Availability of vaccines against major animal diseases in the European Union

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Summary

This paper presents the results of a survey in which countries within the European Union and the European Economic Area were requested to provide information on the availability of vaccines against 47 major diseases of animals as part of the DISCONTOOLS project within the European Technology Platform for Global Animal Health. The objective of the survey was to help identify those diseases to which priority should be given by both the public and private sectors in terms of developing new tools to assist in their control. The survey also provides information on the availability of vaccines authorised at national level against the diseases concerned which may be useful in the event of a disease emergency or to enhance preparedness.

Keywords

Introduction

An extensive survey on the availability of vaccines against a number of the major diseases of animals in the European Union (EU) and the European Economic Area (EEA) was conducted as part of the DISCONTOOLS project, which is a five-year joint initiative of industry and a wide range of stakeholders that is being carried out within the framework of the European Technology Platform for Global Animal Health (ETPGAH) (1). The results of the survey form part of a gap analysis to be used to prioritise the diseases considered within the project. The ETPGAH project is a public-private partnership that aims to accelerate the access to market of products that are important for animal health within the EU. The DISCONTOOLS component of the project aims to prioritise the diseases considered important so that resources can be directed most effectively. The existing availability of a vaccine against a disease, or the lack thereof, is an important factor in prioritising resources to develop new vaccines.

As of January 2010, the DISCONTOOLS disease list included 47 diseases caused by various aetiological agents, including viruses, bacteria, parasites and prions. Some of the entries in the list represent a group of diseases, e.g. transmissible spongiform encephalopathies (TSEs), or a class of infectious agents, e.g. nematodes, rather than a particular condition or aetiological agent. Thus, for some entries, a high number of vaccines exist, whilst for others, either vaccines do not exist or immunisation is not an option for control. In order to ascertain if vaccines were marketed or otherwise made available, the National Competent Authorities (NCAs) responsible for veterinary medicinal products in each Member State of the EU and in each EEA country were requested to provide comments on the availability of vaccines against the listed diseases. As far as the authors are aware, this is the only database providing detailed information on the availability of vaccines for this range of animal diseases in the EU.

Access to information on vaccine availability could be of vital importance in an animal disease emergency. To address a variety of needs in animal health, different products are authorised in the Member States of the EU and information on the availability of these products is useful to a range of stakeholders. During an outbreak, the NCA may grant an emergency permit to use a particular product, so knowing that such a product is authorised in another EU Member State can simplify and accelerate the procedure by which vaccines may be made available. Currently, there is no centralised database of the availability of veterinary medicinal products at a European level,
Generally, the diseases on the list can be divided into three categories:

- diseases for which commercial vaccines are widely available across the EU
- diseases for which no vaccine has been reported to be available
- diseases for which vaccines are available only in certain countries.

The first two groups are more predictable, since it is commonly known for which diseases there are a lot of products on the market and for which diseases no vaccine has been reported to be available. The availability of vaccines against diseases from the last group is subject to factors such as national legislation and the current disease status. The same can be said about diseases affecting multiple species – vaccines are available for some species, but not for others. The last group includes diseases for which there is no commercial product but for which vaccines are available in a national laboratory or are under research.

The diseases from the first group, together with examples of widely available commercial vaccines, are listed in Table I. This list is not intended to be exhaustive and it is recognised that many additional products are available in the different countries, often from national producers. The survey provides information on vaccines for which a marketing authorisation exists and does not reflect whether the vaccine is actually marketed. In addition, although some of the products listed in Table I are authorised by means of a ‘Centralised’ marketing authorisation issued by the European Commission and valid in all Member States of the EU, the products concerned are not necessarily actually marketed in all Member States.

Aetiological agents/diseases that fall in the second group and for which countries reported that no vaccine is available in the EU/EEA are:

- African swine fever
- tuberculosis
- contagious bovine pleuropneumonia (CBPP)
- Campylobacter
- coccidiosis (in all species other than poultry, see Table I)
- cryptosporidiosis
- cysticercosis
- echinococcosis/hydatidosis
- hepatitis E
- leptospirosis in sheep and horses
- liver fluke

Although the European Medicines Agency is developing such a database – Eudrapharm (www.eudrapharm.eu). The World Organisation for Animal Health (OIE) mentions in its disease cards the types of vaccines that exist, without specifying where they are available or giving any product details (7). The commercial names of vaccines and their respective marketing authorisation holders (MAHs), sometimes accompanied by more details, can be found in diverse compendia, e.g. the National Office of Animal Health (NOAH) Compendium published in the United Kingdom (4) or the database of the Paul-Ehrlich-Institut in Germany (5), but that information is on a national level. A further limitation is that most existing databases, printed or electronic, are in national languages. Information on vaccine availability for certain diseases can be found in scientific articles, but such information is often not comprehensive. This article is therefore intended to provide information on vaccine availability within the EU and EEA countries.

Methods

A survey was conducted in February 2010 involving all EU Member States and two of the three EEA countries, namely, Norway and Iceland. A questionnaire, in the form of a Microsoft Excel spreadsheet, was sent to the Heads of Medicines Agencies and to the members of the Immunologicals Working Party (IWP) of the European Medicines Agency (EMA), which provides recommendations to the EMA Committee for Medicinal Products for Veterinary Use (CVMP). The January 2010 version of the disease list of the DISCONTOOLS project (2) was used as a basis. The questionnaire was designed to focus attention on those diseases for which information would be most useful and the IWP members were invited to provide comments and additional information rather than simply list product details.

Results

The response rate to the survey was good, with only three of the 29 countries not responding. The responses provided a very good overview of the vaccines available in Europe. In addition to the list of products, many contributors provided valuable comments, such as information on disease status and national legislation, and on products known to be ‘in the pipeline’ or still under research. Thus, not only did the current situation become clear, but also some future trends could be seen. Overall, it can be said that the survey was successful, both in terms of response rate and the volume and quality of the information gathered.
– nematodes (other than \textit{Dictyocaulus viviparus})
– Nipah virus
– peste des petits ruminants
– transmissible spongiform encephalopathies
– swine vesicular disease
– trypanosomosis.

About one third of these diseases are parasitic – coccidiosis, cysticercosis, echinococcosis, liver fluke, nematodes and trypanosomosis, some of them affecting multiple species – and commercial vaccines against parasites have proved difficult to develop. Exceptions are the vaccine against coccidiosis in poultry (see Table I) and vaccines against parasitic bronchitis in cattle caused by the nematode \textit{Dictyocaulus viviparus}, which was included in the third category of diseases, i.e. vaccines available only in certain countries. A further particular case is \textit{Mycoplasma mycoides mycoides}, the aetiological agent of CBPP – it is included as an antigen of the vaccine Agalax Tres by Syva, which is authorised in Spain, but indicated for sheep and goats.

Comments on the diseases in the third group are listed below, including product details where available.

\textbf{African horse sickness (horses)}

No commercial products are available in Europe, but a vaccine from the Onderstepoort Veterinary Institute in South Africa is available, for which several Member States reported that emergency permission may be granted in exceptional circumstances.

\textbf{Anthrax (cattle and small ruminants)}

Vaccines authorised nationally for emergency use are shown in Table II.

\textbf{Avian influenza (poultry)}

Poulvac FluFend (Fort Dodge) and Nobilis Influenza H5N2 (Intervet) are authorised centrally and vaccines authorised nationally for emergency use are listed in Table III.

\textbf{Bluetongue (sheep and cattle)}

BTVPUR AlSap 8 EU (Merial), Zulvac 8 ovis and Zulvac 8 bovis (Fort Dodge) are authorised centrally. Bovilis...
BTV8 (Intervet) and BTVPUR AlSap 2-4 (Merial) have received a positive opinion after assessment by the CVMP. As stated in Table IV, the vaccines available in the Czech Republic, Germany and Italy are fully licensed. In the other listed countries, only temporary permits exist.

### Bovine mycoplasma (cattle)

In Denmark, Myco-Shield Vet (Novartis) is authorised nationally but not marketed.

### Bovine tuberculosis (cattle)

No products are authorised for use against tuberculosis (TB) in cattle in the EU. However, as part of the national scheme for the eradication of bovine TB in Ireland, the development and implementation of a vaccine strategy for use in badgers (reservoir species for the maintenance of bovine TB in Ireland) is ongoing. A suitable candidate vaccine has been identified and efficacy on oral delivery has been demonstrated in a laboratory environment. In the United Kingdom (UK) ‘Badger BCG’ containing Danish strain 131 of *M. bovis* bacillus Calmette-Guérin (BCG), also for badgers, has been provisionally authorised.

### Brucellosis (cattle, small ruminants, pigs, wild boar, dogs)

As can be seen in Table V, available vaccines are mainly indicated for use in small ruminants. There are also some for cattle, but none for pigs, wild boar or dogs.

### Classical swine fever (pigs and wild boar)

Immunisation against classical swine fever is forbidden in all Member States except for Romania. The vaccines authorised there, as well as a vaccine for wild boar available in Bulgaria, can be found in Table VI.

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**Table II**

<table>
<thead>
<tr>
<th>Country</th>
<th>Vaccine</th>
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<tbody>
<tr>
<td>Bulgaria</td>
<td>Antraks (Biofarm Engineering, Bulgaria)</td>
</tr>
<tr>
<td>France</td>
<td>Carbovac (Merial)</td>
</tr>
<tr>
<td>Greece</td>
<td>Unauthorised State Veterinary Laboratory spore vaccine, used in the past in exceptional circumstances</td>
</tr>
<tr>
<td>Hungary</td>
<td>Carbonormuc (S.C. Romvac Company S.A.)</td>
</tr>
<tr>
<td>Italy</td>
<td>Live attenuated anthrax vaccine Sterne, strain 24F2</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Avirulent miltuur vaccin (Lelystad Biologicals BV)</td>
</tr>
<tr>
<td>Romania</td>
<td>Antravac (Institute Pasteur S.A.), Carbonormuc (Romvac Company S.A.)</td>
</tr>
<tr>
<td>Slovenia</td>
<td>3-VAC (VETERINA d.o.o.); indicated for cattle only</td>
</tr>
<tr>
<td>Spain</td>
<td>Vacuna anticarbuncosa unica (Ovejerol), Anthracina (CZ Veterinaria), Antravac (Syva), Univac (Farbiol) (currently suspended), Vaccisor-n (Instituto Llorente) (currently suspended)</td>
</tr>
</tbody>
</table>

**Table III**

<table>
<thead>
<tr>
<th>Country</th>
<th>Vaccine</th>
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<tbody>
<tr>
<td>France</td>
<td>Trovac AIV-H5 (recombinant) (Merital)</td>
</tr>
<tr>
<td>Germany</td>
<td>Gallimune HSN9 (Wisconsin strain) (Merital)</td>
</tr>
<tr>
<td>Italy</td>
<td>PA OLVAC PM+I and PA OLVAC I+E (Fatro), both with a full licence</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Gallimune Flu HSN9 (Merital)</td>
</tr>
<tr>
<td>Portugal</td>
<td>Poulvac i-Al (Fort Dodge)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>Nobilis Influenza, including strains H7N7 and H5N2</td>
</tr>
</tbody>
</table>

**Table IV**

<table>
<thead>
<tr>
<th>Country</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>Temporary licences for vaccines against BTV1: Zulvac 1 ovis, Zulvac 1 bovis (Fort Dodge) and Bluevac 1 (CZ Veterinaria)</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>BioBos BTB8 (Biovetra Ivanovice)</td>
</tr>
<tr>
<td>France</td>
<td>Temporary authorisation for BTVPUR AlSap 1, BTVPUR AlSap 2, BTVPUR AlSap 4, BTVPUR AlSap 2-4 (Merial), Bluevac 1 (CZ Veterinaria), Syvazul-1 (Syva), Zulvac 1 ovis and Zulvac 1 bovis (Fort Dodge)</td>
</tr>
<tr>
<td>Germany</td>
<td>Bluevac-8 (CZ Veterinaria)</td>
</tr>
<tr>
<td>Italy</td>
<td>BTVPUR AlSap 1-8 (Merial), BTVPUR AlSap 2-4 (Merial), BTVPUR AlSap 9 (Merial)</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Provisional permit for use (2008): Bovilis BTB8 (Intervet)</td>
</tr>
<tr>
<td>Portugal</td>
<td>Vaccines used for emergency vaccination: Live bluetongue virus vaccine, serotype 4 (Onderstepoort Vaccine Institute, South Africa), BTVPUR AlSap 4 (Merial), Syvazul-1 (Syva), BTVPUR AlSap 2-4 (Merial), Zulvac-1 bovino (Fort Dodge), Zulvac-1 ovis (Fort Dodge)</td>
</tr>
<tr>
<td>Spain</td>
<td>The following products have a national authorisation for use in exceptional circumstances: Syvazul-1, Syvazul-4, Syvazul-8, Syvazul-1+4, Syvazul-1+8, Syvazul-1+8 ovis one (Syva) Bluevac-1, Bluevac-4, Bluevac-BTV 8; Bluevac-1+4; Bluevac-1+8, (CZ Veterinaria) Zulvac-1 ovis, Zulvac-1 bovino, Zulvac-4, Zulvac-1+8 ovis, Zulvac-1+8 bovis, Zulvac-1+8 (una dosis) (Fort Dodge) BTVPUR AlSap 1, BTVPUR AlSap 4, BTVPUR AlSap 1+8 (Merial) Primun Lengua Azul S1, Primun Lengua Azul S4, Primun Lengua Azul S8, Primun Lengua Azul 1+8, Primun Lengua Azul 1+8 dosis unica (Calier) United Kingdom</td>
</tr>
</tbody>
</table>
information on the legal situation can be found in a paper published by the European Food Safety Authority (3).

**Escherichia coli (multiple species)**

There are many vaccines for cattle and pigs (see Table I). For poultry, besides the centrally authorised Nobilis E. Coli inac (Intervet), there is one nationally authorised product in Italy, BIO NEW B1 COLI+AP (Merial). The vaccines authorised for use in small ruminants are listed in Table VII.

**Foot and mouth disease (cattle, small ruminants and pigs)**

Foot and mouth disease vaccines available nationally are shown in Table VIII.

**Leishmaniosis (dogs)**

There are no commercial vaccines yet available, but in Spain there are products under research and clinical trials have been approved. In France, two vaccines against Leishmania infantum are in clinical trials. A commercial product is known to be available in Brazil – Leishmune (Fort Dodge).

**Leptospirosis (pigs)**

Leptospirosis in cattle and dogs is present in the first category and examples of the many commercial products against the disease in these species can be found in Table I. As no vaccines are available for sheep or horses, the disease has also been included in the second category. For pigs, three commercial vaccines are available, see Table IX. Clinical trials have been authorised in France for Porcilis EPL (Intervet). In Denmark, Lepto Shield™5 is dispensed by the National Laboratory under special circumstances.

**Mastitis (cattle, small ruminants)**

Data on three types of mastitis were gathered – environmental/streptococcal mastitis in cattle, Staphylococcus aureus mastitis in cattle and ‘small ruminant’ mastitis caused by Mycoplasma agalactiae, Mycoplasma mycoides subp. mycoides and Staphylococcus aureus. Startvac is centrally authorised for use against E. coli and S. aureus mastitis in cattle, whereas the products in Table X have national authorisations. Vaccines against small ruminant mastitis are listed in Table XI.

**Nematodes – parasitic bronchitis (cattle)**

Dictyocaulus viviparus, the cause of parasitic bronchitis in cattle, is the only nematode against which a commercial vaccine is available. The vaccine is authorised in the Netherlands, in the form of Bovilis Longworm, and in the UK, in the form of Bovilis Huskvac (Intervet).
Paratuberculosis (Johne’s disease) (cattle)

The availability of vaccines against Johne’s disease varies between Member States. There is one commercial product in France – Neoparasec (Merial), and one in Romania – Parvac (S.N. Institute Pasteur). In Denmark an unregistered vaccine – Mycopar (Fort Dodge) – may be used in special circumstances if permission is granted by the National Laboratory. Gudair (CZ Veterinaria) has provisional authorisations in Cyprus, Greece, the Netherlands, Spain and the UK for use in sheep and goats rather than in cattle.

Q-fever (cattle, small ruminants)

Coxevax (Ceva) has been granted a temporary permit for use in goats in Belgium and the Netherlands. It has also received a positive opinion after evaluation by the CVMP.

Ruminant pox virus infection (sheep and goats)

The only vaccine against sheep and goat pox (capripox) for which information was provided was an unauthorised live vaccine produced by the State Veterinary Laboratory in Greece. The vaccine, which contained the ‘Algiers’ strain, was used until 1983. Also notified under this heading, although indicated for sheep parapoxvirus rather than capripox, was the product Overvac EC (Ovejero) in Spain.

Salmonella (cattle, sheep, pigs, horses)

Many commercial vaccines are available across Europe against salmonellosis in poultry, some examples of which are listed in Table I. Table XII shows nationally authorised products for use in cattle, sheep and pigs, as no vaccine was reported for use in horses.

Discussion

The results of this survey present a ‘snapshot’ of the availability of vaccines against major animal diseases in the EU and EEA countries. Whilst recognising that the situation concerning the availability of particular products varies over time, it is possible to draw some general conclusions. Essentially, there are two main reasons for which vaccines may not be available for certain diseases: (i) it has not yet been technically possible to develop vaccines that provide adequate protection against the aetiological agent (e.g. African swine fever [6]); or (ii) it is possible to develop safe and effective vaccines, but there is insufficient financial incentive to seek authorisation to use the vaccine in the EU (e.g. peste des petits ruminants, Nipah virus). For many such diseases commercial vaccines are available...
in other regions but efforts are seldom made to make them available in Europe in advance of a disease emergency. This situation can change rapidly if there is an incursion of a previously exotic disease, as exemplified recently in the case of bluetongue. Several respondents to the survey mentioned that, although commercial vaccines were not available, the production of autogenous vaccines was permitted under certain circumstances. Autogenous vaccines are extemporaneously manufactured vaccines produced using infectious agents isolated from a particular holding for use on the same holding. Such products serve a useful purpose on a small scale, but they can never replace the need for safe and effective commercial vaccines in the event of a disease emergency.

It is hoped that the results of this survey will be useful in informing prioritisation exercises to identify important diseases against which it would be useful to develop new vaccines. These results also provide a source of information on products that are available at a national level in various EU and EEA countries and that could be used in other countries should the need arise.

La disponibilité des vaccins contre les principales maladies animales dans l’Union européenne

K. Videnova & D.K.J. Mackay

Résumé
Les auteurs présentent les résultats d’une étude conduite dans les États membres de l’Union européenne et de l’Espace économique européen dans le cadre de l’initiative DISCONTOLS de la Plateforme technologique européenne pour la santé animale mondiale (ETPGAH) afin de recueillir des informations sur les stocks de vaccins disponibles contre 47 maladies animales majeures. L’enquête devait permettre de déterminer quelles maladies étaient à considérer en priorité par le secteur privé et les pouvoirs publics pour la mise au point de nouveaux outils de lutte. L’enquête a également permis de recueillir des informations sur la disponibilité des vaccins autorisés au niveau national contre les maladies concernées, ce qui pourra servir en cas d’urgences sanitaires et permettra également d’améliorer la préparation aux situations d’urgence.

Mots-clés
Disponibilidad de vacunas contra enfermedades animales importantes en la Unión Europea

K. Videnova & D.K.J. Mackay

Resumen
Los autores presentan los resultados de un estudio en el que se pidió a los países de la Unión Europea y del Espacio Económico Europeo que facilitaran información sobre la disponibilidad de vacunas contra 47 enfermedades importantes de los animales como parte del proyecto DISCONTOOLS de la Plataforma Tecnológica Europea de Sanidad Animal Mundial. El estudio tenía por objetivo ayudar a determinar las patologías a las que los sectores público y privado debían dar prioridad con vistas a la elaboración de nuevas herramientas con las que ayudar a combatirlas. También se obtuvieron datos sobre la disponibilidad de vacunas autorizadas a escala nacional contra las enfermedades en cuestión que pudieran resultar útiles en caso de emergencia sanitaria o para mejorar la preparación para tal coyuntura.

Palabras clave

References


