

## IFAH-Europe factsheet

### Animal vaccines: development, registration and production

#### Summary

Vaccines are important tools for protecting animal health and welfare. Aside from significant financial investment, the development of a vaccine for a new virus or a new serotype of an existing virus is technically complex taking 5 to 7 years with authorisation taking 1.5 to 3 years.

It takes 6 to 8 months to manufacture a new vaccine. In order to be able to respond to demand, especially in an emergency situation, all stakeholders need to plan ahead such that sufficient quantities of vaccine can be made available in a timely manner to protect animal health and welfare.

#### Introduction

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The goal of IFAH-Europe and its members is to supply safe, efficient, and cost-effective veterinary medicinal products, including vaccines, to prevent and treat animal diseases. These contribute to animal health and welfare as well as to public health and food safety.

Research on vaccines and on the immune system of animals is constantly evolving to provide new products that prevent diseases or have other improved characteristics, such as no cold-chain requirements, ease of administration, or built-in diagnostic features to distinguish vaccinated animals from infected ones.

Vaccination has profoundly influenced and improved world health, and will continue to be a fundamental tool to meet future health challenges. This paper presents an overview of the opportunities and challenging steps to bring animal vaccines to the European market. It highlights the need for stakeholders to plan vaccination policies well ahead of disease threats so that sufficient vaccine will be available on time.

#### About vaccines

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The basic principle of vaccination is that if a small amount of a weakened or inactivated (killed) or parts (protein or genes) of a pathogen<sup>1</sup> is introduced into the body, it stimulates the body's immune system to build up a defensive reaction.

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<sup>1</sup> An organism causing disease, typically a micro-organism such as a virus or bacterium.

The immune system then remembers the pathogen and can defend the body against natural exposure to that pathogen in the future.

Conventional animal vaccines are derived from the pathogen causing the disease and hence are specific for that disease. Both live and inactivated vaccines exist and in either case the ability of the micro-organism to cause an immune response is preserved.

Sometimes only part of the bacterial micro-organism is used or just the toxins secreted by it. These are treated to render them harmless, while retaining their immunising properties and thus neutralising the deleterious effects of a disease.

- Research and innovation

Researchers are in a constant quest for new ways to meet the changing challenges to animal health, which are linked to the evolution and the geographical spread of diseases threatening animals. Recent examples are the highly pathogenic form of avian influenza and the spread of bluetongue disease in sheep and cattle to northern Europe.

Modern techniques, particularly in molecular biology, have greatly improved the available range of vaccines and the methods of administering them; for example, with the introduction of “vector vaccine” technology<sup>1</sup>. New vaccines not only target new diseases, but they can also simplify administration, be it by actively protecting against a variety of diseases in one single product, or by offering a wide variety of application routes: through drinking water, baits, spray, eye drops, via the nose, through the skin, using the classical or needle-free injection technique or by immersion.

- Vaccine types

Live vaccines can be produced using live micro-organisms that have been “attenuated” in some way to make them harmless. Alternatively, vaccines can be produced using killed micro-organisms or just relevant sub-units such as specific proteins by which the immune system can recognise the pathogen. In either case the ability to trigger an immune response is preserved. During production, the micro-organisms are propagated, harvested (whole or specific parts), often purified and formulated to preserve the activity during a reasonable shelf-life.

Attenuated (live) vaccines can be made by culturing these micro-organisms for many generations in laboratory conditions, which encourage their growth while losing their ability to cause disease or by using other modern techniques. The immunity induced by such “live” vaccines is usually strong and long lasting.

Inactivated (killed) vaccines consist of suspensions of the dead micro-organism (or specific parts). For these vaccines the selected strain of micro-organism is grown and

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<sup>1</sup> This technology uses a harmless micro-organism as a carrier of pieces of a disease-causing microorganism.

then killed by heat or chemical treatment. The immunity induced by such vaccines is usually not as strong as from live, attenuated vaccines. Therefore, in inactivated vaccines substances, termed adjuvants, may be added to increase the immune response to the vaccine. Inactivated vaccines are also often used to boost the effect of previous vaccinations.

## Vaccine development

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It takes an average of **5 to 7 years** to develop and obtain a marketing authorisation for a new animal vaccine or a vaccine to protect against a new serotype. Significant investments are required by the animal health industry to address this highly fragmented and dynamically changing market.

Broadly speaking, the R&D process for veterinary vaccines can be divided into several largely consecutive phases, each of which may take years to accomplish:

The main phases are as follows:

- Evaluation of basic research concept
- Feasibility assessment
- Pre-development with elaboration of methods and evaluation of experimental reagents and products
- Industrial product and process definition
- Manufacturing scale-up
- Registration

It is of interest to note that the new product development by itself will not be sufficient to get a vaccine into the market. Additionally, each vaccine launch will inevitably require, in parallel, appropriate manufacturing capacity provisions and the building of appropriate technical expertise, which can add significant costs, complexity and lead times before a new vaccine comes available on the market.

## Vaccine registration

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Before any new vaccine can be placed on the market, it must obtain a marketing authorisation. This involves a stringent, scientific and independent review by the regulatory authorities of data submitted by the manufacturer to ensure **quality, safety and efficacy** of the vaccine.

The process requires applicants to submit a detailed and voluminous 'dossier'. The registration process takes 1.5 to 3 years and generally results in a marketing authorisation that is initially valid for a 5-year period, after which the company has to apply for a renewal.

Some modifications have been made to this process for emergency situations to achieve faster access to urgently needed new vaccines. However, this does not allow a shortening of the development time or a reduction of costs.

## Vaccine production

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Vaccine production comprises various phases, from testing the master seed<sup>1</sup> to the formulation into the finished product and the scaling up of the manufacturing process to meet the doses needed.

Key production phases are:

- Starting material sourcing and control
- Production-seed and active-ingredient production
- Active-ingredient quality control
- Formulation and filling of finished product
- Final production quality control and release (i.e. antigen<sup>2</sup> content, safety and potency testing)
- Packaging and shipment.

From the viewpoint of full-scale production of ready-to-use vaccines, all these steps are critical and often have non-compressible timelines; these can be highly variable depending on the vaccine in question and the number of doses required.

For veterinary vaccines, it takes an average of **6-8 months** to manufacture a new vaccine, which has been developed in order to respond to an emerging pathogen or a new serotype. It is therefore vitally important that plans are made in time to be able to protect animals against disease.

## Conclusion

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Considering the long development and production lead times, it is critically important to anticipate product developments in time to be able to introduce vaccines intended to protect animals against emerging disease. Furthermore, since each vaccine production engages significant resources and costs and requires careful manufacturing planning, it is vitally important that all stakeholders develop vaccination strategies in time to estimate vaccine demand and enable industry to plan supply of appropriate quantities.

**IFAH-Europe and its members are continuously striving to assure efficient new product development and manufacturing, and in collaboration with other animal health stakeholders, increase the availability of vaccines against endemic and new infectious animal diseases covering all significant veterinary pathogens as well as their individual serotypes spreading to Europe.**

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<sup>1</sup> Original culture of the micro-organism.

<sup>2</sup> Component of an invading micro-organism that is recognised by the body's immune system as being 'foreign' and induces an immune reaction.