Vaccine response to the avian influenza A(H7N9) outbreak - step 1: development and distribution of candidate vaccine viruses

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Influenza vaccination is the most important intervention in reducing the impact of influenza, and a key component of the WHO response and preparedness efforts for influenza of pandemic potential, including avian influenza A(H5N1), A(H9N2) and A(H7N9).

Development of candidate vaccine viruses

The first step in the long cycle of vaccine development and production is vaccine virus selection and the development of high-growth reassortants (candidate vaccine viruses (CVVs)). This is a well-established process and has been in place since the 1970s. It was further strengthened during the response to A(H5N1) and pandemic A(H1N1) 2009, mainly through the WHO Global Influenza Surveillance and Response System (GISRS) which currently comprises 150 laboratories in 111 countries.

Since the detection of avian influenza A(H7N9) virus in China, GISRS has been on alert. Through the excellent work undertaken by the WHO Collaborating Centre (WHO CC) in Beijing, viruses have been isolated and shipped to other WHO CCs and Essential Regulatory Laboratories (ERLs) of GISRS for joint virus characterization, development of diagnostic tests, risk assessment and candidate vaccine virus development for pandemic preparedness purposes.

Using the two available technologies, classical reassortment and reverse genetics, the WHO CCs and ERLs are developing high-growth reassortants that are suitable for vaccine development and production. The status of development of CVVs will be updated routinely by WHO for influenza vaccine manufacturers, national/regional regulatory agencies and other interested parties.

Release of candidate vaccine viruses

Candidate vaccine viruses are usually released to interested manufacturers after a series of characterization and safety tests have been completed[1].

However, discussion with experts aimed at enhancing vaccine production readiness has led to a consensus that permits the expedited release of reassortant candidate vaccine viruses before the completion of all safety testing and characterization of the viruses. Specifically, a ***potential*** candidate vaccine virus can be released to a recipient if:

- The reassortant virus has passed the following tests satisfactorily:
    - sequencing of the HA gene

[1] A guidance document describing the required biosafety tests for CVVs derived from avian influenza A(H7N9) will be published on the WHO website shortly.

    - chicken embryo survival testing
- The recipient has BSL3 facilities and appropriate import permit if needed

It should be noted that a virus that has passed the two safety tests described above, will still require handling at a biosafety level equivalent to that applicable for wild-type viruses (BSL-3 at laboratory scale, BSL-3 enhanced for large scale work). Furthermore, without antigenic characterization by one-way and two-way HI tests, no assessment of the antigenic appropriateness of a ***potential*** CVV can be given, and use of such ***potential*** CVVs is conducted at the manufacturer's own risk.

WHO will provide updates on the development and testing of ***potential*** CVVs on its website at: http://www.who.int/influenza/vaccines/virus/en/

Receipt of candidate vaccine viruses

In order to request ***potential*** reassortant candidate vaccine viruses of A(H7N9), vaccine manufactures, research institutes and other interested bodies should send an email to WHO CCs and ERLs of GISRS as listed at: http://www.who.int/influenza/gisrs_laboratory/collaborating_centres/list/en/index.html; in particular, at this stage of development of CVVs, the WHO CC at CDC US (rvd6@cdc.gov) and the WHO ERL at NIBSC UK (Othmar.Engelhardt@nibsc. org), as well as the WHO CC at CCDC China (xinli@cnic.org.cn), the WHO CC at NIID Japan (nobusawa@nih.go.jp) and the WHO ERL at CBER/FDA, US (Zhiping.ye@fda.hhs.gov) which are expecting to have ***potential*** reassortant candidate vaccine viruses of A(H7N9) available shortly.

To receive fully characterized and safety tested reassortant and wild type candidate vaccine viruses of A(H7N9), requests should be sent to WHO CCs and ERLs of GISRS as listed at: http://www.who.int/influenza/gisrs_laboratory/collaborating_centres/list/en/index.html.

A(H7N9) viruses, including reassortant candidate vaccine viruses, are considered PIP Biological Materials and are being shared under the PIP Framework (http://www.who.int/influenza/resources/pip_framework/en/index.html).

For general questions, please email GISRS-WHOHQ@who.int.