
Reports by the Director-General

Summary progress reports

Financing and sustainability of benefits

1. In May 2007, the Health Assembly in resolution WHA60.28 requested the Director-General “to identify and propose, in close consultation with Member States, frameworks and mechanisms that aim to ensure fair and equitable sharing of benefits, in support of public health, ... taking strongly into consideration the specific needs of developing countries”. Specifically, she was requested to facilitate the “acquisition by developing countries of capacity for manufacturing in-country influenza vaccine”, to establish an international stockpile of influenza A (H5N1) vaccine, and to propose “innovative financing mechanisms to facilitate timely and affordable procurement of pandemic vaccines for and by Member States in need”.

Capacity for influenza vaccine production

2. In May 2006, WHO launched the Global pandemic influenza action plan to increase vaccine supply in order to reduce the expected gap between potential vaccine demand and supply during an influenza pandemic.¹ The Director-General convened a technical advisory group on the global action plan, with representatives from developing and industrialized countries, all WHO regions, and countries with and without influenza vaccine manufacturing capacity. It met in Geneva on 19 October 2007 and is scheduled to hold its second meeting in Pune, India, on 26 and 27 November 2008.

3. Details of progress towards achieving the goals of the global action plan, including revision to the original goals as recommended by the technical advisory group, will be published in the 2008 progress report, currently under preparation. In summary, since early 2007 substantial progress has been made to increase the production capacity for influenza vaccines.

- With funds provided by Canada, Japan, the United States of America and the Asian Development Bank, WHO awarded grants of up to US\$ 2 million each to six Member States² to assist them in developing new capacity for manufacturing and production of influenza

¹ Document WHO/IVB/06.13 – WHO/CDS/EPR/GIP/2006.1.

² Brazil, India, Indonesia, Mexico, Thailand, Viet Nam.

vaccines. WHO is pursuing this plan to increase manufacturing capacity in low-income and middle-income countries by:

- continuing the grants to the six new manufacturers;
 - expanding the programme through award of similar grants to new applicants;
 - establishing a manufacturing “hub” in the Netherlands as an available source of technology transfer to answer the problem of scarcity of technology providers.
- New facilities and expansions of existing facilities have been announced, including some in developing countries.
 - Introduction of new adjuvants has lowered the concentration of antigen used per dose.
 - Antigen-production yields have improved.
 - New technologies for vaccine production are advancing.

4. Estimates of the capacity to produce influenza vaccines, including H5N1 vaccines, in order to meet some developing country needs, are being updated with support from the Bill & Melinda Gates Foundation. Preliminary results suggest that currently it would take two to three years to produce sufficient vaccine to vaccinate the world’s population, and that by 2014, provided all planned expansion of production capacity materializes, this time could decrease to just over one year.

H5N1 vaccine stockpile development

5. In November 2007, the Strategic Advisory Group of Experts on immunization (SAGE) recommended that WHO should continue to develop urgently the H5N1 vaccine stockpile, taking into consideration logistical needs and long-term sustainability, and drawing up the associated procedures for procurement, management, governance, regulation and deployment.¹

6. SAGE recommended specifically that the stockpile should hold 150 million doses of H5N1 vaccine with related ancillary equipment. It indicated that up to 50 million doses should be maintained for rapid-response activities to an outbreak with sustained human-to-human transmission of H5N1 virus. An additional 100 million doses should be distributed to low- and middle-income countries for use in nationally-defined essential populations as part of their response to an influenza pandemic if caused by such an H5N1 virus variant.

7. Criteria for acceptance of H5N1 vaccines into the stockpile are under review, including issues such as registration of the vaccines and liability. WHO is working with manufacturers to accelerate regulatory pathways for licensure and prequalification of H5N1 vaccines.

8. Pledges of donations of H5N1 vaccine to the stockpile have been made by GlaxoSmithKline Biologicals (50 million doses) and sanofi pasteur (60 million doses). Other manufacturers are considering making initial donations to the stockpile.

¹ *Weekly Epidemiological Record*, 2008, **83**(1):1-15.

9. Decisions about the release of H5N1 vaccines from the stockpile would depend on the use for which release is being considered:

- for *rapid containment*
- for *protection of essential populations in low- and middle-income countries* the decision would need to be based on the recommendations to the Director-General by the Emergency Committee under the International Health Regulations (2005) once it is determined that an H5N1 influenza pandemic is a public health emergency of international concern.

10. The Secretariat continues to seek guidance from Member States on appropriate and sustainable mechanisms for operating the stockpile, including rules and procedures for deployment, management, oversight, and financing. In addition to a physical stockpile, whose cost is estimated to be US\$ 3000 million over 20 years, two other, cheaper options for the H5N1 vaccine stockpile are being considered:

Option 1. Manufacturers pledge to reserve specified amounts of antigen and adjuvant in bulk form (analogous to current arrangements for WHO stockpiles of yellow fever and meningitis vaccines), with fill and finish operations being undertaken when WHO announces the need for vaccine is identified. Manufacturers would ensure that all products released from the stockpile have at least six months' remaining shelf-life.

Option 2. Manufacturers hold a stockpile of filled and finished vaccine. They would ensure that all products released from the stockpile have at least six months' remaining shelf-life.

Possible financing mechanisms

11. The largest single cost of maintaining an H5N1 vaccine stockpile is related to replenishment of vaccine stocks. The costs of each of the options above vary considerably and may require use of one or more of the following possible financing mechanisms that are being evaluated:

- (a) “*self financing*” – a financial commitment made by some combination of Member States or other parties, under some type of governance mechanism, which would only be accessed in case of need on the basis of a one-time or periodic payment;
- (b) “*casualty insurance*” – an insurer covers the costs at the time of a pandemic in exchange for advance premium payments;
- (c) an “*annuity*” – an upfront payment to one or more insurers in exchange for a guaranteed annual payment, thereby transferring the length of funding risk to an insurer and guarantees the availability of funds for a sufficient period of time, without requiring donors to enter into long-term pledges or risking donor fatigue;
- (d) “*guaranteed line of credit*” – a creditor maintains a line of credit (at preferential terms) that could be called on at the time of a pandemic to be used for financial needs for low- and middle-income countries;
- (e) a “*product warranty*” – manufacturers who undertake to supply vaccines provide for any required replenishment of their vaccine for a period of time in exchange for pre-arranged payments.

12. Other financial mechanisms being evaluated, particularly with the cooperation of the development banks, include catastrophe bonds and tax-channelling commitments in the event of a pandemic.

13. The financing mechanisms above are also being evaluated for their suitability to finance activities in the global action plan as well as the expected costs associated with the procurement of pandemic vaccines.

Continued H5N1 vaccine policy development

14. A working group of the Strategic Group of Experts on immunization on uses of H5N1 vaccines has been convened and will first meet in November 2008 to begin a process of examining whether evidence-based policy recommendations can be made for using H5N1 vaccine as an immunological primer in the current interpandemic period. The working group will consider in particular whether enough evidence is available to recommend: use of H5N1 influenza vaccine in high-risk or other groups in the interpandemic period; use of H5N1 vaccine nearing the end of its shelf-life that is in a WHO stockpile; and increasing the size of the stockpile in order to cover a broader definition of essential populations. The working group's deliberations will be reviewed by the Strategic Group of Experts on immunization, and recommendations are expected to be issued in 2009.

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