Overseas Market Access for Shellfish

December 2009

Dr Catherine McLeod

Dr John Sumner

Dr Andreas Kiermeier

AUSTRALIAN SEAFOOD COOPERATIVE RESEARCH CENTRE

Project No. 2009/752

Government of South Australia

CRC AUSTRALIA

Australian Government
Fisheries Research and Development Corporation

SARDI
SOUTH AUSTRALIAN RESEARCH AND DEVELOPMENT INSTITUTE

The Australian Seafood CRC is established and supported under the Australian Government's Cooperative Research Centres Programme. Other investors in the CRC are the Fisheries Research and Development Corporation, Seafood CRC company members, and supporting participants.

ISBN: 978-0-9756044-8-9

Important Notice

Although SARDI has taken all reasonable care in preparing this report, neither SARDI nor its officers accepts any liability from the interpretation or use of the information set out in the document. Information contained in this document is subject to change without notice.

Table of Contents

Glossary of Terms

AQIS	Australian Quarantine and Inspection Service
EC	European Commission
EFSA	European Food Safety Authority
EU	European Union
OA	Okadaic Acid
SAF	Seafood Access Forum
SARDI	South Australian Research and Development Institute
STX	Saxitoxin

Non Technical Summary

2009/752	Overseas Market Access for Shellfish

PRINCIPAL INVESTIGATOR: Dr Catherine McLeod
SARDI
33 Flemington Street
Glenside, 5065
South Australia

Project Overview

The European Commission (EC) requested the European Food Safety Authority (EFSA) to assess the current European Union (EU) limits for shellfish regarding human health and methods of analysis for various marine biotoxins, including newly emerging toxins. A critical recommendation of the 'EFSA Opinions' is that the regulatory limits should be significantly lower (more stringent) for both Okadaic Acid (OA) (~4-fold lower) and Saxitoxin (STX) (~10-fold lower).

A reduction of the regulatory limits for STX and OA on such a scale would have negative economic consequences for the Australian shellfish industry due to longer production area closures and less product being eligible for sale. In addition to a direct impact on exports to the EU, experience has repeatedly demonstrated that European decisions can impact on other significant markets (including Asia) and Codex may be prompted to change international marine biotoxin guidance levels in response.

This project involved undertaking a technical review of the EFSA risk assessments on STX and OA group toxins (Appendix One). To protect the current level of trade in Australian shellfish the technical review, containing rationale for maintaining current marine biotoxin regulatory limits, was submitted (by AQIS) to the EC for consideration when deliberating on regulatory limit changes.

Objectives

1. Undertake a robust technical review of the EFSA risk assessments on STX and OA group toxins.
2. Submit the technical review and a rationale for maintaining current marine biotoxin regulatory limits to the EC.
3. Convene a working group to determine future steps required to mitigate potential lowering of marine biotoxin regulatory limits.

Outcomes

1. Maintenance of eligibility of Australian shellfish for export and sale on the domestic market (with reference to marine biotoxins).
    - Exports to the EU in 2006/2007 for scallops were valued at around $4,551,000 AUD (187 t). Other molluscs (including oysters and mussels)

were valued at around $1,084,000 AUD (255 t). Due to the occurrence of OA and STX in Australian shellfish, the implementation of reduced regulatory levels would have placed this trade in jeopardy. The maintenance of the regulatory limits achieved via this project has protected the shellfish industry's access and current level of trade with the EU.

- Codex and other non-EU countries have not adopted the recommendations of the EFSA to lower regulatory thresholds for marine biotoxins. This protects the current level of shellfish trade between Australia and other non-EU countries.

2. Improved relationships between the EC and Australian industry, science and regulatory representatives.

   - Several informal meetings and email exchanges have been conducted during the course of this project between various EC officials and Australian scientists and regulators.
   - This has led to improved relationships between parties and heightened awareness of current European shellfish safety legislation and potential changes to the legislation in the future.
   - This will assist in identifying potential EU market access issues for Australian shellfish in the future.

Background

At the request of the European Commission (EC), the European Food Safety Authority (EFSA) undertook a series of eight risk assessments on different marine biotoxins in shellfish. The EFSA has suggested that regulatory levels should be significantly lower (more stringent) for OA (4-fold lower), STX (10-fold lower), azaspiracids (5-fold lower) and domoic acid (4-fold lower). In response to the EFSA risk assessments the EC are considering revising the European Union (EU) shellfish legislation to reflect current knowledge. These new regulations will apply to all Australian bivalves (oysters, mussels, scallops), gastropods (abalone) and crustaceans exported to the EU. European decisions can impact on other more important markets, including Asia and the domestic market. The lowering of the regulatory thresholds would have substantive economic consequences for the oyster, mussel, scallop and abalone industries in Australia (refer to 'need' section for further details).

In June 2009 SARDI (through Seafood CRC funded project 2007/782) held a meeting with the EC to gain insights into potential changes in legislation with regard to marine biotoxin regulatory limits. The EC welcomed a submission of Australian peer reviews of the key EFSA risk assessments to assist them in maintaining the current regulatory limits.

This project was undertaken to enable Australia to be at the forefront of an emerging international trade issue with potential for serious impacts on industry. In this project a proactive approach to maintaining the status quo with respect to marine biotoxin regulatory limits was undertaken. The approach involved undertaking a technical peer review of two EFSA risk assessments and submission of these to the EC (via AQIS) for their consideration when revising the EU shellfish legislation.

The project underpins Research Program 2 of the Seafood CRC 'Product and Market Development' and specifically supports Seafood CRC Output 2.4: Optimised Technical Market Access.

Need

The oyster, scallop and mussel industries currently export product to the EU. Due to the periodic occurrence of OA and STX group toxins in Australian shellfish the implementation of reduced regulatory levels would reduce the amount of product eligible for EU export.

Exports of Australian abalone to the EU ceased in 2007, this was in part due to the enforcement of marine biotoxin regulatory limits set by the EC. The wild caught abalone industry is attempting to regain EU market access through determining alternate risk management procedures for marine biotoxins in abalone. The reduction of regulatory levels for marine biotoxins would impinge on future EU access arrangements for Australian abalone (and negatively impact other seafood CRC projects aimed at addressing this problem, specifically project 2008/909).

It is well documented that food safety standards that are mandated in Europe are frequently adopted in Asian countries (including China) and in other countries such as Australia. Table 1 shows an assessment of key Asian markets and the influence

of European food safety standards on Asian regulations. It is important to note that China in particular has based many standards on European food safety legislation and that this trend is likely to continue due to a strong industry desire in China to export seafood to Europe. Codex may also be prompted to change marine biotoxin guidance levels in response to potential EU changes.

Table 1. Summary of food regulatory systems in Asian markets of importance to crustacean exporters.

	Market Access System			
Country	**EU**	**Codex**	**Own**	**Comment**
China	✓	✓	✓✓	EU: PCB, dioxins & micro. Many areas adopt EU for biotoxins. Poorly developed domestic micro stds.
Hong Kong	✓	✓	✓✓	EU: PCB, dioxins, biotoxins & micro.
Taiwan		✓✓	✓	Codex: micro
India	✓	✓✓	✓	Own system is minor, mainly Codex & micro from EU
South Korea	✓		✓✓✓	Largely informed by Japan & micro from EU. Also informed by US requirements (biotoxins/micro)
Indonesia		✓✓✓	✓	Own system only for metals
Japan	✓		✓✓✓	EU: PCB, dioxins & where they don't have own limits. Own requirements viruses and vibrios (over and above EU)
Malaysia		✓✓✓	✓	Own system only for metals
Singapore	✓		✓✓✓	EU: PCB, dioxins & vet drugs. Heavily influenced by EU though. Own requirements on virus and vibrio (over and above EU)
Thailand		✓✓✓	✓	Own system only for metals

Note: Countries default to Codex (or may chose EU) when they don't have their own

Note: Countries may accept exporting countries requirements when they don't have their own

Note: Ticks indicate level of reliance on EU, Codex or 'in house' standards

Widespread adoption of reduced regulatory levels for marine biotoxins would result in increased growing area closures in Australia and less product eligible for sale. The lack of human illness related to the consumption of shellfish from areas in which marine biotoxin management programmes are applied (with the current regulatory limits) suggests that lowering the regulatory levels may be overly precautionary. This project aimed to assist in maintaining the current EU regulatory limits for marine biotoxins to allow the current amount of shellfish to be exported to the EU and avoid other markets being influenced.

Objectives

1. Undertake a robust technical review of the EFSA risk assessments on STX and OA group toxins.
2. Submit the technical review and a rationale for maintaining current marine biotoxin regulatory limits to the EC.
3. Convene a working group to determine future steps required to mitigate potential lowering of marine biotoxin regulatory limits.

Methods

1. Scientific Peer Review

The core aspect of the project was the scientific peer review of the EFSA opinions (risk assessments) on OA and STX (Appendix One). This was undertaken primarily by Dr John Sumner, with statistical and contextual input by Dr Andreas Kiermeier and Dr Catherine McLeod. The peer review followed standard critical assessment practices.

2. Preparation of a submission to the EC

A letter addressed to the EC was prepared. The letter outlined the key findings of the technical peer review and contained a rationale that supported the contention that current regulatory limits for marine biotoxins are adequate to protect human health and should not be lowered. AQIS submitted the peer review and letter to the EC for their consideration.

3. Working Group

Following the submission of the peer review to the EC, a working group was established under the auspices of the Australian Shellfish Quality Assurance Advisory Committee. The working group discussed the EFSA opinions and has agreed to maintain a 'watching brief' (including continued contact with the EC). The working group will report back to the Seafood Access Forum (SAF) at the next meeting in early 2010.

Results

See Appendix One for the key output of this project.

In summary, while the peer reviewers welcomed the EFSA conclusions relating to analytical methods, they found significant weaknesses in a number of aspects of the EFSA panel's assessment of regulatory limits with regards to human health. The peer reviewers found no evidence for the reductions proposed by the EFSA panel, and their findings align with the recommendations of the Codex Committee on Fish

and Fishery Products (Beijing, 2006) that there be no change to the regulatory limit for OA and STX-group toxins in shellfish.

On the basis of the technical review it was recommended to the EC that:

1. Current regulatory limits for STX and OA group toxins are maintained.
2. Consideration be given to allowing HPLC and LC-MS methods that have undergone limited inter-laboratory study to be used as screening methods for determining OA and STX group toxins.
3. Future EFSA opinions be subjected to rigorous peer review by independent scientists.

Benefits/Adoption/Outcomes

1. Maintenance of the current levels of Australian shellfish (oysters, scallops, mussels) eligible for export and sale on the domestic market (with reference to marine biotoxins).
    - Upon receiving the SARDI/AQIS submission (Appendix One), along with submissions from Ireland and the European Mollusc Producers Association, the EC have consulted with the EU Member States and retained the current regulatory thresholds for OA and STX.
    - The EC have requested the EFSA to revise their risk assessment and recommendation of lowering the regulatory thresholds based on some technical factors, including those highlighted in the SARDI review.
    - Exports to the EU in 2006/2007 for scallops were valued at around $4,551,000 AUD (187 t). Other molluscs (including oysters and mussels) were valued at around $1,084,000 AUD (255 t). Due to the occurrence of OA and STX in Australian shellfish the implementation of reduced regulatory levels would have placed this trade in jeopardy. The maintenance of the regulatory limits achieved via this project has protected the shellfish industry's access and current level of trade with the EU.
    - Codex and other non-EU countries have not adopted the recommendations of the EFSA to lower regulatory thresholds for marine biotoxins. This protects the current level of shellfish trade between Australia and other non-EU countries.
    - The EC have facilitated a technical vote of the EU member states on methods of analysis for marine biotoxins. The outcome of the vote was to replace the mouse bioassay as the reference method for lipophilic toxins with an LC-MS method. It is envisaged that the EC legislation will be altered to reflect this decision by June 2010. This will result in a large decrease in false positive results from shellfish harvested in Tasmania and South Australia and a larger proportion of product being eligible for export to the EU.
2. Improved relationships between the EC and Australian industry, science and regulatory representatives.

- Several informal meetings and email exchanges have been conducted during the course of this project between various EC officials and Australian scientists and regulators.
- This has led to improved relationships between parties and heightened awareness of current European shellfish safety legislation and potential changes to the legislation in the future.
- This will assist in identifying potential EU market access issues for Australian shellfish in the future.

Conclusions and Further Development

- This project has assisted in protecting the Australian shellfish industry's EU export market against potential marine biotoxin technical barriers to trade.
- For a relatively small investment (~$8,000 AUD) this project has allowed the continued export of Australian shellfish to the EU, valued at around $5.5 million AUD.
- Informal communication with EC officials should be maintained to assist in early identification of potential technical barriers to trade in the future.
- A watching brief with respect to the actions of Codex (particularly the Fish and Fishery Products Committee) and other non-EU countries with regards to the setting of new marine biotoxin limits needs to be maintained by the Australian shellfish sector and Seafood Access Forum.

Appendix One

SARDI/AQIS submission to the European Commission including an independent peer review of EFSA scientific opinions on saxitoxin and okadaic acid group toxins.

SARDI

SOUTH AUSTRALIAN RESEARCH AND DEVELOPMENT INSTITUTE

Dr Paolo Caricato
European Commission
Health and Consumers Directorate-General
Directorate E - Safety of the Food Chain
E2 - Food Hygiene, Alert System and Training
B232 04/112 B-1049 Brussels
Belgium

SUBJECT: Independent Peer Review of EFSA Scientific Opinions on Saxitoxin and Okadaic Acid Group Toxins

Dear Dr Caricato,

I write to you in regard to the recently published Scientific Opinions on the 'Saxitoxin group' (STX) and 'Okadaic Acid and Analogues' (OA) by the European Food Safety Authority (EFSA) Panel on Contaminants in the Food Chain. A critical recommendation of the EFSA Opinions are that the regulatory limits should be significantly lower (more stringent) for both OA (~ 4-fold lower) and STX (~10-fold lower).

A reduction of the regulatory limits for STX and OA on such a scale would undoubtedly have a negative economic consequence on some sectors of the international shellfish industry. In addition to a direct impact on exports to the European Union, experience has repeatedly demonstrated that European decisions can impact on other significant markets (including Asia) and Codex may also be prompted to change marine biotoxin guidance levels in response. Because of this it is extremely important that any changes that are made to the regulatory limits by DG SANCO are based on robust scientific and technical information.

Due to the importance of the newly proposed regulatory limits an Australian panel of three independent scientists with relevant high-level experience has peer reviewed the EFSA opinions on OA and STX (attached). In summary, while the peer reviewers welcomed the EFSA conclusions relating to analytical methods, they found significant weaknesses in a number of aspects of the EFSA panel's assessment of regulatory limits with regards to human health. The peer reviewers found no evidence for the reductions proposed by the EFSA panel, and their findings align with the recommendations of the Codex Committee on Fish and Fishery Products (Beijing, 2006) that there be no change to the regulatory limit for OA and STX-group toxins in shellfish.

On the basis of the independent peer reviews we recommend to DG SANCO that:

1) current regulatory limits for STX and OA group toxins are maintained
2) consideration be given to allowing HPLC and LC-MS methods that have undergone limited inter-laboratory study to be used as screening methods for determining OA and STX group toxins
3) future EFSA opinions be subjected to rigorous peer review by independent scientists

We understand that DG SANCO is consulting with the European producers, EFSA, the EU National Reference Laboratories and the EU Community Reference Laboratory regarding the practical application of the new limits proposed by EFSA in September 2009. We welcome the consideration of the enclosed independent peer reviews by DG SANCO and other parties as part of the consultation process.

I look forward to hearing from you regarding the outcome of the EFSA recommendations on marine biotoxins in shellfish.

Yours sincerely

Dr Andrew Pointon
Chief, Innovative Food and Plants
South Australian Research and Development Institute

“Marine biotoxins in shellfish – Saxitoxin group: Scientific opinion of the panel on contamination in the food chain” by the European Food Safety Authority (EFSA)

A Review

South Australian Research and Development Institute (SARDI)

September 2009

Government of South Australia

AUSTRALIAN SEAFOOD COOPERATIVE RESEARCH CENTRE

SARDI R&D SOUTH AUSTRALIAN RESEARCH AND DEVELOPMENT INSTITUTE

Contents

Summary

1. The European Commission requested the European Food Safety Authority (EFSA) to assess the current EU limits regarding human health and methods of analysis for various marine biotoxins, including newly emerging toxins.
2. The panel has recommended a reduction in the current EU limit of 800 µg to 75 µg Saxitoxin (STX) equivalents/kg of shellfish meat.
3. If the reduction recommended by the EFSA opinion is accepted by DG SANCO there will be a significant commercial impact on Australian exports of shellfish (scallops, oysters, abalone and mussels) to the EU. Consequently, a review of the scientific and technical factors used by the panel in forming their recommendation was undertaken.
4. This review concludes that there are significant weaknesses in a number of aspects of the EFSA panel's findings, most importantly:
   - the paucity and quality of data supplied by Member States on exposure of consumers to STX-group toxins;
   - the use of biased consumption data;
   - the lack of peer review of the opinion;
   - uncritical evaluation of epidemiology data; most of the incidents cited by the EFSA panel predate implementation of biotoxin management systems in harvesting areas, while recent incidents are most likely due to recreational harvest; and
   - failure to consider the recommendations of the Codex Committee on Fish and Fishery Products (CCFFP) that the current standard, its practical application and demonstrated results, indicate that the level of 800 µg/kg provides adequate protection for consumers. This led the CCFFP to recommend no change to the current level of 800 µg/kg of shellfish meat.
5. Based on the foregoing, this review finds no evidence for the reduction proposed by the EFSA panel and aligns with the recommendations of the CCFFP that there be no change to the regulatory limit for STX-group toxins in shellfish.

1. Background

The European Commission has requested the European Food Safety Authority (EFSA) to assess the current EU limits with regard to human health and methods of analysis for various marine biotoxins, including newly emerging toxins. The EFSA's Scientific Panel on Contaminants in the Food Chain (CONTAM) is undertaking this task with respect to eight different marine biotoxin groups: okadaic acid (OA) group toxins, azaspiracids, yessotoxins, saxitoxins, pectenotoxins, cyclic imines, domoic acid and palytoxins.

In terms of the Saxitoxin (STX) group, the subject of the present document, the panel recommends a reduction in the current EU limit of 800 µg STX equivalents/kg shellfish meat to 75 µg STX equivalents/kg (Anon. 2009).

2. Purpose of the present document

If the reduction recommended by the EFSA opinion is accepted by DG SANCO there will be a significant commercial impact on Australian exports of shellfish (scallops, oysters, abalone and mussels) to the EU. Consequently, a review of the scientific and technical factors used by the panel in forming their recommendation was undertaken.

3. Panel members

The EFSA panel comprised 19 members and was informed by material produced by a 13-person working group, six of whom were also panel members. Surprisingly, the affiliation of panel members is not provided. This would inform on the balance of expertise of the panel, particularly the presence of regulators who could interface between the science and the implementation of the panel's opinion.

The experience of the working group and panel members is reflected by the fact that, collectively, they are authors of 17 of the 124 peer-reviewed papers cited in the literature. These papers deal predominantly with toxicity of the STX-group and with their detection and indicate that the panel was well qualified to respond to the terms of reference listed in Section 4, and particularly elements three and four.

4. Terms of reference of the EFSA panel

The terms of reference as supplied by the Requestor (the European Commission) are as follows:

In accordance with Art. 29 (1) (a) of Regulation (EC) No 178/2002, the Commission asks EFSA to assess the current EU limits with regard to human health and methods of analysis for various marine biotoxins as established in the EU legislation, including new emerging toxins, in particular in the light of:

1. *the report of the Joint FAO/IOC/WHO ad hoc Expert Consultation on Biotoxins in Bivalve Molluscs (Oslo, September 26-30 2004), including the ARfDs and guidance levels proposed by the Expert Consultation,*
2. *the conclusions of the CCFFP working group held in Ottawa in April 2006,*

3. *the publication of the report and recommendations of the joint European Centre for the Validation of Alternative Methods (ECVAM)/DG SANCO Workshop, January 2005,*
4. *the report from CRL Working group on Toxicology in Cesenatico October 2005,*
5. *any other scientific information of relevance for the assessment of the risk of marine biotoxins in shellfish for human health.*

While the Requestor required the EFSA panel to consider the conclusions of the CCFFP working group (TOR 2) it is surprising that the panel was not required to also consider the recommendations of that working group to the 28th meeting of CCFFP in Beijing in September 2006. These recommendations are introduced in Section 7.9 of this report.

5. Conduct of the review

The review was undertaken by appraising the EFSA document within the overall context of:

- 2004: EU Hygiene Package, which set maximum levels for STX
- 2004: Joint FAO/IOC/WHO *ad hoc* expert consultation on biotoxins in bivalve molluscs held in Oslo in September 2004
- 2006: Working group meeting to assess the advice from the joint FAO/IOC/WHO *ad hoc* expert consultation on biotoxins in bivalve molluscs held in Ottawa in April 2006
- 2006: Recommendations of the working group on biotoxins in bivalve molluscs to Codex Committee on Fish and Fishery Products CX/FFP 06/28/6 –Add. 1

To this end, the present report focuses on elements 1, 2 and 5 of the response of the EFSA panel to the Requestor's terms of reference. While the PSP mouse bioassay is widely recognised as providing a high level of public health protection, the broad conclusions of the panel regarding methods of analysis and the appropriateness of high performance liquid chromatographic (HPLC) methods are particularly welcome.

6. Approach of the EFSA panel

The approach of the EFSA panel followed a continuum as described in Sections 6.1-6.4 (below). Because the EFSA panel refer on numerous occasions to findings of the FAO/IOC/WHO expert consultancy, the findings of the latter are included in this review.

6.1 Acute Reference dose

In view of the acute toxicity of STX-group toxins the panel decided to establish an acute reference dose (ARfD) based on their assessment of the available human data. The assessment led to a lowest-observed-adverse-effect-level (LOAEL) of 1.5 µg STX equivalents/kg bodyweight. A safety factor of three was applied to convert the LOAEL to a no-observed-adverse-effect-level (NOAEL), from which an ARfD of 0.5 µg STX equivalents/kg body weight was derived.

The EFSA panel were required (TOR 1) to consider the report of the FAO/IOC/WHO expert consultation, which comprised 37 persons, of whom six were members of the EFSA panel or working group. The expert consultation adopted the same approach as the EFSA panel, except for adopting an LOAEL of 2 µg STX equivalents/kg bodyweight, which resulted in an

ARfD of 0.7 µg STX equivalents/kg body weight. This disparity is not acknowledged in the EFSA summary of the FAO/IOC/WHO report.

6.2 Prevalence and concentration of STX-group biotoxins in shellfish

The EFSA panel requested EU Member States to provide data on STX and analogues, of which seven States responded (data are summarised in Tables 2, 4, 5, 6 and 7 of the EFSA report). Because 90.8% of samples were below 350 or 380 µg/kg shellfish (the LOD) the panel found itself unable to provide a reliable exposure estimate.

Because of insufficient data, the FAO/IOC/WHO panel did not evaluate prevalence and concentration of toxins in bivalve molluscs, focusing instead on levels generally associated with closure of harvesting areas and on maximum reported levels; these were reported as 800-1,000 µg STX/kg and 800,000 µg STX equivalents/kg of shellfish meat, respectively.

6.3 Consumption of shellfish in EU

The panel used data from seven surveys in five European countries: France, Italy, Germany, UK and The Netherlands (summarised in Table 8 of the report). The panel decided to use an intake at the 95th percentile of 400 g shellfish meat in their calculation of a regulatory limit for STX-group toxins in shellfish.

The FAO/IOC/WHO panel quote (without reference) consumption patterns and intakes of shellfish from various European and non-European countries. The 97.5th percentile is derived from data from The Netherlands (380 µg STX equivalents/kg shellfish meat). In total, the FAO/IOC/WHO panel cite three consumption levels when generating their "Derived Guidance Level":

- 100 g (standard portion of used in risk assessment and one which approximated mean consumption)
- 250 g (97.5th percentile for most countries)
- 380g (97.5th percentile for The Netherlands)

6.4 Risk characterisation

The EFSA panel noted the high-end 95th percentile consumption value of 400 g, at the current regulatory limit of 800 µg STX equivalents/kg of shellfish meat, would equate with an intake of 320 µg STX equivalents/kg (around 5.3 µg/kg bodyweight in a 60 kg person).

The panel drew attention to the fact that an ARfD of 0.5 µg/kg shellfish meat is exceeded about ten-fold by the current regulatory limit, for which reason the panel opines that shellfish meat should contain no more than 75 µg/kg.

The FAO/IOC/WHO panel use a similar process to state a "Guidance/Maximum level" based on consumption of 100 g, 250 g or 380 g of 420 µg/kg, 170 µg/kg and 110 µg STX equivalents/kg of shellfish meat, respectively.

7. Assessment of the EFSA opinion

While the EFSA report (and the FAO/IOC/WHO report) has followed a logical process in suggesting a new regulatory limit there are a number of weaknesses in the report, including:

7.1 Paucity and quality of data supplied

Exposure data (Sections 5-7) are pivotal to the panel's opinion, but how representative are data supplied by only 10/27 Member States for prevalence and concentration of toxins, and by only 5/27 States for consumption?

The disparity in consumption patterns between those States which responded is striking. Did only 0.6% of Germans consume shellfish in the mid-1980s? Did only 1.1% of Dutch consumers eat shellfish in 1997-98? How credible are consumption data for France when the INCA 1999 survey in France indicates that 11% of consumers eat shellfish while the CALIPSO survey in 2004 found 96% did?

7.2 Presentation of data

Because of the way exposure data are presented it is difficult for a reviewer to judge where high-level consumption begins. For example it can be adduced that 2/47 consumers in The Netherlands survey estimated their consumption at 465 g and 480 g (95^{th} and 100^{th} percentile, respectively), while seven or eight German consumers ate between 400 g and 1,500 g at one sitting.

These few consumers have a great effect on the mean consumption, which is why median consumption would be helpful, as would additional percentiles below the 95^{th}.

7.3 Lack of a reality check on consumption data

It appears that the EFSA panel accepted consumption data at face value. Can it really be accepted that 5% of German consumers eat between 400 g and 1,500 g of shellfish meat at one sitting? The EFSA opinion (Anon. 2008) on Okadaic acid states (page 29) that mussel meat weighs between 5 g and 6.5 g/piece) which equates to 62-80 mussels (400 g) and 231-300 mussels (1500 g). These are consumption levels which strain credulity.

The EFSA panel considers it likely that the 1,000 g and 1,500 g maxima are probably shell-on values. So why include them when they shift the 95^{th} percentile towards a much higher consumption level? If the 1,000 g and 1,500 g levels are shell-on – is this also the case for the 95^{th} percentiles of 400 g and 465 g for The Netherlands and Germany, respectively? If these values were divided by five (20% meat weight), the 95^{th} percentiles become 80 g for Germany and 93 g for The Netherlands - the same range as the other 95^{th} percentiles quoted in Table 8.

Given the pivotal importance of the 95^{th} percentile, the panel should have validated the high-end consumption figures reported.

The panel may also wish to reconsider their opinion in light of the recent findings on shellfish consumption reported at the 7^{th} International Conference on Molluscan Shellfish Safety (where, incidentally, the EFSA panel also presented their risk assessments on marine biotoxins). In France, Picot *et al.* (2009) surveyed 500 recreational harvesters by food frequency questionnaire (FFQ) and face-to-face interview. Mean harvest was 11.83 g/day and

mean consumption from recreational and retail sources totalled 30.35 g/person/day. The researchers state that recreational harvesters are high consumers of shellfish, consuming almost 16-times more than the general population. The findings of Picot *et al.* (2009) present a reality check worthy of consideration by the EFSA panel.

7.4 Use of biased consumption data

The panel established the 95th percentile from intake data of 1159 consumers of shellfish for whom percentiles can be calculated (France, Germany, The Netherlands). As stated by the panel's report, the 95th percentile of 400 g was "chosen". A cursory examination of Table 8 indicates that the high portion figure results from intake data of two Dutch plus seven or eight German consumers, some of whom apparently ate up to 1,500 g.

The EFSA panel seeks to justify their "choice" by claiming "good agreement" with the FAO/IOC/WHO figure of 380 g for the 97.5th percentile. However, the FAO/IOC/WHO panel consulted the WHO/GEMS Food database and obtained the highest 97.5th percentile of 380 g for The Netherlands. They also obtained 97.5th percentiles of 133 g (Japan), 181 g (Australia), 225 g (USA), 263 g (New Zealand) and 182 g for the maximum intake in Norway. The FAO/IOC/WHO panel stresses the conservatism in the 380 g high portion and continued their risk assessment simulations by using three intake levels: 100 g, 250 g and 380 g.

In addition, many would query whether a 95th percentile of 400 g and a 97.5th percentile of 380 g represent "good agreement", as claimed by the EFSA panel.

The present bias towards high-end consumption would be removed if the EFSA panel excised obviously "wrong" intakes (1,000 g and 1,500 g) and then generated the 95th percentile from intakes of all 1159 consumers for whom data are available. It is likely that the 95th percentile would be much closer to the mean consumption.

7.5 Use of biased concentration data

As part of the assessment process EFSA requested data on the prevalence and concentration of STX-group toxins in shellfish from all Member States. Ten Member States provided such data, which was taken at various points in the marketing chain, as random and targeted samples and as samples taken when contamination was suspected.

There can be no suggestion that these samples properly represent production and it is highly likely that there is a bias towards sampling stock suspected of containing toxin. What can be said is that 90.8% of samples were below 350 or 380 µg/kg shellfish (the LOD) and a further 4.5% were between the LOD and 800 µg/kg shellfish. The 95th percentile is, therefore, below the current regulatory limit.

The present bias towards high-end concentration would be removed were a properly-designed survey of shellfish at the market level were undertaken. In addition, because any revised level is to be applied across 27 Member States and is likely to be adopted by other countries (in order to meet EU import requirements) it seems logical to use as representative a dataset as possible.

7.6 Lack of peer review

It is surprising that EFSA procedures would allow a risk assessment to be published without peer review. By way of comparison, the FAO/WHO "Risk assessment of *Vibrio parahaemolyticus* in raw oysters" was reviewed by twenty peer reviewers from fifteen countries, each of whom was independent of the drafting group. Their comments amounted to 44 pages of A4 paper and each comment required a response by the drafting group. Each response was then transmitted to the reviewer, who was given further opportunity to comment. The review process required by FAO/WHO was arduous but led to significant improvements in the final text.

This review finds it highly likely that the chosen 95th percentiles for consumption and concentration of toxin would have incurred substantial enquiry.

7.7 Epidemiology

Section 11 (Observations in humans) presents a summary of STX-group toxin epidemiology data for the period 1953-2005. The panel details uncertainties associated with estimating STX intake in human case reports, which are manifested in Figure 9 where, in some incidents there is little difference in estimated toxin intake between "no effect" and "extreme severity".

In an appreciation of the text provided by the EFSA panel it should be noted in amplification that:

- The vast majority of incidents cited by the EFSA panel predate the implementation of PSP management plans in harvesting areas.
- Recent cases (post-1990) all have very small numbers of affected individuals suggesting harvesting by recreational gatherers, rather than commercial harvest.

7.8 Risk estimate used in the study

The panel found that a reliable estimate of exposure to STX-group toxins in the market place was not feasible. The fact that there have been no recent reports of PSP from consumption of shellfish in European countries seems to have been discounted without demur, the panel citing the absence of a formal reporting system.

7.9 Failure to consider the recommendations of the CCFFP working group held in Ottawa in April 2006

The working group made their report to the 28th session of CCFFP held in Beijing in September 2006. It is valuable to quote verbatim (with two sentences highlighted in bold type) their comments and recommendations for no change to the regulatory limit:

5.7 SAXITOXINS (STX) group

41) Summary of Analysis from the Expert Consultation

The Expert Consultation acknowledged data quality challenges in completing this risk assessment. While select unpublished studies were included in this evaluation (along with published sources), the experts recommended that further unpublished data be collected and evaluated with an aim to further increase the accuracy of the assessment. The

impact/influence of the long-standing enforced tolerance limit of 0.8mg/kg STX.2HCl equiv., established for consumer protection, was also not considered.

42) WG Comment(s)

The WG considered the long history of success (nearly 50 years) using an action level of 0.8 mg/kg with the mouse bioassay, with no human illnesses (from commercially harvested product).

The WG discussed available methodology, in particular the fact that the Lawrence LC-FL method had recently undergone inter-laboratory validation and that it could be considered as a Codex Type II method. The WG also discussed the need for other methods that could be used for routine monitoring, such as mouse bioassay, receptor binding assay, etc.

43) Recommendation(s)

1. ***The WG recommends that the Codex standard (section I-5) maintain the action level currently identified for PSP as 0.8 mg/kg STX.2HCl equiv.***
2. *The WG recommends to CCFFP that the Codex standard (section I-7.7) identify the Lawrence LC- FL method as a potential reference method (Codex Type II) subject to review by CCMAS. The Lawrence LC-FL method was recently approved by AOAC as an official method of analysis.*
3. *The WG recommends that Codex identify the range of methods currently available to effectively detect saxitoxins, including the mouse bioassay, the receptor binding assay, immunochemical, LC- FL and LC-MS methods for consideration as Type III methods. These methods should be recommended by CCFFP to the CCMAS for review and designation.*

8. Conclusions

The EFSA panel has fulfilled all the terms of reference set out by the Requestor and *inter alia*, provided an opinion for a significant reduction in the regulatory limit, from 800 µg STX equivalents/kg of shellfish meat to 75 µg STX equivalents/kg of shellfish meat. Pivotal to the suggested reduction was the choice of 95th percentile levels for intake (400 g). Criticism of the data from which this value was derived and of the panel's approach to setting it has been detailed in Section 7 of this review.

Clearly, if the European Commission were to accept the opinion of the EFSA panel there would be significant impact on the global shellfish industry. But there seems little evidence that public health, either in the EU, or globally, is much affected by STX contamination of shellfish. The statement by the CCFFP working group of "*the long history of success (nearly 50 years) using an action level of 0.8 mg/kg with the mouse bioassay, with no human illnesses from commercially harvested product"* is instructive and it is surprising that the EFSA panel did not address this recommendation.

This review concurs with the recommendations of the CCFFP.

References

Anonymous. 2008. Marine biotoxins in shellfish – okadaic acid and analogues: Scientific opinion of the panel on contamination in the food chain. The EFSA Journal, 589:1-62.

Anonymous. 2009. Marine biotoxins in shellfish – saxitoxin group: Scientific opinion of the panel on contamination in the food chain. The EFSA Journal, 1019:1-76.

Picot, C., Nguyen, T., Carpentier, Roudot, A. and Parent-Massin, D. 2009. A shellfish consumption survey in recreational harvesters in Brittany (France). Proceedings, 7th International Conference on Molluscan Shellfish Safety. Nantes, June 2009.

Acknowledgment

This review was supported by funding from the Australian Seafood Cooperative Research Centre (CRC). The CRC receives funding from the Australian seafood industry and from the Australian Federal and State governments.

Review Panel

Dr Andreas Kiermeier is the Program Leader of the South Australian Research and Development Institute's Food Safety Research Program and an Honorary Senior Lecturer with the University of South Australia. In 2008 he led a review of the Victorian Shellfish Quality Assurance Program (Australia).

Dr Catherine McLeod is a Senior Scientist (Shellfish Safety) at the South Australian Research and Development Institute and an Honorary Research Associate at the University of Tasmania. She currently leads a research programme focused on the food safety of shellfish, including risk assessment of saxitoxins in Australian abalone.

Dr John Sumner is an Honorary Research Professor at University of Tasmania, Australia. He is a member of the FAO/WHO drafting group on microbial risk assessment "Vibrios in seafoods", a consultant to Fisheries Division, United Nations Food and Agriculture Organisation, Rome and undertook the Australian National Seafood Risk Assessment.

“Marine biotoxins in shellfish – Okadaic acid and analogues: Scientific opinion of the panel on contamination in the food chain” by the European Food Safety Authority (EFSA)

A Review

South Australian Research and Development Institute (SARDI)

September 2009

Government of South Australia

AUSTRALIAN SEAFOOD COOPERATIVE RESEARCH CENTRE

SARDI R&D SOUTH AUSTRALIAN RESEARCH AND DEVELOPMENT INSTITUTE

Contents

Summary

1. The European Commission requested the European Food Safety Authority (EFSA) to assess the current EU limits regarding human health and methods of analysis for various marine biotoxins, including newly emerging toxins.
2. The panel has recommended a reduction in the current EU limit of 160 µg to 45 µg okadaic acid (OA) equivalents/kg of shellfish meat.
3. If the reduction recommended by the EFSA opinion is accepted by DG SANCO there will be a significant commercial impact on Australian exports of shellfish (scallops, oysters, abalone and mussels) to the EU. Consequently, a review of the scientific and technical factors used by the panel in forming their recommendation was undertaken.
4. This review concludes that there are significant weaknesses in a number of aspects of the EFSA panel's findings, most importantly:
   - the paucity and quality of data supplied by Member States on exposure of consumers to OA-group toxins;
   - the use of biased consumption and concentration data;
   - the lack of peer review of the opinion;
   - uncritical evaluation of epidemiology data; and
   - failure to consider the recommendations of the Codex Committee on Fish and Fishery Products (CCFFP) that the current standard, its practical application and demonstrated results, indicate that the level of 160 µg/kg provides adequate protection for consumers. This led the CCFFP to recommend no change to the current level of 160 µg/kg of shellfish meat.
5. Based on the foregoing, this review finds no evidence for the reduction proposed by the EFSA panel and aligns with the recommendations of the CCFFP that there be no change to the regulatory limit for OA-group toxins in shellfish.

1. Background

The European Commission has requested the European Food Safety Authority (EFSA) to assess the current EU limits regarding human health and methods of analysis for various marine biotoxins, including newly emerging toxins. The EFSA's Scientific Panel on Contaminants in the Food Chain (CONTAM) is undertaking this task with respect to eight different marine biotoxins: okadaic acid (OA) group toxins, azaspiracids, yessotoxins, saxitoxins, pectenotoxins, cyclic imines, domoic acid and palytoxins.

In terms of the OA-group toxins (the subject of this document) the panel recommends a reduction in the current EU limit of 160 µg OA equivalents/kg shellfish meat to 45 µg OA equivalents/kg (Anon. 2008).

2. Purpose of the present document

If the reduction recommended by the EFSA opinion is accepted by DG SANCO there will be a significant commercial impact on Australian exports of shellfish (scallops, oysters, abalone and mussels) to the EU. Consequently, a review of the scientific and technical factors used by the panel in forming their recommendation was undertaken.

3. Panel members

The EFSA panel comprised twenty members and was informed by material produced by a 16-person working group, seven of whom were also panel members. Unusually, no information is provided on the affiliation of panel members; this information would inform on the balance of expertise of the panel, particularly the presence of regulators who could interface between the science and the implementation of the panel's opinion.

The experience of the working group and panel members is reflected by the fact that, collectively, they are authors of 19 of the 83 peer-reviewed papers cited in the literature. These papers deal predominantly with toxicity of DSP toxins and with their detection and indicate that the panel was particularly well qualified to respond to the terms of reference listed in Section 4, and particularly elements three and four.

4. Terms of reference of the EFSA panel

The terms of reference as supplied by the Requestor (the European Commission) are as follows:

In accordance with Art. 29 (1) (a) of Regulation (EC) No 178/2002, the Commission asks EFSA to assess the current EU limits with regard to human health and methods of analysis for various marine biotoxins as established in the EU legislation, including new emerging toxins, in particular in the light of:

1. *the report of the Joint FAO/IOC/WHO ad hoc Expert Consultation on Biotoxins in Bivalve Molluscs (Oslo, September 26-30 2004), including the ARfDs and guidance levels proposed by the Expert Consultation,*
2. *the conclusions of the CCFFP working group held in Ottawa in April 2006,*

3. *the publication of the report and recommendations of the joint European Centre for the Validation of Alternative Methods (ECVAM)/DG SANCO Workshop, January 2005,*
4. *the report from CRL Working group on Toxicology in Cesenatico October 2005,*
5. *any other scientific information of relevance for the assessment of the risk of marine biotoxins in shellfish for human health.*

While the Requestor required the EFSA panel to consider the conclusions of the CCFFP working group (TOR 2) it is surprising that they were not required to also consider the recommendations of that working group to the 28th meeting of CCFFP in Beijing in September 2006. These recommendations are introduced in Section 7.10 of this report.

5. Conduct of the review

The review was undertaken by appraising the EFSA document within the overall context of:

- 2001: Draft legislation notified on regulatory levels for DSP group of toxins in shellfish (SANCO/2227/23001 Rev 3).
- 2004: EU Hygiene Package, which set maximum levels for DSP.
- 2004: Joint FAO/IOC/WHO *ad hoc* expert consultation on biotoxins in bivalve molluscs held in Oslo in September 2004.
- 2006: Working group meeting to assess the advice from the joint FAO/IOC/WHO ad hoc expert consultation on biotoxins in bivalve molluscs held in Ottawa in April 2006.
- 2006: Recommendations of the working group on biotoxins in bivalve molluscs to Codex Committee on Fish and Fishery Products CX/FFP 06/28/6 –Add. 1.

To this end, this report focuses on elements 1, 2 and 5 of the response of the EFSA panel to the Requestor's terms of reference. The broad conclusions of the panel regarding the inadequacy of mammalian bioassays and the appropriateness of liquid chromatographic-mass spectrometric (LC-MS) methods are particularly welcome.

6. Approach of the EFSA panel

The approach of the EFSA panel followed a continuum as described in Sections 6.1-6.5 (below). Because the EFSA panel refer on numerous occasions to findings of the FAO/IOC/WHO expert consultancy, the findings of the latter are included in this review.

6.1 Acute Reference dose

In view of the acute toxicity of the OA-group toxins, the panel decided to establish an acute reference dose (ARfD) based on their assessment of the available human data. The assessment led to a lowest-observed-adverse-effect-level (LOAEL) of 50 µg OA equivalents/person, which approximates 0.8 µg OA equivalents/kg bodyweight for a 60 kg adult. A safety factor of three was applied to convert the LOAEL to a no-observed-adverse-effect-level (NOAEL), from which an ARfD of 0.3 µg OA equivalents/kg body weight was derived.

The above approach was also used by the FAO/IOC/WHO expert consultation, which used exactly the same value for LOAEL and NOAEL to reach an ARfD of 0.33 µg OA equivalents/kg body weight.

6.2 Prevalence and concentration of OA-group biotoxins in shellfish

The EFSA panel requested EU Member States to provide data on OA and analogues, of which ten States responded (data are summarised in Table 3 of the EFSA report). The panel utilised these data to derive a concentration at the 95th percentile of 240 µg OA equivalents/kg of shellfish meat.

Because of insufficient data, the FAO/IOC/WHO panel did not evaluate prevalence and concentration of toxins in bivalve molluscs, focusing instead on levels generally associated with closure of harvesting areas and on maximum reported levels; these were reported as 160-1,000 µg OA equivalents/kg and 36,000 µg OA equivalents/kg of shellfish meat, respectively.

6.3 Consumption of shellfish in the EU

The panel used data from seven surveys in five European countries: France, Italy, Germany, UK and The Netherlands (summarised in Table 10 of the report). The panel decided to use an intake at the 95th percentile of 400 g shellfish meat in their calculation of a regulatory limit for OA-group toxins in shellfish.

The FAO/IOC/WHO panel quote (without reference) consumption patterns and intakes of shellfish from various European and non-European countries. While the 97.5th percentile for The Netherlands is chosen (380 µg OA equivalents/kg of shellfish meat) two other consumption levels are also used in FAO/IOC/WHO modelling (see Section 6.4).

6.4 Dietary exposure to OA-group toxins at the top end

Because OA-group toxins have acute toxic effects, the EFSA panel multiplied the 95th percentile values for concentration and consumption (400 g x 240 µg OA equivalents/kg) to derive an exposure of 96 µg OA equivalents/kg per person.

The FAO/IOC/WHO panel cited three consumption levels when generating their "Derived Guidance Level":

- 100 g (standard portion often used in risk assessment and one which approximated mean consumption)
- 250 g (97.5th percentile for most countries)
- 380 g (97.5th percentile for The Netherlands).

6.5 Risk characterisation

The EFSA panel noted the high-end 95th percentile consumption value of 400 g, at the current regulatory limit of 160 µg OA equivalents/kg of shellfish meat, would equate with an intake of 64 µg OA equivalents/kg (around 1 µg/kg body weight in a 60 kg person). Using a high-end (95th percentile) value for concentration, a 400 g intake would equate with 96 µg OA equivalents/kg (around 1.6 µg/kg body weight in a 60 kg person).

The panel drew attention to the fact that an ARfD of 0.3 µg/kg shellfish meat is exceeded about three-fold by the current regulatory limit and 5-fold by the 95th percentile, for which reason the panel opines that shellfish meat should contain no more than 45 µg/kg.

The FAO/IOC/WHO panel use a similar process to state a "Guidance/Maximum level" based on consumption of 100 g, 250 g or 380 g of 200 µg/kg, 80 µg/kg and 50 µg OA equivalents/kg of shellfish meat, respectively.

7. Assessment of the EFSA opinion

While the EFSA report (and the FAO/IOC/WHO report) has followed a logical process in suggesting a new regulatory limit there are a number of weaknesses in the report, including:

7.1 Lack of transparency

In Sections 5, 6 and 7 critical data are quoted in a way which does not allow a reviewer to properly assess them. This is particularly important in Section 7 where Table 10 is based on un-referenced reports and hides critical information such as:

- Who carried out the surveys?
- How were they done (selection of survey group etc)?
- Are the data still relevant (e.g. German data are more than two decades old)?
- What is the meaning of the information contained in parentheses following each country ("FFQ", "7 days", "2 days")?
- Which shellfish are surveyed in each country?
- For toxin occurrence data provided by member states, how many samples were recorded during closures or suspected incidents, when sampling could be more frequent?

7.2 Paucity and quality of data supplied

Exposure data (Sections 5-7) are clearly pivotal because the panel derives 95th percentiles from them. But how representative are data supplied by only 10/27 Member States for prevalence and concentration of toxins, and by only 5/27 States for consumption?

The disparity in consumption patterns between those States which responded is striking. Did only 0.6% of Germans consume shellfish in the mid-1980s? Did only 1.1% of Dutch consumers eat shellfish in 1997-98? How credible are consumption data for France when the INCA 1999 survey in France indicates that 11% of consumers eat shellfish while the CALIPSO survey (no date supplied) found 96% did?

7.3 Cryptic presentation of data

Data for consumption and for prevalence and concentration of toxins, would be less cryptic if they were augmented by including the median (in the case of consumption) plus 75th and 90th percentiles. This would allow a reviewer to judge where high-level consumption begins.

For example, it is clear that 2/47 consumers in The Netherlands survey estimated their consumption at 465 g and 480 g (95th and 100th percentile, respectively). Equally, it appears that seven or eight German consumers ate between 400 g and 1,500 g at one sitting.

These few consumers have a great effect on the mean consumption, which is why median consumption would be helpful, as would additional percentiles below the 95th.

7.4 Lack of a reality check on consumption data

It appears that the EFSA panel accepted consumption data at face value. Can it really be accepted that 5% of German consumers eat between 400 g and 1,500 g of shellfish meat at one sitting? The EFSA report states (page 29) that mussel meat weighs between 5 g and 6.5 g/piece) which equates to 62-80 mussels (400 g) and 231-300 (1500 g). These are consumption levels which strain credulity.

The EFSA panel considers it likely that the 1,000 g and 1,500 g maxima are probably shell-on values. So why include them when they shift the 95th percentile towards a much higher consumption level? If the 1,000 g and 1,500 g levels are shell-on – is this also the case for the 95th percentiles of 400 g and 465 g for The Netherlands and Germany, respectively? If these values were divided by five (20% meat weight) the 95th percentiles become 80 g for Germany and 93 g for The Netherlands - the same range as the other 95th percentiles quoted in Table 10.

Given the pivotal importance of the 95th percentile, the panel should have verified the high-end consumption figures reported.

The panel may also wish to reconsider their opinion in light of the recent findings on shellfish consumption reported at the 7th International Conference on Molluscan Shellfish Safety (where, incidentally, the EFSA panel also presented their risk assessments on marine biotoxins). In France, Picot *et al.* (2009) surveyed 500 recreational harvesters by food frequency questionnaire (FFQ) and face-to-face interview. Mean harvest was 11.83 g/day and mean consumption from recreational and retail sources totalled 30.35 g/person/day. The researchers state that recreational harvesters are high consumers of shellfish, consuming almost 16-times more than the general population. The findings of Picot *et al.* (2009) present a reality check worthy of consideration by the EFSA panel.

7.5 Use of biased consumption data

The panel established the 95th percentile from a subset of intake data of 1159 consumers of shellfish for whom percentiles can be calculated (France, Germany, The Netherlands). As stated by the panel's report, the 95th percentile of 400 g was "chosen". A cursory examination of Table 10 indicates that the high portion figure results from intake data of two Dutch plus seven to eight German consumers, some of whom ate up to 1,500 g.

The EFSA panel seeks to justify their "choice" by claiming "good agreement" with the FAO/IOC/WHO figure of 380 g for the 97.5th percentile. However, the FAO/IOC/WHO panel consulted the WHO/GEMS Food database and obtained the highest 97.5th percentile of 380 g for The Netherlands. They also obtained 97.5th percentiles of 133 g (Japan), 181 g (Australia), 225 g (USA), 263 g (New Zealand) and 182 g for the maximum intake in Norway. The FAO/IOC/WHO panel stresses the conservatism in the 380 g high portion and continued their risk assessment simulations by using three intake levels: 100 g, 250 g and 380 g.

In addition, many would query whether a 95th percentile of 400 g and a 97.5th percentile of 380 g represent "good agreement", as claimed by the EFSA panel.

The present bias towards high-end consumption would be removed if the EFSA panel excised obviously "wrong" intakes (1,000 g and 1,500 g) and then generated the 95th percentile from intakes of all 1159 consumers for whom data are available. It is likely that this 95th percentile would be more realistic.

7.6 Use of biased concentration data

As part of the assessment process EFSA requested data on the prevalence and concentration of OA-group toxins in shellfish from all Member States. Ten Member States provided such data, which was taken at various points in the marketing chain, as random and targeted samples and as samples taken when contamination was suspected.

There can be no suggestion that these samples properly represent production and it is highly likely that there is a bias towards sampling stock suspected of containing toxin; the problem is compounded in Table 9 where the 95th percentile is derived.

The present bias towards high-end concentration would be removed if a properly-designed survey of shellfish at the market level were undertaken. In addition, because any revised level is to be applied across 27 Member States and is likely to be adopted by other countries (in order to meet EU import requirements) it seems logical to use as representative a dataset as possible.

7.7 Lack of peer review

It is surprising that EFSA procedures would allow a risk assessment to be published without peer review. By way of comparison, the FAO/WHO "Risk assessment of *Vibrio parahaemolyticus* in raw oysters" was reviewed by twenty peer reviewers from fifteen countries, each of whom was independent of the drafting group. Their comments amounted to 44 pages of A4 paper and each comment required a response by the drafting group. Each response was then transmitted to the reviewer, who was given further opportunity to comment. The review process required by FAO/WHO was arduous but led to significant improvements in the final text.

This review finds it highly likely that the chosen 95th percentiles for consumption and concentration of toxin would have incurred substantial enquiry.

7.8 Epidemiology

Section 11 (Observations in humans) presents a summary of OA-group toxin epidemiology data for the period 1976-2006, in which nine incidents are described involving 780-880 individuals. This represents a known global total over three decades, with most consumers suffering short-term gastro-intestinal symptoms.

The EFSA panel comment that information on doses and profiles in these reports is very limited. In addition, it should be noted, as amplification of the panel's text, that:

- In one of the incidents, 200 individuals were affected following consumption of crustaceans (brown crabs) self-harvested from Norwegian waters. It is questioned

whether this information is relevant to the EFSA brief since EU Directive 2002/225/EC does not regulate DSP toxins in crustaceans.

- It is possible that incidents may have occurred in an era before shellfish management plans had been implemented (e.g. in Japan in 1976-77).
- In another incident, to celebrate the opening of a new mussel farm in Norway in 2001, more than half of the seventy guests developed DSP symptoms. The comment by Aune *et al*. (2001) that "the organisers were warned about the risk" points to a lack of adherence to normal biotoxin management systems.
- Other incidents resulted from recreational harvest e.g. in Portugal in 2001, six cases followed consumption of razor clams and one case followed consumption of crabs (COT, 2006).

While the EFSA panel's focus appears to have been on dietary intake of OA-group toxins, the panel should also balance their text by noting whether biotoxin management systems were in place in the incidents they described and whether areas were subjected to voluntary or mandatory closure at the time.

In summary, it may be asked whether a handful of recorded incidents over a 30-year period of global consumption of shellfish, with most suffering relatively mild, short-term symptoms represents such a hazard to necessitate the significant reduction in allowable limit proposed by the EFSA panel.

7.9 Risk estimate used in the study

The EFSA panel made the decision to generate a risk estimate describing the probability of a consumer ingesting more than 96 µg of OA toxins from one serving, based on the 95th percentiles for intake and concentration generated by their study. The chance is 20% which, given the billions of servings of shellfish consumed annually in Europe might be expected to result in a large number of illnesses. That such is not the case reflects the overall fragility of the EFSA opinion.

7.10 Failure to consider the recommendations of the CCFFP working group held in Ottawa in April 2006

The working group made their report to the 28th session of CCFFP held in Beijing in September 2006. It is valuable to quote verbatim (with two sentences highlighted in bold type) their comments and recommendations for no change to the regulatory limit:

OKADAIC ACID (OA) group

35) Summary of Analysis from the Expert Consultation

The Expert Consultation's conclusions were based on real cases of human illnesses. Both Japanese and Norwegian data were used.

36) WG Comment(s)

The WG discussed the action levels used in various countries and the level of consumer protection which they have provided to date. ***The current standard, its practical application***

and demonstrated results indicate that the level of 0.16 mg/kg provides adequate protection for consumers.

The WG noted that the most current procedures, including those to be used in alternative chemical and biochemical methods, include hydrolysis of naturally occurring esters of the OA-group. The toxicity of these substances has proven to be significant and in some cases even the dominant fraction of total OA-group toxicity. This would result in a more relevant and ultimately more conservative strategy than reduction of the action level.

The WG agreed that, where instrumental methods are used, the hydrolysis of naturally occurring esters should be an essential part of the methodology.

37) Recommendation(s)

1. ***The WG recommends that the Codex standard (Section I-5) identify an action level for OA equivalents of 0.16 mg/kg.***
2. *The WG recommends that the Codex standard (Section I-7.7) identify a range of methods available to effectively detect OA, including the mouse bioassay, in vitro functional assays (e.g., PP2A-based assays), ELISA, LC-FL and LC-MS methods as potential alternative approved methods (Type III). These methods should be recommended by CCFFP to the CCMAS for review and designation.*
3. *The WG recommends that Codex standard (Section I-7.7) identify LC-MS method as a potential reference method (Type II).*

8. Conclusions

The EFSA panel has fulfilled all the terms of reference set out by the Requestor and *inter alia*, provided an opinion for a significant reduction in the regulatory limit, from 160 µg OA equivalents/kg of shellfish meat to 45 µg OA equivalents/kg of shellfish meat. Pivotal to the suggested reduction were the choice of 95th percentile levels for concentration (240 µg OA equivalents/kg shellfish meat) and intake (400 g). Criticism of the data from which these values were derived and of the panel's approach to setting them has been detailed in Section 7 of this review.

Clearly, if the European Commission were to accept the opinion of the EFSA panel there would be significant impact on the global shellfish industry. But there seems little evidence that public health, either in the EU or globally, is much affected by OA contamination of shellfish. It is true that nine incidents were cited over a 30-year period by the EFSA panel and it is equally true that other incidents will have gone undetected. But a risk assessment which asks for an estimate of annual cases of DSP expected in the EU should precede any change to regulatory limit. It goes without saying that such a risk assessment would have high-quality exposure data: a market survey of prevalence/concentration of OA-group toxins coupled with up-to-date intake data. The present EFSA opinion can claim neither of these prerequisites and it is instructive that the Codex Committee on Fish and Fishery Products recommends no change to regulatory levels for OA-group toxins.

This review aligns with the recommendations of the CCFFP.

References

Anonymous. 2008. Marine biotoxins in shellfish – okadaic acid and analogues: Scientific opinion of the panel on contamination in the food chain. The EFSA Journal, 589:1-62.

Aune, T., Torgersen, T., Aasen, J., Castberg, T., Naustvolt, L-J. and Woll, A. 2006. Risk assessment of DSP toxins in brown crabs (*Cancer pagurus*). In: Proceedings, 5th International Conference on Molluscan Shellfish Safety. Galway, June 2004.

COT (Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment. Statement on risk assessment of marine biotoxins of the okadaic acid, pectenotoxin, azaspiracid and yessotoxin groups in support of human health. Available at URL: http://www.food.gov.uk/multimedia/pdfs/cotstatementlipophilic200616.pdf

Picot, C., Nguyen, T., Carpentier, Roudot, A. and Parent-Massin, D. 2009. A shellfish consumption survey in recreational harvesters in Brittany (France). Proceedings, 7th International Conference on Molluscan Shellfish Safety. Nantes, June 2009.

Acknowledgment

This review was supported by funding from the Australian Seafood Cooperative Research Centre (CRC). The CRC receives funding from the Australian seafood industry and from the Australian Federal and State governments.

Review Panel

Dr Andreas Kiermeier is the Program Leader of the South Australian Research and Development Institute's Food Safety Research Program and an Honorary Senior Lecturer with the University of South Australia. In 2008 he led a review of the Victorian Shellfish Quality Assurance Program (Australia).

Dr Catherine McLeod is a Senior Scientist (Shellfish Safety) at the South Australian Research and Development Institute and an Honorary Research Associate at the University of Tasmania. She currently leads a research programme focused on the food safety of shellfish, including risk assessment of saxitoxins in Australian abalone.

Dr John Sumner is an Honorary Research Professor at University of Tasmania, Australia. He is a member of the FAO/WHO drafting group on microbial risk assessment "Vibrios in seafoods", a consultant to Fisheries Division, United Nations Food and Agriculture Organisation, Rome and undertook the Australian National Seafood Risk Assessment.