

How to implement influenza vaccination of pregnant women

An introduction manual
for national immunization programme managers
and policy makers



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Abbreviations

AEFI	Adverse event following immunization
ALRI	Acute lower respiratory infection
cMYP	Comprehensive multi-year plan
DQS	Data quality self-assessment
EPI	Expanded programme on immunization
ERL	Essential Regulatory Laboratory
GACVS	Global Advisory Committee on Vaccine Safety
HA	Haemagglutinin
HIV	Human immunodeficiency virus
HSA	Health surveillance assistant (Malawi)
ICC	Inter-agency coordinating committee
IEC	Information, education and communication
ILI	Influenza-like illness
KABP	Knowledge, attitudes, beliefs and practices
LMIS	Logistics management information system
M&E	Monitoring and evaluation
NIC	National Influenza Centre
NITAG	National Immunization Technical Advisory Group
PAHO	Pan American Health Organization
PIE	Post-introduction evaluation
RMNCAH	Programme manager for reproductive, maternal, newborn, child and adolescent health
RMSD	Regional Medical Supply Division (Sri Lanka)
SAGE	WHO's Strategic Advisory Group of Experts on Immunization
SARI	Severe Acute Respiratory Infection
TT2+	Reported number of second, third, fourth and fifth doses of TT administered to pregnant women during a calendar year
UNICEF	United Nations Children's Fund
VVM	Vaccine vial monitor
WHO	World Health Organization

1. Executive summary

WHO's influenza recommendations aim to protect vulnerable high-risk groups from severe disease[1]. In 2012, WHO published a position paper on influenza vaccine which identified pregnant women as the highest priority group for countries considering initiation or expansion of programmes for seasonal influenza vaccination. Influenza vaccination of pregnant women will protect both the mother and her young infant against influenza as there is no licensed vaccine available for neonates up to 6 months after birth [2]. Giving influenza vaccines to pregnant women is safe and has proven to be efficacious, preventing laboratory-confirmed influenza in 35–70% of mothers and 28–61% of infants under 6 months of age [3–5]. Maternal influenza vaccination programmes have the potential to augment/reinforce existing vaccination programmes and the maternal and child health infrastructure as well as to establish a delivery platform for future vaccines targeting these high-risk groups. In addition to protecting against yearly influenza outbreaks, a seasonal influenza vaccination programme can support countries' planning efforts for a potential pandemic by increasing their capacity to produce or procure vaccines, to register and distribute them, to conduct targeted vaccine delivery, and to monitor vaccination coverage and effectiveness [6].

Vaccination programmes should be based on scientifically sound and cost-effective approaches. It is essential that sufficient human resources and training capacity are present when planning the introduction of a new vaccine. For maternal immunization, a communication strategy should be in place to address potential concerns about the use of the vaccine in pregnant women. As expanded service delivery may put additional stress on health systems, decision-makers should assess the impact of the vaccine's introduction on the interconnected components of the health system.

Structure of the manual

This manual has two main parts:

- decision-making at country level, aimed at policy-makers (section 4), and
- issues concerning vaccine introduction planning and implementation, aimed at national immunization programme managers and immunization partners (sections 5–7).

Annexes at the end of the manual and links throughout provide planning and assessment tools for policy-makers and programme managers.

Main points addressed in the manual

1. Background and rationale for implementation of maternal influenza vaccination.
2. Key policy decisions in considering vaccination implementation.
3. Practical guidance for vaccine programme implementers, including: tools for planning the introduction of the vaccine (addressing infrastructure and supply chain management), staff training and communication strategies, and monitoring and evaluation.

2. About this manual

Objective

This manual serves as a primary resource and a catalogue of optional tools to help users to decide, plan and implement maternal influenza vaccination strategies and to foresee and address potential challenges related to decision-making or implementation. The manual aims to guide countries by providing principles and considerations to support decision-making and introduction planning rather than prescribing introduction measures that may not be applicable in some country contexts.

The manual focuses on the introduction of maternal influenza vaccination with inactivated seasonal influenza vaccine (subsequently referred to as “influenza vaccine”), and aims to:

- inform discussions on policy and assist with decision-making processes for introduction of influenza vaccine compared to other health interventions;
- provide an operational design framework for a delivery system for influenza vaccines for pregnant women;
- provide suggestions for developing a service delivery plan, including using local/regional influenza epidemiology and seasonality trends to guide vaccine provision, timing and strategies;
- provide an overview of monitoring and evaluation considerations specific to maternal influenza vaccination.

In addition, this manual outlines:

1. how to integrate influenza vaccine into an existing antenatal care system, and
2. how to prepare the national immunization programme to expand its activities in order to target pregnant women (Figure 1).

Audience

This document has two main parts:

1. decision-making at country level, and
2. planning and implementing the introduction of the vaccine.

The section on decision-making is aimed primarily at policy-makers; the sections on planning, training and communication, and monitoring and evaluation aim to support national immunization programme managers and their partners, such as programme managers for reproductive, maternal, newborn, child and adolescent health.

Figure 1. Sections of this manual

Recommended sequence for reading this documents

This document can be read either as a whole or by consulting individual chapters, depending on the reader's requirements. At the end of each (sub)section, information boxes point to the tools that are described in that section.

Related document

Readers are strongly recommended to familiarize themselves with the following documents before reading this manual:



Principles and considerations for adding a vaccine to a national immunization programme: from decision to implementation and monitoring. Geneva: World Health Organization; 2014.

http://www.who.int/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines, accessed 9 November 2017.

This is a generic guide that describes the process for introducing new vaccines and includes the latest guidance and tools for:

- vaccine decision-making
- economic analyses
- developing an introduction plan
- cold chain management

- integrated disease control and health promotion
- communications
- monitoring and evaluation
- vaccine safety.



Pan American Health Organization. Maternal and Neonatal Immunization Field Guide for Latin America and the Caribbean. PAHO. Washington DC 2017.

http://www.paho.org/hq/index.php?option=com_docman&task=docview&gid=40767&Itemid=270, accessed 9 November 2017.

This practical guide has been developed for the WHO Region of the Americas and may also be applicable to other regions. It provides useful information on maternal immunization, including influenza vaccine and other vaccines.

3. Background and rationale

WHO's influenza recommendations aim to protect vulnerable high-risk groups from severe disease [1]. WHO published a position paper on influenza vaccine in 2012, identifying pregnant women as the highest priority group for countries considering the initiation or expansion of programmes for seasonal influenza vaccination. Influenza vaccination of pregnant women will protect both the mother and her young infant against influenza [2]. Currently there is no licensed vaccine available for the first 6 months of life. The administration of influenza vaccines to pregnant women is safe and has been shown to prevent laboratory-confirmed influenza in 35–70% of mothers and 28–61% of infants under 6 months of age [3–5]. Other groups considered at increased risk from influenza infection include children aged less than 5 years, older persons, and persons with chronic underlying health conditions (e.g. HIV/AIDS or other immunosuppressive conditions, asthma, and chronic heart or lung diseases). Health-care workers are also a key target group for vaccination because they are at increased risk of infection and because they risk transmitting influenza to patients [3]. More background information on influenza, influenza vaccine and maternal vaccination can be found in Annex 1.

Establishing a maternal influenza vaccination programme can build on successful experiences of introducing tetanus toxoid vaccination for women of reproductive age, and can help establish programmes for future vaccines specifically for pregnant women. In addition to protecting against yearly influenza outbreaks, a seasonal influenza vaccination programme can support countries' planning efforts for a potential pandemic by increasing their capacity to produce (where applicable) or procure vaccines, to register and distribute them, to conduct targeted vaccine delivery, and to monitor vaccination coverage, safety and effectiveness [6].

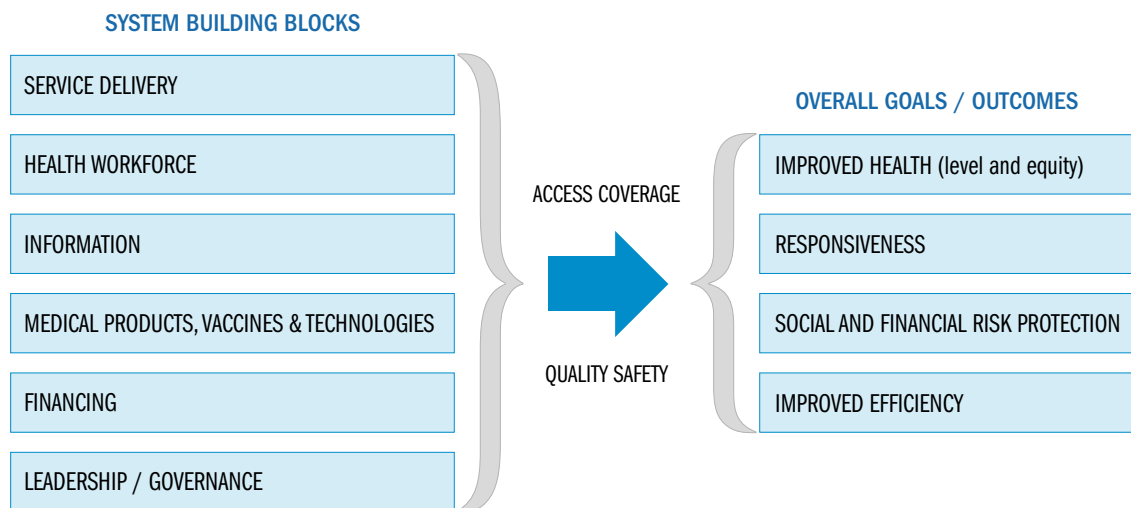
Compared with other vaccines, the introduction of maternal influenza vaccine requires specific consideration of timing of vaccine delivery, health-care worker training and communication, and implementation planning. There are a number of reasons for this:

1. Vaccination in every pregnancy is recommended for two main reasons, namely:
 - The immune response to infection declines over time.
 - Influenza viruses can undergo changes which require a reformulation and redistribution of influenza vaccine at least annually.
2. Some countries may not have clear seasonal patterns of influenza transmission. In these countries, on the basis of seasonality data and the composition of circulating viruses, managers of National Immunization Technical Advisory Groups (NITAGs) and of Expanded Programme on Immunization (EPI) programmes must select the optimal vaccine formulation and decide on the timing of vaccination efforts, particularly in non-temperate regions.
3. Health worker training and overall communications on maternal influenza vaccination must carefully address safety issues and efficacy information.

4. Vaccination programmes must be based on scientifically sound and cost-effective approaches; sufficient human resources and training capacity must be included in the planning.
5. Existing vaccine delivery and maternal and child health care infrastructure should be considered wherever these are likely to maximize the reach of immunization programmes.

As expanded service delivery may put additional stress on health systems, decision-makers should assess the impact of the vaccine's introduction on the interconnected health system and its components which must function together effectively (Figure 2).

Figure 2. The WHO Health Systems Framework¹



¹ Examples of opportunities to strengthen immunization and health systems can be accessed in: Principles and considerations for adding a vaccine to a national immunization programme: from decision to implementation and monitoring. Geneva: World Health Organization; 2014 (http://www.who.int/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines, accessed 9 November 2017).

4. The decision to implement influenza vaccination of pregnant women

The decision to add a vaccine to a country's immunization programme should be guided by prioritization of health interventions in the light of available resources. This means optimizing the response to the most relevant public health needs and selecting interventions that are affordable and cost-effective (section 4.1).

This section uses WHO concepts on introducing vaccines into national immunization programmes and health systems in order to help decision-makers appropriately prioritize the introduction of influenza vaccine or expand an existing influenza vaccination programme to include pregnant women [7]. In addition, this section includes discussion of the decision to use antenatal care services as a potential delivery channel for influenza vaccine. In places where evidence is not readily available and efforts to generate it may be significant, policy-makers and programme planners must decide whether to carry out studies to find out the burden of influenza and/or use data from other countries or regions.

4.1. Decision-making process

As with other vaccines, the Ministry of Health should request the NITAG to conduct a review of local and global evidence. This includes disease characteristics (e.g. influenza disease burden among pregnant women and children under 6 months of age, influenza virus seasonality and antigenicity), vaccines and immunization characteristics (e.g. effectiveness and safety characteristics of available vaccines), economic and operational considerations (e.g. vaccine availability, affordability, vaccine costs and resource use, economic impact), and health policy and programmatic issues (e.g. interaction with other interventions, feasibility, acceptability) (Figure 3). Where available, the NITAGs may draw some of the information required from national influenza centres that are tasked with monitoring influenza virus composition in a number of countries (Box 1).

A review of existing vaccination activities (e.g. maternal tetanus toxoid or other vaccination efforts targeting pregnant women) may provide useful information on delivery of vaccine via the antenatal care system. Such a review of existing delivery strategies should include coverage rates, vaccine acceptability and any logistical challenges identified.

Box 1. National influenza centres

To monitor and respond to the changes in the influenza virus antigenic structure and the subsequent necessity to change vaccine compositions, a large number of countries have established a national influenza centre (NIC) to collect and characterize virus specimens in their country and perform other analyses to inform the decisions of WHO and partners on the composition of the next year's influenza vaccine. In many countries, virological surveillance is complemented by more systematic influenza surveillance for severe acute respiratory illness (SARI) and influenza-like illness (ILI).

An NIC in a country – or in a neighbouring country – can support evidence-based recommendations by providing data on the influenza disease burden and seasonality to the NITAG or other relevant national decision-making body. Involving these and other centres in NITAG discussions is key to bringing together all relevant information that is needed for the decision-making process.

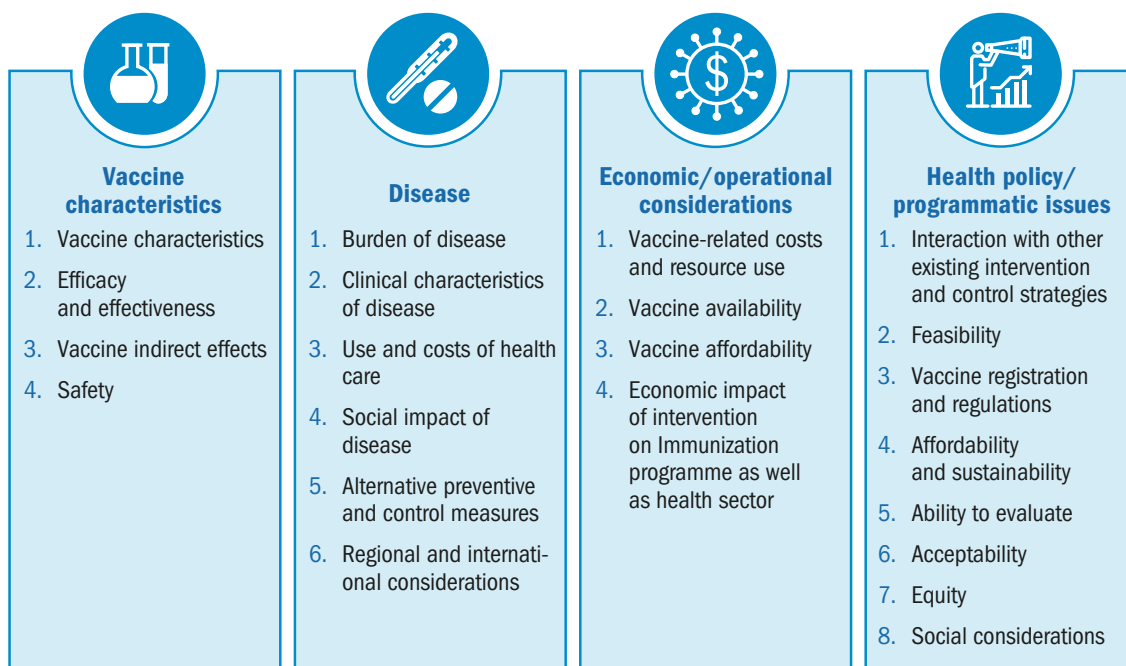
A list of NICs, WHO collaborating centres and Essential Regulatory Laboratories (ERLs) can be found at the following links:

- http://www.who.int/influenza/gisrs_laboratory/national_influenza_centres
(accessed 9 November 2017)
- http://www.who.int/influenza/gisrs_laboratory/collaborating_centres
(accessed 9 November 2017)

NITAGs² or equivalent technical advisory bodies can provide transparent and independent recommendations to the Ministry of Health. Additional information should be considered by the Ministry of Health from other relevant groups of which can be either members of NITAGs (core, ex-officio, or liaison members) or should be involved in development of NITAGs recommendations through participation in working groups. These can include other ministries (e.g. Ministry of Education, Ministry of Defence, Ministry of Finance) as well as from academic, scientific and professional groups (e.g. antenatal care providers such as obstetricians, midwives and family or general practice physicians), professional associations (e.g. associations of gynaecologists, paediatricians), civil society organizations, the private sector, and high-level national stakeholders that could champion and disseminate information on maternal influenza vaccination. In particular, the inclusion of professional organizations (e.g. general practitioners, gynaecologists, midwives) is relevant to ensure agreement with national recommendations and professional buy-in during the further roll-out of the programme. The objectivity and independence of NITAG members will enhance the group's credibility and strengthen the argument for securing funding from national authorities or donors for the introduction of the vaccine based on an evidence-based recommendation.

2 See: http://www.who.int/immunization/sage/national_advisory_committees (accessed 9 November 2017).

Figure 3. Elements that should be assessed, discussed and addressed by NITAGS during the introduction of maternal influenza vaccination



Source: Adapted from: Elements to consider in developing a framework for issuing immunization related policy recommendations. Agence de Médecine Préventive; 2015 (<http://www.nitag-resource.org/media-center/document/882>, accessed 9 November 2017).

On the basis of the evidence reviewed, the EPI manager and the programme manager for reproductive, maternal, newborn, child and adolescent health (RMNCAH) or equivalent should provide recommendations on the planning of vaccine introduction to the Minister of Health who ultimately takes the decision to introduce the vaccine. Where available, an Interagency Coordinating Committee (ICC) or equivalent body, made up of representatives of the Ministry of Health, WHO, UNICEF, and other domestic and external partners, should, as a multidisciplinary group, help to guarantee coordination of implementation among partners and ensure funding within the national agenda for implementing influenza vaccination.

4.2. Considerations for decision-making

Chapter 2 of WHO's *Principles and considerations for adding a vaccine to a national immunization programme: from decision to implementation and monitoring*³ outlines the general decision-making process. Considerations specific to maternal influenza vaccination are provided in the following sections of the present manual. Complementing this section, Annex 3 includes a checklist specifically relating to the decision to introduce maternal influenza vaccination.

³ Principles and considerations for adding a vaccine to a national immunization programme: from decision to implementation and monitoring. Geneva: World Health Organization; 2014 (http://www.who.int/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines, accessed 9 November 2017).

Country Experience: Thailand – considerations to support decision-making on introducing influenza vaccination for pregnant women

Thailand introduced influenza vaccine for high-risk target groups in 2008 following preparedness planning discussions on pandemic influenza in relation to the occurrence of H5N1 avian influenza in 2004. The vaccination target groups included pregnant women, older persons, children aged 6 months to 2 years, and persons with chronic medical conditions.

The programme was implemented within the national immunization programme, using established decision-making processes and mechanisms involving the NITAG. The aims of the influenza vaccination programme were to reduce the health burden from seasonal influenza, to simultaneously create demand to sustain vaccine production capacity, and to maintain public acceptance of influenza vaccine.

Apart from disease burden considerations, the decision-making process included a cost-benefit and cost-effectiveness analysis of the planned programme. This resulted in a proposal on influenza vaccine capacity investments which was presented to the government. The decision-making process also included an assessment of the financial capacity and strengths of the existing immunization programme. The programme was deemed manageable under the universal health coverage budget (for influenza vaccination) and the revenue of the Government Pharmaceutical Organization (for influenza vaccine production). Measurement of the strength of the national immunization programme for the introduction of influenza vaccine included assessment of the system for vaccine delivery, vaccine logistics, training and supervision, public communication, programme monitoring and evaluation.

Source: Dr Supamit Chunsuttiwat, Department of Disease Control, Ministry of Public Health, Thailand.

4.2.1. Disease burden analysis

Influenza viruses are responsible for substantial morbidity and mortality in high-, middle- and low-income countries. These viruses typically cause acute, systemic, self-limiting illness that resolves in 7–10 days but that may also lead to serious outcomes (e.g. acute lower respiratory infections, or ALRI, in young children) [8], and including death and increased risk of hospitalization of pregnant women. Most data on the influenza disease burden come from high-income countries with well-established surveillance systems. Studies among pregnant women in high-income settings show higher influenza-associated hospitalization rates compared to non-pregnant women. The risk of influenza-associated complications in pregnancy increases with gestation. Pregnant women with underlying medical conditions such as asthma, diabetes and obesity have a higher influenza-associated morbidity compared to pregnant women without such underlying conditions [1, 9, 10].

Other illnesses that are prevalent in low-resource settings may additionally increase the impact of influenza disease; for instance, evidence from South Africa indicates that people living with HIV infection have a substantially higher mortality from influenza [11]. Moreover, annual seasonal influenza mortality rates for HIV-positive and HIV-negative pregnant women in a study in South Africa were 74.9 deaths per 100 000 person-years compared to 1.5 deaths per 100 000 person-years respectively [12]. Overall, the South Africa study found that pregnant women were 2.8 times

(all-cause HIV-adjusted and age-standardized RR, 2.8; 95% confidence interval [CI], 1.7–3.9) more likely to die from influenza than non-pregnant women [12]. However, those who seek outpatient care, or who are hospitalized, or who die pose only a fraction of those suffering from illnesses associated with influenza. Thus only a small proportion of all influenza cases are actually reported. This “tip of the iceberg” phenomenon is common to many illnesses (e.g. diarrhoeal diseases) and is increased in many settings by the lack of reliable point-of-care diagnostic testing, limited access to care facilities and suboptimal reporting. Strengthening disease surveillance, enhancing diagnostic testing capacity for influenza and reinforcing surveillance should be considered during the decision-making and planning processes for maternal influenza vaccine introduction in order to better estimate the burden of disease and its economic consequences (Toolbox A). Countries without robust surveillance can consider estimating the proportion of maternal mortality due to influenza like illness or confirmed influenza.

Country Experience: Use of disease burden analysis in Maharashtra, India

Maharashtra is one of the most developed and populous states of India with a population of over 110 million. Disease burden studies carried out in a rural population in Maharashtra indicate that the annual rate of hospitalizations due to influenza was 46.8 per 10 000 persons during the 2009 A(H1N1) pandemic and 40.5 per 10 000 during the post-pandemic period. During the peak of acute respiratory illnesses (i.e. during the monsoon period), 20% of all hospital admissions were found to be influenza-positive.

In March 2015, more than 200 influenza-associated deaths, of which 22 were pregnant women, were reported, causing public concern and media attention. In April 2015, a Maharashtra Communicable Disease Prevention and Control Technical Committee was set up by Government of Maharashtra to provide guidance and recommendations on the prevention and control of various communicable diseases, including influenza. The committee included members from the National Center for Disease Control, the National Institute of Virology, the Indian Medical Association, the State Family Welfare Bureau and the Department of Medical Education and Research. A retrospective analysis of data conducted by the committee indicated that, between 2009 and 2015, pregnant women accounted for 9.84% (214 out of 2175) of all influenza-related deaths. The great majority of deaths (97%) among pregnant women occurred during the second and third trimesters. On the basis of these data, and since maternal immunization could lead to protection of children against influenza in the first months of life, the State of Maharashtra accepted the committee’s recommendations and decided to introduce free voluntary influenza vaccination for second- and third-trimester pregnant mothers and other risk groups.

The state approved funds for procurement of influenza vaccines and for an Information, Education and Communication (IEC) campaign. The campaign was inaugurated by Maharashtra’s Minister of Health in six selected vaccination centres in the state in July 2015. Vaccination centres were established in all major maternity homes, and separate desks for influenza vaccination were created in antenatal care clinics.

Sources: Dr Pradeep Awate, Directorate of Health Services, Government of Maharashtra, India; Dr Mandeep Chadha, National Institute of Virology, Indian Council of Medical Research; Dr Lalit Kant, Public Health Foundation of India; Dr Subhash Salunke, Public Health Foundation of India.

4.2.2. Vaccine efficacy and effectiveness

Measuring the efficacy and effectiveness of inactivated influenza vaccine and forming generalizable conclusions about it is challenging because of both the difficulty of identifying the burden of influenza disease and the difficulty of matching the vaccine to the circulating strains which may vary each year (Toolbox B). Reports from two recent randomized controlled clinical studies in South Africa (2013) and Bangladesh (2014) [3, 14] indicated an efficacy in the range of 35–70% in pregnant women and 28–61% in infants less than 6 months old when tested against laboratory-confirmed influenza disease.

4.2.3. Vaccine safety

The robust safety profile of multiple inactivated influenza vaccine preparations over many decades, and the potential complications of influenza disease during pregnancy, support the WHO recommendations that pregnant women should be vaccinated against influenza [15]. As with most live-virus vaccines, live attenuated influenza vaccines are not currently indicated for use in pregnant women.


Seasonal influenza vaccines do not usually contain adjuvants, although some newer influenza vaccine formulations may have novel adjuvants that increase the immune response. Among these are oil in water microemulsions such as MF59 and ASO3. Evaluation of the reproductive and developmental toxicity of MF59 alone and of a candidate MF59-adjuvanted H5N1 vaccine in animals demonstrated no evidence of teratogenicity or impact on fetal or early perinatal development. The utilization of MF59 adjuvanted vaccines during the 2009 H1N1 influenza pandemic allowed for the evaluation of their safety and efficacy in different populations, including pregnant women.

Toolbox A



WHO's **Manual for estimating disease burden associated with seasonal influenza** [13] provides a comprehensive assessment of disease burden associated with the respiratory manifestations of influenza – i.e. influenza-like illness (ILI), severe acute respiratory infection (SARI) and hospitalized severe acute lower respiratory illness (ALRI). The manual can help countries obtain a conservative estimate, based on a proportion of the overall disease burden associated with influenza, using existing data sources and taking into account their limitations. When introducing maternal influenza vaccination, the manual can serve to estimate the influenza disease burden and can help identify areas where sentinel influenza surveillance can be established or improved.

See: Manual for estimating disease burden associated with seasonal influenza. Geneva: World Health Organization; 2015:

 http://apps.who.int/iris/bitstream/10665/178801/1/9789241549301_eng.pdf (accessed 9 November 2017)

Toolbox B



The WHO field guide **Evaluation of influenza vaccine effectiveness** supports the generation of reliable national data on the impact of influenza vaccine and provides advice on the design of observational influenza vaccine effectiveness studies.

See: Evaluation of influenza vaccine effectiveness: a guide to the design and interpretation of observational studies. Geneva: World Health Organization; 2017:

 <http://apps.who.int/iris/bitstream/10665/255203/1/9789241512121-eng.pdf> (accessed 9 November 2017)

However, decreased immunogenicity responses have been reported in previously naive pregnant women when compared to non-pregnant women. Therefore, inactivated vaccines with novel adjuvants considered for pregnant women may need to be considered and evaluated individually given their recent introduction. The Global Advisory Committee on Vaccine Safety issues regularly recommendations on the use of these novel vaccines. (Toolbox C).

No adverse reactions have been reported from co-administration with other vaccines given during pregnancy, such as tetanus.

Toolbox C



The WHO Global Advisory Committee on Vaccine Safety (GACVS) report on **Safety of immunization during pregnancy** presents an overview of relevant safety data found in the literature on the use of influenza vaccine in pregnant women.

See: Safety of immunization during pregnancy: a review of the evidence. Geneva: World Health Organization; 2014

➡ http://www.who.int/vaccine_safety/publications/safety_immunization_pregnancy (accessed 9 November 2017)

The **Global manual on surveillance of adverse events following immunization** provides guidance on setting up surveillance systems for adverse events following immunization (AEFI) with standardized methodologies and tools.

See: Global manual on surveillance of adverse events following immunization. Geneva: World Health Organization; 2014 (revised 2016)

📄 http://www.who.int/entity/vaccine_safety/publications/Global_Manual_revised_12102015.pdf (accessed 9 November 2017)

Information sheets on observed rates of vaccine reactions of influenza vaccine provide details found in the literature on rates of vaccine reactions in pregnant women.

See: WHO vaccine reaction rates information sheets. Geneva: World health Organization; various dates.

➡ http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets (accessed 9 November 2017)

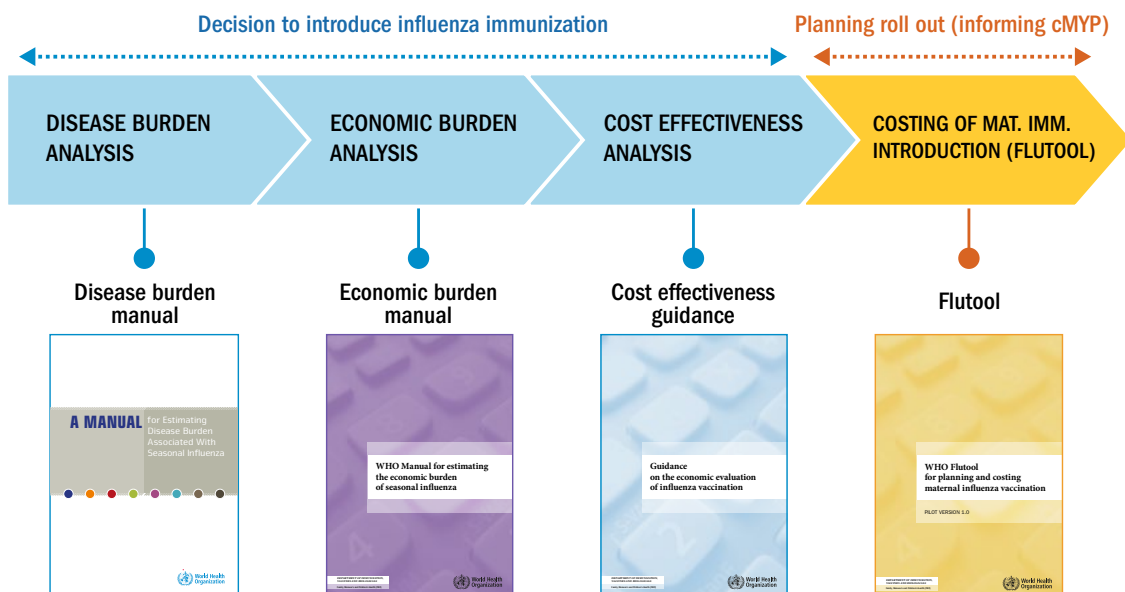
Maternal Immunization Safety Monitoring in Low- and Middle-Income Countries:

➡ <http://gapps.org/docs/MaternalImmunizationSafetyMonitoringInLMICs.pdf> (accessed 9 November 2017)

4.2.4. Economic analysis

Figure 4 outlines several guidance documents that can support countries to assess the economic and social benefits of introducing maternal influenza vaccination or to expand existing vaccination targeting pregnant women.

Figure 4. Elements in the decision and planning process for maternal influenza vaccine introduction



WHO's *Manual for estimating disease burden associated with seasonal influenza in a population* is summarized in section 4.2.1. The economic tools are outlined in subsections 4.2.4.1 to 4.2.4.3.

4.2.4.1. Estimating the economic burden of seasonal influenza

National governments require data on the economic burden of influenza disease in their countries in order to inform the allocation of limited resources and prioritization of interventions in the health sector. As recommended in the *WHO guide for standardization of economic evaluations of immunization programmes* [16, 17], evaluations should ideally adopt a societal perspective, including all relevant costs and consequences of delaying the decision (Toolbox D). The economic burden of influenza encompasses multiple dimensions such as direct costs to the health service and households (e.g. hospitalization and outpatient care costs), indirect costs due to productivity losses, and broader detriments to the wider economy [18].

Toolbox D



WHO's *Manual for estimating the economic burden associated with seasonal influenza* outlines key conceptual frameworks, best-practice approaches and practical guidance to estimate the overall influenza economic burden. The manual's Excel-based analysis tool can be used to generate disease-burden estimates guided by the step-by-step manual (see section 4.2.1).

➡ http://www.who.int/entity/immunization/research/development/influenza_maternal_immunization/en/index2.html

4.2.4.2. Economic evaluation of influenza vaccination

While analyses of cost-effectiveness of seasonal influenza vaccination have been widely assessed in high-income countries, there have been relatively few economic assessments of the value of seasonal influenza vaccination in low-resource settings [19–22]. One recent study from Mali indicated that maternal influenza immunization can be cost effective if vaccine is obtained, managed and administered at a pricing level adapted to the country context [40]. Results of economic evaluations (e.g. cost–utility analyses) should be considered for comparison of influenza vaccination with equivalent evaluations of other health programmes, to promote efficient allocation of resources in the health-care sector (Toolbox E).

Toolbox E



To optimize cost-effectiveness evaluation in national settings the *WHO Guidance on the economic evaluation of influenza vaccination* provides analysts with robust analytical methods and outlines relevant issues that can arise when evaluating influenza vaccination strategies.

➡ http://www.who.int/entity/immunization/research/development/influenza_maternal_immunization/en/index2.html

4.2.4.3. Estimating costs of introducing influenza vaccination of pregnant women

When introducing a new vaccine, the associated costs (e.g. vaccine purchase, transportation, waste) should be estimated, as should the long-term financial requirements for the introduction (Toolbox F). Pregnant women are usually already reached by antenatal care services at health facilities. If these services have the capacity to include influenza vaccination they should be included in the planning of further implementation of maternal influenza vaccination delivery. For further information on selection of delivery strategy, see section 4.3.

Toolbox F



The WHO **FLUtool** helps to project total costs of influenza vaccine introduction for pregnant women by type of delivery strategy over a period of up to five years. The FLUtool can also inform multi-year planning efforts in countries and is consistent with, and complements, the cMYP costing tool. The FLUtool can be used to assess the total costs of a phased or nationwide introduction and to estimate the costs per pregnant woman immunized.

➡ http://www.who.int/entity/immunization/research/development/influenza_maternal_immunization/en/index2.html

In order to assess the financial sustainability of maternal influenza vaccination programmes within the immunization activities of a country, the vaccine's introduction into national cMYPs should be guided by the **comprehensive Multi-Year strategic Plans (cMYP) tool and user guide**.

See: WHO-UNICEF guidelines for comprehensive Multi-Year Planning for immunization. Geneva: World Health Organization; 2014 (Document WHO/IVB/14.01)

➡ http://www.who.int/immunization/programmes_systems/financing/tools/cmyp (accessed 9 November 2017).

Toolbox G



Section 3.8 of **Principles and considerations for adding a vaccine to a national immunization programme** provides advice on advocacy, communications and social mobilization measures.

See: Principles and considerations for adding a vaccine to a national immunization programme: from decision to implementation and monitoring. Geneva: World Health Organization; 2014

➡ http://www.who.int/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines (accessed 9 November 2017).

A report by the WHO Strategic Advisory Group of Experts on Immunization (SAGE) Working Group on Vaccine Hesitancy includes survey questions to assess the underlying determinants of vaccine hesitancy.

See: Report of the SAGE Working Group on Vaccine Hesitancy. Geneva: World Health Organization; 2014

📄 http://www.who.int/immunization/sage/meetings/2014/october/1_Report_WORKING_GROUP_vaccine_hesitancy_final.pdf (accessed 9 November 2017).

WHO commissioned a cross-sectional, mixed-methods study in Pune district (India) in 2012–2013 [23–26] to examine factors affecting urban and rural uptake of pandemic influenza vaccines in 2009. Subsequently, a protocol was developed not only to assess community awareness and acceptance but also clinicians' awareness, priority and prescribing practices for influenza vaccination of pregnant women. The protocol has been tested in a pilot study to promote antenatal influenza vaccination (AIV) in Pune city. The approach is generic and adaptable for implementation in other settings. It involves assessing clinicians' and community views about AIV, explaining the rationale for recommended policy to clinicians and discussing findings from a qualitative survey of women and spouses in their communities of practice. The impact of engaging clinicians is assessed by monitoring their clinic vaccination rates and comparison with control clinics without such engagement activities.

➡ http://www.who.int/entity/immunization/research/development/influenza_maternal_immunization/en/index3.html

4.2.5. Vaccine acceptance

In some contexts, individuals or groups may initially refuse, or be hesitant to accept, vaccination of pregnant women. An understanding of perceptions and acceptance of influenza vaccination among pregnant women, their families, their health-care providers and the public can be a relevant consideration when deciding on the introduction of vaccines. In particular, the awareness, attitudes, priority and prescribing practices of antenatal health-care providers have to be taken into account (Toolbox G).

4.3. Delivery strategies

Depending on the local context, countries may wish to apply various approaches for vaccinating pregnant women. The decision should be based on epidemiology and seasonality of the disease (see section 5.4), choice of optimal immunization strategies to reach the target population, financial resources, existing infrastructure and workforce, and availability of the vaccine. Responsibilities will need to be clearly defined on the basis of local contexts to ensure that health-care workers are aware of who is vaccinating and who should refer women for vaccination.

One or several of the following delivery strategies should be chosen, depending on the degree of desired coverage, optimal use of available resources, and potential disruption of established services:

- vaccination campaigns;
- routine vaccine delivery incorporated into antenatal care, primary care, HIV care, at preconception or family planning visits, and/or at well or sick child visits to health-care facilities;
- vaccine delivery through outreach.

To reinforce vaccination efforts, delivery approaches can be co-delivered with other health interventions to pregnant women (e.g. TT/dT/Tdap vaccination, iron, folic acid, health education) and, where possible, to their children (e.g. vitamin A, deworming, growth monitoring) to reduce costs to the health-care system [27]. Strategies including co-delivery with other interventions need to be assessed with regard to their ability to reach a critical number of pregnant women during the projected delivery times for influenza vaccination.

4.3.1. Campaigns

Up to now the most common approach used for seasonal influenza vaccination target groups, including pregnant women, is via campaigns shortly before or at the beginning of an influenza season. Campaigns can vary in approach, ranging from intensive communication or social mobilization efforts that encourage pregnant women to go to health centres to be vaccinated, to organized mass vaccination campaigns that directly provide influenza vaccine to pregnant women and may facilitate access to remote populations. Some of the factors to consider when deciding whether to conduct vaccine delivery as a campaign are included in Box 2.

Campaign-style delivery can put pressure on or even disrupt routine services with limited capacity. Their use should be considered following an assessment of delivery service capacities in place, as well as scheduling and duration of the campaign. If antenatal care services are involved in the

campaign, close coordination between the EPI manager and the RMNCAH manager is essential to allow for capacity assessment, planning of roll-out and distribution of responsibilities among stakeholders at all levels.

Using annual vaccination weeks or vaccination days in countries with clearly defined seasonal influenza peaks is helpful to raise awareness of the vaccination and consequently can help to increase vaccination coverage. Building maternal influenza vaccination on existing strategies to reach pregnant women, such as child health days, can further improve reaching these target groups.

To protect pregnant women after the main seasonal peak, a combined approach, offering influenza vaccine through health facilities routinely throughout the influenza season, can help ensure coverage of pregnant women whose pregnancy was not identified during the campaign. (See Pan American Health Organization. Maternal and Neonatal Immunization Field Guide for Latin America and the Caribbean. PAHO. Washington DC 2017. http://www.paho.org/hq/index.php?option=com_docman&task=doc_view&gid=40767&Itemid=270, p. 53–54).

Country Experience: Moldova

In the WHO European Region, influenza vaccination is mainly provided through pre-seasonal campaigns using existing immunization services. With such an approach, establishing a functional referral system to bridge antenatal care services to immunization services is critical to ensure sufficient uptake.

In the Republic of Moldova, maternal influenza vaccination began in 2009 as part of the broader disease control strategy of pandemic influenza in high-risk populations. Microplanning for maternal influenza vaccination and vaccine forecasting were integrated into the broader EPI vaccine planning activities. Vaccine financing is provided by the national health insurance company while vaccine procurement is integrated with the central procurement services of the Ministry of Health. Management functions, including guidance, training, planning, coverage monitoring, supervision and vaccine supply are performed by epidemiologists from national and district public health centres.

Influenza vaccination is provided during a short period of time before the influenza season begins. It is delivered through the existing immunization system (i.e. through general practitioners, family doctors and nurses) as is the case in several European countries. In Moldova this approach has led to a modest uptake of influenza vaccine among pregnant women. In implementation planning discussions, the establishment of a functional referral system bridging antenatal care services to immunization services is considered a critical factor for increasing vaccination uptake.

Source: Maternal influenza vaccine delivery in Moldova: a case study from the WHO Regional Office for Europe.

Box 2. Campaigns

When deciding whether to conduct vaccine delivery as a campaign (seasonal or outreach), policy-makers and EPI managers should consider several factors that may affect the capacity needed and the budget required of the immunization programme. The questions below highlight some issues that decision-makers should consider with regard to campaign-style delivery of maternal influenza vaccination:

- TIMING:** What is the timing/seasonality of the circulating influenza virus in the country? How many months in advance (e.g. at least 3 months) should the campaign be planned? Has a strategy been developed to address logistics issues related to vaccination timing? Have other health strategies or events (e.g. vaccination days) that could cause interference or promote synergy been identified? (see section 5.4)
- SUPPLY CHAIN:** Is vaccine locally produced or procured outside the country? Is vaccine procurement ensured sufficiently in advance (e.g. 6–12 months)? Do current surveillance measures allow vaccine match to be identified? Has a planning group been set up to plan the annual switch to the most recent vaccine formulation? Do storage and distribution systems have sufficient capacity to distribute within the projected period?
- USE of EXISTING SERVICES:** Can lessons learned from existing vaccination campaigns or seasonal health campaigns serve to inform seasonal influenza vaccination of pregnant women? Could leaders and staff from these campaigns (e.g. deworming, vitamin A supplements, HIV screening) be involved to champion or otherwise support the implementation of the influenza campaign in pregnant women.
- HEALTH SYSTEM CAPACITY:** Is the capacity (e.g. human resources, supply chain, cold chain) of existing health campaign services (screening, vaccination, treatment) sufficient to include maternal influenza vaccination?
- SAFETY and SYSTEM EFFICIENCY:** Is a pregnancy registry and monitoring system available to support monitoring and evaluation? If not, how can systems (registry and vaccination cards) be developed to monitor coverage? Is an AEFI reporting system in place? How can pregnant women best be reached?
- RESOURCES AND COSTS:** Has the country evaluated the impact of other health campaigns and estimated their costs. Can these cost estimations be used to estimate the costs of influenza vaccination campaigns? What is the expected impact of a campaign in the coverage of other vaccines and services (in particular services for pregnant women)? Are existing resources (vaccinators, cold chain, distribution system) sufficient to ensure implementation of influenza vaccination of pregnant women?

4.3.2. Routine vaccine delivery

Pregnant women can be targeted through routine antenatal care; preconception or family planning visits; visits to health-care facilities with their children (e.g. routine childhood immunization); outpatient care (general practice, gynaecology, family planning, high-risk clinics); and any other health settings where pregnant women might seek care for themselves or their children.

WHO estimates that antenatal care visits are attended by an estimated 82% of pregnant women globally [28]. During these visits, health-care worker recommendations could support generation of demand for influenza immunization and could address hesitation or concerns of patients. Antenatal health-care workers should either refer patients for influenza immunization at immunization centres or, if they have sufficient capacity, deliver influenza vaccine directly to pregnant women.

Combining influenza vaccination with other vaccination efforts (e.g. tetanus), programmes such as “clean cord care instruction”, family planning services, HIV testing and treatment sites, or well child care visits beyond regular vaccination activities, may further increase influenza vaccine uptake. Integration of influenza vaccination with other health care services including antenatal care should take into account the following considerations below to maximize health resource utilization and service uptake, while minimizing system costs (Box 3). In addition, when vaccination interventions are combined with respected and desired health services such as antenatal visits, vaccine hesitancy may be minimized.

Box 3. Combining influenza vaccination with antenatal care services

When deciding to integrate vaccine delivery into antenatal care services, policy-makers must consider several factors that may affect the capacity of existing systems or lead to additional costs. The questions below address some of these factors.

- TIMING:** Can/should vaccine be made available all year round in tropical areas with varying influenza virus circulation, or in areas with limited access to vaccinating pregnant women? (see section 5.4)
- SUPPLY CHAIN:** Do other antenatal interventions have supply chains that are logistically similar to those of seasonal influenza vaccination? If yes, can both be combined into one supply chain without hampering introduction or coverage of either intervention?
- USE of EXISTING SERVICES:** Can vaccination be provided with other health interventions given during an antenatal visit (e.g. co-administration with tetanus toxoid vaccine)? If so, are system planners and primary health-care providers engaged in planning efforts at an early stage? Is there a high drop-out rate of visits or late arrival at antenatal care service clinics that may affect coverage/uptake?
- HEALTH SYSTEM CAPACITY:** Is the capacity (e.g. human resources, supply chain, cold chain) of antenatal care services sufficient to provide other antenatal interventions and influenza vaccination together? If not, what additional resources are needed to avoid overburdening existing systems and do the benefits associated with offering influenza vaccination as an antenatal service balance with the additional resource requirements?
- SAFETY and SYSTEM EFFICIENCY:** Is there a possibility to introduce/use an existing home-based record⁴/antenatal care record of the mother in order to help health facilities avoid unintended re-vaccination of women who received vaccine in a campaign or at another health facility? Should the vaccination status of the mother appear on the vaccination card of the baby?
- BURDEN ON HEALTH SYSTEM:** Could joint administration of influenza vaccine with other interventions promote or detract from utilization of the other interventions?
- ADDITIONAL COSTS:** What would be the costs of the additional outreach activities required to reach sufficient coverage among pregnant women? What time, infrastructure and cost will be required to train staff on vaccination procedures, potential AEFI, benefits of influenza vaccination for pregnant women, and data collection and reporting for monitoring uptake?

⁴ See: Home-based records. (http://www.who.int/immunization/monitoring_surveillance/routine/homebasedrecords, accessed 9 November 2017).

Country Experience: Maternal tetanus vaccine delivery in Sri Lanka: a case study

Experiences describing the use of maternal influenza vaccination in low- and middle-income resource settings have not yet been extensively documented. Although influenza vaccine differs from tetanus vaccine in terms of procurement, distribution and administration, this example from Sri Lanka on routine use of tetanus vaccine targeting pregnant women helps to illustrate some programmatic aspects when using antenatal care services as the delivery platform.

Sri Lanka's national immunization programme introduced tetanus toxoid vaccination in pregnancy in 1969 through integrated immunization and maternal and child health services. This approach helped to:

1. significantly reduce service delivery costs,
2. provide pregnant women with equitable access to tetanus vaccinations, and
3. eliminate neonatal tetanus.

Maternal tetanus vaccination is provided through the widespread, nationwide antenatal care clinics by family health workers. A well-established system monitors and evaluates maternal tetanus vaccination with technical support from Medical Officers of Health, regional epidemiologists and the medical officers responsible for maternal and child health at the field level. Provincial and regional directors oversee implementation in their respective provinces and districts. A specialized vertical epidemiology unit and the Family Health Bureau provide policy guidance, technical support, supportive supervision and programme evaluation from the national level.

The decision to use antenatal care services as a delivery platform was supported by the high attendance of pregnant women (75.4% register before 8 weeks of gestation, 94.8% attend antenatal care clinics at least once in their pregnancy, and there are an average 6.6 antenatal visits per pregnant woman according to the Ministry of Health).

In terms of supply and logistics, tetanus vaccines are procured centrally by the Ministry of Health and distributed to the Regional Medical Supply Divisions (RMSDs) in each district. RMSDs distribute vaccines and other supplies to Medical Officer of Health offices with storage facilities. From these offices, tetanus toxoids are supplied daily to antenatal care clinic services in the field. Health-care facilities with antenatal care clinics receive vaccines directly from the RMSDs. Vaccine movement registers at the clinic and ministry levels and monthly stock returns of vaccines are used to monitor vaccine stock and requisitions.

An immunization information management system is available to report maternal tetanus vaccine coverage data from the clinic to the national level via Medical Officer of Health offices and districts. A separate AEFI reporting system disseminates and consolidates AEFI reported to the district and national levels from hospitals and by family health workers. At the field level, family health workers have data on:

1. the estimated number of pregnant women,
2. the number of registered pregnant women, and
3. the number of pregnant women under care.

These figures are used as denominators to monitor coverage of maternal tetanus vaccination. The Family Health Bureau receives information on the vaccination status of mothers at delivery. The coverage is reviewed in monthly Ministry of Health conferences, quarterly reviews of regional epidemiologists and annual district EPI reviews. In 2013, the Ministry of Health reported that 91% of pregnant women receiving tetanus vaccination at antenatal care clinics in the government sector had been protected (TT2+) while the percentage protected among reported deliveries was 99.9%.

Source: WHO Regional Office for South-East Asia.

4.3.3. Outreach

Outreach activities can help to maximize coverage of maternal influenza vaccination and are essential for reaching populations with limited access to health facilities. Outreach in this context refers to any strategy that requires health-care workers to transport and deliver vaccination services to a variety of sites (other than the normal outlets for vaccination) to target pregnant women. Outreach can be achieved through vaccination posts, specialty service sites such as HIV testing or treatment facilities, or through educational and work facilities, community centres, support or self-help groups for pregnant women, and other places where pregnant women tend to gather. If outreach is done through routine EPI, its outreach guidelines, targets and schedule will need to be adapted accordingly in order to align with the other services being utilized; equivalent documentation within the respective delivery system's planning framework will need to be established in collaboration with the EPI manager.

Country Experience: Malawi

While Malawi has yet to introduce maternal influenza vaccination, the country is often lauded for its success in implementing maternal vaccination against tetanus which affects both mothers and, through them, their infants.

Maternal neonatal tetanus was eliminated in Malawi over a decade and a half ago [29]. The Ministry of Health launched a national initiative, *The "Road Map" for Accelerating Reduction of Maternal and Newborn Mortality and Morbidity in Malawi* [30], which strongly promoted the utilization of quality antenatal care by pregnant women and supported the EPI guidelines for administering up to five doses of tetanus toxoid vaccine to pregnant women and women of reproductive age.

Malawi's strategy to achieve high tetanus vaccination coverage is based on a strong emphasis on facility-based delivery, where tetanus vaccine is often integrated into routine antenatal care services. Providing these services in combination can be mutually reinforcing (e.g. saving time and effort for recipients and health-care workers, overcoming hesitancy of one service through perceived benefits of the other, and providing incentives to recipients if both services are received together). While the majority of maternal tetanus vaccination is provided in health facilities, the vaccination is also made available in communities through outreach services. These outreach sessions, which are largely provided by a cadre of paid extension workers (called health surveillance assistants, or HSAs) from the respective community, are combined with health services targeting children less than 5 years of age. The sessions are provided in communities at regular intervals (e.g. the first Thursday of every month) and in the same location (e.g. a church, school, or a shelter built specifically for the purpose).

The additional availability of health services close to communities, along with the familiarity of the HSAs and the regularity of the services, contributes to both acceptance and use, ultimately resulting in high vaccination coverage. In 2014, WHO estimated that 90% of pregnant women aged 15–49 years of age in Malawi received at least one protective dose of tetanus toxoid in their last pregnancy. This indicates that reaching a majority of pregnant women with tetanus toxoid vaccine in Malawi is feasible and acceptable.

Source: Formative research conducted by PATH and the Centre for Social Research, University of Malawi, through the WHO-PATH Maternal Influenza Immunization Project, 2015.

In most countries, outreach activities are a routine part of vaccine delivery. These activities often contribute to meeting coverage targets and can improve equity of access for women living in remote areas or those in underserved or hard-to-reach groups. However, outreach can substantially increase financial cost. Where resources are limited, the use of a costing tool capturing the financial impact of outreach activities is recommended to help decide whether outreach can be considered as a complementary vaccine delivery strategy or if delivery should be limited to health facilities (see section 4.2.4.3).

5. Planning vaccine introduction

To meet the demands and challenges identified in the decision-making process, detailed planning processes are needed to further refine the delivery strategy, vaccination schedule, logistics and financial considerations. This section provides suggestions, guidance and tools that specifically support the planning process for implementing influenza vaccination of pregnant women.

5.1. Vaccine introduction plan


The general concept of developing a vaccine introduction activity within the annual EPI operational plan is outlined in chapter 3.1 of the WHO guide *Principles and considerations for adding a new vaccine to a national immunization programme: from decision to implementation and monitoring*. (For quick access to the template, instruction manual and a vaccine introduction checklist tool, see the toolbox below).

A vaccine introduction plan, integrated into the overall annual plan for immunization and ante-natal care, can help programme planners to ensure that all critical activities are implemented prior to the introduction of influenza vaccine (Toolbox H). Such activities include training of staff shortly before the influenza season, adapting cold chain capacity to seasonal vaccine provision, and distributing roles and responsibilities between immunization and collaborating health-care service providers (e.g. antenatal care).


Toolbox H



Annex 3. Template for a new vaccine introduction plan of WHO's new vaccine introduction guidance⁵ provides a generic template to guide countries in developing a practical plan for introducing a new vaccine.

 http://www.who.int/entity/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines/Annex3_NVI_Template_EN.doc (accessed 9 November 2017).

Annex 4. New vaccine introduction checklist, activity list & timeline of WHO's new vaccine introduction guidance⁵ provides advice on planning and budgeting activities, distribution of roles and responsibilities, and timelines.

 http://www.who.int/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines/Annex4_Instructions.pdf (accessed 9 November 2017).

Corresponding **Checklist tool**.

 http://www.who.int/entity/immunization/programmes_systems/policies_strategies/vaccine_intro_resources/nvi_guidelines/Annex4_checklist_en.xls (accessed 9 November 2017).

5 Principles and considerations for adding a vaccine to a national immunization programme. Annex 4. Geneva: World Health Organization; 2014 (http://apps.who.int/iris/bitstream/10665/111548/1/9789241506892_eng.pdf, accessed 9 November 2017).

Complementing the new vaccine introduction guidance available from WHO, the checklist in Table 1 may be useful to complete the planning and implementation process for a maternal influenza vaccination roll-out.

Table 1. Maternal influenza vaccination programme checklist

To account for the specifics of maternal influenza vaccination, elements of the supplementary checklist below should be taken into consideration when completing the new vaccine introduction checklist ⁵ .	
Fundamental health system infrastructure	
1. National antenatal care guidelines are consistent with WHO recommendations on antenatal care ⁶ .	✓
2. Surveillance system is in place for influenza activity, including defining start and end of the influenza season, to inform selection of the most appropriate vaccine formulation and timing of influenza vaccination.	✓
Maternal influenza prevention and control policy planning infrastructure	
3. A functional multidisciplinary coordination group is in place to discuss and promote access to a new target population of pregnant women, or women of reproductive age, enabling the formation of partnerships which support and shape the national agenda.	✓
4. Maternal influenza vaccination strategies, in addition to regular vaccination activities, include collaborative efforts with stakeholders from reproductive health (midwives, nurses, obstetrician-gynaecologists, women's health physicians), adolescent health, sexually transmitted disease and HIV prevention and treatment sectors, and stakeholders from other areas that could support vaccination outreach efforts in the community.	✓
5. Maternal influenza vaccination, including communication and vaccine safety, is included in the national immunization plan. In countries where influenza vaccination is in place, the plan should advise how the official vaccination schedule should be modified to include the vaccination of pregnant women.	✓
Implementation of maternal influenza vaccination	
6. Existing training plans should be expanded to include training of antenatal care staff and other health-care providers who would be involved in vaccination of pregnant women.	✓
7. Communication strategies are in place to educate pregnant women, health staff and communities about the benefits of vaccinating pregnant women against influenza, and to respond to rumours and potential concerns about the safety of the vaccine.	✓
Monitoring and evaluation	
8. A system to monitor influenza vaccine coverage in pregnant women, including denominator data, is in place. Early coordination efforts are undertaken with national departments of statistics to prepare information and adverse event reporting forms and tools for registering immunization-related information. Additionally, the electronic data management systems are adapted to include pregnant women receiving influenza vaccine.	✓
9. Numerator/denominator is defined to calculate coverage (see section 7.1).	✓
10. Surveillance strategies or plans developed for monitoring of AEFI, including reactogenicity and maternal, obstetric, fetal and neonatal events.	✓

6 WHO antenatal care randomized trial. Manual for the implementation of the new model. (Document WHO/RHR/01.30). Geneva: World Health Organization; 2001 (http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/RHR_01_30/, accessed 9 November 2017).

Pregnancy, childbirth, postpartum and newborn care. A guide for essential practice. Geneva: World Health Organization; 2015 (http://www.who.int/maternal_child_adolescent/documents/imca-essential-practice-guide/, accessed 9 November 2017).

5.2. Long-term planning

As with any vaccine, planning efforts need to be reflected in the national cMYP (Toolbox I). Specifically for maternal influenza, planning efforts may also be included in the country's maternal and child health-care plan. To inform long-term planning, the FLUtool (section 4.2.4.3) can be used by national officials to estimate the introduction costs for maternal influenza vaccination over several years and to feed these into the cMYP and/or into the annual plan of the EPI.

Toolbox I



WHO-UNICEF guidelines for developing a comprehensive multi-year plan (cMYP). Geneva: World Health Organization; 2013

➡ http://www.who.int/immunization/programmes_systems/financing/tools/cmyp (accessed 9 November 2017)

5.3. Phased introduction

Nationwide implementation of a vaccine is usually preferred because of economies of scale, equity considerations, and the larger impact expected with a national introduction. However, in large countries, the complexities and potential lack of experience in providing vaccines to pregnant women may be a barrier to introducing influenza vaccine to this group. A phased introduction, in one or several districts with different characteristics (e.g. urban/rural, high/low coverage), can help to identify potential bottlenecks and facilitate the subsequent scale-up at a national level.

A phased introduction delivering influenza vaccine on a small scale may be useful to:

- test programmatic feasibility by determining the costs of vaccine introduction as well as the human and financial resources needed to support optimal delivery;
- pilot and refine training and communication plans and materials to fit the local context;
- determine and test strategies on how to best access pregnant women and monitor vaccination in this group;
- provide a proof of concept for the proposed delivery strategies when current national capacities can support only a limited number of provinces or districts and demonstrating proof of concept may serve to secure external funding;
- evaluate attitudes, acceptability and barriers in the community, pregnant women, and among health professionals – to help refine communication strategies.

5.4. Scheduling the vaccination

5.4.1. Adapting delivery strategies to influenza seasonality


WHO recommends the use of the most recent vaccine formulation available. Following strain selection and recommendation by WHO, influenza vaccine is formulated by manufacturers as Northern Hemisphere (NH) and Southern Hemisphere (SH) vaccine and is – depending on regulatory approval and delivery times – accessible to countries around September (NH) or April (SH).

- In *temperate regions*, shortly after the respective hemisphere’s vaccine is available, vaccination is usually offered during a specific period before the start of the influenza season and can be offered to pregnant women through routine immunization during the remaining influenza season.
- In *tropical and subtropical regions* where there is often a secondary peak, information on the country’s influenza seasonality and virus characteristics should be used to choose either NH or SH vaccine [31, 32] (Toolbox J). If influenza vaccination campaigns are used, they should be timed before the main peak of the influenza season. Where no data on national influenza seasonality are available, countries can use estimates from countries with similar seasonality. For a list of countries see publication *Seasonal influenza vaccine policy, use and effectiveness in the tropics and subtropics* (Toolbox J). In practice, where coverage during several peaks is not feasible, influenza vaccine campaigns are often timed prior to onset of the primary seasonal peak⁷. In such cases, offering routine coverage with remaining vaccine over several months can help to improve coverage among pregnant women.
- In some *countries close to the equator*, influenza virus circulates all year round, without distinct seasonal peaks, requiring additional considerations on vaccine composition, availability and programmatic issues. Offering vaccination through routine delivery services offers protection from circulating viruses over an extended period of time. The feasibility and ability of this delivery strategy would, however, need to be assessed on the basis of vaccine availability and local programmatic considerations (see section 4.3.2). Vaccine production and regulatory approval processes typically lead to “availability gap months” of approximately three months per year for each SH or NH vaccine (see Figure 5).

Toolbox J



Seasonal influenza vaccine policy, use and effectiveness in the tropics and subtropics. Geneva: World Health Organization; 2016

 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4910173/pdf/IRV-10-254.pdf>
(accessed 9 November 2017)

Considerations of strategies to provide influenza vaccine year round. *Vaccine*. 2015; 33(47):6493-8

➡ <http://www.sciencedirect.com/science/article/pii/S0264410X15011640>
(accessed 9 November 2017)

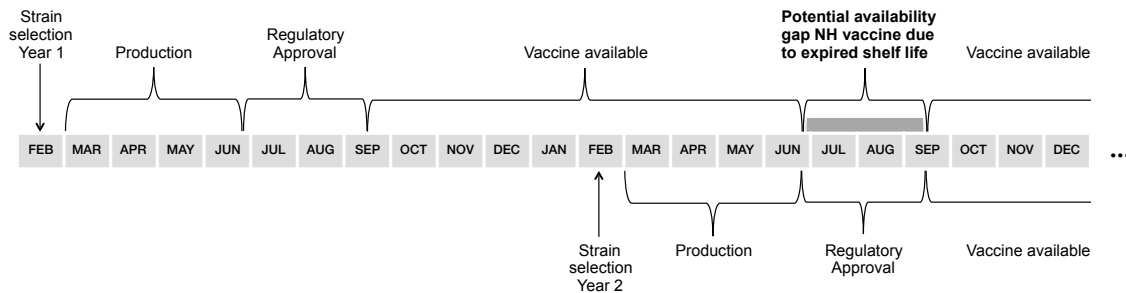
Suggestions on when to vaccinate in the tropics

➡ <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0153003>
(accessed 9 November 2017)

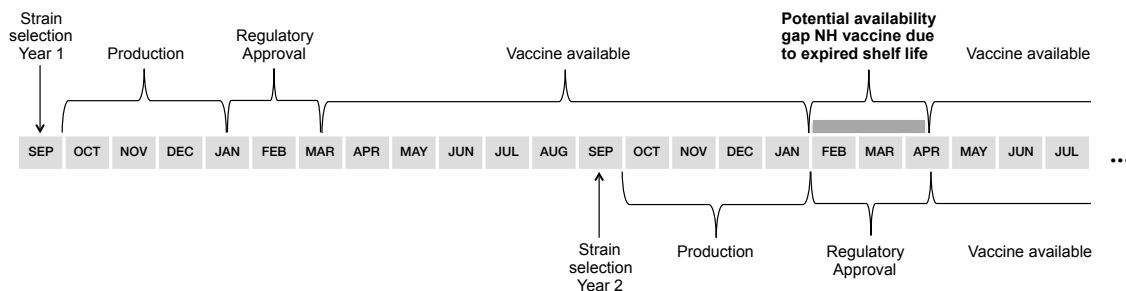
⁷ WHO Expert Group Meeting on Seasonal Influenza Vaccine Composition for Tropics and Subtropics : meeting report. Geneva: World Health Organization; 2015 (http://apps.who.int/iris/bitstream/10665/183954/1/WHO_HSE_PED_GIP_EPI_2015.1_eng.pdf, accessed 9 November 2017).

Figure 5. Availability gaps of Northern and Southern Hemisphere vaccines

Northern Hemisphere vaccine



Southern Hemisphere vaccine



Lessons learned from practical experience of how to ensure vaccine supply year-round are not yet available. To ensure use of the latest vaccine formulation available, countries can opt to alternate between NH and SH formulations throughout the year as each becomes available. However, this option would require significant logistical capacities to replace the vaccine formulation in use with the most recent formulation becoming available. Another option is an extension of shelf-life of influenza vaccine to ensure vaccine supply year-round. This would require agreement between the vaccine manufacturer and regulators of the producing and ordering country. As a third option, local vaccine manufacturers can adapt their production timing to meet local vaccination needs. For more detail on such approaches, see *Considerations of strategies to provide influenza vaccine year round* listed in the Toolbox J.

5.4.2. Timing of vaccination during pregnancy

WHO recommends vaccination of pregnant women at any stage during pregnancy to protect both the mother and, through her, her young infant. This recommendation is supported by two considerations: vaccination at an early stage provides benefits to the pregnant woman, and immunization in the later trimesters of pregnancy maximizes protection to the newborn [32, 34–36]. The optimal timing for influenza vaccination for pregnant women is just before the influenza season starts, thus providing protection during the peak of the influenza season.

A single-dose injection is typically sufficient to provide protection against influenza virus infection in pregnant women for the period of the influenza season.

In practice, pregnant women may have limited access to influenza vaccination in low-resource settings. Only an estimated 54% of pregnant women attend at least four recommended antenatal visits, whereas an estimated 82% benefit from at least one antenatal visit [28]. This limits the opportunity to reach a large number of pregnant women with the vaccine prior to the influenza season. In areas of limited antenatal coverage, it may be preferable to recommend vaccination at the first (and possibly only) antenatal care visit or at another medical consultation during pregnancy with the formulation of the influenza vaccine available at the time of the year [32].

5.5. Vaccine procurement and supply chain management

5.5.1. Vaccine procurement

Procurement of influenza vaccine should in general be based on forecasting, tendering, contracting and ordering procedures similar to those for other vaccines in the immunization programme (Toolbox K). Forecasting is critical to prevent stock-outs or overstocks of the vaccine. Forecasting is based on the estimated number of pregnant women, the estimated vaccine uptake and wastage (unused vaccine in both opened [multi-dose] and unopened vials).

The accuracy of vaccine forecasting and needs estimation depends on both the level of implementation and the time period for estimation. It is necessary to track the actual consumption of influenza vaccine and to monitor stocks at different levels of the supply chain and at health facilities in order to redistribute them according to actual consumption during the time the vaccine is available.

The price of influenza vaccine can vary according to several factors, and should be taken into consideration when deciding to procure the vaccine. The WHO Vaccine Product Price and Procurement (V3P) database provides information on vaccine prices. Influenza vaccine formulations and presentations (multi-dose or single dose) should be selected that are least likely to result in programmatic errors and that correspond to the training levels and capacities of the health-care workers providing immunization, particularly when delivered through a previously unused channel.

When selecting the vaccine to be used in a campaign, ease of use of a vaccine should be balanced against risk of wastage. It is particularly important to keep in mind the following: vial size (doses/vial), vaccine delivery method (injectable vaccine), vaccine wastage versus missed opportunities for vaccination (e.g. health-care workers reluctant to open and be forced to discard the remainder of a multi-dose vial in case of low-volume of pregnancy visits in a clinic setting.)

Toolbox K



Vaccine procurement guidance. Webpage.
Geneva: World Health Organization

➡ <http://who.int/immunization/programmes/systems/procurement>
(accessed 9 November 2017)

UNICEF Supply Division

➡ <http://www.unicef.org/supply>
(accessed 9 November 2017)

List of prequalified influenza vaccines. Geneva:
World Health Organization

➡ https://extranet.who.int/gavi/PQ_Web
(accessed 9 November 2017)

Vaccine Product, Price and Procurement (V3P)
web platform. Geneva: World Health Organization


➡ <http://www.who.int/immunization/v3p>
(accessed 9 November 2017)

Toolbox L



WHO's **Switch from tOPV to bOPV: guidelines for developing national operational plans** provide information on how to establish management structures and plan and implement a vaccine switch. The guidelines can be used as blueprint for the development of an influenza switch plan.

See: Switch from tOPV to bOPV: guidelines for developing national operational plans

 http://www.who.int/immunization/diseases/poliomyelitis/endgame_objective2/oral_polio_vaccine/OPVSwitch-Guidelines_nat_plans_Mar2015.pdf (accessed 9 November 2017)

Tools supporting effective vaccine management (EVM):

E-learning course

➡ http://apps.who.int/immunization_delivery/systems_policy/logistics/evmlearning/index_0_1_1.php (accessed 9 November 2017)

EVM assessment tools

➡ http://www.who.int/immunization/programmes_systems/supply_chain/evm/en/index3.html (accessed 9 November 2017)

EVM training materials

➡ http://www.who.int/immunization/programmes_systems/supply_chain/evm/en/index1.html (accessed 9 November 2017)

EVM Standard operating procedures

➡ http://www.who.int/immunization/programmes_systems/supply_chain/evm/en/index2.html (accessed 9 November 2017)

Compilation of cold chain and logistics tools (supply chain sizing tool, logistics forecasting tool, vaccine volume calculator and user guide, cold chain inventory tool)

➡ http://www.who.int/immunization/programmes_systems/supply_chain/resources/tools/en/index5.html

Guidance specific to cold chain:

- EVM Vaccine management handbook:

- Containers and coolant packs

-  http://apps.who.int/iris/bitstream/10665/183584/1/WHO_IVB_15.03_eng.pdf

- Temperature monitoring:

-  http://apps.who.int/iris/bitstream/10665/183583/1/WHO_IVB_15.04_eng.pdf

- WHO aide-memoire for prevention of freeze damage to vaccines. Document WHO/IVB/07.09. Geneva: World Health Organization; 2009

-  http://apps.who.int/iris/bitstream/10665/69673/1/WHO_IVB_07.09_eng.pdf (accessed 9 November 2017).

- Cold Chain Equipment Manager (CCEM). Seattle (WA): PATH; 2012

- ➡ <http://www.path.org/publications/detail.php?i=1569> (accessed 9 November 2017).

5.5.2. Logistics/Cold chain management

The handling of influenza vaccine does not differ from handling of other vaccines used in the cold chain. The influenza vaccine must be kept between +2 and +8 °C. Compared with the use of most other routine vaccines, influenza vaccine use is typically limited to few months before and during the circulation of the influenza virus. All levels of the immunization programme should therefore have adequate and functioning storage and transport capacity for the additional influenza vaccine volume, and capacity to manage a vaccine that would have to be replaced at least annually.

Accurate data will be needed to assess expected coverage, wastage and storage volume. The *Vaccine management handbook*, a component of the EVM Initiative, provides planners of vaccine introduction at national and subnational levels with technical advice on immunization logistics. Given the price of influenza vaccine, the annual need to update the vaccine, and the limited period of use, poorly managed logistics systems can lead to interrupted vaccination activities, non-availability of immunization-related supplies and overstocking of influenza vaccine, which can result in significant operational programme costs. Logistics management information system (LMIS) data should be regularly assessed to ensure adequate vaccine wastage rates, stock and waste management. Including influenza vaccine in the country's LMIS requires updating vaccine order forms, vaccine and injection equipment stock records, wastage reports, and its inclusion in temperature monitoring and alarm systems.

To manage the annual switch from the influenza vaccine formulation currently in use to the new vaccine formulation for the next season, a national influenza vaccine switch plan should be developed through close collaboration between policy-makers, EPI, and RMNCAH programme managers and logisticians. This plan should set the dates for the vaccine switch and should define the management structures necessary to align supply, communications, logistics, process monitoring and reporting. For further information, see WHO's *Guidelines for developing National Operational Plans for the Switch from tOPV to bOPV* in Toolbox L.

5.5.3. Safe injection practices and waste management


Influenza vaccine is comparable to other vaccines with regard to safe injection practices and waste management. If provided through seasonal campaigns rather than year-round routine delivery, influenza vaccine will put temporary stress on waste management. Managers should plan to integrate the ordering and distribution of injection and waste-disposal equipment with the management of other vaccines used in the country (Toolbox M).

Health-care worker training must include safe injection practices in order to prevent reuse and needle-stick injuries. The WHO Safe Injection Global Network (SIGN) handbook provides information and tools for avoiding unsafe practice issues. See section 6.1 for additional detail on staff training.


Toolbox M




Safe management of wastes from health-care activities. Second edition. Geneva: World Health Organization: 2014

 http://apps.who.int/iris/bitstream/10665/85349/1/9789241548564_eng.pdf (accessed 9 November 2017).

WHO guideline on the use of safety-engineered syringes for intramuscular, intradermal and subcutaneous injections in health-care settings. Geneva: World Health Organization: 2015

 <http://apps.who.int/iris/bitstream/eam/10665/250144/1/9789241549820-eng.pdf> (accessed 9 November 2017).

Vaccine volume calculator

 http://www.who.int/immunization/programmes_systems/supply_chain/resources/tools/en/index4.html

6. Training and communications

6.1. Training

Country Experience: Introducing influenza vaccination for pregnant women in the Republic of Kazakhstan

The Government of the Republic of Kazakhstan introduced recommendations for influenza vaccination of pregnant women in 2011. Vaccination is recommended for pregnant women in the second and third trimesters and is provided from 1 October to 31 December at primary health care clinics as part of the country's antenatal care programme.

The vaccination programme in Kazakhstan has been highly successful in overcoming barriers to vaccination uptake among pregnant women which have been observed in many countries of the WHO European Region. The achievements of the maternal influenza vaccination programme in Kazakhstan are the result of a number of training and communication initiatives involving both vaccine providers (health-care workers) and vaccine recipients (pregnant women), combined with strong commitment and support from the government and the Ministry of Health. Specific activities to promote influenza vaccination for pregnant women have included:

- workshops to enable health-care workers to develop theoretical and practical skills on the epidemiology, clinical picture, laboratory diagnosis, treatment and prevention of influenza in pregnant women;
- training of immunization nurses to ensure safe vaccination;
- annual awareness campaigns for women of reproductive age through a programme named *Young Mother*, as well as communication using different mass media outlets.

Since the introduction of the vaccination programme, the proportion of pregnant women vaccinated against seasonal influenza has increased significantly – from 4.6% in 2011–2012 to 92.3% in the 2015–2016 influenza season. Analysis of surveillance data indicated a decrease in the incidence of acute respiratory infections and confirmed influenza over this period not only among pregnant women but also among young infants.

Source: Committee of Consumer Rights Protection, Ministry of National Economy of the Republic of Kazakhstan

6.1.1. Training of immunization programme and health staff

In order to appropriately time, fund and implement training efforts, training plans need to be developed, budgeted and included in the maternal influenza vaccine introduction plan, as well as in subsequent annual workplans and the cMYP. Integration of training efforts into the broader framework of existing training plans and policies in the national health plan can be useful to limit costs. For campaign-style dissemination, the timing of the training should ideally be planned to take place as pre-service training and early programme in-service training.

Training plans should include an assessment of the existing knowledge, skills and practices of health-care workers to identify training needs and tailor the curriculum to target audiences. It is recommended that training on influenza vaccination should be integrated into existing training efforts or be part of ongoing supplementary training within supportive supervision visits to minimize the absence of health-care workers from their work.

All health-care workers should be trained in communicating information on the benefits and risks of influenza vaccine to the pregnant woman and family members (or other people) who accompany her, and in response to questions. For immunization programme staff, no additional skills are required for intramuscular influenza vaccine administration compared to other injected routine vaccines. Antenatal care workers should be involved in maternal influenza vaccination and therefore require training in vaccine administration and communication skills to encourage uptake among pregnant women. Health-care workers should apply strategies to mitigate pain during immunization sessions⁸. Encouraging vaccination of health-care workers themselves may encourage uptake among pregnant women, but this would require that the vaccine is available or recommended for health-care workers (Toolbox N).

Training in preparation for maternal influenza vaccination should cover:

- specific information on influenza disease in pregnant women and their infants (manifestations, disease burden, seasonality);
- specific information on influenza vaccine for use in pregnant women and their offspring (composition, safety, efficacy, potential side-effects, injection site, use with other vaccines such as tetanus);
- the vaccine delivery strategy, microplanning, and the calling and recalling system, including tracking those who are not vaccinated;
- timing and scheduling of vaccination and updating of vaccination records (if provided through antenatal care visits, national data on antenatal care coverage should inform the timing of immunization of pregnant women; in places where pregnant women often attend only one antenatal care visit, they should be offered vaccination at this visit (see Ref. [32]);
- proper storage, preparation and administration of influenza vaccine are essential to ensure the quality of influenza immunization in view of the sensitivity of the vaccine to heat and freezing (see Toolbox L);
- briefing on updated vaccination records and tally sheets, reporting of doses and potential updates in the reporting of, and communications regarding, AEFI in pregnant women (see section 7.3);
- messaging on how to introduce maternal vaccination to increase vaccine acceptance and educate pregnant women and their families, including communication of risk and benefits of the vaccine, and to answer frequent questions;
- locally-adapted guidance on how to communicate with pregnant women and their families in a manner that generates trust and provides reassurance (e.g. by demonstrating good listening and offering appropriate responses to questions);
- procedures for monitoring coverage and vaccine wastage rates;
- guidance on integrating the use of the vaccine with existing vaccines (e.g. tetanus).

⁸ Reducing pain at the time of vaccination: WHO position paper – September 2015. Wkly Epidemiol Rec. 2015;39(90):505–16 (<http://www.who.int/wer/2015/wer9039.pdf>, accessed 9 November 2017).

Toolbox N



Principles and considerations for adding a vaccine to a national immunization programme. Geneva: World Health Organization; 2014

http://apps.who.int/iris/bitstream/10665/111548/1/9789241506892_eng.pdf (accessed 9 November 2017)

Section 3.7 provides information on training and supervision of health personnel.

Tailoring Immunization Programmes for Seasonal Influenza (TIP FLU). A guide for increasing health care workers' uptake of seasonal influenza vaccination. Copenhagen: World Health Organization Regional Office for Europe: 2015

➡ <http://www.euro.who.int/en/tailoring-immunization-seasonal-influenza-health-care-workers> (accessed 9 November 2017)

Tailoring Immunization Programmes for Seasonal Influenza (TIP FLU). Understanding health care workers' uptake of seasonal influenza vaccination in Montenegro: a case study for policy-makers and programme managers. Copenhagen: World Health Organization Regional Office for Europe: 2015

http://www.euro.who.int/__data/assets/pdf_file/0007/281860/Tailoring-Immunization-Programmes-Seasonal-Influenza-TIP-FLU.pdf (accessed 9 November 2017)

Mid-level management modules (Cold chain, Partnering with communities, Immunization safety, Supportive supervision, Monitoring the immunization system, Making a comprehensive annual national immunization plan and budget, The EPI coverage survey, Making disease surveillance work)

➡ <http://who.int/immunization/documents/training/> (accessed 9 November 2017)
Specific modules for use in the WHO African Region are also available.

Global Learning Opportunities for Vaccine Quality (GLO/VQ)

➡ http://who.int/immunization_standards/vaccine_quality/gtn_index/ (accessed 9 November 2017)

Vaccine safety

- Global manual on surveillance of adverse events following immunization. Geneva: World Health Organization; 2014

http://who.int/vaccine_safety/publications/Global_Manual_on_Surveillance_of_AEFI.pdf (accessed 9 November 2017)

- National public health officials, immunization programme managers, members of AEFI review committees can benefit from face-to-face training offered by WHO

➡ http://who.int/vaccine_safety/initiative/tech_support/ (accessed 9 November 2017)

- E-learning courses on vaccine safety basics for vaccinating staff, but also for national public health officials, immunization programme managers, and members of AEFI review committees

➡ http://who.int/vaccine_safety/initiative/tech_support/ebasic/ (accessed 9 November 2017)

Immunization in practice: a practical guide for health staff, cold chain, safe injections, microplanning to reach communities, managing immunization sessions, monitoring and evaluation, partnering with communities

➡ <http://who.int/immunization/documents/training/> (accessed 9 November 2017)

RED (Reaching Every District) strategy

- Microplanning for immunization service delivery using the Reaching Every District (RED) strategy. (Document WHO/IVB/09.11). Geneva: World Health Organization; 2009

<http://who.int/entity/immunization/documents/RED-strategy-document.pdf> (accessed 9 November 2017).

Monitoring charts

- Immunization monitoring charts (CD-ROM)

➡ <http://who.int/immunization/documents/training/en/index2.html> (accessed 9 November 2017)

6.1.2. Building knowledge among health professionals

Health-care workers are one of the target groups recommended for vaccination against influenza by WHO. However, even in settings with a robust medical education infrastructure, information on maternal vaccination may be limited and may prevent health professionals (gynaecologists, obstetricians, midwives, nurses, family/general practitioners and other health staff) from providing reliable information on the benefits and risks of maternal influenza vaccination [37].

Informed health professionals (e.g. gynaecologists, obstetricians, family practitioners, midwives, nurses) are more likely to recommend influenza vaccination and are better positioned to inform pregnant women and their families and thus help to improve vaccine uptake in pregnant women and women of reproductive age [38]. Including information on vaccination of pregnant women in pre-service curricula for medical schools, nursing schools and other training institutions targeting health professionals may help to establish knowledge for future providers of maternal immunization.

6.2. Communication and vaccine acceptance

Ongoing communication between the programmes for immunization, antenatal care, women's health, and/or sexual and reproductive health and the different levels of government is essential to boost acceptance and facilitate high vaccination coverage. Communication approaches should be outlined in a systematic communications plan, developed with inputs from a technical committee for communications and vaccine hesitancy, and should be informed by a study of public knowledge, attitudes, beliefs and practices (KABP).

Comprehensive influenza vaccination communications activities should be included in the annual EPI plan and should be part of an existing national communications strategy to sustain political support and public trust. The strategy should identify and address target audiences at national, regional and local levels, appealing to physicians, health-care staff (particularly those with limited immunization experience), opinion leaders, communities, pregnant women and their families, medical and nursing associations, women's rights and gender equity advocates, civil society organizations, government officials, parliamentarians, and the media. The development of messaging that is tailored and targeted to each main audience group will also be relevant.

The key components of a communications plan to support influenza vaccination for pregnant women include: communication objectives, target audiences, summary findings of a KABP (if completed), key messages tailored to each target audience, approaches/channels for information dissemination and engagement, timing of communication activities, and methods for measuring and evaluating the communication activities (Toolbox O).

Coordination between programmes is important to ensure proper technical content of the messaging, to choose appropriate channels for dissemination and to achieve shared endorsement of the communications strategy. A multidisciplinary technical committee for communications may best inform the development of such a communications plan. The group should include technical experts (maternal and child health, influenza immunization) as well as communication and social mobilization experts. Partner organizations (e.g. WHO, UNICEF), civil society representatives, different sectors of societies, pregnant women, their families, communities, women's associations, religious groups and health-care workers should be able to provide inputs to adapt

communications to local contexts. A KAPB study may help to identify misperceptions of the severity of influenza disease in pregnant women, gaps in public knowledge about the vaccine, and attitudes and acceptance issues regarding the vaccine [41–48]. The KAPB will be essential to informing parts of the communications plan, such as selection of channels for information dissemination, as well as message development for target audiences.

Workshops or briefings with journalists or other critical stakeholder groups (e.g. medical associations, parents' groups) should be organized if possible. Such workshops may be an opportunity to inform about, consult on and generate buy-in for the new programme and immunization activities, especially with influential groups. Workshops can be a means for the Ministry of Health to share information proactively about the introduction of the influenza vaccine and explain the concept of protecting both pregnant women and, through them, their infants. During the implementation of maternal influenza vaccination efforts, the media and key stakeholders should be regularly informed of progress and can help establish the vaccine as a routine intervention in the country.

Toolbox 0



Immunization coverage survey methods and resources

➡ http://www.who.int/immunization/monitoring_surveillance/routine/coverage/en/index2.html (accessed 9 November 2017)

Tailoring immunization programmes for seasonal influenza (TIP FLU). A guide for promoting uptake of maternal influenza vaccination. Copenhagen: World Health Organization Regional Office for Europe: 2017

📄 http://www.euro.who.int/__data/assets/pdf_file/0004/346369/Whodesignvfinal_august.pdf (accessed 9 November 2017)

Vaccine. Special Issue on Vaccine Hesitancy. 2015;33(34):4155–218

➡ <http://www.sciencedirect.com/science/journal/0264410X/33/34> (accessed 9 November 2017)

Vaccine safety events: managing the communications response. A guide for Ministry of Health EPI managers and health promotion units. Copenhagen: World Health Organization Regional Office for Europe; 2013

📄 http://www.euro.who.int/__data/assets/pdf_file/0007/187171/Vaccine-Safety-Events-managing-the-communications-response.pdf (accessed 9 November 2017)

E-learning course on vaccine safety basics. Module 6: Communication

➡ <http://vaccine-safety-training.org/overview-and-outcomes-6.html> (accessed 9 November 2017)

7. Monitoring and evaluation

7.1. Monitoring of coverage

Information on influenza vaccines administered to pregnant women should be integrated into existing immunization registries, vaccination/antenatal care home-based records, community registers and tally sheets. Monitoring of vaccination coverage of pregnant women should be an integral part of the antenatal care and immunization monitoring mechanism.

Monitoring activities can include:

- use of centralized nominal records, if available, to monitor coverage [39];
- routine reviews of immunization registries and aggregation and reporting practices, including vaccination status of the mother recorded on the vaccination card of the infant if possible;
- review of antenatal records to ensure influenza vaccination is included in the antenatal care register, antenatal care card and vaccination card tally sheets (routine reports from health or antenatal care centres can provide relevant information about immunization coverage; careful assessment is required due to the risk of reporting from multiple sources);
- immunization coverage surveys such as DHS or MICS about vaccines received during pregnancy that systematically interview women who were pregnant for the past 12 months or that target women who were pregnant during the period of influenza vaccine administration.

Vaccination coverage strategies should be reported by all countries using the denominator of live births. Additional manipulations of the denominator can be used to check programmatic performance or determine in-country statistics. Depending on the vaccination strategy, countries may wish to modify the denominator they use to calculate vaccination coverage:

- In temperate countries with seasonal influenza epidemics, an annual campaign before the start of the transmission season will capture only those women who identify as pregnant and attend antenatal care during the 3–4-month period during which the vaccine is provided to protect against circulating influenza. Therefore, influenza vaccine coverage will not exceed 50% if the denominator used is all pregnant women in a year. In order to monitor effectively the proportion of eligible pregnant women who are vaccinated, system performance should be measured using the number of pregnant women attending antenatal care during the campaign period or the estimated pregnant population during the campaign period (estimated from monthly health facility denominators for maternal tetanus vaccination or antenatal care attendance).
- In tropical countries with moderate transmission throughout the year or multiple seasonal peaks, influenza vaccines can be distributed through routine delivery throughout the year or in biannual campaigns. For vaccine delivered throughout the year, the annual health facility denominators for maternal tetanus vaccination or antenatal care attendance could be retained. For biannual campaigns, either this denominator or the

denominators identified for annual campaigns above could be applied to the number of months during which influenza vaccine is available in the year. For example, if two campaigns were conducted of 3-months duration, each vaccine would be available for 6 months of the year and the number of pregnant women attending care during those 6 months (or half the annual maternal tetanus/antenatal care attendance denominator) would be an appropriate denominator to measure vaccine coverage.

- If vaccination strategies target only those women in the second and third trimester, using an entire year birth cohort as the denominator will underestimate the coverage. Instead, if possible, then only women who are registered at health facilities as pregnant in second or third trimester during the influenza vaccination should be included in the denominator. (See 2016 WHO Manual for Assessing Influenza Vaccination Coverage in Target Groups included in Toolbox P below).
- Suggested indicators for vaccination of pregnant women are proposed in Box 4.

Box 4. Indicators that may be relevant for monitoring maternal influenza vaccination

Specific indicators should be established for the newly-introduced influenza vaccine and should subsequently be included in the monitoring and evaluation planning of the immunization programme. The following indicators are suggested by the writing group of this manual for consideration in the monitoring and evaluation plan:

- percentage of pregnant women vaccinated against influenza;
- percentage of pregnant women with a minimum of four antenatal care visits;
- percentage of pregnant women with an antenatal care visit in the first trimester;
- percentage of newborns or young infants of mothers vaccinated against influenza⁹.

7.2. Disease surveillance

Baseline data is needed at programme outset so countries understand their burden of disease and subsequently can estimate the potential impact of the programme.

WHO's publication *Global epidemiological surveillance standards for influenza* provides information on case definitions and epidemic thresholds developed by WHO's Global Influenza Programme. WHO also offers summaries of global surveillance based on data gathered through global and regional data-sharing platforms and direct reports from Member States.

For practical use, the WHO manual on *Estimating disease burden associated with seasonal influenza* provides tools and methods to estimate disease burden on the basis of available surveillance data.

Further guidance and tools to set up, monitor, report on and analyse disease surveillance at district and national levels are offered in WHO's *Training for mid-level managers series, Module 8* (Toolbox Q).

⁹ These data can be collected at birth or during the DTP1 visit.

Where resources permit, establishment of sentinel sites should be considered for collecting virus samples and to assess vaccine impact by comparing vaccine coverage in laboratory-confirmed versus test-negative cases (Toolbox Q). Collaborating with WHO surveillance and epidemiology networks such as the SARI Sentinel Surveillance Network (SARINet) or the African Network for Influenza Surveillance and Epidemiology (ANISE) can support countries by allowing data analysis based on sufficient sample sizes from their member countries.

Toolbox P



Immunization in practice series, module 6: Monitoring and using your data


 http://www.who.int/immunization/monitoring_surveillance/resources/IIP_Module7.pdf

Training for mid-level managers. Module 7: The EPI coverage survey. (Document WHO/IVB/08.07). Geneva: World Health Organization; 2008.

 http://who.int/immunization/documents/MLM_module7.pdf (accessed 9 November 2017)

Provides a step-by-step walkthrough, including relevant guidance and tools, to plan and conduct a coverage survey of newly introduced vaccine at district, and also national, level and to analyse data.

Immunization summary: statistical reference containing data through 2013. New York (NY): United Nations Children's Fund; 2014.

 http://www.who.int/immunization/monitoring_surveillance/Immunization_Summary_2013.pdf (accessed 9 November 2017)

Gives an overview of immunization schedules which provide other vaccines in pregnancy.

WHO reference for estimating influenza vaccination coverage among target groups.

 http://www.euro.who.int/__data/assets/pdf_file/0004/317344/Methods-assessing-influenza-vaccination-coverage-target-groups.pdf.


Pan American Health Organization. Maternal and Neonatal Immunization Field Guide for Latin America and the Caribbean. PAHO. Washington DC 2017.

 http://www.paho.org/hq/index.php?option=com_docman&task=doc_view&gid=40767&Itemid=270

Toolbox Q



Global epidemiological surveillance standards for influenza. Geneva: World Health Organization; 2014

 http://who.int/influenza/resources/documents/influenza_surveillance_manual (accessed 9 November 2017)

WHO influenza surveillance updates

 http://who.int/influenza/surveillance_monitoring/updates/latest_update_GIP_surveillance/en (accessed 9 November 2017)

Manual for estimating disease burden associated with seasonal influenza. Geneva: World Health Organization; 2015

 http://apps.who.int/iris/bitstream/10665/178801/1/9789241549301_eng.pdf (accessed 9 November 2017)

Training for mid-level managers series. Module 8: Making disease surveillance work. (Document WHO/IVB/08.08). Geneva: World Health Organization; 2008.

 http://who.int/immunization/documents/MLM_module8.pdf (accessed 9 November 2017)

7.3. Adverse events following immunization (AEFI) surveillance

When delivering influenza vaccine to pregnant women, a surveillance system to monitor and investigate possible AEFI should include the following objectives:

1. Detect and identify problems with vaccines which could be due to the product, its quality or an immunization error in the programme.
2. Evaluate the rate of reactions to the vaccine observed in that specific population and compare it to the expected vaccine reaction rates reported in literature.
3. Ensure that coincidental events are not mistaken for vaccine reactions and affect the confidence in the immunization programme.
4. Facilitate the investigation and causality assessment of individual AEFI reports that are collected when implementing the programme.
5. Identify events that may indicate a previously unknown or unexpected vaccine reaction that can be investigated in more depth.
6. Create awareness of immunization safety in the community and share this information with other programmes and with WHO.

The national immunization programme should work with the national regulatory authority and the district and subnational stakeholders to define the roles and responsibilities that will be assigned to each other. Establishing background rates of expected events prior to programme roll out, based on national data or data found in literature can put into perspective the occurrence of reported AEFI. A checklist for the immunization safety surveillance system can be found in Table 7 of the *Global manual on surveillance of adverse events following immunization* (see Toolbox R).

All vaccine recipients who present to the health-care system or are reported from the community as having an event (including minor events) perceived to be related to the influenza vaccine should be reported to the influenza vaccine immunization programme and surveillance system using the standard AEFI reporting form that has been adapted to include details on pregnancy (Annex 7).

For serious AEFI that are investigated, the causality should be assessed by a group of experts, as described in the *Causality assessment of an adverse event following immunization (AEFI): user manual for the revised WHO AEFI causality assessment classification* (see Toolbox R).

Toolbox R



Global manual on surveillance of adverse events following immunization. Geneva: World Health Organization: 2014

➡ http://www.who.int/vaccine_safety/publications/aeft_surveillance (accessed 9 November 2017)

Causality assessment of an adverse event following immunization (AEFI): user manual for the revised WHO AEFI causality assessment classification. Geneva: World Health Organization: 2013

➡ http://www.who.int/vaccine_safety/publications/gvs_aefi (accessed 9 November 2017)

WHO forms guiding the investigation and causality assessment of AEFI

➡ http://www.who.int/vaccine_safety/initiative/investigation (accessed 9 November 2017)

7.4. Post-introduction evaluation and National Immunization Programme reviews

National Immunization programme (NIP) reviews typically assess the strengths and weaknesses of an immunization programme at national, subnational and service delivery levels with the purpose of providing evidence for the programme's strategic directions and priority activities. Related assessments, such as post-introduction evaluations (PIE) are recommended to be performed 6 to 12 months after introduction of a new vaccine into a national programme. Influenza vaccine introduction should be assessed by performing a PIE. PIE is intended

to assess the extent to which the vaccine introduction was successful, review any challenges related to its implementation and recommend measures, if any, which need to be taken in order to improve the introduction efforts, e.g. in the areas of management, supply chain, monitoring and data quality.

A PIE should ideally be combined with a planned NIP Review, and performed at all levels of the health system. It is conducted by using standard questionnaires and checklists, assessing experiences and practices of using the new vaccine, details of vaccine storage, transport and logistics, reviewing of data and records, and including – at the service delivery level – observation of delivery practices and obtaining direct feedback from clients and vaccinees. The questionnaires, data collection forms and report templates (see Toolbox S) provide further detailed instructions.

WHO has developed an influenza-specific PIE tool that can be adapted to each country's context and to specific vaccine formulations and presentations. The influenza PIE tool also takes into account the seasonality of disease and vaccine administration, characteristics of specific target populations, coordination needs between the NIP, the antenatal care and other health programmes, communications and training aspects, vaccine safety as well as specific surveillance, monitoring and evaluation needs. This tool also provides a systematic approach to comparing findings across countries and to sharing country experiences. A PIE will also provide valuable lessons for the continued use of influenza vaccine, and for the interaction of influenza vaccination with other maternal immunization activities and related health services.

For further information on the adapted PIE tool, please contact influenza@who.int.

Toolbox S



New vaccine post-introduction evaluation tool. (Document WHO/IVB/10.03). Geneva: World Health Organization; 2010

➡ http://www.who.int/immunization/monitoring_surveillance/resources/PIE_tool (accessed 9 November 2017)

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➡ <http://www.who.int/immunization/documents>

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Annex 1. Q&A: influenza disease, vaccine and maternal immunization

Influenza disease

- **Which virus is causing influenza disease?**

Influenza viruses belong to the family orthomyxoviridae and are classified as A, B or C. Influenza A and B viruses are responsible for most seasonal epidemics of human disease that range from asymptomatic infection and febrile upper respiratory disease to influenza pneumonia, exacerbation of chronic illness, bacterial super infection, and severe illness including death. Influenza C viruses rarely cause disease in humans. Influenza A viruses circulating among animal species can serve as a source of novel viruses to which humans have little or no immunity, and are responsible for periodic worldwide influenza pandemics.
- **Why is it difficult to protect humans against influenza disease?**

Influenza virus has a high likelihood of mutation and undergoes frequent genetic reassortment. Frequent minor structural changes in the influenza A strains' protein structure ("antigenic drift") enable the virus to evade immune recognition and cause repetitive influenza outbreaks. Reassortment of different influenza A subtypes can lead to major changes ("antigenic shift") in the influenza type A haemagglutinin (HA) antigen, which can result in viruses capable of causing large regional outbreaks or a global pandemic. There are two major lineages of influenza B viruses that cause human disease.

Influenza vaccine

- **Is influenza vaccine a new vaccine?**

Vaccines against influenza first became available in the 1940's. Currently, two types of influenza vaccine are available: inactivated and live-attenuated (cold adapted). Three types of inactivated influenza vaccines are produced – egg-based, cell-based, and recombinant (through reverse genetics). While both the egg-based and cell-based approaches use vaccine strains produced in eggs, the recombinant approach uses molecular technology to produce the antigens. Both inactivated and live-attenuated influenza vaccines are being made and used, with the former administered by injection and the latter administered via the intranasal route.
- **Can live attenuated vaccines be administered to pregnant women?**

In general, live attenuated vaccine viruses could potentially cross the placenta and infect the fetus if given to pregnant women. Even though this risk is largely theoretical, most live attenuated vaccines are contraindicated or not recommended during pregnancy. Inactivated influenza vaccines are considered safe during pregnancy. For a discussion of specific influenza vaccine safety data see section 5.5 of this document.
- **How effective is influenza vaccine?**

The efficacy of influenza vaccine in low-resource settings was assessed in a proof-of-concept study in Bangladesh in 2004–2005. The study found that influenza vaccines decreased febrile respiratory illness by 29% among infants and by 36% among mothers. Vaccine efficacy against laboratory-confirmed influenza among infants of vaccinated mothers was 63%. Three randomized controlled clinical trials from Mali, Nepal and South Africa showed a vaccine efficacy in preventing laboratory-confirmed influenza – which was mostly mild influenza infection – ranging from 35% to 70% in mothers and from 28% to 61% in infants less than 6 months of age [3–5].

Maternal immunization

- Maternal influenza immunization refers to vaccination during pregnancy in order to provide protection to **both** the mother and her child. Several publications have summarized the evidence of the risks of maternal influenza disease for the mother and the fetus, particularly in the second and third trimester, and others have established the safety and effectiveness of immunization of pregnant women with inactivated influenza vaccines [1, 35]. As infants often cannot form sufficiently protective immune responses to specific vaccine antigens until weeks after birth, there is an "immunity gap" during which the newborn infant is extremely vulnerable to a number of otherwise vaccine-preventable diseases. Immunization during pregnancy allows adequate amounts of protective antibodies to be passively transferred on from the mother to the fetus, protecting the neonate from disease until active immunization of the infant can be accomplished. Passive antibody transfer from vaccinated mother to fetus is critical for the protection of the infant during the first 6 months of life, before it can get vaccinated with influenza vaccine.
- **Are there alternative preventive treatment options to protect children that are vulnerable to disease in their first months of life?**

Maternal immunization is considered for vaccine-preventable diseases that are associated with risk of severe outcomes in young infants, including influenza, tetanus and pertussis. There are no other preventive options that directly protect young infants.

Annex 2. National immunization programme readiness criteria

Criteria for assessing the national immunization programme readiness for new vaccine introduction

1. Obtaining full benefit from existing vaccines

- An immunization multi-year plan and annual work plans are in place, with regular updating of policies.
- Immunization coverage reflects satisfactory access and limited drop out. Each NIP should set its own coverage targets in the MYP considering the regional targets and global targets in GIVS.
- Specific objectives are met or well under way for already existing vaccines. For example timely (i.e. within 24 hours) coverage with HepB birth dose is achieved where relevant, catch-up measles vaccination has been conducted, or two-dose measles strategy has been established.

2. Financially sustainable programme

- The NIP is able to mobilize and use resources for existing programme strategies with secure current and future financing.
- MYPs include a budget linked with the national health budget to secure vaccine supply and other costs.
- There is a capacity to expand the programme without threatening financial sustainability.

3. Functional cold chain

- National cold-chain policy and vaccine management systems include an updated cold-chain inventory as well as plans for the maintenance and replacement of equipment.
- The cold chain has adequate volume capacity and performance for existing vaccines at all levels.
- Cold space is able to meet any additional demands of the new vaccine, with an adequate spare capacity to meet campaign or unforeseen needs.

4. Well managed vaccine stock

- There are two-year to five-year forecasts for all existing vaccines (including planned/ likely campaigns) and the new vaccines, including the transition period when existing vaccines are being replaced.
- There is effective monitoring of wastage for all vaccines, with acceptable levels of wastage compared to coverage.
- Vaccine stock-outs at national or subnational levels are infrequent.

5. Safe immunizations and monitoring of adverse events

- All vaccines are given with auto-disable (AD) syringes.
- Proper diluents and reconstitution methods are used for lyophilized vaccines.
- There is capacity to procure, distribute and dispose of additional injection materials for new vaccine.
- There is capacity to investigate and respond to adverse events following immunization.

6. High quality disease surveillance

- There is timely, reliable and comprehensive surveillance for major vaccine- preventable diseases.
- There is surveillance with pre-introduction baseline data to monitor impact of new vaccine.

Source: Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation. Geneva: World Health Organization; 2005 (http://www.who.int/immunization/hpv/plan/vaccine_introduction_guidelines_who_2005.pdf, accessed 9 November 2017).

Annex 3. Checklist to assist in the decision of whether to introduce maternal influenza vaccination

Priority of intervention

- **Consultation process:**
 - Have recommendations from NITAGs and other advisory bodies such as NICs been considered in the decision-making process?
 - Have other health programmes, in particular the antenatal care services, been consulted?
 - Have key decision-makers from all relevant ministries and medical professional bodies been involved in the final decision-making process to introduce the vaccine?
- **Burden of disease:** What is the magnitude of influenza disease (incidence, prevalence, related morbidity and mortality in the population, particularly among pregnant women and children less than 6 months of age)? Which estimates from other sources could be used if direct estimates of disease burden are not available? (For more details, see section 4.2.1.)
- **Vaccine safety and efficacy:** Are local data on vaccine safety and efficacy in pregnant women available? If not, have reviews and summaries of available data been consulted? (For more details, see sections 4.2.2 and 4.2.3.)
- **Economic and financial criteria:** What is the economic burden of the disease? How cost-effective is the vaccine? What is the impact of vaccine introduction on the national budget? Can the vaccine introduction costs be covered with additional national or external financing? (For more details, see section 4.2.4.)
- **Prioritization arguments:** How will introduction of an influenza vaccine compare with other interventions? What are the pros and cons of the distinct interventions available?
- **Acceptance:** What is the perception of the severity of the disease and the vaccine in society and how does it compare to other public health concerns? (For more details, see section 4.2.5.)
- **Sustainability:** How can the vaccination be sustained over a longer period of time? (For more details, see section 4.2.3.)
- **Political priorities:** Is there support from leadership and governance mechanisms to enable the introduction of the intervention?

Programmatic feasibility

- **Comprehensive multi-year plan:** Is a cMYP in place? Are annual plans being regularly updated? Does the current cMYP include a provision for maternal influenza vaccination? (For more details, see section 4.2.)
- **Characteristics of vaccine presentation:** How many types of influenza vaccines have been licensed by the national regulatory authority? Of the product options available on the market, what is the number of doses per vial? Which one(s) will be preferred to fit in with the national schedule?
- **Vaccine supply, budgeting and financing:** What is the expected cost of the vaccine, and which are the sources that are expected to cover those costs (government/health insurance/donors)? Is the vaccine prequalified by WHO? Is it licensed by the national regulatory authority? Can enough vaccine be made available through the selected purchase mechanism (is there a danger of stock-outs)?
- **National regulatory authority approval:** Has the vaccine been approved by the national regulatory authority? Is the WHO recommendation on use of the vaccine in pregnant women being supported by the product label or national policy recommendations?
- **Vaccine delivery:** What resources (financial and human) are required to deliver the vaccine? Which delivery strategies are available (e.g. routine delivery through the antenatal care system, etc.)? Which of these strategies is the most compatible with existing vaccine delivery infrastructure and cold chain capacity; which one is the most affordable, cost-effective and sustainable; and which one is able to achieve the highest possible coverage?
- **Cold chain and logistics:** The existing system needs to be assessed with regard to its current capacity and ability to make the vaccine accessible to all pregnant women in the country.
 - Is the cold chain equipment up to date, well maintained and with enough residual capacity to take up an additional vaccine at all levels?

- Are adequate measures in place to ensure temperature monitoring (overheating/freezing of vaccine)?
- Is there sufficient capacity to store injection materials for an additional vaccine?
- Have vaccine stock-outs been observed? If yes, have these occurred frequently?
- Is wastage from injection material with an additional vaccine being introduced expected to fall within acceptable wastage levels? Is a wastage monitoring system in place? (For more details, see section 5.5.3)
- **Vaccination programme performance/integration of delivery services into antenatal care:** Prior to vaccine introduction, the readiness of the national immunization programme to take up maternal influenza vaccination should be analysed. For a readiness assessment checklist, see Annex 2. Areas that need to be strengthened should be identified in order to sustain the impact of influenza vaccine introduction and not weaken the overall programme.
 - Has a situation analysis been conducted to determine the size and distribution of the health workforce?
 - Is the health workforce sufficiently able to provide the current health services? Can a vaccine be added to the programme with the existing workforce strength?
 - Can sufficient training be provided to the personnel providing the health services? Is this costed in the new vaccine introduction plan and budgeted in the cMYP?
- **Coverage in target group:**
 - Are data available showing immunization coverage of any vaccines already given to pregnant women (e.g. tetanus, pertussis or Td)?
 - Have coverage rates for other vaccines used in the immunization programme met national targets and not decreased over the past 5 years?
- **Reporting requirements:** Can the use of maternal influenza vaccination be incorporated into existing reporting forms used in the country? Do new reporting mechanisms have to be established (e.g. if the vaccine is provided through antenatal care channels)?
- **Timing for programme delivery:** Are epidemiological data available that can help define the seasonal/year-round occurrence of circulating influenza?

Source: Adapted with permission from: Pan American Health Organization

***Adverse event(s):**

Maternal AE:

- Severe injection site reaction (specify): _____
 - lasting >3 days beyond nearest joint
- Fever $\geq 38^{\circ}\text{C}$ (highest temperature recorded: _____ $^{\circ}\text{C}$)
- Allergic reaction (specify): _____
- Anaphylaxis
- Other systemic reaction (specify): _____
- Maternal infection/sepsis: _____
- Diagnosis of new onset medical condition (specify): _____

- Worsening of existing medical condition (specify): _____
- Other (specify).....

Obstetric AE/outcomes of pregnancy:

- Miscarriage/spontaneous abortion@
- Stillbirth@
- Preterm labour (GA at onset: _____)
- Preterm delivery@ (GA at delivery: _____)
- Preterm prolonged rupture of membranes (GA at onset: _____)
- Complications of delivery (specify): _____
- Event leading to emergency delivery/C-section (indication): _____
- Other obstetric complications in mother (specify – e.g. hypertensive disorder, haemorrhage, abruptio placenta, etc): _____

Infant AE:

- Preterm birth (Gestational age: _____)
- Low birth weight (<2500 g)
- Very low birth weight (<1500 g)
- Extremely low birth weight (<1000 g)
- Small for gestational age (SGA): _____

- Congenital anomalies @ (specify): _____
- Neonatal encephalopathy: _____
- Neonatal infection/sepsis (specify): _____
- Respiratory distress (specify): _____
- Metabolic disorders (specify): _____
- Neonatal death@

- Other neonatal medical conditions in newborn (specify) _____

Date AEFI occurred (DD/MM/YYYY): __ / __ / __

Time _____

Describe AEFI (Signs & symptoms):

***Serious: Yes / No;** ➔ If Yes Death Life-threatening Persistent or significant disability Hospitalization Congenital anomaly Other important medical event (specify –).....

***Outcome:** Recovering Recovered Recovered with sequelae Not recovered Unknown

Died If died, date of death (DD/MM/YYYY): __ / __ / __ Autopsy done: Yes No Unknown

Past medical history (including history of similar reaction or other allergies), concomitant medication and other relevant information (e.g. other cases). *Use additional sheets if needed :*

First decision-making level to complete:

Investigation needed: Yes No

If Yes, date investigation planned (DD/MM/YYYY): __ / __ / __

IMPORTANT: All serious AEFI, including conditions marked with @ should be investigated in detail using a separate AEFI investigation form (Annex 5)

National level to complete:

Date report received at national level (DD/MM/YYYY): __ / __ / __

AEFI worldwide unique ID :

Comments:

****Compulsory field***

Annex 5. Sample AEFI investigation form

AEFI INVESTIGATION FORM

– Adapted for pregnant or postpartum women and their fetus or newborn

(Only for Serious Adverse Events Following Immunization – Death / Disability / Hospitalization / Congenital Anomalies / Cluster and pregnancy-related events that meet criteria for Serious Adverse Events)

Section A Basic details					
Province/State	District	Case ID			
Place of vaccination (✓): <input type="checkbox"/> Govt. health facility <input type="checkbox"/> Private health facility <input type="checkbox"/> Other (specify) _____					
Vaccination in (✓): <input type="checkbox"/> Campaign <input type="checkbox"/> Routine <input type="checkbox"/> Other (specify) _____					
Address of vaccination site:					
Name of Reporting Officer:			Date of investigation: ___ / ___ / _____		
Designation / Position:			Date of filling this form: ___ / ___ / _____		
Telephone # landline (with code):			Mobile:		e-mail:
This report is: <input type="checkbox"/> First <input type="checkbox"/> Interim <input type="checkbox"/> Final					
Patient Name			Sex: <input type="checkbox"/> M <input type="checkbox"/> F		
(use a separate form for each case in a cluster)					
Date of birth (DD/MM/YYYY): ___ / ___ / _____					
OR Age at onset: ___ years ___ months ___ days					
OR Age group (mother): <input type="checkbox"/> < 18 years <input type="checkbox"/> 18–39 years <input type="checkbox"/> > 40 years					
Patient's full address with landmarks (Street name, house number, locality, phone number etc.):					
Name of vaccines/diluent received by mother	Date of vaccination	Time of vaccination	Dose (e.g. 1 st , 2 nd , etc.)	Batch/Lot number	Expiry date
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
Type of site (✓) <input type="checkbox"/> Fixed <input type="checkbox"/> Mobile <input type="checkbox"/> Outreach <input type="checkbox"/> Other _____					
Date of first/key symptom (DD/MM/YYYY): ___ / ___ / _____ Time of first symptom (hh/mm): ___ / ___					
Date of hospitalization (DD/MM/YYYY): ___ / ___ / _____					
Date first reported to the health authority (DD/MM/YYYY): ___ / ___ / _____					
Status on the date of investigation (✓): <input type="checkbox"/> Died <input type="checkbox"/> Disabled <input type="checkbox"/> Recovering <input type="checkbox"/> Recovered completely <input type="checkbox"/> Unknown					
If died, date and time of death (DD/MM/YYYY): ___ / ___ / _____ (hh/mm): ___ / ___					
Autopsy done? (✓) <input type="checkbox"/> Yes (date) _____ <input type="checkbox"/> No <input type="checkbox"/> Planned on (date) _____ Time _____					
Attach report (if available)					

Section B Relevant patient information prior to immunization		
Criteria	Finding	Remarks (If yes provide details)
Past history of similar event	Yes / No / Unknown	
Adverse event after previous vaccination(s)	Yes / No / Unknown	
History of allergy to vaccine, drug or food	Yes / No / Unknown	
Pre-existing illness (30 days) / congenital disorder	Yes / No / Unknown	
History of hospitalization in last 30 days, with cause	Yes / No / Unknown	
Patient currently on concomitant medication? (If yes, name the drug, indication, doses & treatment dates)	Yes / No / Unknown	
Family history of any disease (relevant to AEFI) or allergy	Yes / No / Unknown	
For adult women <ul style="list-style-type: none"> • Currently pregnant? Yes (GA in weeks) _____ / No / Unknown • Currently breastfeeding? Yes / No <p><i>If patient is currently pregnant or has delivered recently, please refer to Appendix 1 for additional information that should be obtained and additional investigations that are recommended</i></p>		
For infants <p>The birth was <input type="checkbox"/> full-term <input type="checkbox"/> preterm <input type="checkbox"/> post-term. Birth weight: _____</p> <p>Delivery procedure was <input type="checkbox"/> Normal <input type="checkbox"/> Caesarean <input type="checkbox"/> Assisted (forceps, vacuum etc.) <input type="checkbox"/> with complication (specify) _____</p>		
Section C Details of first examination** of serious AEFI case		
Source of information (✓ all that apply): <input type="checkbox"/> Examination by the investigator <input type="checkbox"/> Documents <input type="checkbox"/> Verbal autopsy <input type="checkbox"/> Other _____ If from verbal autopsy, please mention source _____		
Name of the person who first examined/treated the patient: _____ Name of other persons treating the patient: _____ Other sources who provided information (specify): _____		
Signs and symptoms in chronological order from the time of vaccination: 		

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Name and contact information of person completing these clinical details:	Designation:	Date/time
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**** Attach copies of ALL available documents (including case sheet, discharge summary, case notes, laboratory reports and autopsy reports) and then complete additional information that is NOT AVAILABLE in existing documents, i.e.**

- ***If patient has received medical care*** – attach copies of all available documents (including case sheet, discharge summary, laboratory reports and autopsy reports, if available) and write only the information that is not available in the attached documents below
- ***If patient has not received medical care*** – obtain history, examine the patient and write down your findings below (add additional sheets if necessary)

<p>Provisional / Final diagnosis:</p>
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Section D Details of vaccines provided at the site linked to AEFI on the corresponding day

Number immunized for each antigen at session site. Attach record if available.	Vaccine name									
	Number of doses									
<p>a) When was the patient (mother) immunized? (✓ the <input type="checkbox"/> below and respond to ALL questions)</p> <p><input type="checkbox"/> Within the first vaccinations of the session <input type="checkbox"/> Within the last vaccinations of the session <input type="checkbox"/> Unknown</p> <p>In case of multidose vials, was the vaccine given <input type="checkbox"/> within the first few doses of the vial administered? <input type="checkbox"/> within the last doses of the vial administered? <input type="checkbox"/> unknown?</p>										
b) Was there an error in prescribing or non-adherence to recommendations for use of this vaccine?									Yes* / No	
c) Based on your investigation, do you feel that the vaccine (ingredients) administered could have been unsterile?									Yes* / No / Unable to assess	
d) Based on your investigation, do you feel that the vaccine's physical condition (e.g. colour, turbidity, foreign substances etc.) was abnormal at the time of administration?									Yes* / No / Unable to assess	
e) Based on your investigation, do you feel that there was an error in vaccine reconstitution/preparation by the vaccinator (e.g. wrong product, wrong diluent, improper mixing, improper syringe filling etc.)?									Yes* / No / Unable to assess	

f) Based on your investigation, do you feel that there was an error in vaccine handling (e.g. break in cold chain during transport, storage and/or immunization session etc.)?	Yes* / No / Unable to assess
g) Based on your investigation, do you feel that the vaccine was administered incorrectly (e.g. wrong dose, site or route of administration, wrong needle size, not following good injection practice etc.)?	Yes* / No / Unable to assess
h) Number immunized from the concerned vaccine vial/ampoule	
i) Number immunized with the concerned vaccine in the same session	
j) Number immunized with the concerned vaccine having the same batch number in other locations. Specify locations: _____	
k) Is this case a part of a cluster?	Yes* / No / Unkn
i. If yes, how many other cases have been detected in the cluster?	
a. Did all the cases in the cluster receive vaccine from the same vial?	Yes* / No / Unkn
b. If no, number of vials used in the cluster (enter details separately)	

****It is compulsory for you to provide explanations for these answers separately***

Section E Immunization practices at the place(s) where the concerned vaccine was used
(Complete this section by asking and/or observing practice)

Syringes and needles used:

- Are AD syringes used for immunization?

Yes / No / Unknown

If no, specify the type of syringes used: Glass Disposable Recycled disposable Other _____

Specific key findings/additional observations and comments:

Reconstitution: (complete only if applicable, ✓ NA if not applicable)

• Reconstitution procedure (✓)	Status		
	Same reconstitution syringe used for multiple vials of same vaccine?	Yes	No
Same reconstitution syringe used for reconstituting different vaccines?	Yes	No	NA
Separate reconstitution syringe for each vaccine vial?	Yes	No	NA
Separate reconstitution syringe for each vaccination?	Yes	No	NA
• Are the vaccines and diluents used the same as those recommended by the manufacturer?	Yes	No	NA

Specific key findings/additional observations and comments:

Section F Cold chain and transport
(Complete this section by asking and/or observing practice)

Last vaccine storage point:

- | | |
|--|--------------------|
| • Is the temperature of the vaccine storage refrigerator monitored? | Yes / No |
| ○ If "yes", was there any deviation outside of 2–8 °C after the vaccine was placed inside? | Yes / No |
| ○ If "yes", provide details of monitoring separately. | |
| • Was the correct procedure for storing vaccines, diluents and syringes followed? | Yes / No / Unknown |
| • Was any other item (other than EPI vaccines and diluents) in the refrigerator or freezer? | Yes / No / Unknown |
| • Were any partially-used reconstituted vaccines in the refrigerator? | Yes / No / Unknown |
| • Were any unusable vaccines (expired, no label, VVM at stages 3 or 4, frozen) in the refrigerator? | Yes / No / Unknown |
| • Were any unusable diluents (expired, manufacturer not matched, cracked, dirty ampoule) in the store? | Yes / No / Unknown |

Specific key findings/additional observations and comments:

Vaccine transportation:

- | | |
|--|--------------------|
| • Type of vaccine carrier used | |
| • Was the vaccine carrier sent to the site on the same day as vaccination? | Yes / No / Unknown |
| • Was the vaccine carrier returned from the site on the same day as vaccination? | Yes / No / Unknown |
| • Was a conditioned ice-pack used? | Yes / No / Unknown |

Specific key findings/additional observations and comments:

Section G Community investigation (Please visit locality and interview parents/others)

Were any similar events reported within a time period similar to when the adverse event occurred and in the same locality?
Yes / No / Unknown If yes, describe:

If yes, how many events/episodes?

Of those effected, how many are

- Vaccinated: _____
- Not vaccinated: _____
- Unknown: _____

Other comments:

Section H Other findings/observations/comments

Appendix 1. Recommended additional investigations for pregnant or postpartum women and their fetus or newborn

Aim of the investigation: To determine if there is an association between influenza vaccine and the reported adverse event in the pregnant or postpartum woman and her fetus or newborn.

Additional relevant information from the mother prior to immunization

Confirmation of the pregnancy and gestational age at the time of immunization

Obstetric history (parity, maternal medical complications in prior pregnancies such as hypertensive disorders [e.g. eclampsia/HELLP syndrome], gestational diabetes, history of previous fetal losses, type and number, premature delivery, LBW or SGA infants, neonatal death)

Conditions that increase the risk for obstetric complications during this pregnancy (e.g. incompetent cervix, placenta previa, oligo-polyhydramnios, etc)

Maternal nutritional status

Maternal health status at the time of vaccination, including documentation of maternal vital signs and presence/absence of signs and symptoms of acute or active disease

Fetal health status at the time of vaccination, including documentation of a live fetus, and presence/absence of fetal anomalies (based on obstetric examination, prenatal testing and obstetric ultrasound when available)

History of adverse reactions to vaccines, particularly influenza vaccines

Receipt of other vaccines concomitantly or within a month prior to and after vaccination with influenza vaccine

Concomitant medications, including immunomodulatory agents, and indication

Existing medical conditions (prior to pregnancy)

Active/recent maternal infection with HIV, Hep B, Hep C, TB, Malaria, STI, other chronic infections (results of prenatal testing for these)

Maternal Group B Streptococcus status

Maternal use/abuse of alcohol, drugs, nutritional or other supplements

Receipt of blood products within a month prior to or after vaccination

Rh isoimmunization

Other nonmedical events that could have led to the AE (eg. trauma, occupational or environmental factors, etc)

Additional findings to be verified on clinical examination

Vital signs

- Physical examination:
- Examination of injection site for oedema, induration, fluctuance, necrosis, and regional lymphadenopathy

Complete physical examination

Obstetric examination

- Doppler fetal heart tones and/or ultrasound

Clinical signs and symptoms consistent with active/new medical condition including infectious and non-infectious conditions

Additional laboratory tests to be done to assist with diagnosis and identify possible cause of the adverse event during pregnancy or postpartum:

- Basic haematology, peripheral smear, chemistries (hepatic and renal function), urine
- Serologies for specific pathogens
- Viral and bacterial pathogen identification from pertinent sources by appropriate stains, cultures, molecular techniques or serologies as available
- Histopathology of relevant tissues, including the placenta

If autopsy is conducted – special forensic tests recommended:

On the Mother / Newborn

- Gross anatomy
- Histopathology
- Pathogen identification through appropriate stains, cultures, or molecular methods

On the products of conception

- Gross anatomy
- Histopathology
- Pathogen identification through appropriate stains, cultures, or molecular methods

