

Japan's comments on the Report of the meeting of the OIE Aquatic Animal Health Standards Commission in September 2021

(Annex 20) Infection with koi herpesvirus

Table 4.1. OIE recommended diagnostic methods and their level of validation for surveillance of apparently healthy animals and investigation of clinically affected animals

[illegible]

(Comments)

Because of the following reasons, Japan would like to request the rationale for the validation of conventional nested PCR being rated Lv1, "++" and "+++" in Table 4.1.. Japan is not content with the current draft.

The drafted validation for the conventional nested PCR seems to refer to the PCR method reported by Englesma et al. (2013), and Engelsma et al. (2013), which do not report specificity and sensitivity of the assay. According to the OIE Manual 2019, Lv 1 requires “Analytical specificity (2.1.2.)” and “Analytical sensitivity (2.1.3)”. Therefore, Japan considers lower score namely one plus (“+”), which is “May be used in some situations, but cost, reliability, lack of validation or other factors severely limits its application”, should be appropriate for the conventional nested PCR.

However, the drafted validations for the method are "++" and "+++" which indicate “Suitable method(s) but may need further validation” and “Recommended method(s) validated for the purpose shown and usually to stage 3 of the OIE Validation Pathway” respectively.

If the OIE drafted the validations based on the other scientific documents, please show all of them for re-evaluation by all OIE members.

(Reference)

OIE Manual 2019. PRINCIPLES AND METHODS OF VALIDATION OF DIAGNOSTIC ASSAYS FOR INFECTIOUS DISEASES

(https://www.oie.int/fileadmin/Home/eng/Health_standards/aahm/current/chapitre_validation_diagnostics_assays.pdf)

Proposed amendments and comments on (4.4.2. Real-time PCR) (Insertion/~~Deletion~~)

Furthermore, it should be noted that there is evidence that the published conventional PCR and real-time PCR methods, developed for the detection of KHV DNA in fresh tissue samples from clinically diseased carp, fail to detect other strains of cyprinid herpesvirus closely related to koi herpesvirus ~~some KHV genotypes~~ in clinically affected fish (Engelsma et al., 2013). ~~Until this is resolved, in geographic locations where these variants may be present it is highly recommended that the assay described by Engelsma et al. (2013) is used i.e. it is recommended to use the nested or one tube semi-nested PCR assay or increase the cycle number of the single round assay to detect the virus in apparently healthy carriers.~~

(Comments)

Japan would like to suggest replacing “some KHV genotypes” with “other strains of cyprinid herpesvirus closely related to koi herpesvirus”. Also, Japan would like to delete the sentence which starts with “Until this is resolved”. The reasons of these suggestions are follows;

- There is insufficient scientific evidence which supports that the virus reported by Engelsma et al. (2013) is a KHV. The title of the paper (Engelsma et al. 2013) is “Detection of novel strains of cyprinid herpesvirus closely related to koi herpesvirus”, and taxonomic classification of the novel strains of cyprinid herpesvirus is not clear.
- The virus reported by Engelsma et al. (2013) has not been registered in the ICTV, an international database of viruses. In addition, the infectious virus particle has not been isolated from diseased fish and its pathogenicity is unknown.
- The paper (Engelsma et al. 2013) says, “Further sequencing is required to establish the true genetic relationship of the novel strains to CyHV3”, in the results and discussion section of the paper.

Considering the above-mentioned, it is required to collect sufficient information such as the taxonomic classification and pathogenicity before the OIE Manual drafts diagnostic methods for detecting "other strains of cyprinid herpesvirus closely related to koi herpesvirus".

Proposed amendments and comments on (4.4.3. Conventional PCR) (~~Deletion~~)

~~Engelsma et al. (2013) reported that the published single-round PCR methods traditionally thought to be the most sensitive for detection of KHV DNA in fresh tissue samples fail to detect some KHV genotypes in clinically affected fish. Therefore, the assay described by Engelsma et al. (2013) is highly recommended when detecting KHV genotypes. By extending the number of cycles or using the nested second round of amplification the assay may also be suitable to detect virus in sub-clinical carriers. This method and other commonly used PCR protocols are shown in Table 4.4.3.1.~~

(Comments)

Japan would like to suggest deletion of this entire section 4.4.3 and the row for Engelsma et al. (2013) of Table 4.4.3.1.

The reason is as mentioned in our comments on paragraph 4.4.2., namely, there is insufficient scientific evidence which supports the notion that the virus reported by Engelsma et al. (2013) is a KHV.

Proposed amendments and comments on (5. Test(s) recommended for surveillance to demonstrate disease freedom in apparently healthy populations) (Insertion/~~Deletion~~)

Real-time PCR is the recommended test for surveillance in apparently healthy animals to declare freedom from infection with KHV. However, there have been unpublished observations that the method may not detect the other strains of cyprinid herpesvirus closely related to koi herpesvirus KHV-variants that were described by Englesma et al. (2013). ~~In geographic locations where these variants may be present, the conventional nested PCR published by Englesma et al. (2013) should also be considered.~~

(Comments)

Japan would like to propose replacing “KHV variants” with “other strains of cyprinid herpesvirus closely related to koi herpesvirus”. Also, Japan would like to suggest deletion of the sentence starting with “In geographic locations where”.

As mentioned in comments on paragraph 4.4.2. there is insufficient scientific evidence which supports that the virus reported by Englesma et al. (2013) is a KHV. Also, as stated in the title of the paper by Engelsma et al. (2013), their reported virus is not clearly and scientifically classified.

(5. THE OIE AQUATIC ANIMAL HEALTH CODE – 5.2 Text for Member Information)

Proposed comments on 5.2.1.1. Infection with carp edema virus (CEV)

The Commission reviewed the latest scientific evidence and noted that infection with CEV continues to be reported to impact production and cause mortality events in wild and farmed populations but the severity of the impacts is unclear.

The Commission did not agree with a comment that infection with CEV did not meet the definition of an emerging disease, and reiterated that detections of infection with CEV should be reported to the OIE as an emerging disease, in accordance with Article 1.1.4. of the Aquatic Code.

The Commission encouraged Members to investigate mortality and morbidity events in carp, emphasizing that a better understanding of the virus is essential for efforts to control its possible spread and impacts on carp populations.

The Commission will continue to monitor the global situation for infection with CEV and seek further information from scientists working on the disease.

(Comments)

Japan supports the notion that the OIE should collect knowledge on the global situation and scientific evidence in order to clarify the severity of the impact of CEV.

However, because of the following two reasons, Japan considers that CEV does not meet the OIE's definition of an emerging disease and Japan disagrees that CEV is considered an emerging disease. As there is insufficient information on CEV, Japan thinks that information from various countries should be collected by the OIE and then the OIE should scientifically examine it if CEV meets the OIE's definition of an emerging disease.

- The 2021 September report of the OIE Aquatic Commission states that "the severity of the impacts is unclear" for CEV. This indicates that CEV does not meet a condition of "diseases, which have significant impact", which is mentioned in the OIE's definition of emerging diseases.
- In response to the 2021 February report, [Japan has submitted scientific rebuttal to Commission's proposal that CEV would be an emerging disease. However, in the OIE Aquatic Committee's September report, there is no scientific response to Japan's rebuttal.](#) The discussion of whether CEV is an emerging disease is not settled.

Thus, the 2021 September report does not describe any rationales. Japan kindly seeks for not only the Commission's views [but also the rational response.](#)

(Reference 1) OIE's definition of an emerging disease

EMERGING DISEASE

means a disease, other than listed diseases, which has a significant impact on aquatic animal or public health resulting from:

- a) a change of known pathogenic agent or its spread to a new geographic area or species; or
- b) a newly recognized or suspected pathogenic agent.

(Reference 2) Japan's comments on the Report of the meeting of the OIE Aquatic Animal Health Standards Commission in February 2021

Japan expresses our appreciation for providing the list of papers (Annex 8), which are rationales for that the Commission proposes that infection with CEV would be an emerging disease.

However, the papers also indicate that CEV does not meet the OIE's definition* of an emerging disease. Thus Japan reiterates that CEV is not an emerging disease for the following reasons.

- Japan considers that CEV does not meet the condition a) of an emerging disease. Any notable change of CEV has not been reported. Then, the several articles the OIE provided have reported that the CEV has already detected in several geographic regions. For example, 'Carp edema virus from three genogroups is present in common carp in Hungary (ADAMEK et al. 2018)' says, "The hypothesis of a prolonged presence of CEV in European carp populations and suggest that previous outbreaks of KSD were not recorded or misdiagnosed."
- Japan also considers that CEV does not meet the condition b) of emerging diseases. It is true that the number of publications on CEV detection has increased in recent years; however, this is possibly due to the cascading discovery of CEV by researchers who had been previously unaware of its existence and became interested in the disease.
- In fact, according to scientific articles, CEV like virus was detected from archived samples for spring carp mortality syndrome (SCMS) in England in the late 1990s (Way et al. 2015) and in the Netherlands in the early 2000s (Haenen et al. 2016). In addition, this disease was reported as a viral disease for carp since 1970s in some scientific papers. While CEV is detected in several European countries, CEV is not currently included in the EU listed diseases (EU 2018/1882).