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Conference report

Strengthening the influenza vaccine virus selection and development process

Outcome of the 2nd WHO Informal Consultation for Improving Influenza Vaccine Virus Selection held at the Centre International de Conférences (CICG) Geneva, Switzerland, 7 to 9 December 2011☆

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1. Introduction

Influenza vaccination remains the cornerstone of global, regional and national public health efforts to reduce the impact of both recurrent influenza epidemics and infrequent pandemics. Effective influenza vaccination programmes rely upon the availability of vaccines that are well matched to the latest antigenic variants, and upon timely and equitable access to such vaccines. At the heart of influenza vaccine production lies the vaccine virus selection and development process (Fig. 1) implemented and coordinated by the WHO Global Influenza Surveillance and Response System (GISRS).[2]

Since 1952, the GISRS has evolved into the key global mechanism for continually monitoring influenza activity, and for assessing the risks posed both by seasonal epidemics and by animal influenza viruses with the potential to cause a pandemic. As awareness of these risks has risen, and as the burden of disease caused by influenza has become clearer, the demands placed on the GISRS have increased, especially over the last decade. In 2003, the re-emergence of human cases of H5N1 influenza highlighted the importance of strengthened pandemic influenza preparedness and response capacities, which were subsequently enshrined in the updated International Health Regulations (2005). The marked expansion of the GISRS – primarily as a result of increases in the number, geographical coverage and capacities of National Influenza Centres (NICs) – and the more prominent coordinating role of WHO proved to be fully justified when the system was tested by the 2009 H1N1 pandemic. In 2011, the historic adoption of the Pandemic Influenza Preparedness (PIP) Framework for the sharing of influenza viruses and access to vaccines and other benefits reflected growing recognition of the importance of the timely sharing and characterization of viruses, and the equitable provision of effective vaccines against both seasonal and pandemic influenza.

Since the early 1970s, WHO has provided formal recommendations on influenza vaccine composition based on the year-round GISRS surveillance of changes in the characteristics and epidemiological impact of circulating viruses. WHO recommendations for seasonal influenza vaccines must be made 7–8 months in advance of the northern and southern hemisphere influenza seasons (Fig. 2) in order to accord with a strict timetable involving the provision of candidate vaccine viruses, regulatory decision-making, and the manufacture, validation and distribution of vaccines.

The principal criteria for recommending a vaccine virus change include evidence of the emergence and geographical spread of a variant (or novel) virus with an antigenically distinct haemagglutinin (HA) protein – the component of prime importance in immunity. Changes in the amino acid sequence of HA, especially at known antigenic, receptor-binding or glycosylation sites, provide additional evidence for differentiating and characterizing new variants. Other criteria include evidence of poor recognition of the HA of circulating viruses by antibodies in sera obtained from recipients of the current vaccine.

Despite the severe time constraints involved, WHO has a long history of success in recommending influenza vaccine compositions that have closely matched the combination of viruses circulating in subsequent influenza seasons. Between the introduction of the first trivalent vaccine in 1978 and the end of 2011, a total of 43 changes were recommended by WHO – 20 to the A(H3N2) component; 9 to the A(H1N1) component; and 14 to the influenza B component (Fig. 3).

Retrospective studies of field vaccine effectiveness during epidemic periods have indicated that well-matched seasonal influenza vaccines have prevented cases of influenza-like illness (ILI) in approximately 70% of vaccine recipients aged 15–64 years, with lower effectiveness observed among older individuals [1]. However, reduced effectiveness has been observed for vaccines which only poorly match the circulating viruses, as occurred in the winter of 1997–98 following the late emergence of A/Sydney/5/97-like viruses in mid 1997. Given the strict timelines involved, any deficiencies or difficulties which adversely impact upon the early detection and characterization of new variants can thus severely

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[2] Formerly known as the Global Influenza Surveillance Network prior to the adoption of the World Health Assembly Resolution WHA 64.5 on 24 May 2011. As of May 2013, the GISRS consisted of 141 National Influenza Centres (NICs) in 111 countries, six WHO Collaborating Centres (WHOCCs), 12 WHO H5 Reference Laboratories and four WHO Essential Regulatory Laboratories (ERLs).

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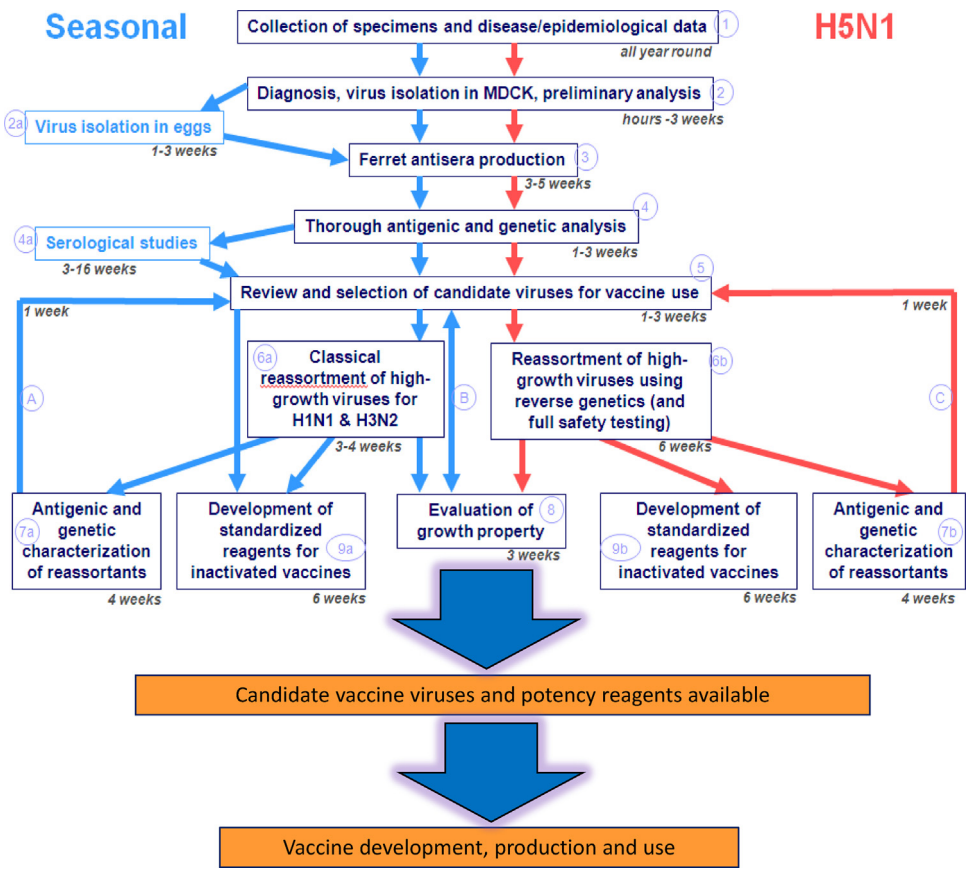

Fig. 1. The influenza vaccine virus selection and development process. "Selection" can be considered to include steps 1–5. Following the review and selection of candidate viruses for vaccine use, the process of vaccine virus development begins.

undermine the timely development of appropriate WHO recommendations and the prompt availability of suitable candidate vaccine viruses.

In recent years, long-standing gaps in the geographical coverage of surveillance activities and delays in virus characterization have increasingly been compounded by technical difficulties in the assays used to determine the antigenic characteristics of circulating viruses. In addition, limitations in understanding the impact of different degrees of antigenic change and the quality and breadth of the immune response to current vaccines have the potential to

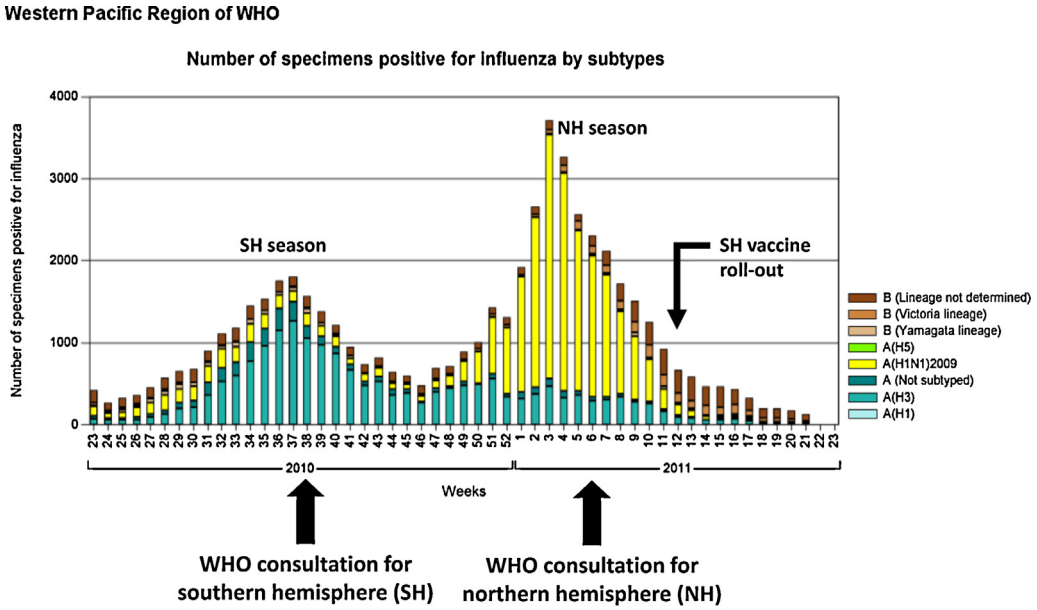

Fig. 2. Timing of vaccine virus recommendations in relation to the incidence of influenza in the WHO Western Pacific Region, and use of vaccine in the southern hemisphere in 2011.