Understanding vaccines and vaccination programmes

Protecting the health of poultry through vaccination has been an essential part of poultry production for more than 50 years. Vaccination is the final act of a very long, meticulous process of vaccine production starting with research and development, manufacturing, and regulatory work and ending in the delivery of a safe and effective vaccine to the farm gate.

Since vaccination failures are most often the result of not understanding vaccines and how they need to be administered carefully in order to establish an optimal immune protection in the flock, this chapter is important for those who will be administering vaccines to gain an understanding of vaccines, how they are used, and when they should (or should not) be used.

The key feature of this chapter is to give a complete perspective of what vaccines should be used. Since this booklet is designed for the poultry industry in both New Zealand and the South Pacific countries, we will make clear vaccination recommendations that account for the differences in the risks to exposure and incidence of poultry diseases based on geography and what pathogens are prevalent. We incorporate new terminology that calls for 'core' and 'non-core' vaccination programmes to differentiate the vaccines that are essential from those that are optional or not required based on the likely risk of a specific poultry disease.

Looking at Vaccines

From the early days of vaccine research in the 18th and 19th centuries, vaccines have continued to become increasingly sophisticated as we gain better insights into diseases, pathogens, and immunity mechanisms. Along with new vaccine technologies, there have been continual improvements in not only vaccine safety and efficacy, but also we have learned how to 'engage' the immune system more effectively to promote more appropriate immunity and optimise immune protection.

In veterinary vaccine use, the poultry industry adopted vaccination early on having largely led the way in developing vaccine technologies as the intensification of the poultry industry continued to demand better vaccines with more simple methods for mass vaccination in increasingly larger flock sizes. As a result, the poultry industry has been able to adopt vaccination as a key measure in disease prevention along with good biosecurity and husbandry practices. We now enjoy an extensive range of vaccines that are safe to use and highly effective in protecting against a wide range of poultry diseases.

So, how are poultry vaccines made?

As we have pointed out, it is a very long and expensive process to research, develop, and manufacture a vaccine. Vaccine development has many stages to go through before a successful vaccine can finally be ready for use. To show the complexity of the process, figure 1 (right) provides, in flowchart format, a description of the basic steps needed to bring a vaccine into fruition.

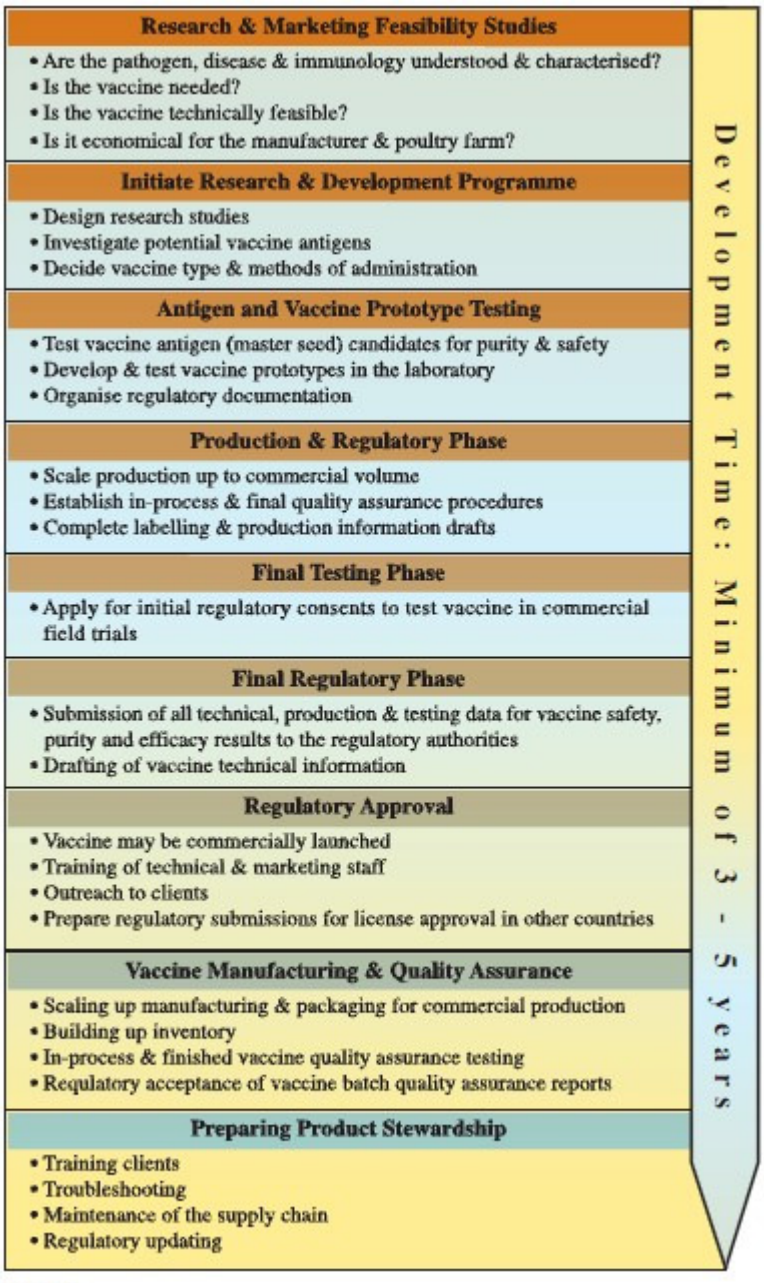


figure 1

Immunity and Poultry Health (3)

Once a disease and its pathogen have been fully characterised, 'vaccinologists', who are usually trained immunologists and microbiologists, search for the strain (or strains) of the pathogen that will make the best candidate as a vaccine that will trigger a safe and effective protective immunity. The organism that is able to trigger such an immune response is known as an antigen. We use the term vaccine antigen when referring to the organism that will be used in the vaccine.

Vaccine development starts with finding and selecting an organism as an appropriate vaccine antigen candidate. It begins with first understanding the characteristics of the pathogenic organism, how it causes disease, what strain (or strains) of the organism would potentially make a good vaccine antigen, and how they interact with the immune system to generate an immune response.

A critical issue at this point is to decide whether the vaccine should be a live or inactivated (killed) antigen. Most live vaccine antigens are attenuated, i.e. have modified virulence, so they are not able to create disease, but still can elicit a robust immune response.

As we noted previously, live vaccines are generally used where a cell mediated response is the most advantageous. An important aspect of live vaccines is that they are highly stable and do not revert to virulence.

The vaccine researcher will have to decide on critical issues before a prototype vaccine is ready for testing.

First, the vaccine must strike the right balance between safety and efficacy. In terms of safety, the vaccine must not cause the disease, a loss of performance, or side effects. Efficacy measures how well the vaccine protects against a disease. Figure 2 demonstrates how a vaccine must be able to stimulate sufficient immune protection without compromising the safety and welfare of the chicken.

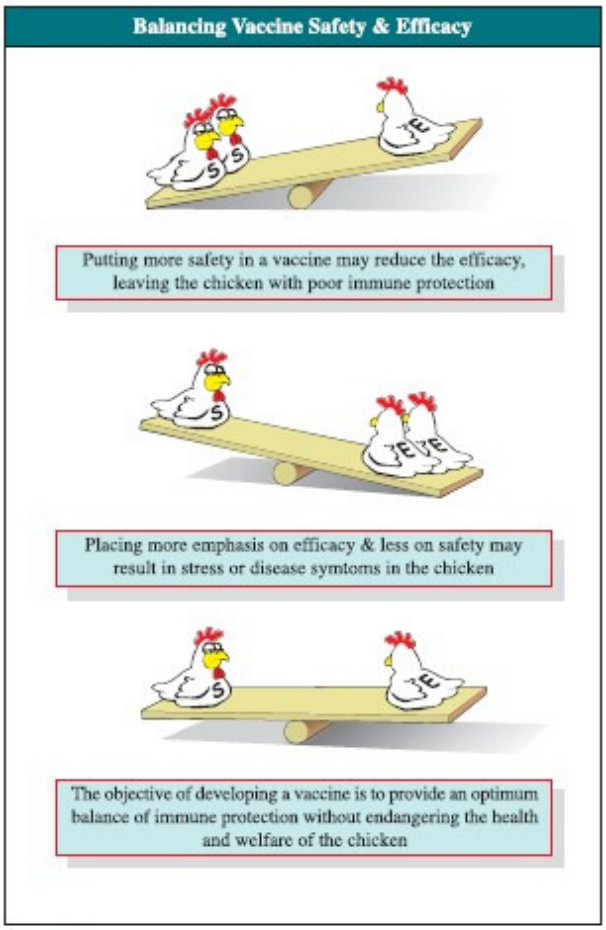
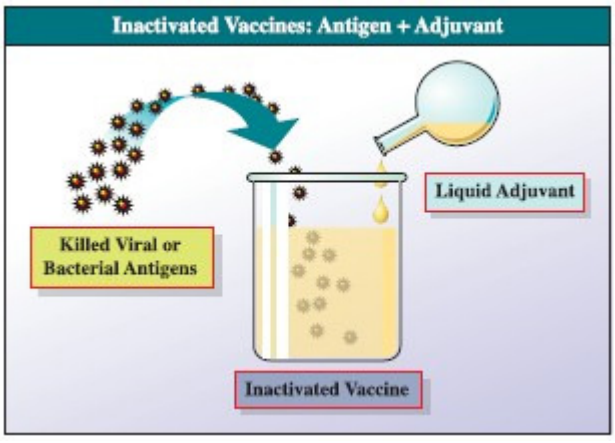


figure 2

To improve vaccine safety, researchers modify the vaccine strain by selecting a mild strain or using methods to reduce the virulence of the selected strain. While reducing the virulence, it is important to retain the vaccine strain's ability to stimulate an immune response. A more virulent strain may induce more antibody production but it may overwhelm the chicken's defences and cause disease. The goal is to find the right balance between the highest level of immune protection with the least amount of stress to the chicken.

Inactivated or killed vaccines are preferred when long-lasting antibody protection is the most appropriate kind of immune protection required to protect against a disease. In poultry, inactivated vaccines are primarily administered to pullets before point-of-lay. Inactivated vaccines normally contain an adjuvant, an additive designed to attract the chicken's immune system to slowly absorb the vaccine antigen and thus trigger a long duration of immunity to protect long-lived breeder and layer hens through their production. These types of vaccines are also important for triggering the passive immunity required for protecting newly hatched chicks, as was discussed in Immunity & Poultry Health (2).



Vaccines require a large volume of pure antigen. Inactivated vaccines require much more antigen than live vaccines, as when the antigen is killed, it can no longer reproduce itself. Thus, inactivated vaccines have to include far more antigen in order to trigger a sufficient immune response.

Manufacturing vaccine antigen is the most critical step in vaccine production. For the vaccine strains to grow, they depend on some

kind of medium in which to grow. Viruses need cells to grow in. Bacteria will generally utilise a broth medium made up of nutrients that the bacteria cell requires to grow and reproduce itself. Most poultry viruses are grown either in a culture of poultry tissue cells or in chicken embryos. Importantly, medium nutrients, tissue cultures, and chicken embryos must be free of any other poultry pathogens. Chicken tissue cultures and embryos are therefore sourced from Specific Pathogen Free flocks that are tested weekly to confirm freedom from contamination by other pathogens. Vaccines are tested again before commercial release.

Once a prototype vaccine is finally prepared, it undergoes extensive testing. Tests start with small clinical trials in the laboratory and, if looking successful, they will be scaled up to increasingly larger trials that will mimic large commercial-scale poultry production. At this time, vaccine production methods are tested and scaled up so large volumes of vaccine can be manufactured.

Extensive testing of vaccine is required to ensure it is safe (it does not cause disease or other ill effects), it is not contaminated with other pathogens, and it is efficacious (able to generate protective immunity). Testing occurs at every step of development and production to ensure every batch of vaccine passes its quality tests.

A most critical part of vaccine development is the regulatory process. The vaccine manufacturer prepares a comprehensive dossier that covers all aspects of the vaccine's origins, development process, production process, quality assurance and efficacy testing. In the country of origin, a national authority responsible for veterinary vaccine approval reviews these dossiers and issues a licence of approval.

For instance, in the United States, this is carried out by the Animal and Plant Health Inspection Service of the U.S. Department of Agriculture. For New Zealand, veterinary vaccine approvals are the responsibility of the Agricultural Chemicals and Veterinary Medicines Group of the New Zealand Food Safety Authority. The regulatory processes are designed to be rigorous and are particularly focused on product safety and assuring the vaccine has been proven to generate protective immunity. The holder of the approval license is then responsible for the stewardship of the product up to the time it is shipped to the client to ensure the vaccine is in proper condition for use.

How do vaccines work?

The objective of a vaccine is to create protective immunity against a specific disease. Generally speaking, the best immunity is one that mimics how the immune system builds up resistance against a natural infection.

The key to successful immunisation is to build up the immunity prior to a chicken being exposed to a disease, as it takes time for the immune system to respond to a vaccine. If we do not vaccinate soon enough, the pathogen may be able to overwhelm what immunity has been started and cause disease.

Vaccination and Immune Memory

There is a common misconception that immunity is only about increasing antibody levels and therefore raising immunity protection levels. This is only one piece of the immunity story. There is much, much more.

Creating immunity is all about changing the capacity and performance of the immune system in four different dimensions:

- **Volume**
- **Speed**
- **Avidity** (adhering to pathogens)
- **Location**

When we vaccinate a chicken for the first time, we are priming the immune system to recognise an invading pathogen and begin setting up the effector cells, cytotoxic T cells and antibody-producing plasma cells, as well as the memory T and B cells that will retain the recognition ability. For most poultry vaccinations, this priming of the immune system will not provide sufficient protection and we need to administer a secondary vaccination or 'booster shot' in order to build up sufficient immunity.

Secondary (booster) vaccination shifts all four dimensions of the immune response into a higher gear from what was created by the vaccination primer:

- **Volume:** The number of immune cells can increase 1000 fold.
- **Speed:** It only takes half as long to create new effector cells, thus the speed of the immune response is essentially doubled.

- **Avidity:** Properly primed and boosted immune cells have a far greater ability to adhere to invading pathogens and process them for elimination.
- **Location:** Primed immune cells migrate towards the most likely tissue sites of infection.

We quickly learn from this that the timing of vaccinations is crucial. As it takes time for the immunity to develop, vaccine manufacturers carefully research the optimal time for administering the primary and subsequent booster vaccinations in order to create an optimal immune response. If we are either too early or too late with secondary vaccinations, we may fail to reinforce the immune response sufficiently and be disappointed by the poor immune protection.

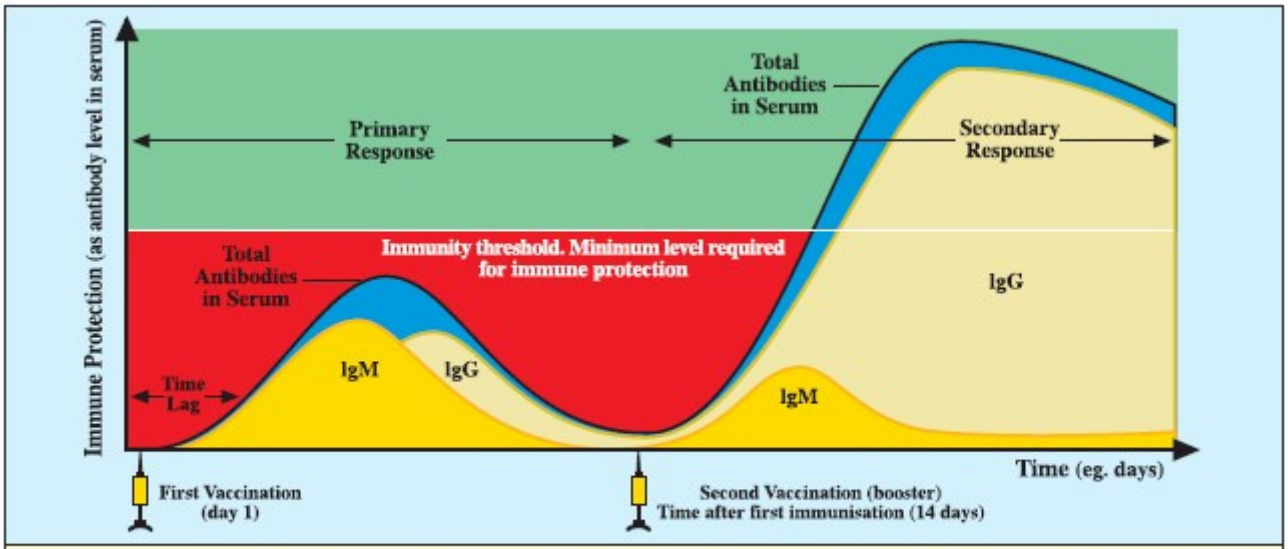


figure 3

As a result, we learn that it may take some time to build up satisfactory immunity. After a primary vaccination, we may need to have an interval of 2 to 4 weeks before giving the booster vaccination, and then it may be another two weeks before the chicken becomes fully immune.

What this means is that we have to vaccinate sufficiently in advance of a potential infection in order to have good immunity.

This 'immunity gap' is one of the reasons we vaccinate breeder hens to help build passive immunity with antibodies in the yolk to help protect chicks until the chick's own immune system is mature enough to create its own active immunity from vaccination.

Immunologists use the term 'duration of immunity' to define how long a protective immune response will last. The length of time of protection will vary considerably between types of vaccines. Some vaccines may give only a few weeks' duration of immunity while others may last several months. This helps explain why each vaccine will have its own specific instructions on vaccination administration.

The primary goal of establishing a vaccination programme is to minimise any 'immunity gaps' by closing the window before possible infections may occur, i.e. by vaccinating sufficiently early to build immunity before infections become a problem.

Thus, the vaccine and timing of the vaccination become crucial factors for us to consider.

Deciding What Vaccines Are to be Used

Every poultry farm will have different vaccination requirements as needs will depend on the type of poultry (breeder, layer, broiler), the age of the chicken, and the incidence of disease.

Long-lived breeders will have different needs than long-lived commercial egg layers. Cage operations will have different requirements from barn and free-range operations. Short-lived broilers present an entirely different set of vaccination needs.

Immunity and Poultry Health (3)

In New Zealand and the South Pacific countries, we are more fortunate than many other poultry producing countries due to the lack of serious disease issues and our isolation from other continents. Such freedom from the ravages of many virulent diseases is an enormous economic advantage in terms of performance. It allows us a degree of 'natural biosecurity' of distance. However exotic diseases can still be a threat. Some diseases, such as Infectious Bursal Disease, have become endemic in the South Pacific (though fortunately eradicated from New Zealand).

To ensure we are only vaccinating for what we need, poultry vaccination programmes may be categorised into three levels based on the risk of disease and the immediate need to prevent the disease by vaccination:

Core Vaccinations: These are vaccinations to prevent the generally ubiquitous diseases from occurring despite the normal level of good biosecurity, hygiene and husbandry standards.

Non-Core Vaccinations: These are vaccinations added to the core vaccination programme due to a higher risk of exposure to certain diseases caused by geographic location in an endemic disease zone, type of bird (e.g. long-lived versus short-lived) or a generally lower level of biosecurity, hygiene and husbandry in an operation.

Not Recommended Vaccinations: These are vaccinations that are not required as the farm may be in a disease-free region, e.g. the South Island's freedom from Infectious Laryngotracheitis virus (ILT). Vaccination would be legally allowed but it would be superfluous and of no value.