REPORT OF THE OIE AD HOC GROUP ON SUSCEPTIBILITY OF MOLLUSC SPECIES TO INFECTION WITH OIE LISTED DISEASES¹

May–June 2021

This report covers the work of the OIE ad hoc Group on Susceptibility of mollusc species to infection with OIE listed diseases (the ad hoc Group) who met electronically between May and June 2021.

The list of participants and the Terms of Reference are presented in Annex I and Annex II, respectively.

Methodology

The ad hoc Group applied criteria, as outlined in Chapter 1.5. Criteria for listing species as susceptible to infection with a specific pathogen of the OIE Aquatic Animal Health Code (the Aquatic Code), to potential host species in order to determine susceptibility to infection with abalone herpesvirus². The assessments were done using a three-stage approach, as outlined in Article 1.5.3. of Chapter 1.5., and further considerations are described below:

1) Stage 1: Criteria to determine whether the route of transmission is consistent with natural pathways for the infection (as described in Article 1.5.4.):

Consideration was given to whether experimental procedures mimic natural pathways for disease transmission. Consideration was also given to environmental factors given that these may affect host response, virulence and transmission of infection with abalone herpesvirus.

The table below describes the sources of infection accepted by the ad hoc Group for the assessments as well as some considerations when applying Stage 1 to support susceptibility to infection with abalone herpesvirus.

<table>
<thead>
<tr>
<th>Source of infection</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Natural exposure included situations where infection had occurred without experimental intervention (e.g. infection in wild or farmed populations) OR</td>
<td>Invasive studies by intramuscular injection were not considered a natural route for transmission (Corbeil et al., 2017 and Bai et al., 2019).</td>
</tr>
</tbody>
</table>

¹ Note: This report should be read in conjunction with the September 2021 report of the Aquatic Animal Commission, where the Commission’s considerations and comments are noted. The Commission’s report can be found at https://www.oie.int/en/what-we-do/standards/standards-setting-process/aquatic-animals-commission/#ui-id-2, and the proposed draft chapter can be found in its annex 14.

² The nomination and classification status of abalone herpesvirus has been accepted by the International Committee on Taxonomy of Viruses (ICTV) as Haliotid herpesvirus 1 (HaHV-1) and represented as the unique member of the genus Aurivirus (family Malacoherpesviridae, order Herpesvirales).
2. Non-invasive experimental procedures: cohabitation with infected hosts; infection by immersion.

2) Stage 2: Criteria to determine whether the pathogenic agent has been adequately identified (as described in Article 1.5.5.):

The ad hoc Group noted that unambiguous pathogenic agent identification might not have been carried out in older publications because molecular techniques were not available at the time. In these circumstances a weight of evidence approach, whereby the combined information from subsequent studies and additional information provided by the authors, was considered and used to conclude sufficiency of pathogen identification.

The table below describes the pathogen identification methods accepted by the ad hoc Group for the assessments as well as some considerations when applying Stage 2 to support susceptibility to infection with abalone herpesvirus.

<table>
<thead>
<tr>
<th>Pathogen Identification</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Species-specific real-time PCR (for example ORF 49, 66 or 77) OR 2. Conventional PCR based on DNA polymerase and terminase region with subsequent sequence analysis (Chen et al., 2012) OR 3. In situ hybridisation (ORF 66).</td>
<td>Although several genotypic variants have been reported based on genome sequence analyses, studies considering only a single variant were taken into consideration. Molecular data associated with microscopical examination (ISH) and transmission electron microscopy (TEM) was preferable but not compulsory to confirm the presence of the pathogen.</td>
</tr>
</tbody>
</table>

3) Stage 3: Criteria to determine whether the evidence indicates that presence of the pathogenic agent constitutes an infection (as described in Article 1.5.6.):

Criteria A to D, as described in Article 1.5.6, and presented below, were used to determine if there was sufficient evidence for infection with abalone herpesvirus in the suspected host species:

A. The pathogenic agent is multiplying in the host, or developing stages of the pathogenic agent are present in or on the host1;

B. Viable pathogenic agent is isolated from the proposed susceptible species, or infectivity is demonstrated by way of transmission to naïve individuals;

C. Clinical or pathological changes are associated with the infection;

D. The specific location of the pathogen corresponds with the expected target tissues.

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1 For the purposes of the assessments for susceptibility to infection with abalone herpesvirus, replication ‘on the host’ was not considered to apply.

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Evidence to support criterion A alone was sufficient to determine infection. In the absence of evidence to meet criterion A, satisfying at least two of criteria B, C or D were required to determine infection.

The table below describes the criteria for assessment of Stage 3 to support susceptibility to infection with abalone herpesvirus.

<table>
<thead>
<tr>
<th>Evidence for infection</th>
<th>A: Replication</th>
<th>B: Viability / Infectivity</th>
<th>C*: Pathology / Clinical signs</th>
<th>D: Location</th>
</tr>
</thead>
</table>
| 1) TEM observation of different developmental stages of the virus (nucleo capsids, empty capsids) OR 2) Demonstration of increasing copy number over time with real-time PCR (targeting DNA)⁴ | 1) Experimental cohabitation (Bai et al., 2019) OR 2) Experimental immersion challenge system (Corbeil et al., 2012a). | 1) Clinical signs, such as:  
   a) Weak or loss of righting reflex  
   b) Reduced or loss of pedal adhesion  
   c) Mortality OR 2) Macroscopic lesions, such as:  
   a) Swollen mouth and prolapsed odontophore (Hooper et al., 2007)  
   b) Mantle recession (Chang et al., 2005)  
   c) Foot contraction OR 3) Microscopic lesions, such as:  
   d) Necrosis of cerebral ganglion and nerve bundles in the muscle of the foot  
   e) Increased cellularity (hemocytes and glial cells) accompanying lesions. | 1) Cerebral and/or pleuropedal ganglion or peripheral nerve bundles (tissue may include surrounding muscle tissue) OR 2) Haemocytes (infiltrated in other tissues such as the hepatopancreas and mantle). |

* Pathology/Clinical signs may be non-specific, variable and include some or all of the characteristics listed.

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⁴ Demonstration of increasing copy number over time with real-time PCR (targeting DNA) was identified as a criterion for replication. However, the ad hoc Group did not find any references to this criterion in the papers reviewed.
Results

The ad hoc Group agreed that the four species currently included in Article 11.1.2. as susceptible to infection with abalone herpesvirus, i.e. Small abalone (Haliotis diversicolor), Greenlip abalone (Haliotis laevigata), Blacklip abalone (Haliotis rubra) and hybrids of Greenlip x Blacklip abalone (Haliotis laevigata x Haliotis rubra), meet the criteria for listing as susceptible to infection with abalone herpesvirus in accordance with Chapter 1.5. of the Aquatic Code and were proposed to remain in Article 11.1.2.

No new species were found to meet the criteria for listing as susceptible species to infection with abalone herpesvirus.

Two species, Japanese abalone (Haliotis discus) and Rainbow abalone (Haliotis iris) were assessed as having incomplete evidence of susceptibility and were proposed to be included in the second paragraph of Section 2.2.2. of Chapter 2.4.1., Infection with abalone herpesvirus, of the Aquatic Manual.

Assessments

The table below describes the different scores and outcomes of the assessments undertaken by the ad hoc Group.

<table>
<thead>
<tr>
<th>Score</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Species assessed as susceptible (as described in Article 1.5.7.). These species were proposed for inclusion in Article 11.1.2. of Chapter 11.1., Infection with abalone herpesvirus, of the Aquatic Code and Section 2.2.1. of Chapter 2.4.1., Infection with abalone herpesvirus, of the Manual of Diagnostic Tests for Aquatic Animals (the Aquatic Manual).</td>
</tr>
<tr>
<td>2.</td>
<td>Species assessed as having incomplete evidence for susceptibility (as described in Article 1.5.8.).</td>
</tr>
<tr>
<td>3.</td>
<td>Species assessed as not meeting the criteria or for which there was unresolved or conflicting information. These species were not proposed for inclusion in either the Aquatic Code or the Aquatic Manual. The exceptions were species where pathogen-specific positive PCR results had been reported, but an active infection had not been demonstrated. These species were proposed for inclusion in the second paragraph in Section 2.2.2., Species with incomplete evidence for susceptibility, of Chapter 2.4.1., Infection with abalone herpesvirus, of the Aquatic Manual.</td>
</tr>
<tr>
<td>4.</td>
<td>Species assessed as non-susceptible.</td>
</tr>
<tr>
<td>NS</td>
<td>Species not scored due to insufficient or irrelevant information.</td>
</tr>
</tbody>
</table>

The assessments for host susceptibility to infection with abalone herpesvirus together with the outcomes and relevant references are shown in the table below.
<table>
<thead>
<tr>
<th>Family</th>
<th>Scientific name</th>
<th>Common name</th>
<th>Subspecies (if applicable)</th>
<th>Stages 1: Route of infection</th>
<th>Stage 2: Pathogen identification</th>
<th>Stage 3: Evidence for infection</th>
<th>Outcome</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haliotidae</td>
<td><em>Haliotis diversicolor</em></td>
<td>Small abalone</td>
<td><em>Haliotis diversicolor</em></td>
<td>N</td>
<td>Conventional PCR &amp; sequencing</td>
<td>ND</td>
<td>ND</td>
<td>YES</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Haliotis diversicolor</em></td>
<td>N and E and E</td>
<td>Real-time PCR ORF 66</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Haliotidae</td>
<td><em>Haliotis laevigata</em></td>
<td>Greenlip abalone</td>
<td><em>Haliotis laevigata</em></td>
<td>N</td>
<td>NO&lt;sup&gt;5&lt;/sup&gt;</td>
<td>ND</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Haliotis laevigata</em></td>
<td>E</td>
<td>Real-time PCR ORF49 and ORF 66</td>
<td>ND</td>
<td>ND</td>
<td>YES</td>
</tr>
<tr>
<td>Haliotidae</td>
<td><em>Haliotis rubra</em></td>
<td>Blacklip abalone</td>
<td><em>Haliotis rubra</em></td>
<td>E</td>
<td>Real-time PCR ORF49</td>
<td>ND</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Haliotis rubra &amp; Haliotis rubra conicopora</em>&lt;sup&gt;6&lt;/sup&gt;</td>
<td>E</td>
<td>Real-time PCR ORF49 and ORF 66</td>
<td>ND</td>
<td>ND</td>
<td>YES</td>
</tr>
<tr>
<td>Haliotidae</td>
<td><em>Haliotis laevigata x H. rubra</em></td>
<td>Hybrid (greenlip x blacklip)</td>
<td><em>Haliotis laevigata x H. rubra</em></td>
<td>E</td>
<td>Real-time PCR ORF49 and ISH ORF66</td>
<td>YES</td>
<td>ND</td>
<td>YES</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Haliotis laevigata x H. rubra</em></td>
<td>E</td>
<td>Real-time PCR ORF49</td>
<td>ND</td>
<td>YES</td>
<td>YES</td>
</tr>
</tbody>
</table>

<sup>5</sup> The Hooper et al., 2007 paper is scored as a 1 based on the molecular information provided from the same source population from Corbeil et al., 2016.

<sup>6</sup> Corbeil et al., 2016 tested both *H. rubra* and *H. conicopora*. *H. conicopora* is considered as a junior synonym of *Haliotis rubra conicopora*.

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<table>
<thead>
<tr>
<th>Score 3</th>
<th>Haliotidae</th>
<th>Haliotis discus</th>
<th>Japanese abalone</th>
<th>Haliotis discus hannai</th>
<th>N</th>
<th>Real-time PCR ORF49</th>
<th>ND</th>
<th>ND</th>
<th>ND</th>
<th>ND</th>
<th>3</th>
<th>Gu et al., 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Haliotidae</td>
<td>Haliotis iris</td>
<td>Rainbow abalone</td>
<td>E</td>
<td></td>
<td>Real-time PCR ORF66 and ISH ORF66</td>
<td>ND</td>
<td>ND</td>
<td>YES</td>
<td>YES</td>
<td>1</td>
<td>Corbeil et al., 2017</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>E</td>
<td></td>
<td>Real-time PCR ORF66</td>
<td>NO</td>
<td>ND</td>
<td>NO</td>
<td>NO</td>
<td>4</td>
<td>Neave et al., 2019</td>
</tr>
</tbody>
</table>
Assessment Table Key

N: Natural infection
E: Experimental (non-invasive)
EI: Experimental (invasive)
YES: Demonstrates criterion is met.
NO: Criterion is not met.
ND: Not determined.

Note:
The scientific names of the species are in accordance with the World Register of Marine Species (WoRMS) https://www.marinespecies.org/index.php.
The common names of mollusc species are in accordance with FAOTERM (http://www.fao.org/faoterm/collection/faoterm/en/). Where the common mollusc name was not found in FAOTERM, the naming was done in accordance with https://www.sealifebase.ca.

Comments on the ad hoc Group’s rationale and decision-making:

General comments

The ad hoc Group agreed to focus on studies published from 2000 onwards, when molecular testing was available. Papers published in earlier years were referred to when necessary to increase confidence of an assessment or when no recent paper was available for the assessment of a specific host species. When necessary to corroborate pathogen identification, the ad hoc Group:

(1) contacted authors of the studies to further describe pathogen identification methods, or

(2) utilized molecular information from parallel or subsequent studies on the same source population.

Although several genotypic variants have been reported based on genome sequence analyses (Cowley et al., 2011 and Corbeil et al., 2016), the ad hoc Group did not assess susceptibility of host species to the virus at the variant level and considered that it was sufficient to regard a species susceptible when it meets the criteria even for a single variant.

The ad hoc Group agreed that either two papers with a score of ‘1’, or a single study with corroborative evidence, were enough to conclude susceptibility of a species. However, additional studies were still reviewed to check for any conflicting evidence. When additional papers were identified but the species had already been determined as susceptible by at least two other papers, these papers were still included in the list of references.

Species-specific comments

- The ad hoc Group considered publications on subspecies of Haliotis discus and Haliotis diversicolor (An et al., 2013 and Wang et al., 2004a) and these publications suggested that the subspecies of haliotids in other literature may not be an accurate reflection of subspecies taxonomic relationships. Based on this finding, the ad hoc Group did not assess subspecies of Haliotis discus or Haliotis diversicolor. Information about these subspecies has been included in the table of assessments for clarity, but the assessments were completed at the species level.

- Haliotis conicopora is indicated in WoRMS (https://www.marinespecies.org/index.php) as a junior synonym of Haliotis rubra conicopora and as a result has been assessed as Haliotis rubra.

- Haliotis discus was assigned an outcome of ‘3’ due to unresolved conflicting information. One paper reported only PCR positives and the other paper supported non-susceptibility. Additional papers were assessed but did not provide further information for the final outcome as they were prior to 2000 and did not include pathogen identification. The ad hoc Group proposed to include Haliotis discus in Section 2.2.2., Species with incomplete
evidence for susceptibility, of Chapter 2.4.1., Infection with abalone herpesvirus, of the Aquatic Manual based on the PCR positive (Gu et al., 2019).

- *Haliotis iris* was assigned an outcome of ‘3’ due to unresolved conflicting information. One paper reported natural low infection in only a few of the animals exposed by immersion and the other paper supported non-susceptibility. Only two papers were available for review for *Haliotis iris* and based on the Corbeil et al., 2017 paper indicating the PCR positive as well as weak signal by ISH in the target tissue of naturally infected (by immersion) animals, the ad hoc Group proposed to include this species in Section 2.2.2., Species with incomplete evidence for susceptibility of Chapter 2.4.1., Infection with abalone herpesvirus, of the Aquatic Manual.

**Listing of susceptible species at a taxonomic ranking of Genus or higher**

- The ad hoc Group considered Article 1.5.9., Listing of susceptible species at a taxonomic ranking of Genus or higher, in Chapter 1.5., Criteria for listing species as susceptible to infection with a specific pathogen of the Aquatic Code, but considered it was not applicable for the hosts of abalone herpesvirus identified at this time as the susceptible species were limited to one Family, Haliotidae.

**References:**


Other references reviewed by the ad hoc Group but not referred to in the assessment table above:


Annex I

OIE AD HOC GROUP ON SUSCEPTIBILITY OF MOLLUSC SPECIES TO INFECTION WITH OIE LISTED DISEASES
May–June 2021

List of participants

MEMBERS OF THE AD HOC GROUP

Dr Isabelle Arzul (Chair)
IFREMER
Laboratoire de Génétique et Pathologie de Mollusques Marins
17390 La Tremblade
FRANCE
Tel.: +33 5 46 76 26 10
iarzul@ifremer.fr
isabelle.arzul@ifremer.fr

Dr Robert Adlard
Marine Biodiversity at Queensland Museum Network
PO Box 3300, South Brisbane
BC
Queensland 4101
AUSTRALIA
robert.adlard@qm.qld.gov.au

Dr Changming Bai
Yellow Sea Fisheries Research Institute, CAFS
Division of Maricultural Organism Disease control and Molecular Pathology
No. 106 Nanjing Road
Qingdao, 266071
CHINA (PEOPLE’S REPUBLIC OF)
baiqm@ysfri.ac.cn

Dr Lori Gustafson
Surveillance Design and Analysis
USDA/APHIS/VS/CEAH
2150 Centre Ave, Bldg B
Mail Stop 2E6
Fort Collins, CO 80526-8117
UNITED STATES OF AMERICA
lori.l.gustafson@usda.gov

Dr Karin B. Lohrmann
Departamento de Biología Marina
Facultad de Ciencias del Mar, Universidad Católica del Norte,
Larrondo 1281, Coquimbo
CHILE
klohrman@ucn.cl

REPRESENTATIVE OF THE AQUATIC ANIMAL HEALTH STANDARDS COMMISSION

Dr Kevin William Christison
Department of Forestry, Fisheries and the Environment
Directorate: Aquaculture Research and Development
Private Bag X 2
Vluebaer, 8018
SOUTH AFRICA
KChristison@environment.gov.za

OIE HEADQUARTERS

Dr. Bernita Giffin
Scientific Coordinator for Aquatic Animal Health
Standards Department
b.giffin@oie.int

Dr Stian Johnsen
Chargé de mission
Standards Department
s.johnsen@oie.int
Background

Chapter 1.5, Criteria for listing species as susceptible to infection with a specific pathogen, was introduced in the 2014 edition of the Aquatic Code. The purpose of this chapter is to provide criteria for determining which host species are listed as susceptible in Article X.X.2 of each disease-specific chapter in the Aquatic Code. The criteria are to be applied progressively to each disease-specific chapter in the Aquatic Code.

These assessments will be undertaken by ad hoc Groups and the assessments will be provided to Members for comment prior to any change in the list of susceptible species in Article X.X.2 of the disease-specific chapters in the Aquatic Code.

For species where there is some evidence of susceptibility but insufficient evidence to demonstrate susceptibility through the approach described in Article 1.5.3, information will be included in the relevant disease-specific chapter in the Aquatic Manual.

Purpose

The ad hoc Group on Susceptibility of mollusc species to infection with OIE listed diseases will undertake assessments for the seven OIE listed mollusc diseases.

Terms of Reference

1) Consider evidence required to satisfy the criteria in Chapter 1.5.

2) Review relevant literature documenting susceptibility of species for OIE listed mollusc diseases.

3) Propose susceptible species for OIE listed diseases for molluscs based on Article 1.5.7.

4) Propose susceptible species for OIE listed diseases for molluscs based on Article 1.5.8.

Expected outputs of the ad hoc Group

1) Develop a list of susceptible species for inclusion in the relevant Article X.X.2. of mollusc disease-specific chapters in the Aquatic Code.

2) Develop a list of species with incomplete evidence for susceptibility for inclusion in Section 2.2.2. of the Aquatic Manual.

3) Draft a report for consideration by the Aquatic Animals Commission at its September 2021 meeting.