Key elements of sustainability for influenza vaccine manufacturing in low and middle income countries

High-Level Report and Checklist

Introduction

The World Health Organization Global Action Plan for Influenza Vaccines (GAP) was initiated in 2006 to address challenges to sustainable influenza vaccine production and uptake in developing countries through three critical avenues to increase equitable access to pandemic vaccines and contributing to international pandemic preparedness efforts:

- Increase of evidence-based seasonal influenza vaccine use,
- Increase of global pandemic vaccine production capacity and strengthening of corresponding national regulatory competency
- Development of new influenza vaccines that have higher-yielding, faster to produce, broader in protection and with a longer duration.

WHO, through its Technology Transfer Initiative, directly supports 14 developing countries to establish or expand influenza vaccine manufacturing within the framework of GAP. The ability to meet the vaccination needs during an influenza pandemic, or “vaccine readiness,” can be achieved through the establishment and maintenance of a regionally-based seasonal influenza vaccine manufacturing capacity.

The Technology Transfer Initiative exists as part of a larger WHO mandate born within the mandate and scope of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI)¹, approved in 2008 by Member states, that encourages an holistic approach to increase innovation for and access to medical products and technologies for diseases disproportionally affecting developing countries.

Within the GSPA-PHI, a prominent role is occupied by transfer of technology as a means to promoting local production in developing countries and improving access to medicines, vaccines and diagnostics. The report Local Production for Access to Medical Products², developed under the scope of the GSPA-PHI, defines transfer of technology “as the transfer of technical information, tacit know-how and performance skills, technical materials or equipment, jointly or as individual elements, with the intent of enabling the technological or manufacturing capacity of the recipients... in a mutually beneficial manner, while promoting public health objectives.”

The framework proposed in the above-mentioned report provides a reference model for Member States to use the “sustainability check-list,” as it describes the importance of policy coherence (especially between industrial and health policy) in local production and the necessity of such coherence in accomplishing public health objectives.

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Various studies have demonstrated that coordination of industrial and health policies with the goal of encouraging local production can lead to improvements in access to medical products, given certain conditions, such as a coherent policy environment, reliable government procurement, product quality assurance, and market certainty.

When established, local production has a large number of potential benefits:

- It can result in potential cost savings due to less expensive, locally produced medical products, if the production scale is sufficiently big.
- The supply of medical products can also be more reliable.
- The products can be of higher quality than certain imports, due to suitability to local culture and conditions.
- It can stimulate local increased innovation capacity and greater development of human capital.
- Some manufactures are able to develop export capacity for their products, improving the national balance of payments.
- Finally, there is potential for employment generation and spill-over effects in other sectors of the economy.

However, in order to achieve these benefits, countries must have policy coherence with regards to local production, ensuring a policy environment that secures increasing financial returns to local enterprises over time. There are strong economic and political drivers to establish and enhance national capacity to manufacture medical products, in addition to the public health objectives, and countries should be aware of these drivers and purposefully work to maintain the sustainability of local production to accomplish public health objectives.

In the particular case of influenza vaccines, a report from the Centre for Global Health Policy at the University of Sussex encouraged the development of sustainable business models for medicines, vaccines, and diagnostics. The report encouraged the promotion of “enhanced regulatory certainty, particularly for manufacturers... of pandemic influenza vaccines,” “strengthening intergovernmental collaboration through global joint programming and greater harmonization of policy priorities, markets and regulation,” and “greater efforts to combine emergency and commercial use applications of products.” Market certainty and reliable government procurement strategies are two important incentives for engaging industry with partnerships for health security.

Local production contributes to health security by maintaining an uninterrupted supply of essential medical products: the long lead times for offshore producers of medical products can cause interruptions in supply. Furthermore, local producers with their potentially more efficient local supply chains can prevent greater disruptions in rural and poor areas.

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The WHO and the United States Department of Health and Human Services (HHS), together with many other stakeholders, are addressing identified technological, political, financial, and logistical issues that affect sustainability of influenza vaccine manufacture in developing countries. This report summarizes complexities and challenges that result from the multi-sectorial nature of influenza vaccine manufacturing. In addition, a checklist has been developed to support policy-makers and influenza vaccine manufacturers to identify their specific issues. The report and check-list address the following areas: policy environment and healthcare system; surveillance system and influenza specific evidence; product development and manufacturing; product approval and regulations; and communication to support influenza vaccination.

Sustainability requires a coherent and coordinated approach to industrial, economic and public health policies, brought forward through transparent and joint actions of all stakeholders (government agencies, manufacturers, international multilateral institutions, donor communities, etc.). There are variables that cannot be influenced by the government or by the manufacturer that need to be factored in during the planning stage. Among these are the population size and the influenza burden in the country: these two variables determine the scale of the vaccine need and influence therefore the vaccination policy that the government can put in place. The Gross Domestic Product (GDP or Gross National Product – GNP) represents another variable that influences public health and industrial policy development, but the government has the capacity to address the economic growth of the country using its economic and fiscal powers. For this reason, government and manufacturers should put in place measures and models for a multi-variable analysis that allows sound decisions that influence the scale of the policies, the manufacturing capacity, and the budget implication.

These report and check list will continue to develop in the future through consultations with experts and they will be enriched by case studies representing options and possible solutions to face the challenges linked to policy making and vaccine manufacturing for influenza. It is important to bear in mind that the specific manufacturing context and products fabricated play a key role in the identification of a successful mix of policies and actions to achieve sustainability.

**Policy environment and healthcare system**

Policies have a central role in strengthening sustainability for any influenza program. International expert bodies, such as the Strategic Advisory Group of Experts (SAGE) on Immunization, GAVI alliance, WHO, etc. all contribute to the international body of health evidence and vaccination recommendations. These recommendations are important to inform national governments and regional priorities. Beyond using the international recommendations and body of evidence, it is encouraged that national governments collect their own disease burden data to make evidence-based adjustments to national policies. By utilizing the evidence collected and using proxies of influenza impact, policy makers may create opportunities to better combat the seasonal influenza burden, as well as prepare the country for an influenza pandemic. By developing multi-purposed health policies, influenza prevention can be incorporated within other health strategies to have greater cumulative impact on the health of

Key elements of sustainability for influenza vaccine manufacturing

populations. By including influenza preventive measures when developing national health policies, for example in prevention and treatment of non-communicable or chronic diseases, countries may achieve cost savings in their health systems.

**Health System and Policies**

- **Ensuring political will** and buy-in is critical in establishing influenza as a national and/or regional priority. The most successful examples of this have been achieved by a local champion who prioritizes influenza prevention and continually keeps influenza on the health agenda.

- **Use international and national influenza recommendations**, such as the SAGE, National advisory committees on immunization, and regional technical advisory group recommendations to support local policy development. Seasonal vaccination policies should be based on the local burden of disease, the vaccine effectiveness among at-risk groups and vaccination cost-effectiveness studies to ensure context-specific issues are considered.

- Develop **coherence among relevant national health policies and programs** that would otherwise function independently. An example of this would be to review influenza-specific policies and programs, alongside existing policies and programs for health-care workers, maternal and childhood immunization, non-communicable diseases and the chronically ill. There may be existing low cost opportunities to leverage access to the country’s identified high-risk target populations.

- It is important for all stakeholders to understand that seasonal influenza vaccine sustainability directly strengthens **national security and pandemic preparedness**. The value generated by seasonal influenza vaccination goes beyond a healthier population and cover also these two fundamental aspects. A solid and regularly updated pandemic influenza preparedness policy and plan should be published and appropriately disseminated to all relevant agencies.

- **Health system infrastructure and human resources with respect to vaccination (vaccine delivery infrastructure)** should be examined comprehensively to identify gaps and opportunities. It is important for government stakeholders and manufacturers to understand the capacity of the cold chain, the availability of health care workers to administer vaccine, the regularly available stock of vaccine in healthcare centers and other distributions sites, and the surge capacity available for a pandemic response. Awareness of the limitations of the existing system can help for planning purposes and possible re-prioritizing of investment into the health system to provide the greatest benefit.

- **Health system financing for influenza vaccine** plays a key role in encouraging population to get vaccinated. The inclusion of seasonal influenza vaccination in health insurance schemes or
directly provided by the public health sector is considered an incentive for seasonal vaccination uptake.\(^7\)

**Policies other than health-specific**

- Some manufacturers have encountered issues that created bureaucratic obstacles that impasse their progress in establishing influenza vaccine production. Manufacturers find themselves navigating the complex of Ministries of Health, Science and Technology, Human Services, Education, Trade, Regulatory, Industry, Finance, Development etc., the policies of which may overlap and not have coherence. It is important that governments consider the multi-sectoral space in which influenza vaccine manufacturing operate to create a fully supportive environment for sustainability. Industrial policies to support the development of a strong bio-pharmacological sector require interagency coordination and strategic vision for economic development.

- Examine the relevant national and regional procurement and distribution policies and look for opportunities and incentives to promote in-country production and sourcing of materials. As WHO pre-qualification becomes more widespread as an indicator of vaccine safety and efficacy, manufacturers may also consider using this mechanism to widen the markets available for their products (see “pre-qualification” under product approval and regulatory section).

- Existing multilateral and bilateral agreements affecting commercialization and the import and export of products can have an impact on the business model, markets and sourcing of technologies and materials available to the manufacturers, and therefore on the sustainability of the local influenza vaccine environment. The government should consider the consequences that these trade agreements have on the economic and public health situation of the country and the manufacturers should be aware of their existence and implication when developing their business strategy.

- Sustainable vaccine manufacturing requires maintaining a skilled local workforce, which is challenging in many areas of the world. Governmental incentives and education policies to prevent brain-drain, or partnerships between manufacturers and academia can help strengthen a vaccine manufacturing workforce.

- Establishing policies to influence the development and size of the GMP bio-manufacturing environment. These policies should touch upon the scientific/academic institutions of the country, the infrastructure to support laboratory research and biologicals manufacturing, the stimulation of up-stream and down-stream research on biologicals etc.

\(^7\) Add publication by Bram Palache about incentives for vaccination (cost of vax and communication campaigns)
Influenza specific evidence

An accurate surveillance system is a key requirement for the early detection of disease insurgence, spread and trend to enable a timely response. The absence of strong data on influenza burden, transmission landscape and antiviral resistance and economic impacts of influenza is an obstacle to establishing evidence-based policies to reduce the impact of influenza nationally and worldwide. In many countries the public perception is that seasonal influenza is a mild illness, with a low to negligible impact on health and economies; however, proxies (such as childhood pneumonia) in the country and morbidity and mortality data from neighboring areas help to understand that seasonal influenza can have a much greater impact. Moreover, rising burdens of non-communicable diseases and growing elderly populations increase the importance of considering seasonal influenza impact on these high risk groups.

The policy maker’s information needs and priorities should be taken into consideration when framing disease burden and cost-effectiveness data from influenza studies. Traditional cost-effectiveness studies take into consideration the typical parameters familiar to public health officials, i.e. health benefits (in terms of DALY and QALY) and averted health costs. In addition, framing evidence for the Minister of Finance or Trade can be powerful by highlighting cost-savings and other economic advantages of supporting influenza vaccination and influenza vaccine manufacturing.

- Governments should establish or utilize an existing surveillance system based on available resources. Sentinel sites, population-based studies, insurance data, hospital and out-patient clinic and regional data are examples of types of surveillance systems typically employed. It is important for countries to establish regular burden of disease data collection that:
  - Provides diagnostic testing for respiratory viruses, allowing collection of data from in- and out-patient facilities;
  - Integrates virological and clinical data with molecular test verification;
  - Provides information on seroprevalence studies, and
  - Provides timely and accessible reporting to detected trends and inform policy decisions.

- Determine what kind of data should be collected, the current informatics systems available and analyze data accurately and appropriately. Once data is collected, it is helpful to report findings to regional/international databases to strengthen regional and international estimates of influenza disease burden. An extensive use should be made of the collected data for example for burden of disease analysis, identification of the required doses to be purchased by the MoH, definition of risk groups etc., and all the results of the analysis should be fully disseminated and made public.

- Invest in local burden of disease and cost-effectiveness studies to build evidence for influenza vaccination policies. Cost-effectiveness analyses are generally prepared using data from many different sources, to create a layered analysis of the burdens and costs, along with cost-savings
Key elements of sustainability for influenza vaccine manufacturing

of particular interventions. Limited specific data can be supplemented with information from other countries, proxy measurements and estimates. WHO can provide general recommendations about disease burden standards and models to inform data collection and study design.

- Consider the priorities, motivations, values and perspectives of the specific decision maker who will review the data analysis, and frame the evidence to be most relevant, “translating” it to highlight the elements that resonate most strongly with the decision makers.

Product development and manufacturing

The development of a solid business plan is essential for the sustainability of the vaccine manufacturing. Through the use of this tool, manufacturer will be guided to analyse the production environment and the marketplace where the product will be sold and used. Aside from the technical and business details of the manufacturing process, the manufacturer should be aware of the international, regional and national context in which it operates. This includes understanding the many rules and restrictions on commercialization, taking advantage of existing associations and networks operating in the influenza vaccine field, and having a pro-active role with all the government agencies supporting the production process.

- Undertake an in-depth analysis of production costs and price of product, considering scale of production, other products produced in the facility, running costs (including labor, utilities, materials), infrastructure costs, etc.

- Ensure a reliable and stable supplies of utilities (water, electricity), developing mechanisms to allow self-sufficiency.

- Secure supply chain for all components, taking into account their costs, their foreseeable substitution and their maintenance. Consider possible challenges to importation and supply chain challenges in the event of a pandemic.

- Identify a technology for which you have freedom to operate (own a license, non-proprietary) and there is a regulatory pathway to approval. Examine the technology used, scale of production and products produced. The technology selected affects the initial investment, the time to market and approval of the product and also the running costs. If the production scale is smaller, the cost of the product will be higher and the positioning on the market will be affected. The identification of market niches specific to the context in which the manufacturer operates could help overcoming the constraints due to the price of the product. Consider also that the chosen technologies affect the time for responding in the event of a pandemic and the ramp up capacity.
• Because of its seasonality, influenza vaccine presents risks of underutilization of human resources and infrastructure, with the consequence of higher production costs. It may be strategic to complement the products manufactured in the facility, and distribute the human resource and infrastructural costs among multiple products to mitigate the business risks.

• Workforce availability is key for a successful manufacturing and commercialization of the product. Skilled workforce needs to be available, which requires planning ahead to face the turnover and ensuring motivating career paths for workforce retention. Strong links and continuous dialogue with academic institutions support the availability of skills necessary to perform appropriately every step of the production process and ensure high managerial competencies.

• Business and marketing strategies are important to identifying desirable and realistic return on investment, based on potential size of the national, regional and international markets. Manufacturers may have an advantage if they focus their initial strategy on globally targeted high-risk populations (like pregnant women, elderly, HCW and the chronically ill) and encourage vaccination policy development at government level whether not already there.

• Control of biological products nearly always involves biological techniques that have a greater variability than physicochemical determinants. In-process controls take on a great importance in the manufacturing of biological products because certain deficiencies may not be revealed by testing the finished product. In the manufacture of biological products full adherence to Good Manufacturing Practice (GMP) is necessary for all production steps, beginning with those from which the active ingredients are produced. Good manufacturing practices and quality control procedures require stringent adherence to standards and international guidelines covering personnel, premises, equipments, animal quarters, production processes, labelling, lot processing and distribution records. Investing adequate resources and dedicating highly skilled personnel to this aspect of manufacturing guarantees a smoother production process and ensures the quality of the final product, reducing the risk of costs linked to substandard quality steps or by-products.

• Clinical trials and vaccine effectiveness studies represent one of the highest costs and require expertise for their design and conduction. A careful planning and a strategic approach to the identification of relevant partners for clinical trial conduction can avoid inefficient and ineffective use of resources. The identification of the target populations and the design of the clinical studies to evaluate effectiveness and safety in those populations help to define the reference market for the product. This also helps to create competitive advantages with the other manufacturers.
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• There are many options that can be used to overcome potential challenges in the various phases of the production process. For example, **Public Private Partnerships or Product Development Partnership** allow the manufacturer to contractually engage with partners that handle specific areas of operation, according to their expertise, to share the risks of development and manufacturing. There are many contractual agreements that can be developed and the manufacturer should explore the available talents and opportunities to address potential challenges in the business model.

• There is a **role for advocacy/category associations/networks** to sustain influenza vaccine manufacturing in developing countries. Many forums exist to discuss economic/industrial activities in developing and emerging economies, and influenza manufacturers can benefit from engaging directly in these fora. There are areas of opportunities for manufacturers to work together, for example workforce skill development and raising seasonal and pandemic influenza awareness as a local, regional and international priority.

**Product approval and regulations**

The assessment, licensure, control, and surveillance of biological medicinal products are major challenges for national regulatory authorities confronted by a steadily increasing number of novel products, complex quality concerns, and new technical issues arising from rapid scientific advances. With the emerging global market, the volume of biological medicinal products crossing national borders continues to rise, and it has become critical that regulatory knowledge and experience can be shared, and approaches to their control are harmonized to the greatest extent possible.

• All countries should have at least a **minimally functional national regulatory authority (NRA)**, and countries producing vaccines need an NRA with more robust abilities to exercise six critical control functions. NRAs need to exercise these control functions in a competent and independent manner, backed up with enforcement power. These six functions are:
  - License of manufacturers and product regulation (a published set of requirements for licensing);
  - surveillance of vaccine field performance (post marketing surveillance)
  - system of lot release;
  - Laboratory access (use of laboratory when needed);
  - regular inspections for GMP;
  - clinical trial approval (evaluation of clinical performance).

From the government perspective, having a functional NRA ensures the **quality, safety and effectiveness of the products** circulating within its borders. A strong and efficient NRA ensures manufacturers that the dossiers presented are analysed in a timely and accurate manner, reducing the time for the product to reach the people in need.
• **Regional harmonization and integration of regulatory approvals** are critical for increasing the market size and sustainability of seasonal influenza vaccines. Efforts to strengthen capacity for national regulation of vaccines and harmonization of rules and regulations at regional level can play a key role to facilitate and improve the accuracy of regulatory work and international capacity building efforts.

• The purpose of the **United Nations prequalification assessment** is to provide assurance that candidate vaccines: (a) meet WHO recommendations on quality, safety and efficacy, including compliance with WHO’s recommended standards for GMP and good clinical practice (GCP); and (b) meet the operational packaging and presentation specifications of the relevant United Nations agency. The aim is to ensure that vaccines provided through the United Nations for use in national immunization services in different countries are safe, effective and suitable for the target populations at the recommended immunization schedules and with appropriate concomitant products. The prequalification procedure established by WHO for vaccines has been effective in promoting confidence in the quality of the vaccines shipped to countries through United Nations purchasing agencies. The procedure is based on the following principles:
  - reliance on the national regulatory authority (NRA) of the country of manufacture, which is required to be “functional”, i.e. meeting the published WHO NRA indicators for prequalification purposes;
  - general understanding of the product and presentations offered, the production process, quality control methods, quality system in place, and available clinical data that are relevant to the target population;
  - assurance of production consistency through compliance with GMP requirements and monitoring of continued compliance with specifications through testing of final product characteristics.

**Communication for influenza vaccination**

Due to the complexities of vaccine manufacture and distribution along with the need for widespread uptake of influenza vaccine, it is critical to have a comprehensive communication plan and well developed infrastructure to assure a maximally effective system of influenza prevention and pandemic preparedness. In essence, a communication plan and its attending infrastructure is about designing, understanding, assessing, and improving all of the linkages in a given human process. Changes in manufacturing processes, government standards, vaccine administration, vaccine schedule etc. affecting the perception that the population and healthcare workers have of the product and the policy need to be linked to timely and effective communication to ensure information is disseminated and decisions understood to prevent negative reactions.
Each governmental, NGO, and private sector unit or organization that is involved in influenza vaccination should be connected in ways that assure timely, meaningful, and appropriate communication takes place to guarantee the best use of resources and the most effective practices.

Risk communication and public campaigns during outbreaks should be developed, conducted, and monitored in the context of local and regional needs, in concert with manufacturers and HCW, to both create the best response and to evaluate for future action.

For a national communication system to be effective, the following functions are required:

- **Communication policy, planning and strategy**: An explicit influenza vaccination policy can achieve several things: it defines a commonly agreed goal; it outlines vaccination priorities and the expected roles of different groups; it reduces vaccine hesitancy and it ultimately builds consensus and informs people. Clear policy guidance based on evidence and data with specific recommendations for seasonal influenza and pandemic influenza is therefore important. Such evidence and policies can advocate for resources and investments and build political will. Communication supports the development and implementation of these policies as well as translating them into a language which will resonate with policy makers, partners and the public.

- **Communication research, monitoring and evaluation**: Just like any other public health intervention, it is essential to develop meaningful and measurable metrics for communication to evaluate progress and results against communication strategy objectives and against agreed public health goals and objectives. Monitoring and evaluating progress and achievements in communication are fundamental to knowing how well communication is doing to contribute to public health outcomes.
  
  It is essential to continuously monitor (listen to) behaviors and “conversations” using various tools (social networks analysis, surveys, interviews, observations, etc.). The on-going “listening” and evaluation results should feed directly into a mechanism to adjust the outreach and decision-making processes at the political, programmatic and technical levels.

- **Partnerships, stakeholders, and public engagement**: Partners are essential to support all aspects of influenza programmes from strategy design to implementation to evaluation. Developing effective partnerships are much easier when there are well-formulated policies leading to clearly defined public health goals, objectives and strategies. An on-going and transparent process for information sharing is vital to build and maintain trustful relationships with the media. The media is one of the many ways to convey information and media engagement strategies need to be part of an integrated communication strategy. Public engagement requires an intimate understanding of influenza vaccinations from the perspective of those who will benefit. How health messages and information are interpreted

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cannot be controlled because it is filtered through individual, family and community experiences and interpretations.

- **Communication capacity building and training**: Building and strengthening communication capacities of different actors and stakeholders who contribute to influenza programmes to meet their goals is key and can be done through targeted and joint partner training. Different professional groups, job functions, individuals, teams and organizations will need different kinds of skills, competencies, tools etc.: Groups targeted for training could be: communication staff; communication focal points; health-care providers; policy makers; administrators; and reporters and media. Resources, tools and scientific expertise need to be made available to all stakeholders, and health officials should make themselves available to help build the understanding of stakeholders and especially the public and the media. Strengthening the link between communication scientists and communication practitioners is to make sure that the discipline informs good practice and good practice in turns shapes the further development of theory and models. Investments in professional development are also essential especially in non-emergency situations before a crisis occurs.

- **Knowledge translation and Information Communication Technologies (ICT)**: Bridging the knowledge practice gap and integrating ICTs to support the four core building blocks of a communication system are key to ensuring that the system is efficient and effective and is in line with the developments and application of tools and technologies outside of the health sector. ICT skills and knowledge are particularly essential for health staff to work in a 21st century information society.
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<tr>
<th>Sustainability Element</th>
<th>Lead Agency or Org</th>
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<th>Does this represent a challenge in your specific context?</th>
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**Policy environment and Health Care System** (government representatives are expected to have the information required below)

**Health System and Policies**

- Political will for in-country influenza vaccine manufacture
- Political will for pandemic influenza preparedness
- International influenza recommendations to shape national policies
- Coherence among relevant national health policies and programs
- Seasonal vaccination policies are based on the local burden of disease, the vaccine effectiveness among at-risk groups and vaccination cost-effectiveness studies
- Seasonal Influenza vaccination and control policies are developed also as means to sustain pandemic preparedness and national security
- The price of the vaccine is not a barrier for the government to provide it for free to the target groups
- Seasonal influenza vaccination is included in health insurance schemes or directly provided by the public health sector
- Vaccine delivery infrastructure is in place and maintained
- The vaccine distribution system is in place and efficient
- There is availability of the vaccine at the hospital,
### Key elements of sustainability for influenza vaccine manufacturing

<table>
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<tr>
<th>Healthcare centers and pharmacies level</th>
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<tbody>
<tr>
<td>Target groups for pandemic influenza immunization have been established and are part of the pandemic preparedness plan</td>
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<tr>
<td>The pandemic influenza preparedness plan takes into consideration the seasonal influenza vaccination policy and the local manufactured product</td>
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<td>The pandemic influenza preparedness policy and plan is regularly updated, published and appropriately disseminated to all relevant agencies</td>
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**Policies other than health-specific**

| Efforts are made to overcome possible bureaucratic obstacles to establish and sustain vaccine manufacturing |  |
| National and regional procurement and distribution policies to promote in-country production and sourcing of materials are developed |  |
| Policies are created to generate skilled local workforce for local vaccine production, also through facilitation of exchanges at national and international level and government grants to further education |  |
| Interactions between academic institutions and local manufacturers are encouraged and facilitated for the development of useful curricula for the vaccine manufacturing sector and for exchange and on the job trainings |  |
| Policies are created to influence the development and size of the GMP bio-manufacturing environment |  |
| Understanding of how the multilateral and bilateral agreements affect commercialization and import and export of products |  |
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<td><strong>Influenza-Specific Evidence</strong> (government representatives are expected to have the information required below)</td>
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<td>Surveillance system for virological surveillance in place (sentinel cites, technology and human resources)</td>
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<td>There are clear and well-functioning procedures for communication of alerts from sentinel sites to central level (information transmission chain tested and updated)</td>
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<td>Accurate and timely surveillance reporting</td>
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<td>Design of data collection driven by surveillance objectives.</td>
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<td>Annual surveillance reports with risk factor data produced</td>
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<td>Data aggregated and reported on international data sharing platforms</td>
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<td>The burden of influenza is known in the country</td>
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<td>Cost-effectiveness of seasonal influenza vaccine in target groups is known</td>
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<td>Data on impact of influenza is expressed in a way that resonates with priorities of policies makers</td>
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<td><strong>Product development and Manufacturing</strong> (this section is answered by local manufacturers)</td>
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<tr>
<td>Business plan based on analysis of production costs, price of product and return on investment</td>
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<td>Reliable and stable supply of utilities</td>
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<td>A proportion of the revenues is planned to be re-invested in R&amp;D</td>
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<td>Reliable supply chain for all components</td>
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<td>Technologies selected based on cost-benefit analysis of initial investment, operating costs, time to market and product approval</td>
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<td>More than one product manufactured in the vaccine manufacturing facility</td>
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<td>Access to and retention of skilled workforce</td>
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<td>Complies with and is certified for Good Manufacturing Practice (GMP)</td>
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<td>In-house skills to design and administer clinical trials for vaccine product</td>
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<td>A system is in place at the manufacturing or governmental level to monitor adverse events after product commercialization</td>
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<td>Animal facility for the conduction of preclinical studies is available and under GLP</td>
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<tr>
<td>Partnerships with public or private entities to acquire know how and technology, conduct clinical trials, conduct post marketing surveillance, distribute the product, etc.</td>
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<tr>
<td>Participation in manufacturers’ networks or</td>
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</tbody>
</table>
## Key elements of sustainability for influenza vaccine manufacturing

<table>
<thead>
<tr>
<th>Sustainability Element</th>
<th>Lead Agency or Org</th>
<th>Status</th>
<th>Does this represent a challenge in your specific context?</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Currently Exists</td>
<td>In Progress</td>
<td>Does not Exist</td>
</tr>
</tbody>
</table>

### Product Approval and Regulations

(this section is answered by representatives of the national regulatory authority)

- National Regulatory Authority (NRA) “functional” in WHO – Pre-Qualification terms
- NRA staff trained and re-trained continuously
- Effective working relation between manufacturers and NRA
- Effective exchanges among NRA staff and other governments and international organization
- Manufacturer’s full awareness of regulatory requirements for the product in the country
- Manufacturer’s full awareness of the requirements to submit a dossier for WHO Prequalification (PQ)
- Regional regulatory approvals harmonized and integrated
## Key elements of sustainability for influenza vaccine manufacturing

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<thead>
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<th>Sustainability Element</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Communication for influenza vaccination (government representatives are expected to have the information required below)</td>
<td></td>
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<tr>
<td>key functions established and strong relationships among stakeholders with a public communication role</td>
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<tr>
<td>Well-trained and skilled communication staff</td>
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<tr>
<td>Operational research and metrics for influenza communication outcomes</td>
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<tr>
<td>Mechanisms for ongoing listening/feedback to update communication strategies and tactics</td>
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<tr>
<td>Integrated communication strategy with other policies (with clear behavioral objectives for priority groups)</td>
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<tr>
<td>Routine use of sound communication methodologies, tools and scientific expertise</td>
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<tr>
<td>Regular evaluation of public campaigns and feedback to stakeholders</td>
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<tr>
<td>There is awareness among the public and the healthcare workers of the benefits of seasonal influenza vaccination</td>
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</tbody>
</table>