

CODEX ALIMENTARIUS COMMISSION

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DISCUSSION PAPER ON REVISION OF THE *GUIDELINES ON THE APPLICATION OF THE GENERAL PRINCIPLES OF FOOD HYGIENE TO THE CONTROL OF VIRUSES IN FOOD (CXG 79-2012)*

(Prepared by Canada and the Netherlands)

Codex Members and Observers wishing to submit comments on the discussion paper should do so as instructed in CL 2022/50/OCS-FH available on the Codex webpage/Circular Letters 2022

INTRODUCTION

1. At the 51st Session of the Committee on Food Hygiene (CCFH51)¹, the CCFH forward work plan was revised to include the *Guidelines on the Application of General Principles of Food Hygiene to the Control of Viruses in Food (CXG 79-2012)* (hereafter referred to as “the guidelines”) for possible revision based on new information available on norovirus (NoV). Canada, with support from the Netherlands, offered to prepare a discussion paper on the possible revision of the guidelines for consideration by the Committee. Due to the virtual nature of CCFH52 an abridged agenda was proposed. It was decided that new work proposals, including discussion papers, would be considered at CCFH53.

BACKGROUND

2. The primary purpose of the guidelines is to provide direction on how to prevent or minimize the presence of human enteric viruses in foods, more specifically, hepatitis A virus (HAV) and NoV. These guidelines are applicable to all foods, with a focus on ready-to-eat food, from primary production through to consumption, for the control of human enteric viruses.

3. The current guidelines also contain an annex on the *Control of Hepatitis A Virus (HAV) and Norovirus (NoV) in Bivalve Molluscs (Annex I)* and an annex on the *Control of Hepatitis A Virus (HAV) and Norovirus (NoV) in Fresh Produce (Annex II)*. These annexes provide additional recommendations for control of these viruses in specific commodities.

4. During the FAO/WHO Expert meeting on “Viruses in Food”² in 2008, NoV and HAV were determined to be the viruses of greatest concern from a food safety perspective based on the incidence of reported foodborne disease, the severity of disease, including mortality, and their potential for transmission via foods. The food commodities of greatest public health concern were identified as prepared (ready-to-eat) foods, bivalve molluscs, and fresh produce.

¹ REP20/FH paragraph 118

² FAO/WHO [Food and Agriculture Organization of the United Nations/World Health Organization]. 2008. Viruses in Food: Scientific advice to support risk management activities: meeting report. Microbiological Risk Assessment Series. No. 13.

BASIS FOR POSSIBLE REVISIONS OF THE GUIDELINES

Scope

5. *Viruses*: Based on a preliminary review of data compiled by the Public Health Agency of Canada from 2008 to 2020, NoV and HAV continue to be the viruses of greatest concern from a food safety perspective. In addition, hepatitis E cases have been increasing in some countries and studies have identified specific food commodities as vectors of transmission (Di Cola et al., 2021). In Europe, foodborne transmission of hepatitis E virus (HEV) appears to be the major transmission route and hepatitis E cases have been increasing (EFSA, 2017). HEV foodborne outbreaks are mostly linked to undercooked pork liver and pork liver containing products (Di Cola et al., 2021; PAIFOD, 2020). While HEV genotypes 1 and 2 (HEV-1, HEV-2) are transmitted through contaminated water in low- and middle-income countries, genotype 3 (HEV-3) and, in some countries, genotype 4 (HEV-4), are transmitted through zoonotic and foodborne pathways and are more prevalent in high-income countries. Pork and pork products can become contaminated through two routes (i) intrinsic contamination because a pig is systemically infected with HEV-3 and (ii) extrinsic contamination with HEV-3 due to cross contamination with faeces, bile or blood (Bouwknegt et al., 2013). As contamination sources of zoonotic foodborne viruses such as HEV-3 and HEV-4 are different from HAV and NoV, guidelines on prevention and intervention measures specific to HEV-3 and HEV-4 might be needed.

6. *Commodities*: A preliminary review of the publicly available international foodborne outbreak data from 2008 to 2020 identified prepared (ready-to-eat) foods, bivalve molluscs, and fresh produce still to be significant food commodities of public health concern (PAIFOD, 2020). In addition, over the past decade, frozen fruits have been a major vehicle of foodborne illnesses, mainly attributed to HAV and NoV infections (Nasheri et al., 2019; Di Cola et al., 2021). Compared to fresh produce, frozen produce represents an additional public health risk because its long shelf life (two years) allows for prolonged temporal exposure (Ruscher et al., 2020; Bernard et al., 2014). In addition, because frozen produce can be distributed over larger geographical distances, there is the potential for spatially extended virus exposure. Dispersed temporal and spatial exposure can lead to large and diffuse outbreaks that are difficult to trace back. Therefore, additional food commodities might need to be included in the guidelines.

7. Based on this preliminary information, a more in-depth review of the foodborne viruses and relevant food commodities of highest public health concern could be useful to determine if the guidelines would benefit from the addition of new guidance.

Process and disinfection

8. A review of the scientific evidence on the efficacy of interventions in the food continuum would be useful to determine whether there is new information that should be considered for inclusion in the guidelines, such as for process-specific control systems (e.g., time and temperature recommendations for heat treatment), processes for the control of foodborne viruses (e.g., high-pressure processing and cold-plasma), recommendations for surface disinfection, and developments in hand-disinfection and food handler hygiene (Ezzatpanah et al., 2022a; Ezzatpanah et al., 2022b).

Testing of foods for foodborne viruses

9. The introduction section of the guidelines briefly discusses the testing of foods for foodborne viruses:

“Evidence of viral contamination is primarily based on the detection of viral RNA/DNA since many foodborne viruses cannot be reliably cultured in vitro. Quantitative and semi-quantitative real time reverse transcription polymerase chain reaction (real time RT-PCR) methods have been developed for various food/virus combinations that are sensitive and specific. Detection of viral RNA/DNA does not discriminate between infectious and non-infectious virus particles and test results are subject to variability depending on the food product, the distribution of virus within the food matrix and the presence of PCR inhibitors. Importantly, there is a degree of uncertainty as to how the lower limits of detection relate to product safety. Molecular technologies should be fully validated and the intended use and interpretation clearly defined. Ideally, the testing laboratory should be accredited”.

10. Since the 2008 FAO/WHO expert meeting, new detection and quantification methods for enteric viruses (i.e., HAV and NoV) have been developed and validated in interlaboratory studies. Several validated methods are available for the detection of the viral genome in specific food commodities (e.g., oysters, mussels, raspberries and lettuce), including the two-part technical method for the detection (ISO 15216-2:2019) and quantification (ISO 15216-1: 2017) of HAV and NoV in food matrices. This method, however, does not address viral infectivity and does not provide the resolution required for investigating viral foodborne outbreaks or source attribution.

11. Other technical advancements include: integrated methods using RT-PCR detection of viral RNA and cell cultures to prove HAV infectivity (Jiang et al., 2004); methods using intercalating dyes to discriminate between viral genomes originating from infectious or heat-treated viruses (Fraisie et al., 2018; Randazzo et al., 2018); and bead-based methods allowing the isolation of intact viral particles from food (Suresh et al., 2019; Nasheri et al., 2020). These methods are not suitable for routine screening purposes but can be used to assess the potential infectivity of the virus recovered from foods. Digital PCR technology has been reported as an efficient methodology to enable the direct quantification of viruses and could be used to reduce the effect of PCR inhibitors on viral detection (Fraisie et al., 2017; Martin-Latil et al., 2016).

12. Finally, since 2012, research groups have successfully developed *in vitro* cultivation systems for some NoV strains (Jones et al., 2015; Ettayebi et al., 2016; Bhar and Jones, 2019; Estes et al., 2019; Ettayebi et al., 2021). Studies have demonstrated the ability to culture NoVs using stem cell derived human enteroids or B cells, thus presenting the potential to evaluate the infectivity of NoVs without the need to extrapolate from experiments using surrogate viruses. However, there are still many challenges to be resolved with these *in vitro* NoV cultivation systems.

13. Based on this information, a review of the analytical methods for relevant enteric viruses in food commodities could be useful.

Control of HAV and NoV in bivalve molluscs

14. As mentioned in annex I of the guidelines, the main hazard known for the production of bivalve molluscs is microbiological contamination of the waters in which they grow. It is important to ensure the seawater quality of growing areas to prevent or minimize viral contamination of bivalve mollusc growing areas. A sanitary survey of growing areas should be conducted prior to the commencement of growing and/or harvesting operations to provide information on the water quality of growing areas. One of the factors to be addressed during a sanitary survey is existing microbiological data from water quality or shellfish monitoring undertaken in the same or adjacent areas.

15. In the guidelines, it is mentioned that the level of faecal contamination may indicate the potential for the presence of human enteric viruses. Generally, *Escherichia coli*/faecal coliforms are used as indicators of faecal contamination in water. However, it has been reported that the occurrence of human enteric viruses, including NoV, does not correlate well with traditional indicators, such as total coliforms, faecal coliforms or *E. coli* (Baggi et al., 2001; Ottoson et al., 2006).

16. Studies have been conducted on the use of bacteriophages as indicators of human enteric viruses. For example, male-specific coliphages (MSCs) have been suggested as potential surrogates for NoV (Lasobras et al., 1999; Simpson et al., 2003; McMinn et al., 2017). Since the publication of the guidelines in 2012, a meta-analysis of the reduction of NoV and MSC concentrations in wastewater treatment plants (WWTPs) found a significant correlation between the mean log₁₀ reduction of NoV genotype II and MSCs within the same WWTP (Pouillot et al., 2015). This meta-analysis also showed that within WWTPs there is a highly significant correlation between the mean log₁₀ reduction in NoV genotype II and the mean log₁₀ reduction in MSCs. Additionally, the results from a recent quantitative risk assessment of NoV illness from consumption of raw oysters in the United States and in Canada support the potential use of MSCs as a surrogate for NoV contamination of oysters for surveillance or performance objectives (Pouillot et al., 2022). Other published results indicate that coliphage monitoring in water could be a useful approach to prevent NoV contamination in shellfish (Cho et al., 2018). Hodgson et al. (2017) also published a review on bacteriophages as enteric viral indicators in bivalve mollusc management, which discusses the rationale and supporting evidence for using bacteriophages as indicators for the contamination with human enteric viruses in shellfish under a variety of conditions. Moreover, pepper mild mottle virus, a non-enveloped single-stranded RNA virus, may be used as an indicator of human fecal contamination in aquatic environments and water treatment systems (Kitajima et al., 2018; Jafferli et al., 2021).

17. Further, risk assessment models have been developed since the publication of the guidelines, including the quantitative risk models developed by the Joint United States-Canada Risk Assessment on NoV in Bivalve Molluscan Shellfish (Pouillot et al., 2022). The focus of this risk assessment was to illustrate how influencing factors, such as environmental parameters and WWTP types, interact and to characterize the relative order of magnitude of the impact of each parameter on the predicted risk of NoV infection. The region- and season-specific predictions of the model provide risk managers with a better characterization of the risk and the elements that contribute to potential risk of NoV infection.

18. In addition, since the publication of the guidelines, FAO has published *Technical Guidance for the development of the growing area aspects of bivalve mollusc sanitation programmes (2018)*. This technical

guidance aims to facilitate implementation of the *Codex Standard for Live and Raw Bivalve Molluscs* (CODEX STAN 292-2008) as well as guidance for the *Codex Code of Practice for Fish and Fishery Products*.

19. Based on this preliminary information, a review of the scientific evidence on the potential utility of viral indicators or other indicators of contamination could be useful. In addition, a review of the various risk assessment models with a view towards constructing more applicable models for wide use among member countries, including a simplified risk calculator, could be explored.

Control of HAV and NoV in fresh produce

20. As mentioned in Annex II of the guidelines, fresh produce may become contaminated with viruses through contact with contaminated water or infected food handlers. If virus-contaminated fresh produce is then chilled to be sold as frozen product, it may lead to outbreaks that are geographically and temporally dispersed. The current guidelines do not provide specific criteria on the required water quality. A risk-based approach and assessment of the fitness of the water for the purpose intended could be articulated for more clarity (FAO and WHO, 2019). Therefore, the ongoing CCFH work on the draft *Guidelines for the safe use and reuse of water in food production* as well as the reports from the JEMRA meetings on the prevention and control of microbiological hazards in fresh fruits and vegetables (part 1, 2, 3 and 4) should be taken into account if the guidelines for the control of viruses are updated.

RECOMMENDATION

21. CCFH is invited to consider the above information and determine whether additional information from JEMRA is required on one or more of the following elements listed below, to be used as basis to determine if new work on the revision of the guidelines is necessary:

- an up-to-date review of the foodborne viruses and relevant food commodities of highest public health concern;
- a review of the scientific evidence on prevention and intervention measures and the efficacy of interventions in the food continuum;
- a review of the analytical methods for relevant enteric viruses in food commodities;
- a review of scientific evidence on the potential utility of viral indicators or other indicators of contamination; and
- a review of the various risk assessment models with a view towards constructing more applicable models for wide use among member countries, including a simplified risk calculator.

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