CONSIDERATIONS FOR REGULATION OF AQUACULTURE VACCINES IN THE AMÉRICAS
I. Introduction
Aquaculture is an economically important activity for several countries in the Americas. There is considerable potential for future expansion and diversification; however, potential losses due to viral and bacterial infectious diseases are a major concern. Some of these diseases can be prevented by vaccination. Aquaculture producers, therefore, require timely access to safe and efficacious vaccines and other animal health products, to help protect aquatic animal health and welfare, and to reduce the financial risks from diseases.

This overview document outlines some recommended approaches for standardizing the regulatory controls, technical standards, documentation, and regulatory approval processes for vaccines and related veterinary biologics that are intended for use in aquaculture. It provides general background information and recommendations, with the objective of facilitating the pre-licensing review and approval processes, as well as avoiding duplication of post-licensing regulatory oversight for regulatory agencies of CAMEVET member countries.

II. General regulatory considerations
In many countries, the government agencies that regulate animal health products for terrestrial animals generally also have the necessary enabling legislation and delegated authority to implement regulatory controls for the manufacturing, importation, and distribution of vaccines and other animal health products for diagnosis, treatment, prevention, and control of infectious diseases in aquatic animals. However, the agencies that are responsible for regulating terrestrial animal health products may not have implemented specific regulations or technical standards for regulating aquaculture products. Nevertheless, many of the key elements of the regulatory frameworks, technical standards, and quality assurance systems that have been developed and implemented for terrestrial animal vaccines can be readily applied or adapted for regulation of aquatic animal vaccines.

In the following document, the terms "aquatic animal vaccine" and “aquaculture vaccine” are intended to refer to products that are comprised of naturally occurring or synthetic biological substances, or a mixture of biological substances, that are manufactured, sold or represented for use in prevention or control of a specific infectious disease in aquatic animals, and which act primarily through stimulation of an acquired immune response. Terms such as "licensing", “permitting”, "registration", or “marketing authorization” may be used synonymously to mean regulatory approval or permission to manufacture, import, distribute, release or use a veterinary vaccine within a jurisdiction. These regulatory approvals may be granted through issuance of licences, permits, or other documents. Various restrictions or conditions may be applied, and should be clearly stated on the regulatory approval document.

In some countries, there may be a perceived overlap or gap in regulatory authorities for regulating aquaculture vaccines because the existing animal health legislative authorities for regulating vaccines for terrestrial animals may not explicitly include authorities for regulating aquaculture vaccines, or a different regulatory agency may be responsible for implementing the controls for aquatic animals and their products. Another factor to consider is that the enabling legislation and regulatory agencies covering aquaculture may be situated in a different Ministry,
such as the Department of Health, Agriculture, Environment, or Fisheries. This may necessitate a Memorandum of Understanding or other arrangement to delineate the division of regulatory responsibilities between agencies.

The technical and jurisdictional challenges for regulation of aquaculture vaccines may be further complicated by the fact that aquaculture may comprise a relatively small segment of the agriculture sector in a country, and there may be no licensed domestic manufacturers of aquaculture vaccines, so all aquaculture vaccines are imported. Consequently, it may not feasible for each individual country’s regulatory agency to invest in developing a regulatory infrastructure, and maintaining the necessary specialized technical expertise that would be required to autonomously develop and implement the necessary science-based regulatory controls for the aquaculture vaccine sector.

III. Technical considerations for regulation of vaccines for use in aquatic animals

In general, the principles and approaches that are employed for regulation of veterinary vaccines for terrestrial animals can be adapted to regulation of vaccines for aquatic species. However, due to differences in immunological responses and aquaculture health management practices, as well as differences in manufacturing and testing procedures, some modifications may be required for regulation of aquaculture vaccines.

Vaccination is relatively widely used for commercially raised fin fish species, such as Atlantic salmon, catfish, and tilapia to stimulate an active humoral and cellular immune response. However, the roles of the innate and acquired immune system in disease resistance for fin fish are less well characterized than in terrestrial species. Crustaceans such as crayfish, lobsters, and shrimp, and molluscs such as clams, scallops, oysters, and mussels have a much less well developed immune system that is primarily based on innate immune responses, therefore conventional vaccines that are intended to elicit an acquired humoral or cellular immune response may not be efficacious for crustaceans and molluscs, unless they activate the innate immune responses.

In comparison with the relatively advanced state of knowledge of the pathogenesis of diseases affecting avian and mammalian domestic species, considerably less is known about the pathogenesis of infectious diseases of aquatic animals (which frequently involve emerging pathogens), and the corresponding protective immune response mechanisms. As a result, well-characterized, validated, predictive in vitro tests for assessing vaccine potency or immune responses may not be readily available for use in pre-licensing immunogenicity/efficacy studies or post-licensing batch release potency tests. Consequently, manufacturers and regulatory agencies tend to rely on vaccination-challenge tests to evaluate potency of each serial (batch) of vaccine, using a method of calculating relative percent protection (RPP) or relative percent survival (RPS) which involves comparing the level of protection or survival of vaccinated fish to that of unvaccinated controls.

Vaccination-challenge studies are used to demonstrate efficacy, and they are also currently frequently used as a serial (batch) release potency test. Due to animal welfare concerns, there
is a trend toward replacement of the vaccination-challenge batch release potency tests with *in vitro* antigen detection tests or *in vivo* tests to compare the serologic immune responses in fish vaccinated with a production serial versus the serologic responses in fish vaccinated with a reference serial by comparing pre-vaccination and post-vaccination antibody levels. In the batch release potency tests, the relative potency could be assessed by comparing the potency of a production serial with a reference standard that has been shown to be efficacious in vaccination-challenge tests.

In efforts to reduce the use of aquatic animals for batch release safety tests, the initial stages of *in vivo* batch release potency tests can also serve as a batch release safety test, based on a lack of adverse reactions in vaccinates during the interval between vaccination and challenge.

From an animal welfare refinement perspective, if an *in vivo* vaccination-challenge test must be used for batch release, the challenge dose should be adjusted so it reliably elicits a detectable level of disease in unvaccinated controls, and little or no clinical disease or mortality in vaccinates.

Vaccination-challenge tests require highly specialized aquatic facilities for maintenance of fish, segregation of treatment groups, biocontainment, and decontamination of effluent. Since there is a potential for inadvertent release of aquatic pathogens in effluent, the vaccination-challenge tests present a potential biosafety risk. Consequently, it may not be feasible for individual manufacturers or lead regulatory agencies to maintain aquaculture testing facilities for confirmatory testing. As an alternative, manufacturers may elect to arrange for contract approved laboratories with specialized expertise to conduct pre-licensing testing, validation of *in vitro* potency tests, and post-licensing batch release safety and efficacy tests. For similar reasons, rather than conducting confirmatory batch release testing in government laboratories or 3rd party laboratories, it may be more expedient for regulatory agencies to supplement their pre-licensing review of data with an onsite evaluation of manufacturing and testing procedures, and periodic audit the manufacturer’s batch release testing procedures during facility inspections.

Table 1 lists some of the factors and parameters that must be considered when regulating vaccines intended for use in aquaculture facilities.

**IV. Coordination of regulatory oversight for manufacturing and Importation of veterinary vaccines**

When implementing pre-licensing evaluations, post-licensing regulatory controls, and confirmatory testing for imported products, it may be preferable and more expedient for regulatory officials to take into consideration the regulatory oversight and preceding decisions of other regulatory agencies which may have more familiarity with specific aquaculture vaccines, and to defer some of the direct regulatory oversight to a lead regulatory agency where the manufacturer is located.
The regulatory agency of the country where the manufacturing facility is located is often best positioned to serve as the lead regulatory agency, with primary responsibility for oversight of the manufacturing and testing procedures for the licensed aquaculture vaccines that are produced in the facility. For regulation of imported veterinary vaccines, the responsibility for regulatory oversight may be shared between the regulatory agency in the country where an aquaculture vaccine is manufactured and the regulatory agency in the destination country. The two regulatory agencies would generally function autonomously, however the destination country’s regulatory agency may elect to take the preceding regulatory decisions and ongoing regulatory oversight of the lead regulatory agency into consideration when reviewing licensing applications and post-licensing documentation for imported vaccines, and determining the appropriate level of post-licensing regulatory oversight for a specific product.

This type of collaborative approach, where regulatory agencies of importing countries consider the decisions and regulatory controls of other agencies when establishing import conditions and other post-licensing regulatory controls, would help minimize duplication of pre-licensing evaluations, post-licensing regulatory controls, and confirmatory testing, especially considering the similarity of the controlled conditions of fish breeding in ponds and lakes.

Whenever possible within the scope of their regulatory authorities, individual regulatory agencies should strive to adopt common documentation and technical standards, and consider the preceding approvals in other jurisdictions when reviewing licensing submissions. In doing so, the individual regulatory agencies could maintain overall regulatory authority, and retain varying levels of regulatory oversight for review and approval of pre-licensing submissions, post-licensing batch release, and approval of major changes in manufacturing and testing procedures, but could defer to preceding assessments, testing, and regulatory controls of other agencies, when warranted.

Similarly, to avoid duplication of regulatory oversight for importing countries, the scope, depth, and frequency of manufacturer facility inspections could be modified if a lead regulatory agency or a competent authority from another importing country is conducting periodic, comprehensive, in-depth facility inspections, and the inspection results are available to other regulatory agencies through the regulated manufacturer.

It may be useful for regulated companies to authorize communications and exchange of confidential product review information among regulatory agencies, for the purpose of facilitating the review and approval of supporting documentation, and to avoid duplication of regulatory oversight. This authorization could be done through a broad-based Memorandum of Understanding between regulatory agencies to authorize sharing confidential information on all facilities and products that they both regulate. Alternatively, a more limited type of product-specific authorization could be achieved through a letter from a manufacturer authorizing two regulatory agencies to share confidential information and decision documents pertaining to a specific product or a group of products.

V. General guidance
A. General criteria for product acceptability
   1. The product must be properly characterized in relation to the purity of the seed, safe, potent and efficacious when used in the target species, according to the label directions.
   2. Each biologically active component must be relevant to the infectious aquatic animal disease conditions and aquatic animal genetics in the country or region where the product will be used.
   3. The product must be manufactured and tested by qualified personnel approved by the competent authority, in facilities that are acceptable to the responsible regulatory agencies.

B. Potential reasons to refuse permission to manufacture or import an aquaculture vaccine
   1. Product manufactured in countries where specific transboundary diseases affecting aquatic or terrestrial animals post a risk for contamination of the regulated vaccine, when the manufacturer does not comply with the appropriate biosafety regulations.
   2. Product manufactured with components originating from countries where transboundary diseases affecting aquatic or terrestrial animals pose a risk for contamination of the regulated vaccine.
   3. Product for the prevention or diagnosis of aquatic animal diseases which are under regulatory control or eradication program, or considered foreign to the country or region. Some exceptions may be granted, i.e., for restricted use of vaccines in government control and eradication programs, if deemed in the best interest of the success of the control or eradication program.
   4. Live attenuated vaccine with an unacceptable level of residual virulence, which could present a disease risk to unvaccinated animals of the target species, or in-contact aquatic animals.
   5. Product which has not been demonstrated to be satisfactorily efficacious in the target species.
   6. Product that is deemed to be contrary to the best interests of public health, animal health, environmental protection, or aquatic animal health control or survey programs.

VI. Recommended documents and forms for licensing submissions
The process for licensing aquatic animal vaccines manufactured within a country generally involves a phased, in-depth review of documents by the lead regulatory agency in the country where the vaccine is manufactured. For imported products, which have been previously reviewed and approved by a competent regulatory agency, a complete licensing submission is generally submitted, which includes all key documentation which was submitted to the lead regulatory agency, as well as any key correspondence pertaining to the review and approval by the lead agency. However, the regulatory agency in the destination country may deem it appropriate to take into consideration the preceding decisions and ongoing regulatory oversight of other competent authorities when reviewing licensing submissions, and may, therefore, decide to waive or modify some data review procedures, pre-licensing testing requirements, or post-licensing regulatory controls.
In some circumstances, such as when it is necessary to authorize restricted importation or provisional marketing authorization to facilitate importation or release of a specific serial (batch) of a vaccine for emergency or research use, the manufacturer and importer may be permitted to file an abbreviated licensing submission which provides summary information (i.e. production outline, batch release test results, material of animal origin documentation, labelling). The application for restricted use should cite any previous review and approval in another jurisdiction, including conditional approval. It may need to be supported by other documents or attestations such as an Establishment Licence, Product Licence, Certificate of Licensing and Inspection, Export Certificate, or Certificate of Free Sale pertaining to the individual serial (batch) to be imported, and the method of analysis.

**VII. General requirements for products manufactured for domestic distribution and export**

Vaccine manufacturers are primarily subject to controls under regulations that are administered by the regulatory agency (competent authority) in the country or region where the product is manufactured. This regulatory agency would ordinarily serve as the lead agency responsible for regulating the manufacturing facility and its products. The regulatory agency of importing countries would serve a secondary role, and may delegate some responsibilities to the lead regulatory agency (e.g., pre-licensing master seed testing, pre-licensing serial testing, post-licensing batch release testing, and in-depth facility inspections).

For products manufactured and distributed within a country, a phased review may be carried out, where the initial phase of the new product licensing submission may contain only preliminary data. A Permit to Release Veterinary Biologics (or similar regulatory authorization), is required for the use of experimental products or unapproved products in field studies outside of biocontainment facilities, or if experimental aquatic animals are intended for entry into the food chain. An assessment by the regulatory agency may also be required for products derived from GMOs or when novel micro-organisms or biotechnology-derived products are used.

In addition to a complete product file, the licensing of vaccine manufactured by a domestic veterinary vaccine manufacturer requires the satisfactory inspection and licensing of the manufacturing facilities, data of the master seeds and approval of pre-licensing serials.

Products that are licensed (approved) for distribution within a country would ordinarily also be eligible for export, provided they meet the requirements of the importing country’s regulatory agency. However, some products may be manufactured for export only. In the licensing submission, the manufacturer should specify whether the product will be manufactured “for domestic distribution and export” or “for export only”, as the document requirements and regulatory approval processes would be different for these two types of approvals.

Regulatory agencies of importing countries may take any pertinent regulatory decisions and post-licensing regulatory controls of the lead regulatory agency into consideration when determining the appropriate level of regulatory oversight for a specific imported product.
If approval is granted, various post-licensing restrictions and conditions may be applied. These restrictions and conditions should be clearly listed on a Veterinary Biologics Establishment Licence, Veterinary Biologics Product Licence, Import Permit, Permit to Release Veterinary Biologics, Marketing Authorization, or corresponding document, and explained in supplemental correspondence as required.

**VIII. Special requirements for products manufactured for export only**

For products manufactured “for export only”, the manufacturer is required to submit the production outline, special outlines, and product labelling, as well as supporting data to demonstrate the safety of the product, the purity of the master seeds and the master cell stocks. The manufacturer must provide documentation to demonstrate approval by the regulatory agency in the destination country (e.g., approval letter, copies of approved label, copy of Marketing Authorization or Import Permit) or a statement of intention to license, in the country of destination.

In some instances, a product which is licensed “for export only” may be similar, or identical to a product manufactured for domestic sale, except it may have different quality control specifications or different label claims (i.e., languages, intended species, directions for use, precaution statements) to conform to the importing country’s regulatory requirements. In other cases, it may be a vaccine for use in a species that is not farmed in the country, or a vaccine against an agent that is not present in a country. In the latter case, there would need to be appropriate biocontainment measures (1), and introduction of a potentially virulent vaccine seed organism into the manufacturing facility may be restricted or prohibited. Similarly, there may be restrictions or prohibitions on vaccination-challenge testing.

**IX. Facilities, equipment, and personnel**

All vaccines intended for distribution and use within a country, or for export to other countries, must be manufactured in a facility that has been approved by the lead regulatory agency in the country where the manufacturing facility is located.

The approval of a new vaccine manufacturing facility involves a review of the facility, personnel, manufacturing and quality control/quality assurance documents, and a pre-licensing inspection of all premises where manufacturing, testing, preservation, packaging, labelling, storage and distribution of veterinary vaccines are performed, in compliance with Good Manufacturing Practices that must be certified.

Appropriate quality management programs, quality control programs, laboratory biosafety programs, and preventive control plans must be in employed. The document requirements for aquaculture vaccine facilities and personnel should be the same as for terrestrial animal vaccine manufacturers.

**X. Manufacturing and testing protocols**

Manufacturers should prepare and submit copies of a production outline and related special outlines, in a format acceptable to the regulatory agency. These descriptions of the
manufacturing and testing methods should be sufficiently detailed to enable regulatory evaluators to assess the appropriateness of the manufacturing and testing methods to demonstrate that the product manufacturing methods conforms to the quality standards established for production of the pre-licensing serials.

The production outline may refer to one or more special outlines, or it may cite internationally accepted regulatory requirements and technical standards such as the United States Department of Agriculture Title 9 Code of Federal Regulations (9 CFR), the European Pharmacopoeia, or the World Organisation for Animal Health (OIE) Manual of Diagnostic Tests and Vaccines for Terrestrial Animals and Manual of Diagnostic Tests for Aquatic Animals, as well as applicable standards of the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH), among others.

Once the production outline and special outlines are approved and stamped as satisfactory, one copy of each will be retained on file with the regulatory agency, and one copy will be returned to the manufacturer.

In the interest of standardizing the quality assurance procedures for veterinary vaccines, it would be helpful if manufacturers and regulatory agencies could work toward development and implementation of common technical standards for manufacturing and testing veterinary vaccines, such as the principles and procedures that are outlined in the CAMEVET Guideline for Good Manufacturing Practices for Veterinary Products, or other technical references that may be developed in the future.

In exceptional and justified cases, additional confirmatory testing may be required to meet the requirements of the manufacturer’s domestic regulatory agency or the destination country’s regulatory agency. This testing must be done by a laboratory acceptable to the regulatory agencies, which could include a contract testing laboratory.

Veterinary vaccines may be manufactured and tested in whole or in part in a contractor’s facility that has been previously approved by the lead regulatory agency for the manufacture of veterinary vaccines. In this case, the manufacturer presenting the licensing submission must provide a flow chart indicating the source(s) of all antigens and/or other components. The manufacturer presenting the licensing submission is also responsible for ensuring that all relevant and up-to-date production outlines and special outlines are provided to the lead regulatory agency, as well as the destination country regulatory agency if required as a condition of importation.
XI. Master seeds, master cell stocks, and pre-licensing serials

The following information is required:

1. Master cell stock data: Identity (species, cell type) karyology, freedom from extraneous agents and the corresponding certificates
2. Master seed data: Identity (genus, species, biotype); purity, freedom from extraneous agents; passage number; back passage studies of modified live vaccines; genetic characterization for the master seed, if the product is biotechnology-derived.
3. Manufacturers must submit summary test results to verify serial-to-serial consistency of consecutively produced serials, e.g., three consecutive batches with a minimum size of 10% or 50% of commercial batches, at the discretion of each regulatory agency. These data demonstrate the manufacturer's ability to consistently manufacture serials that meet the established production outline specifications for a pre-licensing reference serial that has been shown to be safe and immunogenic when used according to label recommendations in the target species. Summary test results for consecutively produced pre-licensing serials serve to demonstrate the uniformity of the serials, as an indicator of the manufacturer’s ability to meet the established quality criteria and minimize batch-to-batch variability.

XII. Materials of animal origin documentation

In order to protect animals and the public from transmissible spongiform encephalopathies (TSEs) and from other infectious animal diseases, all materials of animal origin used in the production of veterinary vaccines must be sourced from countries and animals that are acceptable to the lead regulatory agency, as well as the regulatory agencies of the destination country. The manufacturer of the product must require suppliers of raw materials of animal origin, additional documentation to demonstrate the conformity of these materials with the regulations in force in the country of origin and destination, which will be presented to the official authorities at the time of submitting the license in the country of destination.

XIII. Pre-licensing safety and efficacy testing, and post-licensing serial (batch) release testing

Pre-licensing efficacy and safety testing of vaccines for fin fish should be done in the target species, using fish of the minimum recommended size, which are vaccinated with a prototype vaccine in a manner that is representative of the anticipated field use.

For demonstrating efficacy, the prototype vaccine would ordinarily be formulated to the minimum acceptable potency, so that it may be used as a reference serial in post-licensing batch release tests.

For evaluating target aquatic animal safety, preliminary studies are ordinarily conducted in biocontainment facilities, and larger numbers are subsequently tested in field safety tests. The serologic immunogenicity studies to measure antibody responses, or vaccination-challenge efficacy studies to measure clinical protection should be conducted in parallel with the proposed post-licensing batch release tests (in vivo or in vitro). These parallel tests serve to establish the correlation between the proposed batch release potency test and the protective
dose, when the product is tested in vaccination-challenge studies involving a prototype vaccine that will serve as a reference serial.

Studies supporting efficacy and safety must be conducted with serials that are representative of the final product, as described in the submitted production outline. In general, efficacy studies should be conducted with a vaccine containing the minimum allowable potency, and safety studies should be conducted with a vaccine at meets or exceeds the maximum allowable potency, as stated in the approved production outline.

In the interest of reducing the use of fish for batch release testing, if an in vivo test is used, the first phase of the potency test (in the days after vaccination, but before the challenge), can serve as a batch release safety test.

Once consistency of manufacturing has been demonstrated, if a reliable in vitro batch release potency test is available (based serologic antibody responses in vaccinated fish, or a measure of antigen in the vaccine), the in vivo vaccination-challenge potency test may be discontinued and replaced by an alternative test such as a post-vaccination serum antibody assay, or a quantitative in vitro antigen assay.

Individual animal data for all the animals used in the studies are required; however, these data may be presented in summary tables. Copies of individual records and test reports may be required by the lead regulatory agency or destination country regulatory agency, to supplement the information in summary test reports.

XIV. Labelling
Labelling for vaccines intended for use in aquaculture should conform to the harmonized standard requirements that have been established for other types of vaccines.

XV. Summary test reports for serial (batch) release
In vitro testing should be utilized for post-licensing serial release testing, wherever feasible. If animal testing is employed, the 3R principles of reducing, refining, and replacing animal testing should be followed.

Any required batch release test results should be submitted to the regulatory agency on a standardized Manufacturer's Serial Release Test Report that is acceptable to the lead regulatory agency, and the regulatory agency of the destination countries. Test references on serial release test result forms should cite the current production outline and special outline, as filed with the responsible regulatory agencies.
Manufacturers must retain production and testing records for all serials of products that are manufactured or tested within the facility, for at least one year after the expiry date of the batch.

All serials destined for export must be initially released by a company quality assurance official, prior to distribution within the country or export. Regulatory officials of importing countries may allow importation of any released serial of a licensed product, without further restrictions,
or they may approve importation of each serial individually, after review and approval of the manufacturer’s batch release test results.

XVI. Environmental assessment
For any novel or biotechnology-derived product that is intended for release into the environment, the manufacturer cloud be required to assess the environmental impact of the environmental release, by the competent regulatory agency or complementary committee. Since these summary documents are intended for public release, the documents should be prepared in a format that does not disclose any confidential business information. If necessary, a more detailed version for internal reference may be prepared for the regulatory agencies, with request for confidentiality.

XVII. Manufacturer and importer inspections
Regulated products should be shipped directly from the manufacturer or a regulated regional distributor to the designated importer(s) in the importing country. This helps maintain the cold chain, and minimize the transit time between the manufacturer and importer. Veterinary vaccines should be managed in compliance with good storage, transportation, and distribution practices.

The inspection of the manufacturer and importer facilities can be scheduled shortly after the reviewer has concluded the review of the licensing documentation. The manufacturing facility inspection should be scheduled in consultation with the regulated manufacturer, to ensure that pertinent manufacturing and testing activities will be ongoing, and that the appropriate personnel will be available during the inspection, as well as to provide time for the regulated party to assemble any required documentation, such as test results or facility drawing. It also ensures that any key documentation will be available for examination, and helps minimize any disruptions for the manufacturer or importer.

The inspections serve as an onsite evaluation of the manufacturing and testing procedures, as a supplement to the descriptions of the facilities and materials and methods, and personnel that are provided in the licensing submission. The inspections/onsite evaluations are also an opportunity to further discuss and explain the regulatory system and requirements, establish contact with key corporate regulatory personnel, and answer any questions.

XVIII. Adverse reaction monitoring
Prior to licensing or authorizing restricted importation of a vaccine from another country, the regulatory authority in the destination country may request pharmacovigilance data from the manufacturer in the country of origin. This allows the destination country’s officials to review the performance of the vaccine in the originating country, during the time since the product was originally licensed in the country of origin to provide supplemental safety information. This information could be utilized by the regulatory authority to make decisions regarding any special label precautions, conditions, or restrictions that should be implemented as a prerequisite for licensing or importation.
XIX. Post-licensing regulatory oversight
The monitoring will be managed in accordance with the legislation in force in each licensing country.

XX. Table 1. Parameters to consider when regulating vaccines for use in aquatic species

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Aquaculture system water temperature</td>
<td>Cold water (salmon, trout) versus warm water (catfish, carp, tilapia). Since water temperatures can influence pharmacokinetics of clearance of residues, withdrawal times and duration of efficacy for some vaccines may be determined in degree-days, rather than calendar days.</td>
</tr>
<tr>
<td>Species</td>
<td>Fin fish (i.e., trout, salmon, tilapia, catfish, carp) – innate and acquired immunity. Crustaceans (i.e., crayfish, shrimp) – innate immunity. Molluscs (clams, mussels) – innate immunity.</td>
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<tr>
<td>Water salinity</td>
<td>Fresh water pond, fresh water tanks, marine salt water net pens.</td>
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<tr>
<td>Federal disease control program, surveillance</td>
<td>Diseases may be reportable or notifiable.</td>
</tr>
<tr>
<td>Pathogen</td>
<td>Virus, bacteria, protozoa, fungus, endoparasite, ectoparasite.</td>
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| Epidemiology of disease                        | Endemic/emerging/epidemic
Wild fish may be reservoir, or susceptible to transmission from farmed fish. Human health risk - food borne disease risk for some zoonotic diseases. |
| Target species                                  | Major use, major species versus minor use, minor species.                    |
| Intended use of species                         | Commercial food production, sport fishing, or ornamental.                    |
| Minimum size of fish to be vaccinated           | Usually 10-30 gram for salmon. May also vaccinate later in production cycle, or mature broodstock as a booster or according to the protocol proposed and justified by the interested party or the holder of the license. |
| Dose, quantity of vaccine                       | Range from 25 uL (0.025 mL) to 100 uL (0.1 mL) for injectable vaccines or according to the protocol proposed and justified by the interested party or the holder of the license. |
| Route of administration                        | Immersion (dip), intraperitoneal, intramuscular, oral (in feed).             |

XXI. Reference: Containment standards for facilities handling aquatic pathogens
   URL: http://www.inspection.gc.ca/animals/aquatic-animals/imports/pathogens/facilities/eng/1377962925061/1377963021283