CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 7 **CX/FFP 12/32/7-Add.1**

ORIGINAL LANGUAGE ONLY

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FISH AND FISHERY PRODUCTS

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1 – 5 October 2012

Proposed Draft Performance Criteria for Reference and Confirmatory Methods for Marine Biotoxins in the *Standard for Raw and Live Bivalve Molluscs*

COMMENTS AT STEP 3

(Australia and Canada)

AUSTRALIA

General Comments

Australia recognises that there has been considerable comment received on the proposed performance criteria for biotoxins methods and thanks Canada for their co-ordination of the eWG.

Australia believes that the background and general proposed performance criteria/principles should remain in this draft document. However they are not suitable for inclusion in the standard. It should be made clear what is proposed to be inserted into section 1.8.6 of the standard.

Australia suggests that Section 1.8.6 should include:

a. "General method principles and performance criteria as outlined below are determined from the *Codex Alimentarius Commission PROCEDURAL MANUAL, 19th ed."*
b. The general criteria statements as outlined
c. Table 1
d. Guidance on Toxin Equivalency Factors. Australia would prefer not to list any factors, but use a statement such as "Where methods are used that detect multiple toxin analogues, the competent authority should use internationally acknowledged TEF's." A footnote should be inserted to refer to the WHO/FAO website that CCFFP has been advised could be set up listing this factors and other biotoxin method selection information.

Australia would also recommend that guidance is added on an appropriate sampling plan for biotoxins in the standard (note: Section 1.8.6 is not the appropriate place for this advice).

Specific Comments

a) Title

Australia recommends that the following amendments be made to the title:

'Proposed Draft performance criteria for ~~Reference and Confirmatory Methods~~ **approved (Type II and Type III) methods** for marine biotoxins for inclusion in Section I-8.6 in the Standard for raw and live bivalve molluscs.'

Rationale:

1. *To align with reference (type II) and alternative approved methods (type III) as defined in the procedural manual*
2. *This approach gives flexibility for countries to choose their own methods as long as they meet the criteria.*

b) Background

Australia recommends that the following amendments to the text are made:

- 'In view of the difficulties this would present, described below are the proposed general performance criteria and principles ~~for reference methods~~[1] that can be used by competent authorities to select methods that are adequate for monitoring biotoxins for regulatory purposes.'
- *Remove the associated footnote relating to reference methods.*

  ~~'Reference method: Quantitative analytical method of proven reliability characterised by well-established trueness, specificity, precision and detection power. These methods generally haven't been collaboratively studied and are usually based on molecular spectrometry. The reference method status is only valid if the method is implemented under an appropriate QA regime. (Guidelines on Good Laboratory Practice in Residue Analysis CAC/GL 40-1993, Rev.1-2003).'~~

- 'Competent authorities considering the use of a particular method may utilize a screening method as a complement to reference approved methods to gain efficiencies for routine biotoxin monitoring. Competent authorities should evaluate their entire biotoxin testing strategy against the performance criteria outlined herein.'

Rationale:

1. *'Reference' is no longer necessary if the change to the title is accepted.*
2. *Australia deems that evaluating the biotoxin testing strategy against the performance criteria in the document is an unnecessary statement*

c) 'Method Performance Parameters for Marine Biotoxin Methods' Table

- *Australia recommends that the title is changed to the following:*

  'Numerical Criteria values for biotoxins in bivalve shellfish'

  Rationale: to align with the example given in the Codex Procedural Manual
- *Australia recommends that the minimum range for STX is amended to the following:*

  Minimum range of STX is changed from ~~0.26-1.34~~ to **0.4 - 1.2**.

  Rationale: the current value is incorrect as calculated using the procedural manual. This is in agreement with several earlier country comments.

- *Australia recommends that the numerical criteria associated with the individual analogues in Table 1 be removed.*

  Rationale: there can only be criteria developed where a maximum allowable level exists. No such levels exist for individual analogues.

- *Australia recommends that N-sulfocarbomoyl-gonyautoxin-1 (C3) and N-sulfocarbomoyl-gonyautoxin-4 (C4) are added to the the saxitoxin group.*

  Rationale: Although C3 and C4 toxins are of low potency they contribute significantly to the total saxitoxin toxicity in some growing areas.

CANADA

SPECIFIC COMMENTS

1. Canada supports insertion of the proposed text (submitted by the e-WG on reference and confirmatory methods) into section I-8.6. In addition, as there can only be criteria if there is a maximum limit in Codex, Canada would revise the Table originally submitted as Appendix I by the e-WG. Canada

proposes this section be revised to read as follows:

I-8.6 Determination of Biotoxins

~~Provision~~	~~Methodology~~	~~Principle~~	~~Type~~
~~Saxitoxin Group~~	~~AOAC Official Method 2005.6 (Paralytic Shellfish Poisoning Toxins in Shellfish) four matrices and 12 toxins~~	~~LC FL~~	~~II~~

General method principles and performance criteria (General Criteria) are outlined in the Codex Alimentarius Commission PROCEDURAL MANUAL, in the PRINCIPLES FOR THE ESTABLISHMENT OF CODEX METHODS OF ANALYSIS section. Analytical terms are further defined in the Codex document Guidelines on Analytical Terminology (CAC/GL 72-2009). The competent authority is advised to refer to these documents when considering the following marine biotoxin method principles and criteria.

The following marine biotoxin principles and method criteria are a specific application of the General Criteria. The marine biotoxin principles and method criteria, outlined in the Table Appendix I: Method Performance Parameters for Marine Biotoxin Methods, are to be considered by the competent authority to be inclusive of analytic approach.

(a) Selectivity

(i) Group specific i.e., the method used should be applicable to the appropriate toxin group it is testing.

(ii) Preference should be given to methods that can be used to test multiple toxin analogues and, when applicable, multiple toxin groups.

(b) Trueness and Recovery

(i) Group trueness i.e., differences in recovery may exist but is acceptable if the overall trueness (to estimate toxicity) is correct.

(ii) Preference should be given to methods that minimize bias and have minimized recovery corrections.

(c) Precision

(i) Methods that have undergone inter-laboratory or collaborative studies based on internationally recognized protocols (such as AOAC International or Codex GL 64) are preferred.

(ii) Consideration should be given to intra-laboratory or single lab validation studies, using internationally accepted validation protocols or guidelines, which may have been published in peer reviewed journals.

(d) Detection Capability

(i) Methods should be sufficiently capable to detect the named biotoxin components at the performance limits outlined in Appendix I.

(ii) Preference should be given to methods with detection limits less than in (i) thereby providing an early warning.

(e) Quantification

(i) Methods that detect groups of analogues should be capable of estimating total toxicity.

(ii) Preference should be given to methods that can provide biotoxin profile information and should be given to methods that can provide quantitative information.

(f) Scope

(i) The relative toxicity of structural analogues should be considered when determining method performance requirements. Preference should be given to methods that express the values in terms of relative toxicity.

(ii) Preference should be given to methods that detect a greater number of biotoxin analogues within a particular group.

(g) Measurement Uncertainty

(i) The measurement uncertainty associated with all analytical results should be estimated

Appendix I

Method performance parameters for marine biotoxin methods

Toxin Group	Toxin	Units	Maximum Level	Minimum Range	Limit of Detection	Limit of Quantification	Precision at ML	Recovery	Trueness
Saxitoxin	Total toxicity	Mg STXdiHCl eq/kg	0.8	0.24 – 1.36	0.08	0.16	≤ 44%	80-110%	CRM
Domoic Acid	Domoic acid	Mg DA/kg	20	13.2 – 26.8	2	4	≤ 22%	80-110%	CRM
Okadaic Acid	Total toxicity	Mg OA eq/kg	0.16	0.09-0.23	0.016	0.032	≤ 44 %	80-110%	CRM
Azaspiracids	Total toxicity	mg AZA1 eq/kg	0.16	0.09-0.23	0.016	0.032	≤ 44 %	80-110%	CRM
Brevetoxin	Total toxicity	Mg/kg PbTx-2 eq							

2. However, should there be considerable and varied discussion/positions within the Committee on this matter and indications that full agreement would necessitate significant further work, Canada offers an alternative approach for consideration by the Committee. This option would involve this work on developing criteria being put on hold and sections I-5.2 and I-8.6 being revised in a manner similar to what is proposed below.

Reason: While Canada recognizes that significant work has been accomplished to date, with considerable discussion within the e-WG, Canada is of the view that it may be premature to attempt to finalize such a document at this time. There is significant work underway by AOAC and ISO to draft guidelines for the validation of alternative or qualitative methods. In addition, CCMAS itself is discussing how best to adapt and apply the criteria approach to methods. In the future, these two bodies of work would likely be of value to CCFFP in developing suitable method criteria.

Canada also recognizes that there may be a need for further guidance for some competent authorities in choosing appropriate methods. And for this reason, Canada is of the opinion that there are still enhancements that can be made to sections I-5.2 and I-8.6.

Regarding Section I-5.2, it was clear from the discussion within this e-WG that a common understanding on the specific toxins/ analogs of interest for each toxin group was critical. This is a key component needing clarity in the context of choosing a suitable method for regulatory use. Including the e-WG list of analogues into section I-5.2 of the standard would provide added and useful guidance.

Regarding section I-8.6, the suggested wording provides reference to method guidance found in the Procedural Manual of Codex Alimentarius Commission (20th edition), which provides generic criteria for the selection of methods.

Revised to Read:

I-5.2 The following provisions apply to the edible parts of live bivalve mollusc (the whole part or any part intended to be eaten separately).

Name of Biotoxin Group	**Toxins**	Maximum Level/Kg of mollusc flesh
Saxitoxin Group	**Saxitoxin (STX)**	0.8 mg STXdiHCl eq/kg
	Neosaxitoxin (NEO)	
	Decarbamoyl-saxitoxin (dcSTX)	
	Decarbamoyl-neosaxitoxin (dcNEO)	
	Gonyautoxin-1 (GTX1)	
	Gonyautoxin-4 (GTX4)	
	Gonyautoxin-3 (GTX3)	
	Gonyautoxin-2 (GTX2)	
	Gonyautoxin-5 (GTX5)	
	Gonyautoxin-6 (GTX6)	
	Decarbamoyl-gonyautoxin-2 (dcGTX2)	
	Decarbamoyl-gonyautoxin-3 (dcGTX3)	
	N-sulfocarbamoyl-gonyautoxin-2 (C1)	
	N-sulfocarbamoyl-gonyautoxin-3 (C2)	
Domoic Acid	**Domoic Acid (DA)**	**20 mg DA/kg**

Group	**epi-Domoic Acid (epiDA)** [1]	
Okadaic Acid Group	**Total Toxicity**	**0.16 mg OA eq/kg**
	Okadaic Acid (OA)	
	Dinophysistoxin-1 (DTX1)	
	Dinophysistoxin-2 (DTX2)	
	Esters of OA, DTX1 and DTX2 (FA-ESTERS) [2]	
Azaspiracids Group	**Total Toxicity**	**0.16 mg AZA1 eq/kg**
	Azaspiracid-1 (AZA1)	
	Azaspiracid-2 (AZA2)	
	Azaspiracid-3 (AZA3)	
Brevetoxin Group	**Total Toxicity**	**0.8 mg/kg PbTx-2 eq**
	Brevetoxin-1 (BTX1)	
	Brevetoxin-2 (BTX2)	
	Brevetoxin-1 derivatives (devBTX1)	
	Brevetoxin-2 derivatives (devBTX2)	

[1] Method should detect this analyte

[2] Method should detect this analyte directly or after hydrolysis

I-8.6 Determination of Biotoxins

There are a range of qualitative and quantitative methods available and suitable for regulatory use. Competent authorities should select appropriate qualitative and/or quantitative methods in accordance with the General method principles and performance criteria (General Criteria) outlined in the Codex Alimentarius Commission PROCEDURAL MANUAL, in the PRINCIPLES FOR THE ESTABLISHMENT OF CODEX METHODS OF ANALYSIS section. Codex has reviewed and endorsed the following method specific to the Saxitoxin group.

Provision	Methodology	Principle	Type
Saxitoxin Group	AOAC Official Method 2005.6 (Paralytic Shellfish Poisoning Toxins in Shellfish) four matrices and 12 toxins	LC-FL	II