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Reflection paper on data requirements for swine influenza vaccines against pandemic (H1N1) 2009 influenza

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This paper does not open formal consultation but comments are welcome by 31 May 2010. Comments should be provided using this template to Vet-guidelines@ema.europa.eu Fax: +44 20 7418 8447

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[1] The CVMP has agreed during its October 2010 meeting that in light of the latest information no further revision of this reflection paper is currently necessary.

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1. Introduction (background)

Swine influenza is an acute respiratory disease caused by influenza A viruses that belong to Orthomyxoviridae, a family of enveloped negative-sense, segmented, single stranded RNA viruses. Based upon the major differences within the hemagglutinin (HA) and neuraminidase (NA) proteins, 16 HA and 9 NA subtypes have been identified thus far.

It is recognized that influenza viruses evolve by reassortment and/or point mutation, thus giving rise to new viral subtypes with different host tropism. In April 2009, a novel swine-lineage influenza virus capable of rapid human transmission was reported, although infection with pandemic (H1N1) 2009 virus was not connected to pig exposure or to a contemporary infection in the swine population.

The extent of the circulation of the pandemic (H1N1) 2009 virus among pig populations is not known. Pigs have been shown to be fully susceptible by experimental inoculation. In some circumstances pigs have been shown to have been infected by contact with humans infected with the pandemic (H1N1) 2009 virus. Although not yet demonstrated the possibility of cross-species transmission from pigs to humans exists and may lead to unpredictable consequences in terms of risk of human infection by increasing the reservoir of the virus and the potential risk of re-assortment. In the case of the pandemic (H1N1) 2009 virus becoming established in the pig population this could have a negative economic impact on the pig industry.

This reflection paper has been developed in response to the threat of outbreaks of pandemic H1N1 infection in pigs within Europe and to address some specific concerns relating to the development of vaccines intended to protect against the pandemic (H1N1) 2009 infection.

2. Legal basis, scope and introductory remarks

This reflection paper has to be read in conjunction with Title II of the Annex I to Directive 2001/82/EC as amended.

The introduction, general principles and Title II of the Annex I to Directive 2001/82/EC as amended, list the administrative, quality, safety and efficacy data that should be presented in support of an application for a Marketing Authorisation.

The situation in the field does not currently justify the need to implement Article 39(7) of Regulation (EC) 726/2004 in order to allow applications for an authorisation under exceptional circumstances.

The scope of this document extends to the following types of vaccines:

- Inactivated whole virus vaccines
- "Subunit" vaccines containing proteins purified from pandemic (H1N1) 2009 influenza virus or produced in a biotechnology expression system
- Live recombinant viruses or bacteria capable of infecting pigs
- Virus Like Particle (VLP) vaccines

Due to their potential for genetic reassortment and a risk of spontaneous mutations leading to increased pathogenicity, swine influenza vaccines should not contain replication-competent influenza virus.

3. Data requirements

The dossier should provide at least the following data:

3.1. Analytical (Quality) requirements

The compliance with all the requirements of Annex I, Title II of Directive 2001/82/EC as amended shall be demonstrated.

If the vaccine is a conventional inactivated vaccine, the requirements of the Ph. Eur. monograph 0963 "Porcine influenza vaccine (inactivated)" apply. However the Applicant may need to develop alternative and validated tests for the immunogenicity test, batch potency test and potency test taking into account the specific characteristics of the vaccine and challenge strains.

3.2. Safety requirements

The compliance with all the requirements of Annex I, Title II of Directive 2001/82/EC as amended shall be demonstrated.

3.3. Efficacy requirements

The compliance with all the requirements of Annex I, Title II of Directive 2001/82/EC as amended shall be demonstrated. The standard efficacy requirements for conventional swine influenza vaccines should be applied.

Additionally, due to the potential risk that the pandemic (H1N1) 2009 field strains may be transmitted from pigs to humans the level of viral excretion from vaccinated and control animals after challenge should be investigated. Ideally prevention of viral excretion post-challenge is achieved. If it is not possible to achieve this goal the acceptable level of efficacy will be established on a case by case basis using a risk/benefit approach taking into account for example available data on level of reduction of viral excretion. The methods used to detect the post-challenge viral excretion should be validated.

The challenge strain should be a suitable pandemic (H1N1) 2009 strain whatever the origin of the challenge strain and its relevance to circulating field strains should be demonstrated.