Animal vaccination and the veterinary pharmaceutical industry

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Summary
The market for veterinary vaccines is spread across species but it is limited in size and the development of vaccines is becoming more complex and expensive. Vaccines are amongst the most effective means of preventing disease in both animals and humans. In many cases, diseases have been eradicated or their impact on animal health and welfare greatly reduced. It is an ethical responsibility to ensure the availability of a wide range of vaccines even where the market needs to be financially supported, as in the case of less common animal species and those with less common conditions (commonly referred to by the acronym MUMS: Minor Use and Minor Species). Mass slaughter is becoming unacceptable to society and we must move to a ‘vaccinate to live’ policy wherever possible. We need to use vaccines to avoid the high costs of disease and to enhance food safety. In developing vaccines, we need to minimise animal testing. In addition, we need to ensure that the public accept the use of vaccines in food-producing animals as a means of protecting the health and welfare of all animals. As we look to the future, vaccines will be vital to ensure our ability to provide more food to a growing global population. The European Technology Platform for Global Animal Health has a key role to play in identifying key research priorities.

Keywords

The global veterinary vaccine market

In 2004, the international veterinary vaccine market was worth US$3.1 billion (i.e. 21% of the total veterinary medicine market, which is valued at US$15 billion). Forty-one per cent of the market was based in the Americas, 37% in Europe and 22% across the rest of the globe. Table 1 provides a breakdown of the global veterinary vaccines market in terms of species.

<table>
<thead>
<tr>
<th>Species</th>
<th>Value in US$ billions</th>
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</thead>
<tbody>
<tr>
<td>Livestock</td>
<td>1.50</td>
</tr>
<tr>
<td>Poultry</td>
<td>0.68</td>
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<tr>
<td>Other</td>
<td>0.92</td>
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Developing a vaccine: the process

Put simply, the process of developing a vaccine involves identifying a disease target, isolating the disease organism, growing it in eggs or cells, treating it physically or chemically so that it does not cause disease (inactivated vaccines) or attenuating virulent characteristics of the strain (live vaccines) and then administering it to the animal. The result is an immune response that protects the animal against the disease.

Modern genetics technology allows for more possibilities and options such as taking genes from the disease organism, inserting them into harmless viruses, growing the viruses and then administering the live virus to the animal to create the immune response. In addition, genes may be added to a known virus that is harmless, the virus may then be grown, treated in a manner that kills the virus and the resultant material may be used as a vaccine. Finally, a second disease may be identified, genes from the first disease may be added to the second disease, cultivated and the resultant treated material may be used to vaccinate against two diseases.

In many cases, industry develops vaccines in cooperation with universities, institutes and other bodies, thereby combining its expertise with that of third parties. This is increasingly necessary as new scientific disciplines develop (such as in the area of genomics), as it is much more efficient to combine resources than for each party to have its own specialists.

Costs of developing a vaccine: benchmark data

Industry surveys indicate that the time taken to develop a vaccine varies across species. The process may take eight to ten years for brand new products. During this period, the development of the product is coupled with studies to demonstrate the safety, quality and efficacy of the product. The product must be formulated in a way that facilitates use and optimises efficacy, e.g. by including an adjuvant to stimulate a maximum immune response that lasts for a reasonably long period of time.

The cost of this process also varies, but it is estimated that the average cost is US$50 million. As technology develops in complexity, regulatory requirements also become more complex, with both factors leading to an increase in the cost of developing vaccines. This is in contrast to the value of food-producing animals, which is tending to decline over time.

It is clear, therefore, that commercial vaccine production can only be undertaken for diseases that generate sales covering the cost of development, along with some profits. As a result, we have disease problems where the development of vaccines must be supported by public authorities, e.g. anthrax and botulism.

The benefits of animal vaccination

Vaccination is part and parcel of good husbandry and management. Vaccines are amongst the most effective means of preventing disease in both animals and humans. Preventing disease protects the health and welfare of the animals (i.e. less mortality and fewer animals that survive the disease but are negatively impacted for the rest of their life, e.g. with impaired lung function), helps to prevent the spread of disease to humans (e.g. salmonella vaccination ensures high quality food is produced from healthy animals) and helps to protect the environment, as fewer animals are required for food-producing purposes.

Vaccines, coupled with diagnostic tests, eradication programmes and surveillance, help to eradicate diseases, e.g. foot and mouth disease (FMD), rabies and Aujeszky’s disease in many EU countries. They also help to reduce the annual 17% loss of production associated with disease in animals. With globalisation, the potential for diseases to travel with animals, animal products and humans is greatly increased, as was seen during the 2003 outbreak of severe acute respiratory syndrome (SARS), thus the role of vaccines is becoming increasingly important. The European Technology Platform for Global Animal Health (ETPGAH) is actively involved in identifying priority diseases and research needs so that our ability to control diseases into the future will be increased. Coordination of research on a global basis via the ETPGAH has the potential to deliver significant benefits to society in the medium to long term. The advantage of being able to eradicate diseases, e.g. avian influenza, at source and so prevent them becoming global threats is clear and the benefits to society are huge.

Socio-ethical issues

The benefits of vaccination are clear, but there are several issues to deal with when developing vaccines for animals and each will be examined in this section.
Vaccine availability

In the context of vaccines for less common animal species and those with less common conditions (often referred to with the acronym MUMS: Minor Use and Minor Species), the issue of availability is very real. Where there is a rare disease in a major species, such as FMD, anthrax or brucellosis, public funding must be made available if we wish to develop a vaccine as opposed to relying on antibiotic treatment of sick animals. It is ethically unacceptable to allow animals to become ill if we have tools, such as vaccines, to prevent illness. What price is society willing to pay to follow this ethical approach? In the case of minor species such as goats, fish, rabbits or deer, again, third party intervention is necessary if vaccines are to be developed. This could come in the form of public funding or the funding of the development of a vaccine, under contract, by groups of farmers who pool funds. The alternatives to vaccination are to treat animals that become ill or to stop producing some of these species for food purposes.

Mass slaughter

The outbreak of FMD in the United Kingdom (UK) in 2001 (other areas of the globe are likely to be similarly impacted) represented a turning point in policy in the European Union (EU). It is no longer acceptable to the public to engage in the mass slaughter of animals that was witnessed during that outbreak. Instead of focusing exclusively on prevention and eradication, vaccination is now seen as a tool in the armoury to fight exotic diseases. This change in policy has become known as the ‘vaccinate to live’ policy. Whilst a stamping out approach is still the most widely implemented strategy to eradicate disease in the first instance, vaccination is now regarded as an appropriate strategy if initial efforts to eradicate the disease via slaughtering are not succeeding.

Disease costs

The UK FMD outbreak is estimated to have cost £3,800 million (US$5,186 million) (1). The 2003 outbreak of avian influenza in the Netherlands cost at least US$612 million. Also in the Netherlands, the 1997-1998 outbreak of classical swine fever cost US$2.52 billion.

The cost of disease is a complex issue. Direct costs that may arise for the producer include those that result from:

- future cost of promotion to stimulate demand
- cost of lobbying government.

Related sectors are impacted in various ways that may include loss of feed sales, decline in the value of finished product, scarcity of raw materials, loss of markets, etc.

Indirect costs can include:

- government subvention (vaccination programmes, culling, supervision of quarantine areas, compensation for culling, scientific facilities, negotiation of the lifting of sales bans with other countries, etc.)
- loss of tourism revenue (the FMD outbreak in the UK resulted in many areas of the country being placed off limits to tourists)
- loss of overall employment, treatment of people who become ill.

It is clear, therefore, that major disease outbreaks entail significant costs to society. Consequently, the idea of investing significantly in the prevention of disease makes very good economic sense. In this context, many issues need to be considered, including:

a) the availability of vaccines to prevent a disease and the need to invest in better vaccines
b) the availability of strategic reserves of vaccines and/or sera to respond to diseases that occur rarely (FMD)
c) the ability of industry to respond to a surge in demand (as was the case during the recent outbreak of avian influenza) and the need to stimulate production capacity by public intervention such as the regular purchase of strategic reserves.

In the context of avian influenza, the threat of a human pandemic is of great concern. The Spanish flu killed between 20 million and 40 million people in 1918. The Asian flu of 1957 killed between 1 million and 4 million people, as did the 1968 Hong Kong flu. The ability to use biosecurity, stamping out and vaccination to attempt to eliminate avian influenza and so possibly avoid a human pandemic is of major societal importance and once again highlights the value of vaccinating animals. Indeed, we need to consider vaccine use on a global scale to stop diseases at source and so prevent diseases becoming global problems.

Food safety and quality: the value of vaccines

The control of salmonella in the UK, as depicted in Figure 1, indicates the value of vaccination to society in terms of public health. The elimination of FMD from Western Europe, as depicted in Figure 2, highlights the animal welfare value of vaccination. Similarly, from the
viewpoint of protecting health as opposed to treating disease, the decline in the use of antibiotics in Norwegian salmon production after the introduction of appropriate vaccines, as depicted in Figure 3, further highlights the benefits of vaccination.

![Graph](image)

**Fig. 1**
*Source: Advisory Committee on the Microbiological Safety of Food, United Kingdom*

![Graph](image)

**Fig. 2**
**The elimination of foot and mouth disease from Western Europe**
*Source: Intervet, Netherlands*

![Graph](image)

**Fig. 3**
**Norwegian salmon production, consumption of pure antibiotics and the effect of vaccines**
*Source: Norwegian Ministry of Fisheries and Coastal Affairs, 2005*

Clearly, vaccination has a tremendous benefit directly to society, as well as to animal health and welfare. The desirability of using vaccines to minimise the threat of other zoonoses to society is very clear: *Escherichia coli*, campylobacter, listeria, West Nile virus and Lyme disease are cases in point.

**Animal testing**

In developing vaccines, animal testing is needed at various stages in order to assess safety and efficacy. Many of the testing requirements are contained in the European legislative framework, as detailed in the European Pharmacopoeia. Guidelines also exist clarifying when animal tests are required.

It is the wish of everybody concerned to minimise the use of animals in testing vaccines. In order to move forward, we need alternatives that are accepted across the globe. It is of no value to introduce an alternative in one part of the globe if other regions demand the animal-based test. The company is still forced to use the animal test if it wishes to continue to supply its product in the region demanding the test.

In this context, the International Cooperation on Harmonisation of Technical Requirements for the Registration of Veterinary Products (VICH) has a key role to play. VICH has the potential to harmonise regulatory requirements ensuring that the same test procedure is accepted globally – this prevents duplication of testing. In addition, agreement may be reached where testing may be replaced by alternatives not involving animals. Progress through this forum has the potential to deliver global agreement on alternatives to animal testing.
The initiative announced by the European Commission in November 2005 on alternatives to animal testing (European Partnership to Promote Alternative Approaches to Animal Testing [EPPAA]) is also important. The objective of the EPPAA is to replace, reduce or refine the use of animals in testing (this strategy is referred to as the 3 Rs initiative). It is important that we make every effort to replace animal testing, and to this end the Commission and industry from many sectors have combined to jointly work on alternatives.

Over the years, progress has been made. For example, intra-cerebral safety testing in mice in relation to Aujeszky’s disease vaccines has been eliminated.

**Safety of food from vaccinated animals**

A recently published EU study concerning the knowledge of consumers in relation to avian influenza is of interest (2). Fifty-three per cent of the public believe that it is dangerous to eat the meat of a chicken vaccinated against avian influenza. In the UK in 2001, the authorities did not use vaccination to try to stop the spread of FMD as various parties in the UK food chain indicated that they would not handle produce from vaccinated animals. When one examines these two pieces of information together, the need to communicate the safety of food from vaccinated animals becomes evident.

In a context where the public are concerned about the safety of produce from vaccinated animals, the benefits of vaccination, particularly in the context of a major disease outbreak, may not be realisable. Most food animals receive a number of vaccinations during their life to protect them against various diseases and the public usually consume such produce without concern. It may be that they do not realise that animals are vaccinated routinely or they may be more cautious in the context of a disease outbreak that is widely reported in the media and that may or may not have human health implications.

The challenge for both industry and government is to communicate information in a manner in which it will be accepted by society at large and will assure the public that produce from vaccinated animals is safe to eat.

**Future food needs**

Figure 4 indicates the scale of the challenge facing global agriculture if future food needs are to be satisfied. As previously mentioned, animal diseases are responsible for at least a 17% loss in production, and the elimination/reduction of these losses must be a priority.

Meat consumption will increase by a factor of two in developed countries and by a factor of five in developing countries. For milk, the factors are two and five, respectively. For eggs, the factors are three and eight, respectively. Herd health management will be key in attempting to meet this challenge and vaccination will have a central role to play.

As we move into the future, we anticipate, based on historical knowledge, that new diseases will emerge. This is all the more likely as farming intensifies in developing countries and as a result, intensive agriculture comes into contact with wild species. Our ability to be alert for such diseases and to have the scientific capacity and infrastructure to respond to such challenges is critical. The ETPGAH recognises this reality. Amongst its recommendations is the need to ‘identify the threats to Europe from pathogens which are not considered important at present (i.e. horizon scanning) and conduct full risk assessment of potential threats from new and emerging diseases in particular those outside the EU boundaries’ (3). Whilst reference is made to Europe, the recommendation is valid in any part of the globe.

The ETPGAH has also identified ‘societal acceptance of technology’ as an issue that needs attention. The Strategic Research Agenda (SRA) from the ETPGAH proposes research into consumer perceptions and expectations of new technology and factors which affect consumer behaviour in relation to food safety. The SRA also proposes the development of risk communication strategies to communicate with the public in relation to new technology in the most effective manner. Part of this work should be aimed at communicating the fact that food from vaccinated animals is safe to eat.
Conclusion

The development of vaccines is becoming more complex and expensive. The need to ensure the availability of vaccines requires public and producer cooperation. Vaccines deliver considerable benefits to both animals and society at large and have the potential to deliver even greater benefits in the context of the ETPGAH.

Mass slaughter must be avoided if possible and animal health needs to be protected to avoid the huge costs associated with the outbreak of exotic diseases. The development of a wider range of effective vaccines has the potential to deliver benefits to society far in excess of the cost of development and this opportunity should not be missed. Food safety and quality benefits flow from vaccine use and we need to invest in alternatives to animal testing.

Future food needs at the global level highlight the important role and need for new and effective vaccines. The ETPGAH shows the way forward and this development needs to be coupled with effective communication with the public so that new vaccine technologies are accepted.

From the viewpoint of society, vaccination delivers very considerable benefits. The human health benefits of reducing zoonoses are very substantial and need to be communicated in an effective manner. From the ethical viewpoint, we need to protect animal health and welfare by using vaccines to the greatest extent possible. In addition, we need to prove safety and efficacy whilst minimising the use of animals in testing.

La vaccination animale et l’industrie pharmaceutique vétérinaire

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Résumé
Le marché des vaccins vétérinaires s’intéresse à de nombreuses espèces animales mais reste limité en volume et il devient de plus en plus difficile et onéreux de développer de nouveaux vaccins. Les vaccins sont l’un des moyens les plus efficaces de prévenir la maladie chez les animaux comme chez l’homme. Dans bien des cas, la vaccination a permis d’éliminer des maladies ou d’en réduire l’impact sur la santé et le bien-être des animaux. La responsabilité éthique impose de faire en sorte qu’un large éventail de vaccins soit disponible, y compris lorsque le marché doit être soutenu financièrement comme c’est le cas pour les espèces animales plus rares ou les pathologies moins fréquentes désignées par l’acronyme MUMS (Minor Use and Minor Species). L’abattage sanitaire massif étant devenu intolérable pour la société, nous devons évoluer, dans la mesure du possible, vers des politiques de « vaccination pour la vie ». Les vaccins nous permettent d’éviter le fardeau du coût de la maladie et améliorant la sécurité sanitaire des aliments. Le développement des vaccins devra se faire en recourant le moins possible à l’expérimentation animale. En outre, il faudra faire en sorte que le public accepte la vaccination des animaux destinés à la consommation, en tant que mesure destinée à protéger la santé et le bien-être de tous les animaux. Dans une perspective d’avenir, grâce aux vaccins nous serons en mesure d’assurer la sécurité alimentaire d’une population mondiale de plus en plus nombreuse. La plateforme technologique sur la santé animale dans le monde lancée par la Commission européenne a un rôle déterminant à jouer pour fixer les priorités de la recherche.

Mots-clés
Vacunación animal e industria farmacéutica veterinaria

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Resumen
Si bien el mercado de la inmunización veterinaria comprende la lucha contra las infecciones que afectan a muchas especies animales, su talla es limitada y el desarrollo de vacunas cada vez más complejo y oneroso. La vacunación, que es uno de los instrumentos más eficaces para prevenir enfermedades tanto en los animales, como en los seres humanos, ha permitido erradicar muchas enfermedades, o reducir la gravedad de sus consecuencias en la salud y el bienestar de los primeros. Desde el punto de vista ético, debe garantizarse la existencia de una gran variedad de vacunas, aunque para ello sea preciso prestar apoyo financiero al mercado, como en los casos de las especies animales poco comunes y las indicaciones poco frecuentes (denominadas habitualmente con la sigla MUMS, por las iniciales en inglés de “Minor Use and Minor Species”). En la sociedad contemporánea, el rechazo del sacrificio masivo es cada vez mayor; por ello, siempre que resulte posible debe adoptarse una política de vacunación que impida la circulación de los agentes patógenos en los rebaños. La inmunización es necesaria para evitar los elevados costos de las enfermedades y garantizar la inocuidad de los alimentos. También es preciso reducir al mínimo las pruebas en animales durante el desarrollo de vacunas. La vacunación constituye un medio para proteger la salud y el bienestar de todos los animales; por consiguiente, debe darse a comprender al público la necesidad de administrarla a aquellos que se destinan al consumo. Las vacunas serán indispensables para producir las cantidades de alimentos que serán necesarias en el futuro a fin de alimentar a una población mundial cada vez más numerosa. La Plataforma Tecnológica Europea para la Sanidad Animal Mundial desempeñará un papel clave a la hora de determinar los ámbitos de investigación prioritarios.

Palabras clave

References