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CVMP reflection paper on the risks that should be considered prior to the use of unauthorised vaccines in emergency situations

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1. Introduction

Due to the epidemiological situation of major infectious diseases in neighbouring European countries as well as worldwide, there is a continuous risk of outbreaks of new diseases, many of them exotic, in EU Countries. Depending on the level of emergency, the use of vaccines as one of the most effective methods to prevent and manage infectious diseases can be of crucial relevance for the control of outbreaks or the eradication of diseases in livestock animals. Recent experiences have demonstrated the lack of any available authorised vaccines (vaccines with a marketing authorisation (MA) granted by a medicines regulatory authority in accordance with article 5 of Directive 2001/82/EC), when emergency vaccination may be required in the event of serious epizootic disease as stated in Article 8 of Directive 2001/82/EC. In the absence of such authorised products, the use of vaccines without a MA (hereafter referred to as unauthorised vaccines) can be provisionally allowed by Member States and should be considered in advance.

The national medicines regulatory authorities assessing standard marketing authorisation procedures are often not the same ones that will decide upon the use of unauthorised vaccines. Therefore this document is addressed to decision makers (e.g. such as Directorate General for Health and Food Safety at EU level, Ministry of Agriculture, chief veterinary officers, other bodies at national level depending on the country) that may be required to decide if unauthorised vaccines could be used in emergency situations, in particular to outline the risks associated with the use of unauthorised vaccines in response to outbreaks of new diseases.

The document attempts to explain the risks associated with the use of such products by describing the basis by which a standard MA is granted and outlining the risks posed for use of unauthorised vaccines where the complete data for a standard MA (as required by Directive 2001/82/EC) are not available.

2. Content of a full marketing authorisation dossier – non-emergency situations

In non-emergency situations veterinary vaccines should be authorised for their specific uses by a medicines regulatory authority. For an application for a MA to be successful, vaccine manufacturers have to carry out a series of tests and trials in accordance with the requirements of the veterinary medicines legislation. A full MA dossier including quality, safety and efficacy data, as defined in Annex I to Directive 2001/82/EC, is necessary to allow thorough evaluation of the data from these tests and trials by the medicines regulatory authorities and – provided the data show that the benefits outweigh the risks of the vaccine - to grant a marketing authorisation. The assessment of a MA dossier is a complex process that takes into account the legislative framework and the scientific knowledge. As for all medicines, the information on the benefits and risks of vaccines is necessarily limited to the information that is obtained from the available tests and studies available at the time of authorisation.

Summary of product characteristics (SPC)

The SPC is an integral part of any MA. It is drafted by the applicant for the vaccine and agreed by the medicines regulatory authority based on the available information on the product. The SPC reflects the content of the MA dossier and data that were considered sufficient by the medicines regulatory

authority to demonstrate the quality, the safety and the efficacy of the vaccine. The SPC is the basis of information for the end user on how to use the veterinary medicinal product safely and effectively1.

3. Rapid authorisation of vaccines in emergency situations – recent examples

In recent years during the different disease threats that have affected European countries (e.g. bluetongue disease, avian influenza), the medicines regulatory authorities have used the provisions of the "exceptional circumstances" clauses to facilitate rapid authorisation of vaccines in advance of generation of data to meet the full requirements of Annex I to Directive 2001/82/EC. This was possible because within a short time of the disease threat the vaccine manufacturers were able to develop and produce appropriate vaccines at a sufficient level of compliance with the minimum data requirements for authorisation enabling medicines regulatory authorities to conclude that the benefits of the use of these vaccines outweighed the risks and because the SPC of the vaccines clearly indicated what data were missing. However, it should also be noted that in all these cases previous experiences on these types of vaccines had already been gathered by vaccine manufacturers, and as a consequence, used as background to produce the vaccines in the mentioned emergencies.

4. Points to consider for the use of unauthorised vaccines in emergency situations

In an emergency situation, the data usually requested under standard conditions may not be available for a required vaccine, in which case compliance of the MA dossier with the requirements of Directive 2001/82/EC is not possible. Similarly, insufficient data may be available to apply the "exceptional circumstances" clauses for rapid authorisation of vaccines.

In principle, to use an unauthorised vaccine while limiting the level of risk, minimum data on the quality and the safety of the vaccine should be available particularly as regards live vaccines. Special attention should be paid on the presence of extraneous agents, residual virulence as well as on reversion of virulence. Failure to detect these before allowing the use of the vaccine may have negative animal welfare and economical consequences. The spread of vaccine virus or extraneous agents may affect not only the country in which the decision was made but also neighbouring countries.

The decision to use an unauthorised vaccine is based on a benefit-risk assessment that is unique and depending on the circumstances. Because it is not possible to foresee all the situations: level of emergency, type of disease, characteristics of the vaccine (live, inactivated, genetically modified organism,…), consequences of the vaccination, … a priori scoring/ranking of the risks is not feasible. For example, the grounds for a decision to use a vaccine must at least take into account the following criteria:

- the impact of not having a vaccine available to manage an outbreak of a disease in the time needed to generate a complete data set;

- the economic impact of the disease spreading may offset the potential risks of using an unauthorised vaccine unless the use of such a vaccine may potentially induce a safety problem with an important

[1] The content of the SPC is defined in article 14 of Directive 2001/82/EC and is based on the data submitted in the MA dossier according to Annex I of Directive 2001/82/EC.

economic impact (e.g. spread of a new disease, induction of negative effects linked to vaccination such as abortions, impact on production parameters for food producing animals, etc.).

The risks associated with incomplete information

In certain emergency situations, a MA dossier may not be available at all and the manufacturer may only provide a document summarising some characteristics of a vaccine. The choice to use such a vaccine will inevitably be based on incomplete information, with the additional risks this entails. If nevertheless it is decided to use the vaccine, the decision makers should be aware that there are data gaps with regard to quality, safety, efficacy requirements and that the content of the document provided by the manufacturer or of some sections of this document may not have been endorsed by the medicines regulatory authorities.

The most significant risks for use of unauthorised vaccines where the complete or at least the minimum agreed data sets are not available can be summarised as follows:

Data type:	**Risks**
Incomplete manufacturing/ quality data including batch potency test	Extraneous agent contamination (including Transmissible Spongiform Encephalopathies [TSEs]) in vaccine batches resulting in spread of infectious agents and development of disease in vaccinated and non-vaccinated susceptible animals. Residual infectivity due to incomplete inactivation of live organisms with potential for spreading of infection and development of disease in vaccinated and non-vaccinated susceptible animals. Batch to batch consistency may be impacted resulting in vaccines of variable quality in the field and consequently the observed level of safety and efficacy performance. Uncertainty for the sterility of released batches if final product tests are not adequate. Uncertainty regarding the shelf-life of the product. Food safety concerns from harmful residues in meat or dairy products.
Incomplete safety data	Uncertainty of the nature and extent of adverse reactions in vaccinates including young, breeding and pregnant animals. Reversion to virulence of live vaccine strains leading to disease in vaccinated animals and the potential for spread of the vaccine strain to non-vaccinated susceptible animals; Persistence of the vaccine strain in the animal. The appearance of unpredicted side-effects and possibly impact on productivity in food-producing animals. Risk to the user due to unpredictable reactions from self-injection or exposure to the vaccine strain. Unknown impact for the environment from the vaccine strain, adjuvants or excipients. Food safety concerns from harmful residues in meat or dairy products.

Incomplete efficacy data	Lack of confidence that the vaccine will perform as expected. The vaccine may not protect animals adequately or fail to control the disease outbreak. Limited information for the onset and/or duration of protection, thereby leading to uncertainty for managing the outbreak and the timing for re-vaccination if appropriate. Uncertainty on the optimum primary vaccination schedule and booster interval. Lack of certainty on the level of protection of young animals carrying maternally derived antibodies.

A detailed description of the risks associated with the use of unauthorised vaccines is outlined in the annex attached. The table in the annex describes the different sections of the SPC and the link with the data requirements of a MA dossier. The potential risks associated with the use of a product where the relevant data are missing, are also identified.

The need for ongoing evaluation of the use of the product

If the minimum agreed data are not available, it will be difficult to estimate the safety and the efficacy induced by the vaccination; therefore the assessment of the benefit-risk is limited and needs to be re-evaluated on an ongoing basis either using additional data generated from the vaccine manufacturer or from the use of the vaccine in the field.

5. Conclusion

Depending on the nature of the disease and on the type of vaccines that might be proposed by manufacturers, the benefit-risk assessment can be different and the decision to use an unauthorised vaccine should be made on a case by case basis taking into account, amongst others, the potential risks that are listed in this document.

1 Risks associated with incomplete information that would normally support SPC statements for authorised vaccines

SPC section and expected supporting data in MA dossier in accordance with Art. 5 of Directive 2001/82/EC (full application)	Potential risk in connection with the use of vaccines under Art. 8 of Directive 2001/82/EC if information is not available or inadequate
1. NAME OF THE VETERINARY MEDICINAL PRODUCT	
When selecting invented names, care is taken to avoid the use of words or abbreviations, which may give rise to confusion.	*If the name is similar to another product or misleading there could be a risk of the wrong product being used.* *Risk for vaccinated animal and public health*
2. QUALITATIVE AND QUANTITATIVE COMPOSITION	
The SPC presents the qualitative and quantitative composition in terms of the active substances and constituents of the excipient, knowledge of which is essential for proper administration of the veterinary medicinal product.	*In the absence of the detailed composition of the vaccine it is not possible to verify that all the constituents are safe for the vaccinated animals or consumers. Furthermore, if the specifications are unknown the quality control of the finished product will be uncertain and as a result the safety profile and efficacy induced by the vaccination cannot be guaranteed.* *Risk for vaccinated animal and public health*
The description of the manufacturing process is necessary to show that the manufacturing process is controlled and consistent.	*If information on the manufacturer and manufacturing process are not provided, it cannot be assured that the manufacturing process and control tests are adequate and the manufacturing site complies with the standards for EU Good Manufacturing Practice (GMP).* *The quality and consistency of the vaccine that is produced cannot be guaranteed and consequently this may result in a variable and unpredictable safety and efficacy profiles. Local and systemic reactions and the level of expected protection of vaccinated animals may be subject to batch-to-batch variation.* *Risk for vaccinated animal and public health*
The quality of the starting materials used at any stage in the manufacturing process is an essential criteria to assure a satisfactory quality standard of the finished product which is a direct consequence of the consistency of its production. For the starting materials listed in pharmacopeias, the compliance with the requirements of pharmacopeias should be demonstrated.	*With regard to substances of biological origin used at any stage in the manufacturing process, if information is missing, there is a risk that the vaccine might be contaminated with live extraneous micro-organisms including TSEs that may lead to disease in vaccinated or non-vaccinated susceptible animals in the field and pose a threat to public health through transmission of zoonotic agents to consumers of meat and dairy products or*

SPC section and expected supporting data in MA dossier in accordance with Art. 5 of Directive 2001/82/EC (full application)	Potential risk in connection with the use of vaccines under Art. 8 of Directive 2001/82/EC if information is not available or inadequate
The starting materials not listed in pharmacopeias should be controlled and they should be sourced from suppliers/countries with appropriate standards of production and control. The risk depends on the level where data are missing. - for a live vaccine obtained from an attenuated organism, data have to be provided to show a sufficient attenuation in the target species, - for an inactivated vaccine obtained after inactivation of a live organism, data have to be provided to show a complete inactivation, - for materials of biological origin used in the production process (seed materials, serum, trypsin, serum albumin…), the absence of extraneous agents (virus, bacteria, fungi, mycoplasma, parasite, transmissible spongiform encephalopathy agent) has to be demonstrated.	*those in contact with or handling infected animals.* *Risk for vaccinated animal, non-vaccinated susceptible animals and public health*
Control tests during the manufacturing process are carried out in order to ensure the quality of the vaccine. Details on the antigen quantification and on the blending step allow to verify the consistency of the production and hence no variation in the levels of efficacy and safety of all forthcoming batches. The control of inactivation (or detoxification) is essential to ensure that no residual live pathogenic organism or toxic material is present in the vaccine.	*If the controls are not performed, the batch-to-batch consistency of the product cannot be guaranteed. Furthermore, if in process tests are unvalidated or absent from the manufacturing process the safety profile and efficacy of the vaccine cannot be ensured. For inactivated vaccines there is a risk for incomplete inactivation of the organism or toxoid.* *Risk for vaccinated animal, non-vaccinated susceptible animals and public health*
The absence of control tests on the finished product could have an impact on consistency, safety and efficacy.	*If there is no identification of active substance(s) and/or control of the titre or potency of the batch, the efficacy of the vaccine cannot be guaranteed.* *Risk for vaccinated animal, non-vaccinated susceptible animals and public health*
Control of sterility (absence of contaminating micro-organism) and purity (presence only of the micro-organism of interest) ensures the safety of the vaccine. Controls of physico-chemical characteristics (e.g. adjuvant assay, control of preserving agents, residual humidity, pH, visual appearance, viscosity, etc.) and of the batch to batch consistency ensure the correct production of the vaccine and its stability.	*If the biological and physico-chemical characteristics of the finished product are not controlled, it cannot be ensured that the vaccine has been correctly produced and therefore the stability cannot be guaranteed. As a consequence, the safety and the efficacy of the vaccine may be impacted. Furthermore, if the sterility test is unvalidated there is a risk for releasing non-sterile products for field use.*

SPC section and expected supporting data in MA dossier in accordance with Art. 5 of Directive 2001/82/EC (full application)	Potential risk in connection with the use of vaccines under Art. 8 of Directive 2001/82/EC if information is not available or inadequate
	Risk for vaccinated animal, non-vaccinated susceptible animals and public health
3. PHARMACEUTICAL FORM	
This section provides the description of the visual appearance of the veterinary medicinal product's pharmaceutical form as marketed. The visual appearance is a basic parameter which is normally controlled on the finished product because it allows an initial gross identification of defective batches.	*If there is no description of the appearance of the vaccine, the end user cannot be sure that he is using a correct product of appropriate quality and may fail to identify defective batches.* *Risk for vaccinated animal health*
4. CLINICAL PARTICULARS 4.1 Target species	
This section indicates the species including any sub-category. To authorise a species/sub-category of species, there must be enough data to show that the use of the vaccine is safe and efficacious in each species/sub-category of species as it is not possible to extrapolate the safety and efficacy seen in one species/sub-category of species to another one.	*If the vaccine is used for a species or category of animal in which it has not been tested, then it may not be safe or efficacious.* *Risk for vaccinated animal and public health*
4.2 Indications for use, specifying the target species	
All claims made by the applicant with regard to the properties, effects and use of the vaccine must be fully supported by results of specific trials contained in the application for marketing authorisations. The efficacy of the vaccine is normally demonstrated in 'laboratory' conditions by a challenge model aimed to define the onset and duration of immunity for each category of the indicated target species. The efficacy studies should be controlled trials including vaccinated and untreated control animals and using a challenge strain relevant to the epidemiological situation in the field. Normally, unless the applicant is capable to provide a justification, field studies need to be carried out in order to assess the efficacy of the vaccine in real conditions.	*If the efficacy studies are missing, it will not be possible to correctly describe the benefits of the vaccine for each target species / subspecies.* *If decision makers rely only on the claims provided by the applicant which were not critically assessed by medicines competent authorities, the benefits of the vaccine might be overstated. The vaccine may fail to induce immunity as rapidly as claimed or achieve the level and/or duration of protection in some or all the species indicated. The number of doses for primary vaccination may not have been fully evaluated or the interval between boosters resulting in uncertainty in the optimum vaccination schedule for animals in the field.* *If the vaccine is not efficacious, the animals vaccinated may become infected and develop symptoms of the disease. In the case of a vaccine against a zoonotic disease, the absence of efficacy may have an impact on public health.*

SPC section and expected supporting data in MA dossier in accordance with Art. 5 of Directive 2001/82/EC (full application)	Potential risk in connection with the use of vaccines under Art. 8 of Directive 2001/82/EC if information is not available or inadequate
	The influence of maternally derived antibodies (MDA) in young animals may not have been evaluated. *Risk for vaccinated animal and public health*
4.3 Contraindications	
The contraindications correspond to situations which arise from a set of circumstances where the vaccine must not be used for target animal safety reasons. They can only be defined if sufficient safety studies have been performed with the vaccine in various conditions.	*If these data are not available, there is a risk that a safety concern will arise out of the use of the vaccine.* *Risk for vaccinated animal health*
4.4 Special warnings for each target species	
The purpose of this section is to provide clear information on how to ensure correct use of the vaccine in target animals. It also warns end users of possible modifications of the efficacy profile of the product, which may arise in particular situations such as very old or very young animals.	*In the absence of this information the efficacy of vaccination could be compromised in certain situations or in certain species/categories of animal. For example, if no efficacy study is performed in young animals which have maternally derived antibodies, it will not be possible to recommend the use of the vaccine in this category of animals.* *Risk for vaccinated animal health*
4.5 Special precautions for use Special precautions for use in animals	
The purpose of this section is to provide clear information on how to ensure the safe use of the product in target animals When data suggest that the vaccine could impact on immunological functions these should be investigated.	*If such studies are not provided, it will not be possible to give clear advice about the safety of the vaccine.* *If data are missing, potential harmful effects on immunity (immunodepression, absence/reduction of efficacy of other vaccinations, increased susceptibility to field diseases,…) cannot be assessed and the use of the vaccine could lead to serious adverse effects.*
To define the safety profile of the vaccine, the applicant has to provide specific studies for live vaccines. A live vaccine contains an agent that is generally attenuated and less virulent than the field strain that induces the disease. Nevertheless the vaccine strain keeps the ability to multiply in the target species after vaccination and therefore can have a potential impact on	*In the case of strains of live vaccines for zoonotic diseases that are spread in the environment, if no appropriate safety study is provided, the risk for in-contact animals and humans cannot be assessed.*

SPC section and expected supporting data in MA dossier in accordance with Art. 5 of Directive 2001/82/EC (full application)	Potential risk in connection with the use of vaccines under Art. 8 of Directive 2001/82/EC if information is not available or inadequate
the vaccinated animal, on in-contact animals and on the environment. The study of dissemination is the first step before the study of the spread of the vaccine strain: if dissemination in the animal's body is observed, it can be expected that the vaccine strain will spread into the environment. It is necessary to know if the vaccine strain is able to spread from vaccinated to non-vaccinated animals, whether target species or not, especially to those that could be highly susceptible to the vaccine strain.	
The potential for reversion to virulence of an attenuated vaccine strain also has to be assessed. This it is done through the study of serial passages of the vaccine strain in five groups of animals.	*If this study is missing, the stability of attenuation of the vaccine strain cannot be guaranteed and the possibility of reversion to virulence cannot be assessed. If the vaccine is used in the field, it might induce a disease in vaccinated and non-vaccinated susceptible animals.*
In some cases, the possibility of recombination or genetic reassortment of related live vaccine strains should be subjected to a risk assessment and additional safety studies may be required to further evaluate the safety of this use.	*The potential of the live vaccine organism to recombine with field strains leading to new, and potentially virulent, disease strains should be considered for live vaccines that spread from the vaccinated animal.* *Risk for vaccinated animal, non-vaccinated susceptible animals and public health*
Special precautions to be taken by the person administering the veterinary medicinal product to animals	
Risks resulting from the nature of the product, its preparation, its use and its risks resulting from particular characteristics of the user should be stated here together with advice of how these risks should be managed. If applicable, information should also be given for persons in close contact to the treated animal e.g. animal owner, children, immuno-compromised persons, and pregnant women. Where necessary, recommendations to minimise exposure of the product user during administration and, where relevant, during preparation of the product for administration should also be given in this section. Where safety studies of live vaccines for zoonotic diseases have	*In the absence of this type of data, there may be a safety risk for persons administering or in contact with the vaccine.* *Risk for end user and/or the animal's owner*

SPC section and expected supporting data in MA dossier in accordance with Art. 5 of Directive 2001/82/EC (full application)	Potential risk in connection with the use of vaccines under Art. 8 of Directive 2001/82/EC if information is not available or inadequate
demonstrated that there is a spread of the strain into the environment, the risk for the end user and/or the animal's owner has to be assessed and an appropriate warning should be included under this section.	
4.6 Adverse reactions (frequency and seriousness)	
This section should include information on adverse drug reactions attributed to the product when used as recommended. To obtain this information the applicant has to perform studies to demonstrate the safety of the administration of one dose in laboratory and field conditions. The field studies allow to assess the safety of the vaccine in real conditions: large number of animals of different ages and categories, vaccination in different places. The follow up is less stringent than in laboratory conditions but the results should confirm or are complementary of the results obtained in laboratory studies. Safety data for repeated administration should be provided if repeated administration is recommended in the vaccination schedule. If the vaccine is intended for different target species/sub-category of species, the vaccine should be administered to all these species/sub-category as it is not possible to extrapolate the side effects seen in one species/sub-category to another one. The same applies to the route of administration: it is not possible to extrapolate the side effects observed with one route of administration to another route (intramuscular administration, subcutaneous vaccination, spray….).	*If this information is not available then the adverse effects of the vaccine cannot be anticipated or predicted using the various routes of administration. The number and extent of local and generalised reactions may not be known, including the effects on young and pregnant animals or on the productivity of food producing species.* *Risk for vaccinated animal health*
4.7 Use during pregnancy, lactation or lay	
In order to ensure the safe use of the product, the end user must be informed of the recommendations regarding the use of the product in pregnant/lactating animals or laying birds. When data suggest that the vaccine strain or the vaccine components may be a potential risk factor, the examination of reproductive performance must be investigated by the applicant.	*If data are missing, the potential harmful effects on reproductive performances (sterility, abortion, teratogenic effect on the progeny,…) cannot be assessed and as a result the safety of the product in pregnant/lactating animals or laying birds cannot be ensured.* *Risk for vaccinated animal health*

SPC section and expected supporting data in MA dossier in accordance with Art. 5 of Directive 2001/82/EC (full application)	Potential risk in connection with the use of vaccines under Art. 8 of Directive 2001/82/EC if information is not available or inadequate
4.8 Interaction with other medicinal products and other forms of interaction	
A statement in this section indicates compatibility with other veterinary immunological products. In this case, the safety and the efficacy of the products used together must be investigated. In non-emergency situations where studies are not available, this section normally clearly indicates the absence of data.	*If the studies are missing, the potential negative impacts of using the vaccine with other products (increased adverse effects, reduced efficacy of the vaccine or product(s) administered together) cannot be assessed.* *If there is a negative impact on a product used to protect animals against a zoonotic disease there is also a potential risk for public health.* *Risk for vaccinated animal and public health*
4.9 Amounts to be administered and administration route	
This section provides information on the route and site of administration including directions for proper use by the veterinarian, farmer or owner. Any special equipment needed for administration of the product should be described. Where the product is to be administered via the feed, water or aerosol, any dosage adjustment for animals reluctant to eat and/or drink should be specified as well as the conditions of correct delivery in case of mass vaccination. These different parameters have to be tested in controlled studies in order to demonstrate the efficacy of the vaccination protocol proposed by the applicant. As it is not possible to extrapolate the efficacy observed with one route of administration to another route (intramuscular administration vs subcutaneous vaccination or spray, etc.), the SPC can only mention the route of administration that was tested in the efficacy studies.	*If the efficacy studies are missing, it will not be possible to show the benefit of the vaccine and indicate to the end user how to use the vaccine correctly (age of vaccination, dose to administer, route of administration, vaccination schedule) in order to obtain an optimal protection for vaccinated animals.* *Risk for vaccinated animal and public health*
4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary	
The purpose of overdose studies is to detect signs of possible adverse reactions and to identify the dose at which they occur, in order to establish a safety margin. This study is only requested for live vaccines. In this case the microorganism present in the vaccine is able to multiply in the target species after vaccination and the administration of an overdose mimics the worst case	*If this safety study is missing, the assessment of the safety of a live vaccine can be compromised.* *Risk for vaccinated animal health*

SPC section and expected supporting data in MA dossier in accordance with Art. 5 of Directive 2001/82/EC (full application)	Potential risk in connection with the use of vaccines under Art. 8 of Directive 2001/82/EC if information is not available or inadequate
scenario.	
4.11 Withdrawal period(s)	
The withdrawal period is defined as the period between the last administration of the veterinary medicinal product to animals and the production of foodstuffs from such animals.	*If an arbitrary withdrawal period is set not based on sound science the safety for the consumers of meat and dairy products from vaccinated animals cannot be guaranteed.* *Risk for public health*
The components of vaccine intended for food producing animals must be in accordance with Maximum Residue Limits (MRL) regulations.	*If the compliance of the components of the vaccine with MRL regulations is not demonstrated, the safety for the consumers of meat and dairy products from vaccinated animals cannot be guaranteed.* *Risk for public health*
In the case of live vaccines for zoonotic diseases used for food producing animals, the study of dissemination (see under section 4.5) is necessary to detect where the vaccine strain is present in the animal's body and particularly if the organism persists at the administration site.	*If this information is not provided, the risk for the consumer of meat and dairy products from vaccinated animals cannot be assessed and there may be a safety issue for the consumer after exposure to the zoonotic vaccine strain.* *Risk for public health*
5. IMMUNOLOGICAL PROPERTIES	
This section should include a brief description of the immunological properties and characteristics of the active substance(s) and the ATC vet code.	*No specific risk, but the information is useful in understanding the mechanism of protection which may influence the use of the vaccine in the field.*
6. PHARMACEUTICAL PARTICULARS 6.1 List of excipients	
All of the excipients should be listed, expressed qualitatively only	*If the list is not provided, it will not be possible to verify that the excipients included are safe for the vaccinated animals or consumers.* *Risk for vaccinated animal and public health*
6.2 Incompatibilities	
It is not permitted to mix immunological products with other products, except a diluent or other component recommended/supplied for use with the product, unless studies showing compatibility have been provided	*If compatibility is not studied and the immunological product is mixed with another product, the safety and the efficacy of the mixture cannot be guaranteed. If there is a negative impact on a product used to protect animals against a zoonotic disease there is also a potential risk for public*

SPC section and expected supporting data in MA dossier in accordance with Art. 5 of Directive 2001/82/EC (full application)	Potential risk in connection with the use of vaccines under Art. 8 of Directive 2001/82/EC if information is not available or inadequate
	health. *Risk for vaccinated animal and public health*
6.3 Shelf life	
The shelf-life of the vaccine as packaged for sale and after reconstitution or opening of the immediate packaging are mentioned in this section. In the quality part of the marketing authorisation dossier, the applicant has to provide a stability study in real time conditions on a sufficient number of batches. If the vaccine has to be reconstituted prior to administration or administered via the feed, water or aerosol, the applicant has to show that the in use shelf life is compatible with effective administration. If the vaccine contains a preservative, the applicant has to show that its efficacy covers the shelf life and the in use shelf life of the vaccine.	*If stability data are not provided, it is not possible to know how long the vaccine can be stored and how long it is stable after reconstitution or opening of the container. As a result, the use of a vaccine after storage may compromise its efficacy.* *Risk for vaccinated animal and public health*
6.4 Special precautions for storage	
This section contains the information necessary for the correct storage of the product. It should reflect the conditions that were tested in the stability study.	*If the conditions of storage are not defined, the stability and as a result the efficacy of the vaccine cannot be guaranteed. If there is a negative impact on a product used to protect animals against a zoonotic disease there is also a potential risk for public health.* *Risk for vaccinated animal and public health*
6.5 Nature and composition of immediate packaging	
A short but complete description of the immediate packaging used for (and the contents of) the final sales presentation should be provided. This section presents the different presentations of the vaccine that were tested in the quality studies and shown to be appropriate for the correct use of the vaccine.	*If there is no description of the presentations of the vaccine, the end user cannot be sure that he is using the product in the correct container. If there is a negative impact on a product presented in the wrong packaging used to protect animals against a zoonotic disease there is also a potential risk for public health.* *Risk for vaccinated animal and public health*
6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products	
This section should include information necessary for the safe disposal of unused product, and the equipment used for the administration of the product to animals	*If the conditions for a safe disposal are not mentioned, the product may be discarded without sufficient precautions and may contaminate the end user, the animals and/or the environment.*

SPC section and expected supporting data in MA dossier in accordance with Art. 5 of Directive 2001/82/EC (full application)	Potential risk in connection with the use of vaccines under Art. 8 of Directive 2001/82/EC if information is not available or inadequate
	Risk for animal and public health

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