Advances in aquatic animal health within the framework of the World Organisation for Animal Health

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Summary

The World Organisation for Animal Health (WOAH) seeks to improve animal health by promoting safe trade in animals and their products, setting standards for diagnostic methods, detection of emerging diseases and confirmation of listed diseases in clinically affected animals and surveillance in healthy populations. WOAH launched the Aquatic Animal Health Strategy (AAHS) in 2021 in recognition of the growing importance of aquatic animal products in global food security. Disease is currently a major limiting factor in the sustainable growth and development of the aquaculture industry, impacting the industry's ability to increase yields to meet future food demands. A key aim of the AAHS is to ensure that scientifically sound standards are set to manage risks and facilitate safe trade, improve aquatic animal health and welfare, build capacity to strengthen aquatic animal health services at WOAH and ensure that responses to aquatic animal health issues are coordinated and timely, at both regional and global level. This article evaluates some of the latest scientific and policy advances as well as obstacles for the implementation of the AAHS.

Keywords

Aquaculture – Aquatic Animal Health Strategy – Diagnostics – Disease – Emerging disease – One Health – Pathogen – Reference centres – Reporting – World Animal Health Information System.

Introduction

The World Organisation for Animal Health (WOAH) launched its first Aquatic Animal Health Strategy (AAHS) in 2021 in recognition of the growing importance of aquatic animal products in global food security [1]. Fisheries and aquaculture production reached a record 214 million tonnes in 2020, including 87.5 million tonnes of farmed aquatic animals (US$ 264.8 billion), 90.3 million tonnes from capture fisheries (US$ 141 billion) and 36 million tonnes of algae (US$ 16.5 billion). Aquaculture is the fastest-growing food sector globally, with an estimated increase of over 60% in the production of aquatic animals since the 1990s [2-4]. As of 2022, the consumption rate of aquatic foods had doubled over the previous 50 years, and aquaculture production was forecast to grow another 14% by 2030 [2].

Aquatic animal disease is currently a major limiting factor in the sustainable development of the aquaculture industry and its ambition to increase yields to meet future food demands. WOAH seeks to improve animal health by promoting safe trade in animals and their products. The AAHS sets four priorities for collaborative actions to achieve WOAH's mission:

- setting scientifically sound standards to manage risks, facilitate safe trade and improve aquatic animal health and welfare;
- building capacity to strengthen the aquatic animal health services at WOAH;
- providing leadership in global aquatic animal health and welfare;
- enhancing resilience by ensuring responses to aquatic animal health issues are coordinated and timely, at both regional and global level.

The following sections present some of the latest scientific and policy advances as well as obstacles to improving aquatic animal health globally.

Aquatic Animal Health Code and *Manual of Diagnostic Tests for Aquatic Animals*

Trade of live aquatic animals and their products is known to be a major factor in disease spread and emergence. The movement of infected stocks, often illegal or subject to poor biosecurity, has spread disease between farming regions [5,6].

WOAH standards to minimise transboundary disease spread are recognised by the World Trade Organisation's Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement). Standards are set out in the *Aquatic Animal Health Code*

(*Aquatic Code*) [7] and the *Manual of Diagnostic Tests for Aquatic Animals* (*Aquatic Manual*) [8]. These standards are based on the most recent scientific and technical information and should be followed by Members to ensure the prevention, early detection and reporting, and control of pathogenic agents in aquatic animals (amphibians, crustaceans, fish and molluscs) listed by WOAH. Members are required to report to WOAH diseases listed by WOAH (*Aquatic Code*, Chapter 1.3., 'Diseases listed by WOAH') and those that meet WOAH's definition of an emerging disease. WOAH sets out criteria for listing aquatic animal diseases in Chapter 1.2. of the *Aquatic Code*. This list is revised annually; in 2023 it contained 31 aquatic animal diseases (of viral, bacterial, fungal and parasitic origin), 10 of crustaceans, 11 of fish, 7 of molluscs and 3 of amphibians.

WOAH standards relevant to international trade are currently based on a single-pathogen model of disease aetiology and aim to limit the spread of listed pathogens via reporting and controls. However, multifactorial syndromes have serious impacts on production. For example, slow growth syndrome in shrimp results in retarded growth and is the most important production-limiting condition affecting shrimp farming across Asia. Several potential pathogens have been identified from affected shrimp; some appear necessary for disease development but are individually insufficient for manifestation of disease. Such multifactorial disease states require further elucidation. The 'one pathogen, one disease' paradigm is clearly insufficient to explain many disease scenarios [9]. In recent years interest has grown in the concept of the pathobiome, which is described as a collection of organisms associated with reduced health status [10]. It is recognised that many diseases thought to be associated with one primary disease agent are the result of interactions between multiple taxa, the environment and the host – i.e. syndromic or multifactorial disease. Understanding this complex interaction and the changes in pathobiome profile as diseases progress is important to manage the effects of disease and an area requiring further research. WOAH standards and national aquatic animal health legislation are focused, respectively, on pathogens of international and national importance and thus listed and subject to control. Current international standards and national legislation do not, however, account for the broader symbiont profiles that are involved in disease processes, i.e. the symbiont community interacting with its host in the context of all relevant factors (ecological, chemical, physical, genetic, immunological, etc.) [9]. Regulation of syndromic diseases will require supporting evidence to satisfy criteria for listing, such as case descriptions, understanding the 'necessary and sufficient' set of agents/factors that induce a syndromic disease and relevant diagnostic methods. The process is inevitably more complex than generating

evidence of presence for a single pathogen, as is illustrated by work on reduced growth syndromes in (sub)tropical shrimp farming [9], but is required for accurate elucidation of many diseases and development of robust biosecurity safeguards.

Notably, the molecular techniques required for effective investigation of syndromic/pathobiotic disease (i.e. including semi- or non-targeted high-throughput sequencing; see 'Disease reporting' section below) are similar to those that have recently also been of value in detecting and characterising novel pathogens, particularly those genetically distant from their closest relatives [11-14].

Disease reporting

Prompt reporting of the occurrence of listed (and emerging) diseases is fundamental to meeting the AHSS objective of ensuring that responses to aquatic animal health issues are coordinated and timely, at both regional and global level. Information on disease occurrence will be generated by i) structured active surveillance or ii) disease investigations promoted by reports of morbidity or mortality (passive surveillance).

WOAH regularly publishes aquatic animal health situation reports with information on disease events that have been reported by countries and territories through the World Animal Health Information System (WAHIS). WOAH Members accept the obligation to share animal health data on listed and emerging diseases in accordance with WOAH standards. However, the availability and quality of data vary and are dependent on both the level of active surveillance and the competent authority's capacity to respond to disease reports (passive surveillance). The most recent situational report on health of crustaceans highlights that 30% of the countries and territories that share information via WAHIS declare no surveillance for crustacean diseases. Many Members report no information for the listed diseases or have not reported via WAHIS for the last five years, highlighting an important gap in knowledge of disease occurrence and a flaw in the current reporting systems [15]. A similar situation exists for fish and molluscan diseases, with 21% of countries and territories that shared information in WAHIS lacking surveillance data for fish diseases and 43% for molluscan diseases. While surveillance was reported for some of the listed diseases (44% fish and 25% molluscan), only 35% of reporting countries and territories reported surveillance for all listed diseases of fish and 32% for all listed diseases of molluscs [16,17]. A significant number reported no detection for several aquatic animal diseases without declaring any surveillance in place. For some regions many reports were missing, highlighting important gaps in the current

surveillance networks. WOAH can add value to the aquatic animal health data in WAHIS by providing country-specific information on active and passive surveillance.

Advances in diagnostic methods and technologies

Accurate diagnostic methods are the bedrock of scientifically sound standards to manage risks, facilitate safe trade and improve health and welfare [1].

WOAH sets out standards for diagnostic methods or the detection of emerging diseases, confirmation of listed diseases in clinically affected animals and surveillance in healthy populations.

Although imaging techniques such as cytopathology, histopathology and electron microscopy can be time consuming and demand specialised expertise, these techniques are essential to characterise emerging pathogens and offer unique information regarding morphology, viability and host response. Artificial Intelligence can significantly expand the capacity to extract information from digital images. High-throughput sequencing methods have emerged as a revolutionary tool for rapid and reliable whole-genome sequencing of infectious agents. This enables the identification of new or emerging variants and provides crucial genomic data essential for designing and improving polymerase chain reaction (PCR)-based assays.

Concurrently, environmental DNA/RNA (eDNA/eRNA) methods – collectively designated as environmental nucleic acids (eNA) – using pathogen-specific assays (e.g. quantitative PCR) can detect nucleic acid of pathogens in the environment (for example planktonic vectors, dispersal and dormant forms, and extracellular nucleic acids), offering a non-invasive avenue for pathogen detection in healthy populations and early disease warning systems as well as insights into pathogen ecology and transmission [18,19]. The key challenge for informative and reliable application of eNA methods is to design appropriate sensitive and specific assays that have been validated within a system in which the relationship between environmental detection of pathogens and occurrence of disease in their recognised hosts is well calibrated [18]. Positive results using eNA may provide suspicion of infection, confirmation of which requires targeted diagnostic testing of the putative host.

Despite advances in cellular techniques for disease diagnosis, notable limitations persist, for example the absence of proliferative cell lines from bivalve molluscs and crustacea [20].

Real-time PCR or conventional PCR followed by nucleotide sequencing of amplicons frequently serves as a confirmatory diagnostic method for WOAH-listed aquatic diseases. Diagnostic testing for some pathogens can be complicated by the presence of endogenous viral elements (EVEs). Presence of EVEs may lead to false-positive PCR results, highlighting the importance of genomic data, independent confirmatory tests and regular review of diagnostic test methods. Infectious hypodermal and hematopoietic necrosis virus in shrimp is an example of this now addressed by WOAH methods [21-24]. Standards must reflect the limitations of PCR tests and seek to reduce the likelihood of false positives, which may result in unnecessary culling and disinfection measures, economic losses and disruption to trade.

Alternative methods for pathogen detection involving the amplification of specific genomic regions have gained broader acceptance. For instance, loop-mediated isothermal amplification (LAMP) and recombinase polymerase amplification offer the advantage of rapidity and require less costly equipment and reagents. Recent technological advances have led to considerable improvements in point-of-need testing, from LAMP to in-field third-generation sequencing [25]. WOAH also holds a register of diagnostic kits that have been validated as fit for purpose for diagnostic testing; at present only one aquatic disease (white spot syndrome virus) has validated test kits recommended by WOAH.

WOAH also provides standards for monitoring, including for the use of antimicrobials in aquaculture. International collaboration and efforts are crucial to develop tools and practical guidance on the surveillance of antimicrobial resistance in pathogens and the use of antimicrobials in aquatic animals [26].

Emerging diseases

Aquatic animal diseases are frequently observed within the aquatic environment. The emergence of new, previously unknown diseases in aquaculture is expected to increase in parallel with the expansion of the aquaculture industry, impacting food security, livelihoods, biodiversity and economies [27,28]. An emerging disease is defined by WOAH as ‘a new occurrence in an animal of a disease, infection or infestation, causing a significant impact on animal or public health resulting from: a. a change of a known pathogenic agent or its spread to a new geographic area or species; or b. a previously unrecognised pathogenic agent or disease diagnosed for the first time’ [7].

Rapid detection, characterisation and reporting of the causative agents of emerging disease are a crucial first step in their subsequent control. However, there is often a lag phase between the development and the subsequent detection of a new disease/pathogen. Once identified, there may be a lack of diagnostic tools and capability and only limited information on the epidemiology, such as geographic spread, host range and transmission factors, all of which may lead to a delay in decision-making. Disease events that are reported to WOAH are discussed at the biannual meetings of the Aquatic Animal Health Standards Commission and evaluated for whether they meet the criteria for listing. Before listing (and development of an *Aquatic Manual* chapter), technical disease cards may be developed and information is disseminated to WOAH Members to alert them of the potential impact of the disease, encourage reporting to enable collection of additional epidemiological information and advise on potential control measures [28].

For the listing of diseases to be effective at limiting their spread, it is crucial that new and emerging disease threats be notified and listed as soon as they are identified. To date, the processes involved in listing new diseases are slow, with delays often leading to the spread of the pathogen. For example, the microsporidian parasite *Enterocytozoon hepatopenaei* was first identified in 2004 [29] as a low-level incidental infection of *Penaeus monodon* and formally described in 2009 [30]. Twenty years later, this pathogen has emerged to be one of the most important pathogens in *Penaeus vannamei* cultivation in Asia, is now widespread in shrimp aquaculture and continues to spread to new regions [4,9,31,32]. The listing of this disease as an emergent threat may already be too late in some regions but should now limit any further spread.

Reference centres

WOAH has established a global network of Reference Laboratories (38 of which are specialists in aquatic animal diseases) designated for one or more WOAH-listed pathogens. A Reference Laboratory has not been established for all the listed aquatic animal diseases, which can lead to problems for Members in acquiring positive control reference materials and advice.

WOAH Collaborating Centres promote international collaboration for animal health and welfare and are designated for a specific specialty. WOAH has designated five Collaborating Centres that focus on aquatic animal diseases (Antimicrobial Stewardship in Aquaculture, Emerging Aquatic Animal Diseases, Epidemiology and Risk Assessment of Aquatic Animal Diseases (Americas and Europe) and Economics of Animal Health). They support WOAH in the implementation of policies and assist in delivering key

functions, for example the implementation of training programmes, developing regional networks and supporting investigations to build and strengthen capacity in aquatic animal health across the globe.

Standards and processes for declaring disease freedom

Declaration of disease freedom at country, zone or compartment level is at the heart of the WOAH standards to minimise the transboundary spread of animal diseases. Members can protect their health status if they meet WOAH standards for the self-declaration of freedom from specified diseases. The WOAH process for self-declaration has been little used. WOAH does not assess the validity of claims of disease freedom published on its website and, therefore, does not offer any level of accreditation. By contrast, WOAH does provide an official declaration of disease freedom for selected listed terrestrial animal pathogens (e.g. foot and mouth disease).

Disease-free compartments provide an important mechanism to promote safe trade when country or zonal freedom is not possible. The use of specific pathogen free (SPF) stocks is fundamental to achieving disease freedom in biosecure rearing and cultivating facilities that meet WOAH standards (notably, epidemiological isolation) for compartments. SPF animals are free of selected infectious pathogens. Compartmentalisation and SPF stock have primarily been used by the shrimp industry. The benefits of using of SPF stocks are increased production efficiency and enhanced animal health and welfare [22,33]. The shrimp industry historically relied upon wild captured broodstock for the larvae, a high-risk strategy as pathogens were co-introduced [5]. The development of SPF stocks played a key role in developing shrimp aquaculture practices and led to *P. vannamei* becoming the dominant shrimp species farmed across the globe [5,22,33,34]. This use of SPF stocks combined with enhanced biosecurity on farms has been instrumental in reducing the impact of viral diseases in shrimp aquaculture [22]. However, it is important to note that these stocks are free of only selected pathogens, and not necessarily free from new and emerging diseases. Flegel [5] highlighted the risks to the shrimp industry in relying upon SPF stocks and suggested this led to a reduction in routine screening for new and emerging pathogens, for example the screening of postlarvae for potential *Vibrio* species. This may have been a contributing factor in the advent and spread of acute hepatopancreatic necrosis disease. Thus, it is vital that SPF stocks be routinely screened for new and emerging pathogens, and the list of diseases that are screened in SPF stocks should be regularly reviewed [5,22].

A total of 17 active declarations of freedom from aquatic animal diseases have been made by 4 of 183 WOAH Members since January 2022 [35]. By contrast, 70 Members made 234 self-declarations of freedom from terrestrial animal diseases between 2021 and 2022 [36]. Ten of the 17 declarations were made for disease freedom at country level, and 7 for zones (Table I).

Many Members that have not used the self-declaration process claim freedom from specified aquatic animal diseases and regulate importations of live animals, and in some cases products, to protect their status. For example, the United Kingdom claims freedom from viral haemorrhagic septicaemia, infectious haematopoietic necrosis virus and *Gyrodactylus salaris*, among other diseases, and has in place measures to prevent import of live susceptible species from sources of a lower health status. WOAH standards for disease freedom provide a basis for negotiation between trade partners that has been agreed by all Members and recognised by the SPS Agreement.

There is a need to understand and overcome barriers Members face in using the self-declaration process to better support adoption of standards and to minimise disease spread. Section 5 of the *Aquatic Code* ('Trade measures, importation/exportation procedures and health certification') provides a suite of standards to ensure safe trade (e.g. certification, transport, disinfection). Specifically, WOAH could further develop the standards for compartments by explicitly recognising the importance of SPF stock and promote the benefits of compartments in international trade.

One Health aquaculture

WOAH recognises One Health as a collaborative approach to address risks to global health. One Health aims to sustainably balance and optimise the health of humans, animals, plants and ecosystems by recognising their interdependence. Recently, a One Health perspective was developed for managing aquatic animal health, particularly in respect to aquaculture. It proposes a set of success metrics relating to the environment, organisms and humans, fulfilment of which are underpinned by the availability and application of relevant research, evidence, policy and legislation [4]. A 'seafood risk tool' (SRT) has also been devised to operationalise One Health through assessment and mitigation of chemical and pathogen hazards in the aquaculture supply chain [3]. The One Health metrics and SRT could form the basis for the development of WOAH standards or guidance for the adoption of a One Health approach to aquaculture.

Discussion

Any expansion of aquaculture to meet food security demands will need to be sustainable, via improved efficiencies to produce more with less (less land, energy, water, feed and labour), improved animal health (enhanced diagnostics, improved biosecurity and enhanced farmed animal welfare), prevention of pollution and protection of biodiversity (increased controls to reduce environmental impact). Developing countries will require additional support to expand their industry to meet demands for national food production to feed and create jobs for their growing populations [2-4,37-39].

WOAH has established the Observatory to identify and analyse Members' practices in implementing standards. An objective of the AAHS is to work with the Observatory to highlight barriers to the implementation of standards, and specifically disease reporting. This process will highlight what works well and where efforts need to be concentrated to ensure continual improvement of the processes and activities. More broadly, investment is required to both improve sustainability and address barriers to the expansion of the industry. Specifically, investment should be directed at better animal welfare and breeding programmes to provide genetically improved stock for enhanced growth and disease resistance/tolerance, and at further research to better understand syndromic conditions and disease emergence [1-4,40]. Investment in enhanced sustainability should be matched with enforceable legal and institutional frameworks and good governance.

The four key collaborative actions of the AHSS are interlinked and focused on improving aquatic animal health and welfare through standard setting. The standards need to evolve to meet the changing challenges facing the aquaculture industry, and capacity must be developed to support their implementation. WOAH aquatic animal health capacity similarly needs to expand to provide the necessary leadership to promote adoption of the standards, including a rapid response by Members to emerging threats.

WOAH standards fall into two main categories: i) pathogen-specific standards that provide guidance for the detection and reporting of listed pathogens, and criteria that need to be met to demonstrate disease freedom; and ii) standards providing guidance on aquatic animal health management (e.g. welfare, biosecurity, emergency response). While it is recognised that many diseases do not conform to the single-pathogen aetiology paradigm, no alternative to pathogen-specific standards to minimise the spread of disease with trade in animals and their products is currently available. WOAH's activities will inevitably remain focused on a limited number of internationally recognised

diseases. However, Members can list pathogens of national importance and model controls on WOAH standards. Arguably, WOAH needs a more streamlined and rapid process for listing new and emerging diseases to support control measures before they are widely disseminated.

This article has identified how standards for aquatic animal health and welfare could be developed and expanded. Specifically, it highlights weaknesses in international disease reporting and limitations in the use of the currently available data. A shift in emphasis from disease reporting (which is highly contingent on surveillance) to demonstration and self-declaration of disease freedom would support WOAH's core mission to reduce disease spread via international trade.

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Table I

Self-declarations of freedom from aquatic animal diseases made since 2022 and currently active

Member	Self-declared freedom from	From (DD/MM/YYYY)	Country/zone/compartment
Argentina	*Gyrodactylus salaris* (Inf. with)	01/06/2022	Zone
Argentina	Epizootic haematopoietic necrosis virus (Inf. with)	01/06/2022	Zone
Argentina	Infectious haematopoietic necrosis virus (Inf. with)	01/06/2022	Zone
Argentina	Infectious salmon anaemia virus (Inf. with) (HPR-deleted or HPR0 genotypes)	01/06/2022	Zone
Argentina	Viral haemorrhagic septicaemia virus (Inf. with)	01/06/2022	Zone
Colombia	White spot syndrome virus (Inf. with)	14/03/2024	Zone
Colombia	Yellow head disease	23/05/2024	Zone
Korea (Rep. of)	Infectious salmon anaemia virus (Inf. with) (HPR-deleted or HPR0 genotypes)	27/02/2024	Country
Korea (Rep. of)	*Gyrodactylus salaris* (Inf. with)	27/02/2024	Country
Korea (Rep. of)	Abalone herpesvirus (Inf. with)	27/02/2024	Country
Korea (Rep. of)	Infectious hypodermal and haematopoietic necrosis virus (Inf. with)	29/08/2022	Country

Member	Self-declared freedom from	From (DD/MM/YYYY)	Country/zone/compartment
Korea (Rep. of)	Salmonid alphavirus (Inf. with)	01/06/2023	Country
Korea (Rep. of)	Yellow head virus genotype 1 (Inf. with)	23/05/2024	Country
Peru	Yellow head virus genotype 1 (Inf. with)	13/03/2024	Country
Peru	Infectious myonecrosis virus (Inf. with)	13/03/2024	Country
Peru	Taura syndrome virus (Inf. with)	13/03/2024	Country
Peru	Yellow head virus genotype 1 (Inf. with)	13/03/2024	Country

Source: World Organisation for Animal Health [35]