



# Relevance of the availability of effective vaccines in aquaculture

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# 1 Introduction - premise

Vaccination is one of the most effective tools for preventing animal diseases and for promoting animal health and welfare, safe food production and public health. Despite their importance, there are often challenges to ensure that suitable veterinary vaccines are available in a timely manner on the European Union (EU) market.

Veterinary vaccines play a major role in protecting animal health by preventing and controlling serious epizootic diseases. They also have an impact on human health by ensuring safe food supplies and preventing animal-to-human transmission of infectious diseases.

For environment-friendly aquaculture and human health concerns owing to the rise in incidences of antimicrobial resistant microbes and food safety hazards, the vaccination strategies are highly effective and economical in protecting the health of fish and aquaculture animals from various infectious agents.

Advancements in science have paved newer avenues in both basic and applied research areas for developing and designing novel and effective vaccines, as well as improving existing vaccines for rendering protection from various types of infectious diseases.

***Current advances in vaccines and vaccinology offer valuable opportunities to discover new vaccine candidates to protect from fish pathogens not only bacteria and virus but also against mycotic and parasitic agents, for which vaccines are still lacking.***

However, vaccination should be considered part of a comprehensive fish health management scheme, and not the only solution for a disease problem. Vaccination is intended for disease prevention, and not for disease treatment, and can be thought of as “insurance.” To ensure that vaccination will work, producers must weigh carefully the many factors that determine whether a given vaccine will be effective in

a given situation (the particular pathogen and disease, the fish species and age, fish production methods, vaccine route of administration, and economics).

Three initial points of discussion have been identified: possibility of using EU-approved vaccines without using the cascade principle (free circulation), problems with the use of DNA vaccines, harmonization in the production and use of autologous vaccines. Some solutions on how to promote research on vaccines, the existence of a real common market for vaccines in the EU and to facilitate their registration will be addressed.

## 2 Availability of vaccines for aquaculture in the EU and Cascade Principle.

The availability of vaccines, as well as other veterinary medicinal products, for use in farmed aquatic animals is extremely low. This situation is a serious constraint on the prevention and in case of disease, leading to welfare problems and hampering the growth of European aquaculture. The need for the availability of more authorized vaccines to prevent the most common diseases and secure animal welfare has been stressed by several organizations<sup>1</sup>.

Due to the high costs of research, development, authorization and licensing to bring a new Veterinary Medicinal Product (VMP) to market in Europe, the availability of many VMPs, including vaccines, are restricted to certain countries and to certain species. This is due to the fact that the animal health industry needs a return on investment, and aquaculture is seen as a limited market with stringent regulatory procedures. This is especially true for minor indications or minor species.

According to current legislation (Dir. 2001/82/CE) if no authorized VMP exists to treat a condition, a veterinarian may, in particular to avoid causing unacceptable suffering, treat the animals in accordance with the principle of the Cascade. The Cascade is a European legislative provision that allows a veterinarian to prescribe unauthorised medicines that would not otherwise be permitted, namely either a VMP licensed for

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<sup>1</sup> The Federation of European Aquaculture Producers (FEAP), the Federation of Veterinarians of Europe (FVE) and lately the FishMedPlus Coalition.

another species or condition, or a human medicine or VMP authorized abroad or a product made extemporaneously. When no specific withdrawal period is defined, a withdrawal period of 500 degree/days for meat of fish has to be respected. European veterinarians routinely have to resort to the Cascade principle to cure aquatic animals, given the extremely limited availability of VMPs for aquaculture, especially for minor species (all fish species except Salmon and Trout), minor conditions or minor markets (countries with only a very limited aquaculture industry).

With specific reference to the Proposal for a Regulation of the European Parliament and of the Council on Veterinary Medicinal Products (EC COM (2014) 558), some organizations<sup>2</sup> support the new principles it includes, supporting many of the initiatives, such as, for example, the new definitions of “minor use - minor species” and a common EU product database. However, delays in the process of approval of this new Regulation, the fact is that for the moment, and probably for many years in the future, there will continue to be a lack of availability and access to authorized VMPs, including vaccines, for most aquaculture species.

This issue has been extensively debated in the European institutions for a number of years due to the implications for the health and welfare of the fish farmed throughout the Union.

Recently, the European Medicines Agency’s (EMA) Committee for Medicinal Products for Veterinary Use (CVMP) has adopted a set of revised guidelines that clarify the data needed to support an application for a marketing authorisation for veterinary medicines intended for minor uses and minor species, the so-called MUMS, and limited markets (and aquaculture is defined as a limited market).

## 2.1 Issues for debate

- Actually, although the *Cascade* principle is defined in European Legislation (Directive/2001/82/EC), Member States can implement it differently. In practice, some countries have implemented the *Cascade* much stricter than

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<sup>2</sup> FEAP, Copa-Cogeca and FVE.

others, leading to additional hurdles for the movement of MVP between Member States.

- In some Member States, their restrictions on the implementation of the *Cascade* principle make it very difficult to apply it to vaccine prophylaxis as they do not consider vaccines an exceptional therapeutic intervention for severe suffering animal states.
- The withdrawal period of 500 degree/days, as required now in the application of the *Cascade* principle, makes no sense in the case of vaccines for which the withdrawal period is of 0 degree/days for the registered target species.

## 2.2 Proposed solutions

- *Vaccines available and registered in any European Member State, on the basis of the premises, should be legally usable for veterinarians and farmers all over the EU.*
- *A true single market of aquaculture vaccines (VMPs) is needed; enhancing a free circulation of registered vaccines for aquaculture. This should be applied to all vaccines approved by National Competent Authorities.*
- *A truly functional import procedure of VMPs from the European Free Trade Association (EFTA), and certain third countries (e.g. US and Canada), should exist.*
- *The future Regulation on Veterinary Medicinal Products and its implementing acts should take in to account this issue.*

## 3 Research on vaccines and use of DNA vaccines

Vaccines stimulate the immune system to help fight off diseases and the application of these methods to control infectious diseases is growing in importance. Perfecting

the use of adjuvants, delivery systems and new technologies is needed to meet the demand for vaccines in order to ensure the safe supply of healthy fish products.

Research on vaccines in aquaculture should be stimulated on the following topics:

- making some routes of administration more efficient, such as immersion and oral;
- development of new formulations (including adjuvants and carriers) and delivery methods;
- development of vaccines and vaccination strategies dressed for the different types of aquaculture, farmed species, life stages.

Separate chapter is that concerning DNA vaccination which is considered a promising solution to combat pathological fish diseases. The cost of development of these vaccines is high but DNA vaccines may be the only alternative for many viral diseases. In terms of safety, no adverse effects in the vaccinated fish have been observed to date. There is, however, a lack of knowledge regarding its ecological and social implications. The potential benefits of DNA vaccines for farmed fish include improved animal welfare, reduced environmental impacts of aquaculture activities, increased food quality and quantity, and more sustainable production.

As tools for managing aquatic animal disease emergencies, DNA vaccines have advantages in speed, flexibility, and safety. As DNA vaccination is a relatively new technology, various theoretical and long-term safety issues related to the environment and the consumer remain to be fully addressed, although inherently the risks should not be any greater than with the commercial fish vaccines that are currently used.

Present classification systems lack clarity in distinguishing DNA-vaccinated animals from genetically modified organisms (GMOs), which could raise issues in terms of licensing and public acceptance of the technology.

### **3.1 Proposed solutions**

*Given this background, aquaculture industry's priorities regarding vaccines and vaccination strategies, and its information policy towards the customer, is*

*to get good and well-documented information in the near future from the scientific world with the support of an appropriate regulatory framework.*

*The research should be promoted with appropriate calls and should be addressed to solve the needs described above.*

## 4 Harmonization in the production and use of autogenous vaccines

Autogenous vaccines are manufactured from specific pathogens (e.g., bacteria or viruses) isolated from sick fish at a particular fish farming facility. This type of vaccines can help prevent recurrent disease problems, and should be considered a management option.

Autogenous vaccines remain a regulatory issue. They are demanded by practising veterinarians and by fish farmers and in some European countries they are quite widely used.

Because autogenous vaccines are actually exempted from the harmonised regulation at the EU level, they are regulated by individual Member States, the regulation varying from practically no regulatory measures in certain countries to a quite complex and demanding regulation in other. Both risks and benefits are related to these products and they shall be taken into account when regulatory measures are considered. As appropriate and well balanced regulation of autogenous vaccines is deemed necessary, considering the risks related to them, and based on the fact that national regulatory measures could be considered as a trade barrier under certain circumstances, harmonisation of the key issues or legal admission of the nationally based regulatory measures, including movement of these products from the other Member States, should be laid down in the EU legislation.

The European Medicines Agency's EMA Committee for Medicinal Products for Veterinary Use (CVMP) has set up a working group reviewing the requirements for autogenous vaccines in veterinary medicines. The objective of this group is to have, within the legislative framework, harmonised requirements and understanding

regarding “in the same locality”, regarding the concept of epidemiological links between farms, to define good practices regarding the manufacture and control of autogenous vaccines and to make proposals regarding surveillance and use of autogenous vaccines.

## 4.1 Proposed solutions

*Autogenous vaccines complying with basic quality and safety requirements are a very useful tool for fish health and welfare management. It is considered necessary to take into account the specificities of aquaculture when regulating autogenous vaccines. This is relevant due to the fact that the future VMPs legislation will cover autogenous vaccines.*

*VMPs legislation at EU but also at Member States level, in the event that autologous vaccines are the only appropriate solution for the prevention / control of the spread of the disease, provide greater flexibility that, following proven epidemiological connections, should allow their use even in larger areas.*

## 5 Conclusion

For the future of the fish farming industry it is important that vaccines can be an efficient tool in reducing the need to use antibiotics in animals, thereby contributing to the fight against antimicrobial resistance.

The aquaculture profession, the animal health industry, the regulatory authorities, the veterinary profession and researchers should join forces to improve the availability of vaccines for farmed aquatic animals.



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