15 March 2012
EMEA/CHMP/308136/2007
Committee for the Medicinal Products for Human Use (CHMP)

Concept paper on guidance for DNA vaccines

Agreed by GTWP/BWP/SWP/VWP	**July 2007**
Adoption by CHMP for release for consultation	19 July 2007
End of consultation (deadline for comments)	31 October 2007
Adoption by CHMP for re-release for consultation[1]	15 March 2012
Start of public consultation	30 March 2012
End of consultation (deadline for comments)	30 June 2012

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

Keywords	DNA vaccines, bacterial plasmid DNA, prevention of infectious diseases, gene, antigen, biodistribution, persistence, chromosomal integration.

[1] The work on the guideline was interrupted due to the increased workload during the 2009-2010 influenza pandemic. In the meantime, the Agency became aware of further advances in the field of DNA vaccines. Stakeholders are invited again to comment on this concept paper so that advances in science can be taken into consideration for the future guidance.

7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

1. Introduction

DNA vaccines against infectious diseases have been under development for some time and DNA vaccines expressing HIV or malaria antigens have especially been targeted. Although to date no marketing authorisation for such a vaccine for human use has been granted in the EU, the first DNA vaccines for veterinary use, West Nile-Innovator and Apex-IHN, have been authorised elsewhere.

2. Problem statement

Guidance for DNA vaccines is provided in the CPMP note for guidance on the quality, preclinical and clinical aspects of gene transfer medicinal products (CPMP/BWP/3088/99), which came into effect in 2001 and is currently under revision. However, it is stated in Directive 2009/120/EC that "gene therapy medicinal products shall not include vaccines against infectious diseases", and although some principles and requirements of gene therapy apply, the guidance provided in the current gene transfer guideline does not address specific aspects relevant for a DNA vaccine against infectious disease. Whilst little has changed regarding quality aspects of plasmid DNA, considerable experience has accrued regarding their safety at both the nonclinical and clinical levels. The original safety guidance was based upon hypothetical considerations and this should now be updated in light of extensive non-clinical and clinical experience. Quality aspects also can be updated to ensure they are in line with state-of-the-art DNA manufacture and control. Consequently, it is clear that guidance specific for DNA vaccines needs updating, and this should be provided by development of a specific guidance document (annex to the existing Note for guidance or a self-standing guidance document).

3. Discussion (on the problem statement)

Although two veterinary vaccines based upon plasmid DNA have been authorised (outside of the EU), no authorised human DNA vaccine exists. However, there are many under clinical investigation worldwide and include plasmids expressing malarial, HIV, influenza, tuberculosis (TB) and Ebola virus antigens.

Issues that are specific to these vaccines include their mode of manufacture and control, and especially the studies required for preclinical safety testing including biodistribution, plasmid persistence and chromosomal integration. For DNA vaccines, many of the hypothetical concerns that are highlighted in the current note for guidance can now be re-evaluated based on non-clinical and clinical experience gained.

It is also noted that the DNA vaccines being considered here are for use in prophylaxis of infectious disease. Plasmid DNA is also being investigated for therapeutic use and aspects of the guideline might also be applicable to those products, especially their manufacture and quality aspects.

4. Recommendation

It is recommended that guidance on the quality, non-clinical and clinical aspects associated with DNA vaccines is revised. This would be undertaken by a multi-disciplinary drafting group led by the VWP, drawing expertise from the BWP (for quality issues), the SWP (for safety issues), and the GTWP (for non-clinical and clinical issues related to gene therapy products). The guideline would apply to DNA vaccines for prevention and treatment of infectious disease. Points to be covered include scope, genetic development, manufacture, quality control, nonclinical safety testing and clinical assessment specific to these vaccines. While plasmid DNA is the main product discussed in the guidance, other forms of nucleic acid vaccines and micro-organisms such as bacteria intended for transferring plasmid

DNA to human somatic cells *in vivo* for prevention of infectious disease will also be covered. Where appropriate, reference will be made to other supporting guidelines such as those pertinent for nonclinical and clinical aspects of vaccines.

5. Proposed timetable

It is anticipated that a draft guideline will be available 12-18 months after adoption of the concept paper and will be released for 6 months external consultation, before finalisation within a further 6 months.

6. Resource requirements for preparation

Development of the guideline will be led by the VWP in collaboration with the GTWP, BWP and SWP. A coordinating team will be appointed with representation from the above four working parties. Other relevant working parties and external parties will be consulted as needed.

Drafting work will be conducted primarily by email and teleconferences. The VWP, GTWP, BWP and SWP will discuss draft versions at their regular meetings.

7. Impact assessment (Anticipated)

The guideline will give applicants and Regulatory Authorities guidance on the assessment of DNA vaccines. Such a harmonized approach will contribute to the protection of European patients and to foster the development of DNA vaccines within the EU. It will also streamline their clinical development and ultimately marketing authorisation applications via the centralised procedure.

8. Interested parties

Internal/External parties

VWP, GTWP, BWP, SWP, PhVWP, IWP, PDCO

External consultation: pharmaceutical industry, academic networks and learned societies within the EU.

9. References to literature, guidelines etc

None stated.