EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21 April 2016
EMA/CVMP/IWP/867401/2015
Committee for Medicinal Products for Veterinary Use (CVMP)

Concept paper on DNA vaccines non-amplifiable in eukaryotic cells for veterinary use

Agreed by Immunologicals Working Party (IWP)	February 2016
Adopted by CVMP for release for consultation	21 April 2016
Start of public consultation	29 April 2016
End of consultation (deadline for comments)	31 July 2016

The proposed guideline will replace the 'Note for guidance on DNA vaccines non-amplifiable in eukaryotic cells for veterinary use' (EMEA/CVMP/IWP/07/98).

Comments should be provided using this template. The completed comments form should be sent to vet-guidelines@ema.europa.eu

Keywords	DNA vaccines

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1. Introduction

The 'Note for guidance on DNA vaccines non-amplifiable in eukaryotic cells for veterinary use' was adopted in March 2000 and came into effect on 1st January 2001. This document was intended to provide advice to manufacturers seeking marketing authorisation for a nucleic acid vaccine for use in animals when the vaccine consists of a bacterial DNA plasmid. In recent years, experience has been gained within the regulatory network on such vaccines, and aspects of the guideline are now considered to be out-of-date.

2. Problem statement

The 'Note for guidance on DNA vaccines non-amplifiable in eukaryotic cells for veterinary use' is now over fifteen years old, and was developed at a time when development of DNA vaccines was at an early stage and no such vaccines had been commercially developed and submitted for assessment. Considering the scientific developments since then and experience gained, the CVMP/IWP considers that this guideline should be updated in order to reflect current knowledge and ensure continued relevance for development of commercial vaccines.

3. Discussion (on the problem statement)

The use of plasmid DNA as a form of vaccination has progressed considerably over the past decade or so and a substantial number of trials of this type of vaccination are, or have been, undertaken in different targets which have led in some cases to licensed authorisation, although currently there are no Marketing Authorisations for such vaccines in the EU. Additionally, such vaccine constructs are also being utilised for their potential as therapeutic tools against autoimmune diseases and allergies. DNA vaccination involves the inoculation of a gene(s) encoding a relevant antigen against which an immune response is desired, under the control of a promoter, which will permit its expression in the vaccinated animal. This gene construct is usually contained, for manipulation and for manufacturing purposes, within a bacterial plasmid DNA molecule although shortened linear DNA sequences blocked at either end with synthetic hairpin nucleotides have also shown promise. This type of vaccine has potentially important advantages over the direct inoculation of the antigen itself, e.g. it may provide a much wider stimulation of the immune system, both cellular and humoral, including the stimulation of a cytotoxic T cell response. It can also have advantages over the use of a live attenuated micro-organism, e.g. the avoidance of breakthrough of disease arising from inadequately attenuated infectious agents. Furthermore, the manufacture of a plasmid DNA vaccine is likely to be simpler, quicker, more adaptable and cost efficient than for the more traditional forms of vaccine, particularly where there is a need for disease secure containment, with the added benefit that they are likely to have greater stability, making the need for a cold chain less critical as well as providing wider scope to encompass other modes of delivery.

It is therefore an appropriate time to review the guideline with a view to updating it to take account of more recent scientific developments and experience gained. Some examples where revision may be particularly appropriate include, but are not limited to:

- The need for particular consideration of the potential for integration into the host genome.
- Development of improved methods for DNA sequence analysis may provide for better control over identity and genetic stability.
- The relative importance of supercoiled DNA compared to genomic DNA in respect to vaccine, efficacy and for batch quality control.

4. Recommendation

The Immunologicals Working Party recommends revising the 'Note for guidance on DNA vaccines non-amplifiable in eukaryotic cells for veterinary use' to take into account scientific developments since the guideline came into effect and experience gained. Based on this it is considered that the following areas in particular will require amendment: vaccine characterisation, quality control and safety testing.

5. Proposed timetable

April 2016	Concept paper released for consultation
July 2016	Deadline for comments
October 2016	Discussion in IWP
Q2 2017	Proposed date for release of draft guideline for consultation
Q3 2017	Deadline for comments
Q1 2018	Expected adoption by CVMP

6. Resource requirements for preparation

Revising the guideline will involve one rapporteur and one co-rapporteur.

Discussion at 2 – 3 IWP meetings.

7. Impact assessment (anticipated)

It is anticipated that the revised guideline would benefit both industry and regulators due to provision of more up-to-date and relevant guidance on development and manufacture of DNA vaccines.

8. Interested parties

Veterinary pharmaceutical industry and consultants.

Regulatory authorities involved in assessment of Marketing Authorisation applications.

The Ad Hoc Expert Group on Veterinary Novel Therapies group.