked with collagen at concentration of 1.0 mg/L or more. The AWRI concludes that the concentration of residual isinglass in the commercial wine samples is likely to be less than 1 mg/L. This is the same level of residual isinglass that has been reported for bottled beer. Parvalbumin, the protein of concern to fish-allergic consumers, was not detectable in beer samples fined using isinglass prepared according to the old or the new protocol. Although no data on parvalbumin detection was available for wine, there is no reason to expect the findings would be different from beer. Therefore, theoretical levels of parvalbumin, estimated to be 0.001-0.05 µg/L can be extrapolated.

In a recently published study, 16 wines were tested for residues of isinglass (Weber et al 2007). The wines were fined with four commercially available isinglass preparations at 50 or 250 mL isinglass/100 L wine.

³ Search words: beer, ale(s), lager, brewery, allergen(s), allergic, allergenicity, allergies, allergenic, hypersensitivity, sensitive, anaphylaxis, parvalbumin, isinglass.
Databases searched included: Analytical Abstracts, Biological Abstracts, medline, Registry of toxic Effects, Toxline, Food Science & Technology Abstracts, Conference Papers index, Dissertation Abstracts, etc...

No residual isinglass could be detected in any of the wines when a competitive ELISA with LOD $\leq 5 \mu\text{g/L}$ was used. These findings further support results of undetectable isinglass in two samples of isinglass-fined Australian wines.

3.3 Potential allergenicity of isinglass-fined wine

An investigation of potential food allergens in fined wine was reported, including full details of the double-blind placebo-controlled clinical trial and basophil activation analysis (Rolland et al., 2006). The scope of the study included wine fined with isinglass as well as egg and milk-derived processing aids. The data relevant to isinglass is outlined below.

3.3.1 Literature search

A search of the medical literature was conducted by the AWRI on PubMed using the terms ‘wine AND allergy’. The most commonly-reported adverse reactions among alcoholic beverage consumers appear to be associated with sulphite additives. However, the search was unable to identify any documented cases of adverse reactions specifically associated with isinglass.

3.3.2 Double-blind placebo-controlled trial -Exposure to isinglass in fined wine

The clinical study included ten fish-allergic subjects recruited from the Allergy Clinics, Alfred Hospital in Melbourne. The patients (five females and five males) were diagnosed by a clinical allergist with IgE-mediated food allergy, based on a history of anaphylaxis and corresponding demonstration of specific IgE to allergens of fish or by skin prick testing. The exception was one individual who had negative tests for IgE but a positive oral fish challenge. Clinical characteristics of the ten fish-allergic individuals are included in the published study (Rolland et al., 2006).

Control subjects, with no IgE to any of the allergens including fish, were also included in the study.

All subjects avoided antihistamine medications for three days, short-acting bronchodilator therapy for four hours, and long-acting bronchodilator therapy for twelve hours before each visit. Alcohol ingestion was avoided for at least three days before challenge, with subjects fasted for at least eight hours.

Samples from 23 isinglass-fined wines were used in the study. Controls wines were clarified using other non-food protein-processing aids and/or filtration.

Each subject consumed 100 mL (approximately one standard drink) over 10-15 minutes and completed a symptom questionnaire by using a visual analogue scale and repeated it at 15 minute intervals for two hours after challenge. Over the next six days, subjects abstained from alcoholic beverages and recorded any possible late reactions in a diary.

The study reported that one fish-allergic subject developed mild lip numbness, which resolved spontaneously, after ingestion of a control unfined wine. No subjects developed a typical IgE-mediated allergic reaction requiring medical treatment and no diary card abnormalities were noted during follow-up.

3.3.3 *Basophil activation analysis*

An analysis using a modified basophil activation assay was described in the study by Rolland et al. (2006). The study reported that one isinglass-fined wine caused weak basophil activation for two out of ten fish-allergic subjects, but this same wine was also reported to have caused weak activation of basophils from a peanut-allergic subject (who is not allergic to fish). The two fish-allergic subjects showed no clinical adverse reactions to another wine made using isinglass. One of the two fish-allergic subjects showed weak basophil activation to a wine made using non-grape tannin but this subject was not allergic to peanuts or tree nuts.

4 **Conclusion**

The Table to clause 6 in the Standard 1.3.3 (Processing Aids) requires that isinglass is used according to GMP. Adherence to GMP in the use of isinglass as a clarifying agent minimises the potential level of residual isinglass in the final product. Information provided by the Applicant indicates that residual level of isinglass in bottled beer and wine is about 1 mg/L

Low but variable levels of parvalbumin may be present in commercial isinglass. Reducing the level of parvalbumin in isinglass even further is technically achievable by incorporating steps, including further washing, into the GMP for isinglass manufacturing. The Applicant states that the revised GMP is now widely adopted by the isinglass manufacturers which supply the Australian and New Zealand markets. Using currently available detection methods, parvalbumin was not detectable in isinglass-fined beer regardless of whether the isinglass was prepared according to the old or new protocol.

Together, the GMP for the production of isinglass and the GMP for the use of isinglass in the fining of beer and wine, provide a high level of safety that counteracts uncertainties identified in this paper. The uncertainties relate to the newly developed analytical methodologies used in generating the data provided by the Applicant, the lack of information on the prevalence of fish allergy among the adult population in Australia and New Zealand, and the lack of an agreed threshold for parvalbumin.

Therefore, FSANZ considers that consumption of isinglass-fined beer and wine is not likely to present a risk of allergic reactions in fish-allergic consumers.

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Food Technology Report

Summary

Isinglass is derived from fish swim bladders and is used as a clarifying agent in the brewing and wine industry. The rod-like helical structure and amphoteric nature (able to be both an acid and base) of the isinglass collagen are responsible for isinglass's clarification properties. The yeast cells, polyphenolic and protein substances form complexes with the isinglass and settle to the bottom of the fermentation vessels, thereby assisting in clarifying the liquid.

Residual isinglass in packaged beer and wine has been shown to be removed by the filtration process, whereas cask conditioned beer (which is unfiltered) would require sufficient sedimentation time to ensure all the isinglass has time to settle and form a stable mass at the bottom of the cask. Good Manufacturing Practice (GMP) needs to be followed when isinglass is utilised as a clarifying agent to ensure the minimum possible residue of isinglass in the finished product.

The isinglass may potentially contain the protein parvalbumin, a known fish allergen. The level of parvalbumin in the isinglass can be minimised by establishing and adopting a manufacturing Code of Practice which is intended to reduce the level of parvalbumin.

1. Introduction

Isinglass is used extensively as a processing aid in the brewing and wine industry to improve the efficiency of the fining process (also called clarification) of beer and wine. Isinglass has been used for several centuries for this purpose. An estimated 200 tonnes of isinglass is used annually to clarify an estimated 150 million hectolitres of beer worldwide.

2. Production process of isinglass

Isinglass is a collagen derived from dried swim bladders of specific tropical and subtropical fish. The traditional basic production process may vary between manufacturers, which can also depend on the source and species of the fish and does not seem to have a high level of standardisation (EFSA, 2007). The main steps involve blending swim bladders of specified fish to meet quality, functionality, cost and supply; granulation to reduce the size; washing in chilled water, sterilizing in dilute hydrogen peroxide solution and final rinsing with water. The sterilised granulated swim bladder is then further processed to different product forms such as powder, paste, ready-to-use paste and dry parchment or matted form. The three main forms of commercial isinglass are summarised below.

2.1 *Isinglass powder*

The sterilised hydrated isinglass is extruded using narrow apertures, which disrupts the collagen fibres. It is then dried and milled into a powder of less than 1000 microns.

2.2 *Isinglass paste*

The sterilised hydrated isinglass is macerated to less than 1000 microns paste by high shear mixing with the addition of sodium or potassium metabisulphite (as preservative). The paste is standardised to about 10% solids.

2.3 *Ready-to-use paste*

The isinglass paste can be further diluted then acidified with food grade acids to a pH of 2.0-3.0. The solids level is typically 0.3-1.5%. Sulphur dioxide is often used as a preservative.

2.4 *The new manufacturing protocol for isinglass production*

An industry-agreed GMP for isinglass has been adopted by the major suppliers of isinglass to ensure the presence of parvalbumin can be minimised. This GMP includes an additional washing stage using a phosphate buffer and successive washing steps with fresh water, the introduction of a sieving step in the granulation stage to ensure that swim bladder wall size does not exceed 25 mm and the exclusion of certain fish species. Some fish species appear to have low levels of parvalbumin and therefore, have been specifically included in the new GMP (EFSA, 2007).

3. **Physico-chemical characteristics and technological function of isinglass**

3.1 *Functions and characteristics*

A fining agent such as isinglass is added to beer and wine to reduce or remove the presence of one or more undesirable components in order to achieve clarity and potentially improve sensory appeal, flavour and physical stability in the final product (Morris and Main, 1995).

The major component of isinglass is type 1 collagen (95%) along with small amounts of gelatine, its denaturation product (Hickman *et al.*, 2000; EFSA, 2007). The isinglass collagen exists as a rod-like triple helical molecule, amphoteric in nature (able to be both an acid and base) and is thermally labile, denaturing at about 29°C to form the random coils of gelatine (Hickman *et al.*, 2000). However, the fish allergen, parvalbumins, present mainly in fish muscles and at low levels in fish bladders, seems to be heat stable after heating for three hours at 90°C (Arif *et al.*, 2007). The parvalbumin has a pI (isoelectric point) of around 3.9-5.5 (Bugajska-Schretter *et al.*, 2000).

Isinglass collagen has a molecular weight of 800-1300 kDa and contains hydroxyproline in its structure, which is important to its functionality (EFSA, 2007). The rod-like structural integrity of the collagen triple helix was hypothesised to be crucial for efficient clarification (Hickman *et al.*, 2000). However, a more popular hypothesis of the fining activity is based upon charge interactions. The isinglass is assumed to electronically attract yeast cells with negatively charged cell walls and other suspended charged polyphenolic and protein components. These aggregated complexes would then settle to the bottom of the container. In the sediment, further interactions may take place resulting in firm sediment that is resistant to disturbance when the clear beverage is drawn off.

3.2 Clarifying process procedure in the brewing industry

In the brewing process, after fermentation, the beer is cooled to around freezing, which encourages settling of the yeast and causes proteins to coagulate and settle out with the yeast. Similar to the wine production process, it is at this stage that isinglass powder dissolved in dilute solutions of food grade acids is added to the fermented beer to aid in the clarifying process. The pH of beer is typically between 3.9 and 4.6 (Siebert and Lynn, 2005). At this pH, isinglass is positively charged (iso-electric point of isinglass is around 5.5) and thus attracting and aggregating negatively charged particles. However, if the pH of the beer is below 3.5, the fining activity is severely inhibited (Ward, 2008).

For optimum fining performance, beer must be fined at the coldest point in the process. The reason is that if the chill haze (from protein precipitation) is present prior to isinglass addition, it is then readily removed by fining. This is especially important for cask beer, since there are no effective alternatives to the use of isinglass in producing bright unfiltered beer (Ward 2008).

Information provided by the Applicant suggests that the brewing industry typically uses isinglass at a low level of between 10-15 mg/L but this level can potentially go as high as 60 mg/L in some brews. The sediment formed by the collagen and yeast complex is removed by filtration and/or the centrifugation processes, resulting in very low residual levels of isinglass in the final product. Cask conditioned beer does not undergo filtration or centrifugation and relies on gravity settling.

3.3 Clarification function of isinglass in wine production process

The flowchart in Figure 1 below shows generalised processing steps of white wine. The red wine process is expected to be similar. The fining step, where isinglass is usually added, occurs after alcohol fermentation has been completed and before filtration. The main purpose is to aggregate polymeric carbohydrates, proteins and polyphenols to form larger aggregates that sink to the bottom. Such aggregation improves the filtering efficiency as a consequence by initially clarifying the wine (Wucherpfenning, 2003).

Three different types of filters are commonly used in wine filtration; precoat filter, sheet filter and membrane filter, which are membranes of different pore size that can be used to remove particles down to the molecular level from the wine.

After the fining and filtration process, the wine is normally sufficiently clear and has a pH value ranged from 2.8-4.0, depending on the types of wine (Ribéreau-Gayon *et al.*, 2000). Some wines are subjected to further cold stabilisation before they are ready for development to maturity and bottled.

Isinglass is claimed to be a preferred clarification agent compared to egg or casein, because of its mild effect on flavour. Different batches of wine require different amounts of isinglass, as determined by laboratory tests. In Australia, isinglass is typically added at between approximately 20-50 mg/L in the production of wine (Wine Australia, 2008), in New Zealand, use in wine is typically about 6-10 mg/L (New Zealand Winegrowers, 2008) and use in white wine in France is typically between 10-25 mg/L (Ribéreau-Gayon *et al.*, 2000). In both Australia and New Zealand isinglass is considered as the best and most expensive clarifying agent and is not likely to be used in excess if usage is not warranted.

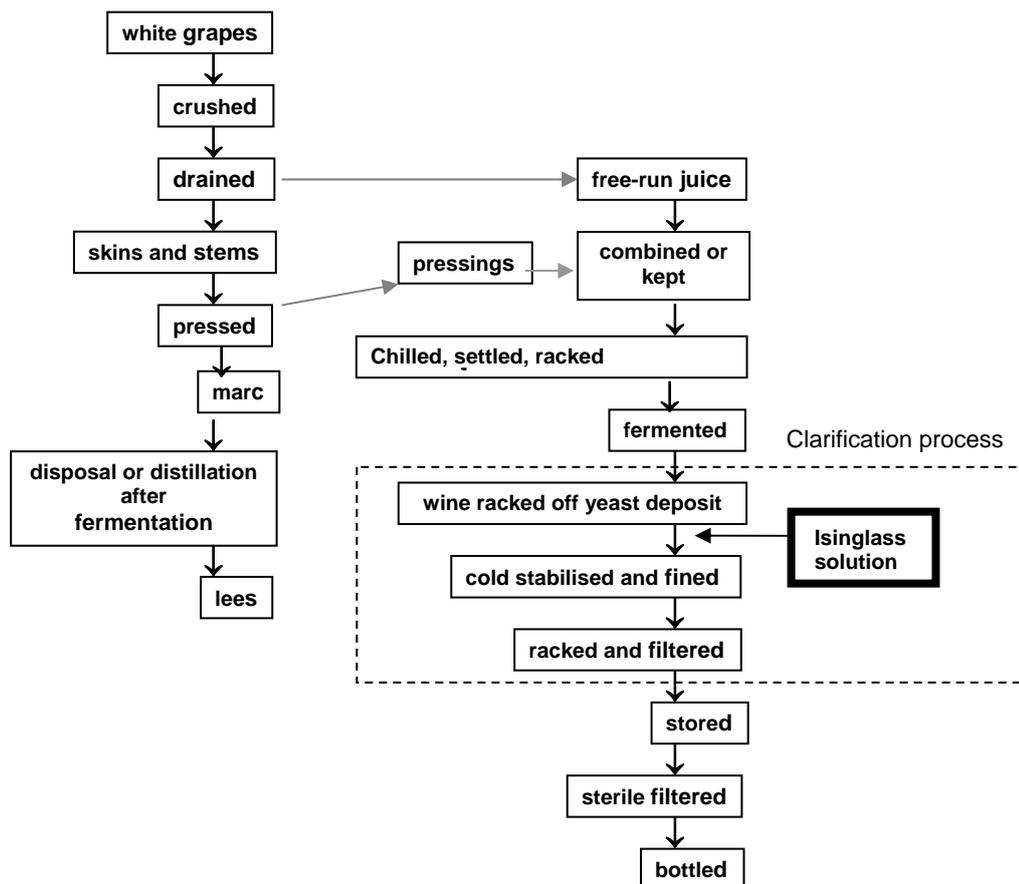


Figure 1: Flow chart of white winemaking stages with the clarification steps indicated in the dotted box (Amended from diagram provided by Winemakers' Federation of Australia, 2005).

3.3 Good Manufacturing practice for usage of Isinglass

Good Manufacturing Practice (GMP) is a requirement in regulating the maximum amount of the isinglass which may be present in a food. The relevant GMP criteria for isinglass are:

- (a) *the quantity added to food shall be limited to the lowest possible level necessary to accomplish its desired effect;*
- (b) *the quantity that becomes a component of food as a result of its use in the manufacture, processing or packaging of a food and which is not intended to accomplish any physical, or other technical effect in the finished food itself, is reduced to the extent reasonably possible; and*
- (c) *the material is prepared and handled in the same way as a food ingredient.*

4. Allergenic residue issues

4.1 Parvalbumin as the allergen

Parvalbumin has been identified as a fish allergen, based mainly on studies of three species of fish: Atlantic salmon, carp and Japanese horse mackerel.

Further immuno-blotting analyses led to the conclusion that parvalbumin is the major fish albumin independent of fish species (Hamada *et al.*, 2001). Parvalbumin is generally associated with skeletal muscle tissue, even though the presence of parvalbumin has previously been detected in swim bladders of fish not used for isinglass manufacture (Feher *et al.*, 1998; Parmentier *et al.*, 2003).

4.2 Reported studies on residues of isinglass in beer and wine

It was reported that the filtration process removed all isinglass residues in filtered beer during the process, tested using a HPLC method that can detect amino acids concentration as low as 3.9×10^{-13} mg/L. However, the study showed that in order for the cask beer to be free of isinglass, sufficient time is required for the sediment to settle properly before dispensing (Chlup *et al.*, 2006).

A recent study investigated the manufacturing processes on the removal of a range of fining agents in four German wines. The wines were dosed with isinglass at 10-50 mg/L and other fining agents at five times their normal dosage levels. ELISA assays were used as the analytical method and detected no isinglass or fish gelatine in wine, except lysozyme and dried egg white, which are soluble in wine. It demonstrated that fining agents used for wine are removed during the manufacturing process or those that are insoluble are removed by filtration (Weber *et al.*, 2007).

5. Conclusion

Isinglass derived from fish swim bladders used as a clarifying agent in the brewing and wine industry may contain parvalbumin. The level of parvalbumin in the isinglass can be minimised by following a GMP that is specifically designed for this purpose.

Residual isinglass has been shown to be removed by the filtration/settling process in wine, in beer that is filtered; and in cask conditioned beer (that is unfiltered) if sufficient sedimentation time is received. It is very likely that parvalbumin with its pI at around 3.9-5.5, could precipitate out in wine and beer, which also has pH around 4 and lower. The precipitated parvalbumin would then settle with the sediment with isinglass-protein complexes or be filtered out by the filtration processes.

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