

CODEX ALIMENTARIUS COMMISSION



Food and Agriculture
Organization of the
United Nations



World Health
Organization

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Agenda Item 7

CX/FH 22/53/7
September 2022

JOINT FAO/WHO FOOD STANDARDS PROGRAMME
CODEx COMMITTEE ON FOOD HYGIENE
Fifty-third Session
San Diego, United States of America
29 November – 2 December 2022 and 8 December 2022

DISCUSSION PAPER ON THE REVISION OF GUIDELINES ON THE APPLICATION OF GENERAL PRINCIPLES OF FOOD HYGIENE TO THE CONTROL OF PATHOGENIC VIBRIO SPECIES IN SEAFOOD (CXG 73-2010)

(Prepared by Japan and New Zealand)

Codex Members and Observers wishing to submit comments on the discussion paper should do so as instructed in CL 2022/49/OCS-FH available on the Codex webpage/Circular Letters 2022

HISTORY

1. The 31st Session of the Codex Alimentarius Commission (CAC) approved the new work proposal submitted by the 39th Session of the Codex Committee on Food Hygiene (CCFH) to elaborate a Code of Hygienic Practice for Pathogenic *Vibrio* Species in Seafood. The drafting work began prior to the CCFH40 with an inter-sessional physical working group (WG) in Japan.
2. At CCFH41, the Committee agreed to forward the renamed Proposed Draft Guidelines on the Application of General Principles of Food Hygiene to the Control of Pathogenic *Vibrio* Species in Seafood to CAC33 for adoption at Step 5/8 (currently CXG 73-2010). In addition, at CCFH40, the Committee agreed to develop an Annex on Control Measures for *Vibrio parahaemolyticus* and *Vibrio vulnificus* in Bivalve Molluscs which CCFH41 recommended for adoption by the CAC at Step 5/8.

CURRENT STATUS

3. Globally, raw shellfish products, represent the most common foodborne source of vibriosis (Newton et al., 2012; Baker-Austin et al., 2018). Over the last decade our understanding of these microorganisms, the risks that they pose, as well as their management continues to evolve. The Joint FAO/WHO Expert Meetings on Microbiological Risk Assessment (MRA) held a meeting on *V. parahaemolyticus* and *V. vulnificus* at the Centre for Environment, Fisheries, and Aquaculture Science (CEFAS), Weymouth, United Kingdom, on 13-15 May 2019 to continue these discussions.
4. The meeting reviewed and updated the existing risk assessment models/tools for *V. parahaemolyticus* and *V. vulnificus* that could be potentially used to address a range of risk management questions in a number of different regions. The report of the 2019 JEMRA meeting was provided in number 35 of the FAO/WHO Microbiological Risk Assessment (MRA) Series titled “Advances in science and risk assessment tools for *Vibrio parahaemolyticus* and *V. vulnificus* associated with seafood: meeting report” (MRA35).¹

ANALYSIS:

5. An analysis was conducted of the current texts in CXG 73-2010 and the scientific advice provided by

¹ FAO and WHO. 2021. Advances in science and risk assessment tools for *Vibrio parahaemolyticus* and *V. vulnificus* associated with seafood. Meeting report. Microbiological Risk Assessment Series No. 35. Rome <https://doi.org/10.4060/cb5834en>

MRA35; the results of this comparison are provided in appendix 1. This analysis identified a number of places where the information provided in CXG 73-2010 could be revised and updated.

RECOMMENDATIONS:

Based on the abovementioned analysis and the potential revisions that have been identified in Appendix 1, it is recommended that CCFH undertake new work to revise and update the appropriate text in CXG 73-2010.

A proposed project document for this work is provided in Appendix 2 for consideration by CCFH53.

APPENDIX 1

Results of the analysis comparing the text from CXG 73-2010 with the report Advances in science and risk assessment tools for *Vibrio parahaemolyticus* and *V. vulnificus* associated with seafood: meeting report (MRA 35)

This Appendix identifies areas of the current CXG 73-2010 text that could be updated and revised to reflect the information provided in MRA 35

Para 1 :

Delete “During the last few years” in the first sentence, Update the contents.

The following information should be added. “The ingestion of a large number of viable cells was thought to be needed for pathogenic *Vibrio* spp. to survive the acidic environment of the stomach and establish an infection. ” There is now recognition that the dose-response may be much lower based on different strains and different virulence profiles, especially with the emergence of highly pathogenic strains.” (cf p.21 MRA35)

Para 5:

The following information should be added: It was previously thought that the ingestion of a large number of cells was needed for pathogenic *Vibrio* spp. to survive the acidic environment of the stomach and establish an infection. However, new and highly pathogenic strains have emerged with a significantly lower infectious dose 50 and different growth characteristics compared to the *V. parahaemolyticus* strains used in the previous risk assessments.

Para 8:

The following information from MRA 35 (page 2) should be integrated in the para 8.

Although detection of tdh- trh- strains among clinical strains has been the source of debate on the pathogenic roles of tdh and trh genes, these genes are still the most appropriate markers of pathogenicity. Other potential markers, such as the type III secretion system (T3SS), have been recognized, perhaps by targeting the cytoskeleton, but their role is not yet fully understood.

Clinical strains of *V. parahaemolyticus* isolated from ill patients tend to produce a variety of recognized virulence factors. Of these, the thermostable direct haemolysin (TDH) (Nishibuchi and Kaper, 1995), responsible for the Kanagawa haemolysis, and the TDH-related haemolysin (TRH) (Honda et al., 1988) are currently the most predictive overall indicators of potential virulence (Baker-Austin et al., 2018; Jones et al., 2012; Pazhana et al., 2014). Most infections are associated with strains that possess these genes, although there are notable published exceptions (Ottaviani et al., 2012). Detection of tdh-trh- strains among clinical strains has been the source of debate on the pathogenic roles of the tdh+ and/or the trh+ genes (FAO/WHO, 2020). Bhoopong et al. (2007) provided solid evidence for the possibility that has long been suspected among clinical microbiologists: the colonies on thiosulphate citrate bile salts sucrose agar (TCBS agar) that are derived from clinical samples may consist of virulent (tdh+ and/or the trh+) and avirulent (tdh-trh-) strains of *V. parahaemolyticus* and accidental isolation of an avirulent (tdh-trh-) strain(s) is actually causing a misleading interpretation of the avirulent (tdh-trh-) strain(s) (FAO/WHO, 2020). Recently, type III secretion systems (T3SS), of which there are two types, have received attention. In particular, those located in the pathogenicity islands associated with the tdh and trh genes are named T3SS2 and are considered to be possible virulence markers (Ceccarelli et al., 2019; Okada et al., 2009). Whole genome sequencing efforts have confirmed that pathogenic isolates of *V. parahaemolyticus* also encode two type III secretion systems (T3SS) (Makino et al., 2003; Richie et al., 2012; Okada et al., 2009) which are multiprotein structures that mediate the translocation of bacterial effector proteins directly into eukaryotic cells (Baker-Austin et al., 2018).

Para 9:

While the pandemic clone ST3 has now spread to countries in at least 5 continents including China, Chile, India, Japan and the Republic of Korea, other pandemic variants have also emerged, such as ST36 (which was identified in the United States of America, Peru, and New Zealand), ST43 and ST636 and have spread rapidly

and globally. In addition, most countries have seen an increase in *V. parahaemolyticus* cases associated with a large genetic diversity of *V. parahaemolyticus* strains.

Para 10

“it is also important to consider post-harvest practices, in particular setting appropriate time-temperature requirements and control measures” should be added.

Para 14

To add: “Recent years have seen an increase in infections associated with these particular strains, and the first outbreak was reported in British Columbia in 2018 with the consumption of herring eggs.” We should consider if we should mention the increase in non O1-non O139 cases and outbreaks, probably related to climate change.

Para 15

Outbreak history and implicated food of food-borne cholera should be reviewed, especially if the statement of “shrimp not linked to cholera outbreaks” is still a relevant statement.

Para 16

Incubation period (26 hours) should be 24 hours.

Add MARTX toxin, RtxA1 information.

The most relevant virulence factors are the capsule and the MARTX toxin (MultiFunctional Autoprocessing Repeat in Toxin), also known as RtxA1 toxin and are involved in sepsis. Other markers could be also used as molecular targets to identify virulent strains, such as the virulence correlated gene (*vcg*) and the pilus-type IV-related gene (*pilF*).

Para 17

The sentence may be deleted, since no further information on biotype 1 is available in the MRA 35.

Para 18

The statement of “outbreak has never been reported.” should be reviewed.

Rationale: There were two outbreaks of *V. vulnificus* in South America, three cases occurring in Peru, without follow-up of the patients (Ibarra et al. 1999) and another outbreak with four cases in Uruguay, as reported by the Ministry of Health in the 2014/2015 summer season in Punta Del Este, resulting in two deaths (Uruguay 2015).

Ref: *Vibrio parahaemolyticus* and *Vibrio vulnificus* in South America: water, seafood and human infections, S.M. Rasz et. al. Journal of Applied Microbiology 121, 1201—1222, 2016

Para 19

Information on virulence correlated gene (*vcg*) (Rosche et al., 2005) and pilus-type IV-related gene *pilF* should be added. Cross references to *par16* should be also added.

Temperature range and salinity range which support growth of *V. vulnificus* should be revised.

“Relaying oysters to high salinity waters (>32 g/l (ppt: parts per thousand) was shown to reduce *V. vulnificus* numbers by 3–4 logs (<10 per g) within 2 weeks.” In the report MRA 35, information on the effects of relaying oyster to *V. vulnificus* was not included.

Para 20

Section 2.2 “2011 RISK ASSESSMENT OF *V. PARAHAEMOLYTICUS* IN SEAFOOD”, Section 2.4 from MRA 35 should be introduced.

Para 21, 22:

No change is needed.

Para 23:

We need to discuss how choleraenic *V. cholerae* should be handled in CXG 73-2010 since information from MRA 35 is very limited.

Para 25:

The definition of “Clean water” should be revised based on the discussions being held to develop the Draft Proposed Guidelines for The Use and Reuse of Water through the electronic working group (Water EWG).

Para 26:

No change is needed.

Para 28:

Pre-harvest time -temperature control could be expanded based on MRA35, page 29

Para 34 and 35:

“clean water” should be discussed and revised if necessary.

Section 4:

No change is needed.

Section 5:

5.2.1 Time and temperature control should be reviewed and revised based on MRA35, page 29

Para 72

This paragraph should be expanded based on information in the “Cryogenic individual quick freezing (IQF) with extended storage” in the MRA35, page 30

Para 73

This paragraph should be expanded based on information in the “High hydrostatic pressure”, “**Low dose gamma radiation Low dose gamma radiation**”, “Mild heat treatment” and “Freezing” in the MRA 35, page 30

Para 74, 75:

No change is needed.

Section 5.5

This section should be reviewed in the light of the ongoing discussion in the CCFH EWG on the safe use and re-use of water.

ANNEX ON THE CONTROL MEASURES FOR *Vibrio parahaemolyticus* and *Vibrio vulnificus* in Bivalve Molluscs

Section 3 should be reviewed and revised based on the information provided in MRA 35.

However, the final decision whether we should keep the Annex 1 should be made during the revision of CXG 73-2010.

A new section on laboratory methods should be considered for inclusion.

PROJECT DOCUMENT

NEW WORK PROPOSAL FOR ON THE REVISION OF GUIDELINES ON THE APPLICATION OF GENERAL PRINCIPLES OF FOOD HYGIENE TO THE CONTROL OF PATHOGENIC VIBRIO SPECIES IN SEAFOOD (CXG 73-2010)**1. Purpose and Scope of the Standard**

The purpose of the work is to revise and update the Guidelines on the Application of General Principles of Food Hygiene to the control of pathogenic *Vibrio* species in seafood (CXG 73-2010) to provide risk management options based on the latest scientific advice from FAO/WHO and to incorporate some relevant aspects of the revision of the General Principles of Food Hygiene (CXG 1-1969)

The intended scope of the guidelines will not be changed from the original guidelines.

2. Relevance and Timeliness

An FAO/WHO expert working meeting² held in 2019 noted several critical developments in the last decade: 1) The emergence of highly pathogenic strains, in particular the Pacific Northwest (PNW) *V. parahaemolyticus* strain (ST36), which have spread to the East coast of the United States of America, Europe, South America and New Zealand. The pandemic spread of these highly pathogenic strains is of global concern for seafood safety. 2) In response to climate change, there has been a significant geographical spread regarding where seafood-associated vibrio infections have been reported, with a general trend in the poleward spread of *V. parahaemolyticus* and *V. vulnificus* cases. Over the last decade in particular, there has been an increase in reported illnesses as well as the geographical spread of foodborne infections associated with these bacteria into regions where reported infections were previously absent. 3) Globally, an increased at-risk population, increased population densities in coastal regions and improvements in diagnosis of infections may also have played a role in accentuating reported cases. 4) A range of new approaches for best practice, such as high pressure treatment, harvesting curfews, relaying and temperature controls appear to offer effective and cost-effective approaches for reducing human health risks postharvest associated with these pathogens. Finally, 5) a range of new methods, such as those utilising genomics and satellite imagery, provide novel means of complementing approaches outlined in previous risk assessment exercises for these globally important foodborne pathogens. New scientific information provided by FAO/WHO justify the need and timeliness of the revision of the Guideline.

New information provided by FAO/WHO can offer significant benefits to competent authorities and food businesses to minimize the risk associated with pathogenic vibrios.

While the fundamental principles in the original document (CXG 73-2010) are likely to largely remain the same, practical guidance covering the specific implementation of control measures will help national competent authorities to reduce the burden of food-borne vibriosis and to ensure fair practice in the international seafood trade.

3. Main aspects to be covered

The new work is intended to update Guidelines on the application of the General Principles of Food Hygiene to the Control of Pathogenic *Vibrio* Species in Seafood based on the latest scientific information. The guidelines will provide guidance on selection of the most appropriate risk management options and risk management tools.

The new work will consider factors relevant to the control of *V. parahaemolyticus* and *V. vulnificus*; including:

- microbiological monitoring methods, particularly molecular-based approaches,
- recently available scientific data, in particular information on new pathogenic strains and their geographical spread and clinical incidence,
- methods for the detection and characterisation of vibrios,
- remote sensing-based techniques to measure variables such as temperature and salinity, climate change,
- practical interventions that can be used to reduce vibriosis risks associated with the consumption of

² FAO and WHO. 2021. Advances in science and risk assessment tools for *Vibrio parahaemolyticus* and *V. vulnificus* associated with seafood. Meeting report. Microbiological Risk Assessment Series No. 35. Rome. <https://doi.org/10.4060/cb5834en>

seafood, include relaying, cooling, post-harvest treatments, etc.

4. An assessment against the *Criteria for the Establishment of Work Priorities*

General Criterion

Consumer protection from the point of view of health, food safety, ensuring fair practices in the food trade and taking into account the identified needs of developing countries

The proposed new work will support competent authorities and food business operators to implement practical interventions that can be used to reduce risk of vibriosis.

Criteria applicable to general subjects

(a) Diversification of national legislations and apparent resultant or potential impediments to international trade.

Additional guidance by Codex might assist countries in amending their legislation to reduce the risk of vibriosis and support fair practice in international seafood trade.

(c) Work already undertaken by other international organizations in this field and/or suggested by the relevant international intergovernmental body(ies).

Codex has already undertaken risk management work on *Vibrio* spp. in seafood.

(e) Consideration of the global magnitude of the problem or issue.

There is some evidence for global spread of pathogenic *Vibrio* strains. Codex guidance is an essential contribution to reducing the global public health burden of vibriosis.

5. Relevance to the Codex strategic objectives

The proposed work is directly related to the purposes of the Codex Alimentarius Commission. Namely, goals one and five of the Codex Strategic Plan 2020-2025, to “Address current, emerging and critical issues in a timely manner” and to “Enhance work management systems and practices that support the efficient and effective achievement of all strategic plan goals”. In particular, this work is relevant to Strategic Objective 1.2 “Prioritize needs and emerging issues” where the outcome is a “Timely Codex response to emerging issues and the needs of members”. This work will address the gap in guidance in particular on the use and consistent application of remote audit and verification systems.

6. Information on the relation between the proposal and other existing Codex documents as well as other ongoing work

The amendment of specific guidance on pathogenic vibrio will complement existing CCFH texts. This includes the General *Principles of Food Hygiene* (CXG 1-1969).

7. Identification of any requirement for and availability of expert scientific advice

Not required at this moment. But during the course of revision, CCFH may need additional scientific advice.

8. Identification of any need for technical input to the standard from external bodies so that this can be planned for

Not required at this time.

9. Proposed timeline for completion of the new work, including the start date, the proposed date for adoption at Step 5, and the proposed date for adoption by the Commission; the time frame for developing a standard should not normally exceed five years.

Subject to the Codex Alimentarius Commission approval at its 46th Session in 2023, it is hoped that the new work can be expedited (i.e. within two sessions of CCFH).