CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 2b) **CX/FFP 12/32/2-Add.1**

JOINT FAO/WHO FOOD STANDARDS PROGRAMME
CODEX COMMITTEE ON FISH AND FISHERY PRODUCTS

Thirty-second Session
Bali, Indonesia
October 2012

MATTERS ARISING FROM THE WORK OF FAO AND WHO

Prepared by FAO and WHO

***Salmonella* in bivalve molluscs**:

1. FAO/WHO had presented an interim report of an Electronic Expert Group on *Salmonella* in bivalves to the 31st Session of Codex Committee on Fish and Fishery Products. A physical meeting of the Expert Group was held at Ottawa, Canada during 20-21 October 2011 to review any additional data available, finalise the analysis and provide a final response to the question posed by the CCFFP. The expert meeting concluded the following:

a. Is there a significant public health risk associated with *Salmonella* in live bivalve molluscs?

A: While bivalve molluscs are known to concentrate pathogenic microorganisms that may be present in their environments, there is little epidemiological evidence of a strong association between bivalve molluscs and salmonellosis for bivalves harvested from areas that are managed for harvesting for direct human consumption (HDHC) by shellfish sanitation programs. In regions of the world where live bivalve molluscs are consumed as a ready-to-eat food, approximately 0.5% to 2% of samples from areas managed for HDHC test positive for *Salmonella*. Despite this, there is little evidence of salmonellosis from bivalves harvested from those areas, though a few outbreaks (in the order of one every few years) and usually involving relatively small numbers (<10) of consumers have been reported.

From the available evidence, it is concluded that live bivalve molluscs harvested from HDHC areas, e.g., managed by shellfish sanitation programs, do not cause frequent outbreaks of salmonellosis.

b. Is the existing Codex microbiological criterion and accompanying sampling plan for *Salmonella* in bivalve molluscs meaningful for public health protection?

A: Two approaches were taken to provide an answer to this question. The first was to compare actual data for parallel testing of both *Escherichia coli* and *Salmonella* prevalence in bivalve molluscs. Specifically, for the data evaluated, *Salmonella* testing in addition to *E. coli t*esting would have increased the number of unacceptable lots detected from 9 to 9.5%. Thus, routine monitoring for *Salmonella* appears to add little further health protection above that which is currently achieved by shellfish sanitation programs, such as those recommended by the Codex *Code of Practice for Fish and Fishery Products* (CAC/RCP 52-2003). Furthermore, on the assumption that faecal indicator criteria provide public health protection against a range of enteric pathogens, the public health benefit of testing specifically for *Salmonella* in bivalves harvested from areas managed for HDHC, is further limited.

The first approach was based on limited data. A second, theoretical, approach was used to analyze the performance of the sampling plan associated with the current microbiological criterion for *Salmonella*. It can be shown that the $n = 5$, $c = 10$, absence in 25 g, sampling scheme cannot reliably (i.e., 95% confidence) detect contamination levels in a lot that have less than 2 to 5 *Salmonella* cells per 200g serving (depending on credible assumptions about the composition of a lot, the compositing of samples, and the distribution of *Salmonella* within a lot). According to the FAO/WHO dose-response

model for *Salmonella*, the probability of illness from ingesting 2 cells of *Salmonella* is predicted to be ~1 in 200[1]. Thus, the sampling plan at best only provides assurance that risk of illness ***will not be greater than*** one in ~200 servings. That probability of salmonellosis is much higher than the frequency that is currently observed from the consumption of live/raw bivalve molluscs. Thus, this second approach also suggests that the existing *Salmonella* criterion provides little or no additional protection from salmonellosis above that which is achieved by current risk management strategies.

2. The conclusions of the expert meeting are included in Annex 1. A technical report which provides a full analysis of the information behind these conclusions is currently under preparation.

[1] The value 1 in 200 should not be understood as a risk estimate for *Salmonella* in bivalves. It only describes the upperbound estimate of risk for a serving from a lot where the ONLY information available on the lot is that it is deemed acceptable by the n=5 (no composting) absence in 25g test.

Vibrio spp in bivalve molluscs:

3. The 42nd Session of the CCFH requested FAO/WHO to continue the work in four steps:

- Step 1: Provide recommendations on a range of test methods for quantifying *V. parahaemolyticus* (total and pathogenic (e.g. *tdh*+, *trh*+) and *V. vulnificus* in seawater and bivalves and facilitate performance evaluation of the proposed methodologies;
- Step 2: Develop data collection strategies (that would facilitate the collection of data) by countries to support the modification/development of models with a broader scope than those which currently exist;
- Step 3: Encourage the collection of data in different regions, in different bivalve species and for geographically diverse strains of pathogenic *V. parahaemolyticus* and *V. vulnificus* according to the data collection strategy and using recommended test methods; and
- Step 4: To modify/develop risk assessment models that could be used to address a range of risk management questions in a number of different regions and products, when adequate data becomes available.

4. An expert meeting was organised in Ottawa, Canada on October 17-19, 2011 to (a) identify possible end uses of *Vibrio* methodologies (b) look at the performance characteristics of available methods and provide recommendations on the requirements for different end uses (c) provide recommendations for collection of data to support national/regional risk assessments. The output of this Expert Meeting and subsequent discussions are being used to develop a "Guidance document" addressing performance characteristics of *Vibrio* methodology and approaches for data collection.

5. As a follow up to this and in starting to address step 3 above, a Regional training Workshop for Asia on *Vibrio* methodologies is scheduled to be held in Singapore during November 19-23, 2012. This is being implemented with support of the International Life Sciences Institute (ILSI). About 14 countries are expected to participate in the training with the expectation that some of the participating countries will use this training to support data collection pertaining to bivalve species produced there.

6. FAO/WHO recognise the need to organise such training in other regions and are actively seeking resources to facilitate this and welcome any support that Members can provide.

Histamine in fish and fishery products

7. During the 31st Session of CCFFP, the Committee accepted FAO/WHO's offer to provide scientific support in addressing the issue of histamine criteria in various fish and fishery products, examining their public health and trade impacts. To facilitate this, FAO/WHO implemented a joint Expert Meeting on the Public Health Risks of Histamine and other Biogenic Amines from Fish and Fishery Products in Rome on 23-27 July, 2012.

8. Currently, Codex standards include histamine criteria under two sections (a) decomposition and (b) hygiene and handling. The meeting concluded that while sensory evaluation remains a highly useful tool for quality control programs, acceptable sensory quality cannot be taken as final assurance of low histamine, nor can low histamine be taken as final assurance that fish is not decomposed. In view of this, the expert meeting decided to focus their advice on histamine limits and related sampling plans to those focused on consumer protection.

9. The meeting concluded that a dose of 50 mg histamine is the no-observed-adverse-effect level (NOAEL) that could be used as the appropriate hazard level and based on a serving size of 250g, calculated the maximum concentration of histamine in a serving that would not cause adverse effect to be 200 mg/kg. Based on data made available by industry, the meeting noted that when food business operators apply good hygienic practices (GHP) and HACCP, an achievable level of histamine in fish products was lower than 15 mg/kg. Since the problem is related to only fish with high histidine levels and the information on the fish species likely to be involved would be important for risk management, the meeting developed the most comprehensive list to date of fish associated with SFP based on data from different parts of the world.

10. The expert meeting concluded that the risk from SFP is best mitigated by applying basic GHPs and where feasible, a HACCP system. Appropriate sampling plans and testing for histamine should be used to validate the HACCP systems, verify the effectiveness of control measures, and detect failures in the system. In order to provide more explicit guidance on sampling approaches, the meeting analysed a range of sampling plans implemented under different scenarios of histamine levels as defined by mean and standard deviation and presented examples of attributes sampling plans appropriate to different levels of tolerance for samples above 200 mg/kg, and for different assumptions about the standard deviation of histamine concentration within lots. The spread of contamination levels in the batch (i.e., standard deviation of contamination levels) has a strong effect on the tolerable average contamination level and, thus, on the number of samples that must be tested to 'accept' the batch. Appropriate selection of the criterion against which test units comprising the sample will be assessed for compliance (m value), can considerably improve the time- and cost-effectiveness of sampling – requiring the least number of samples to be tested to achieve the same level of confidence about the disposition of the lot being assessed.

11. The Executive Summary of the report has been included in Annex II and the final report that will be subjected to editing and formatting is available at http://www.fao.org/fileadmin/user_upload/agns/pdf/FAO-WHO_Expert_Meeting_Histamine.pdf.

Annex 1

Conclusions of the Expert meeting on *Salmonella in bivalve molluscs*

1. There are many potential sources of *Salmonella* contamination in the growing waters of bivalve molluscs, including commercial growing areas. Measures to completely prevent the sporadic occurrence of *Salmonella* in bivalve molluscs are not currently achievable.

2. Environmental parameters such as temperature and salinity are not predictive of *Salmonella* contamination in a growing or harvest area.

3. There is, however, a relationship between the concentration of *E. coli* in a bivalve mollusc sample and the likelihood that it will be positive for *Salmonell*a, although the relationship, and strength of relationship, varies with country and region.

4. In areas that are managed by sanitary surveys and faecal indicator monitoring, the prevalence of *Salmonella* decreases with stringency of classification status. This suggests that HDHC area management based on sanitary surveys and testing for faecal indicator organisms can be an effective means of reducing the risk of salmonellosis associated with consumptions of live/raw bivalve molluscs.

5. Based on available data, the frequency of contamination/detection of *Salmonella* in bivalves sampled from the market and harvested from an area managed for HDHC is 0.5 to 2%.

6. Routine sampling of oysters and large clams usually involves compositing multiple animals into a single sample. As a result, a sample of n=1 may constitute an effective sample of between 10 and 20 animals. Similarly, n=5 may constitute a sample of between 50 and 100 animals. Compositing can dramatically increases the effective sensitivity of the test, depending on:

i) the compositing ratio, and

ii) the level of contamination of the most contaminated animal in each sample.

As such, the sampling plan will either provide very little information (n=5, no compositing, very few detections), or ambiguous information (n=5, with compositing, unclear separation of lots according to risk).

7. Compliance of a sample of bivalves molluscs with a n = 5, c = 0, m = 0/25 g sampling plan theoretically provides 95% confidence that the concentration is less than 2 to 5 cells per 200 g. Based on the FAO/WHO (2002) dose-response model for human salmonellosis, this contamination level corresponds to an approximately 1 in 200 chance of illness from consumption of a bivalve molluscs meal of 200g. In other words, the current criterion can, at best, only provide assurance that the probability of salmonellosis will not be greater than 1 in 200. This assumes that the test method can reliably detect 1 cell in 25 g. In practice, the performance of available test methods is less than that (perhaps only 5 cells per 25 g), i.e., the actual sensitivity of the sampling plan may be up to five-fold lower than the theoretical level.

8. The conclusion in Pt. 7 will be affected by the potential for growth of *Salmonella* in bivalves after harvest. If growth occurred that led to a 10-fold increase in the level of *Salmonella* at the time of consumption compared to the time of testing, the sampling plan provides 95% assurance only that the risk of salmonellosis per bivalve meal from that batch is less than 1 in 20 servings. Data to quantify the likely extent of *Salmonella* growth in bivalves after harvest are not available currently. Other data for prevalence of *Salmonella* at harvest or at market suggest that growth is uncommon and that *inactivation* of *Salmonella* in harvested bivalve molluscs can occur under some circumstances.

9. As inferred in Pt. 6, the predicted efficacy of the sampling plan will be affected by the variability in contamination levels within and between growing areas. The data currently available do not allow the overall effect on efficacy to be determined.

10. It should be noted that testing for faecal indicator organisms provides broad protection from contamination from a variety of enteric pathogens, including *Salmonella*. The incremental value of testing for other pathogens would need to be similarly considered given the primary screening that is provided by the faecal indicator testing.

Annex II

EXECUTIVE SUMMARY OF THE JOINT FAO/WHO EXPERT MEETING ON THE PUBLIC HEALTH RISKS OF HISTAMINE AND OTHER BIOGENIC AMINES FROM FISH AND FISHERY PRODUCTS, JULY 23-27, 2012

1. Scombrotoxin fish poisoning (SFP) (often called "histamine poisoning") is caused by ingestion of certain species of marine fish that contain high levels of histamine and possibly other biogenic amines. Codex Alimentarius through its standards and guidelines aims to provide countries with the basis for which to manage issues such as histamine formation. Several of the existing standards include maximum levels for histamine in different fish and fishery products. The need to harmonize such limits and ensure the associated guidance on the relevant sampling plans and other aspects of sampling resulted in the 31st Session of the Codex Committee on Fish and Fishery Products (CCFFP) agreeing to look into the issue of histamine limits in more detail. The Committee established an electronic Working Group in order to facilitate this work and identified the need for scientific advice from FAO and WHO to support this work.

2. FAO and WHO convened an expert meeting at the FAO headquarters in Rome from 23 – 27 July 2012 to address the public health risks of histamine and other biogenic amines from fish and fishery products. This report summarises the outcome of that meeting.

3. Histamine is produced by bacterial actions, e.g. spoilage and fermentation, in fish species which have a naturally high level of the amino acid histidine. Generally, this takes place at a temperature of more than 25° C over a period of more than 6 hours or for longer at lower abuse temperatures.

4. A hazard identification, where all biogenic amines were considered, concluded that there is compelling evidence that histamine is the most significant causative agent for SFP and that histamine can be used as an indicator of SFP. There are no difficulties in analysing histamine and a number of suitable methods are available. The different species of fish that are reportedly responsible for SFP were identified including those with a high histidine level which have the potential to cause SFP. Noting, that this information should be easily accessible to support risk-based approaches to SFP management, the expert meeting developed the most comprehensive list of fish associated with SFP to date.

5. The hazard characterization concluded that a dose of 50 mg of histamine, which is the no-observed-adverse-effect level (NOAEL), is the appropriate hazard level. At this level healthy individuals would not be expected to suffer any of the symptoms associated with SFP. Also no cumulative effect for consecutive meals with fish was expected, since histamine usually leaves the body within a few hours.

6. Using the available fish and fishery products consumption data combined with expert opinion the meeting agreed that a serving size of 250 g captured the maximum amount eaten in most countries at a single eating event. Based on the hazard level of 50 mg of histamine and the serving size of 250 g, the maximum concentration of histamine in that serving was consequently calculated to be 200 mg/kg. When food business operators apply good hygienic practices (GHP) and hazard analysis critical control point (HACCP), an achievable level of histamine in fish products was reported to be lower than 15 mg/kg, based on data made available by industry (using a test method with a lower detection limit of 15 mg/kg).

7. Recognizing that the purpose of testing is not to control the problem of SFP, but rather to verify that all the necessary control measures have been effectively implemented, identify failures in the system and remove implicated products from the market, different sampling approaches and associated plans were presented. In order to provide more explicit guidance on sampling approaches the meeting analysed a range of sampling plans implemented under different scenarios of histamine levels as defined by the log-transformed mean and standard deviation. Example of attributes sampling plans appropriate to different levels of tolerance for samples above 200 mg/kg, and for different assumptions about the standard deviation of histamine concentration within lots were presented. The sampling plans shown were two class plans and indicate the number of analytical units required to be tested in order to have 95% confidence that the batch as a whole satisfies the desired specified low proportion of samples (such as 1 in 10000) to exceed 200 mg/kg. The spread of contamination levels in the batch (i.e., the log-transformed standard deviation of contamination levels) has a strong effect on the tolerable average contamination level and, thus, on the number of samples that must be tested to 'accept' the batch. Appropriate selection of the criterion against which test units comprising the sample will be assessed for compliance (m value), can considerably improve the time- and cost-effectiveness of sampling – requiring the least number of samples to be tested to achieve the same level of confidence about the disposition of the lot being assessed.

8. The expert meeting concluded that histamine formation and SFP can be easily controlled. The risk from SFP is best mitigated by applying basic GHPs and where feasible, a HACCP system. Appropriate sampling plans and testing for histamine should be used to validate the HACCP systems, verify the effectiveness of control measures, and detect failures in the system. Sensory evaluation remains a highly useful tool for quality control programs, but acceptable sensory quality cannot be taken as final assurance of low histamine, nor can low histamine be taken as final assurance that fish is not decomposed. As a result the conclusion of the expert meeting was to focus their advice on histamine limits and related sampling plans to those focused on consumer protection.

9. Several areas for which further research will be needed have been identified, including the need to clarify the critical role played by histamine and other biogenic amines in the pathogenesis of SFP.