GLOBAL INFLUENZA PROGRAMME

Global Surveillance during an Influenza Pandemic

Version 1

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World Health Organization

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A Introduction

1. Background

Documented pandemics have occurred at intervals of 10 to 50 years since the 16th century including three in the last century.[1] The most devastating of the last three, the 1918 "Spanish Influenza", caused the death of an estimated 20 to 40 million people. The current widespread circulation of highly pathogenic influenza A (H5N1) virus in poultry and its occasional transmission to humans have raised concern that the world is moving closer to the next pandemic. While it is uncertain whether this particular virus will ever acquire the capacity for sustained human-to-human transmission, scientists agree that it is inevitable that another pandemic with an influenza virus will occur. The Severe Acute Respiratory Syndrome (SARS) that emerged in 2002 and 2003 affected 26 countries in less than five months and showed how fast an epidemic with a new pathogen can spread in modern society with air travel. This event also demonstrated the impact a public health crisis can have on a global economy.

Importance of surveillance to detect and respond to a pandemic

Successful containment or control of pandemic influenza will rely on early recognition of sustained human-to-human transmission which requires a system for outbreak detection, rapid data collection, analysis, assessment and timely reporting. Early detection of the start of a pandemic is crucial to rapidly implement measures to stop the pandemic at its source and to prevent millions of deaths, social disruption and economic loss. Modelling studies suggest that mass prophylaxis with antiviral drugs combined with other public health interventions such as movement restriction, social distancing, and vaccination may successfully contain an emerging pandemic. However, such an approach (i.e. rapid containment operation) would need to be implemented within the first few weeks that transmission of a pandemic virus began..[2,3] The goal of rapid containment is to delay, if not stop the pandemic. This will provide additional time for countries to implement public health actions, produce and distribute pandemic vaccines, and allow mobilization of international resources.

As part of national pandemic preparedness planning each country should prepare for enhanced surveillance to (i) detect the emergence of the new disease, (ii) characterize the disease (epidemiology, clinical manifestations, severity) and (iii) monitor its evolution.

Benefits of global pandemic influenza surveillance

An influenza pandemic will affect every country. Standardized and coordinated international information sharing is crucial for crisis management at global and national levels. National authorities will need to know how the pandemic is evolving not only in their own country, but also in neighbouring countries and continents. Sharing of information at global level will be a benefit to all. The continual flow and aggregation of information provided by individual countries will contribute to the development of a global picture (see

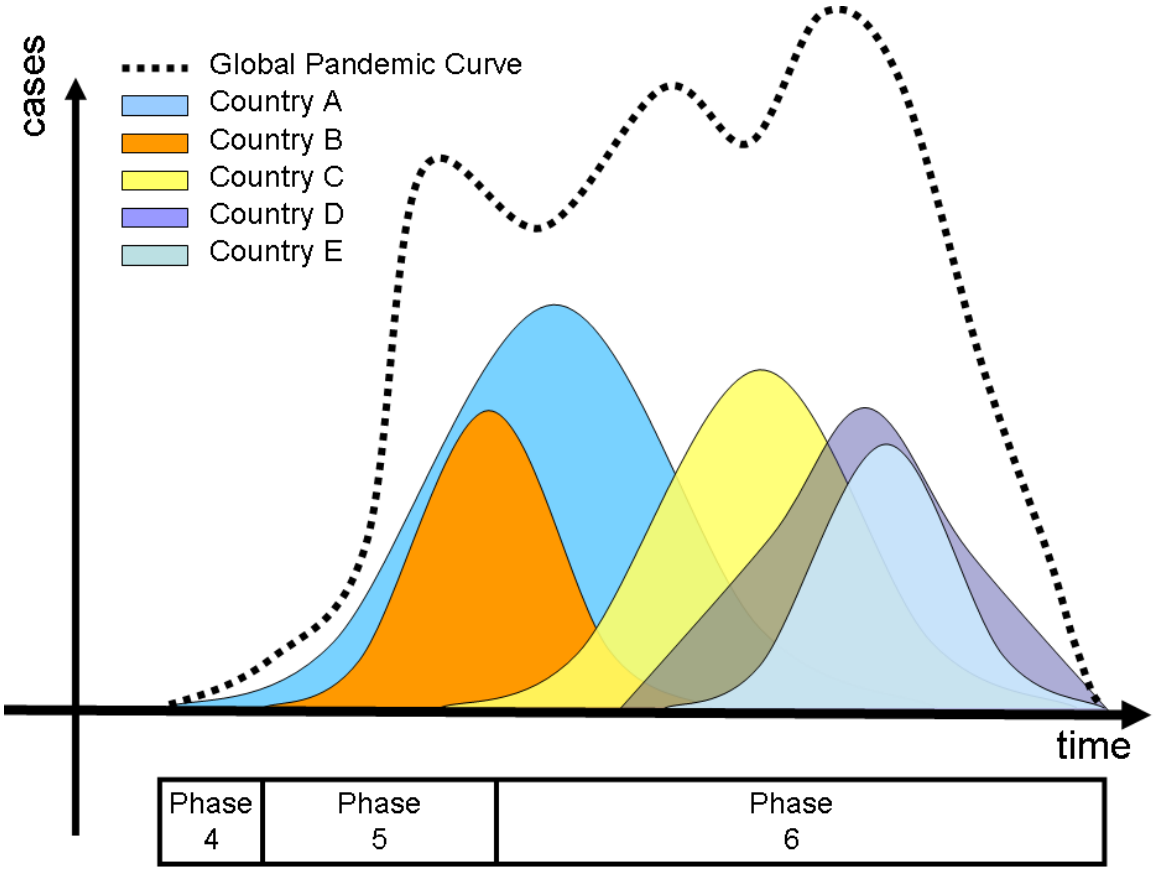
[1] WHO. *Avian influenza:* assessing the pandemic threat. January 2005. WHO/CDS/2005.29. Available at: http://www.who.int/csr/disease/influenza/H5N1-9reduit.pdf Accessed on: 23 June 2008.
[2] Longini IM Jr et al. Containing pandemic influenza at the source. *Science,* 2005, 309:1083–1087.
[3] Ferguson NM et al. Strategies for containing an emerging influenza pandemic in SoutheastAsia. *Nature*, 2005, 437:209–214.

Figure 1) that:

- will result in a rapid accumulation of critical clinical, epidemiological and virological data about the new disease;
- will allow health care providers and public health authorities to modify their strategies for case management, community mitigation, and health resource allocation;
- will disperse the workload among the first affected countries;
- will reduce the impact of inaccurate and unconfirmed rumours;
- will enable WHO to serve as a credible and stabilizing source of information and guidance.

Misinformation or lack of information at global or country level will inevitably result in delays in response, spread of damaging rumours, inadequate resource allocation, misdirected efforts, and ultimately, unnecessary loss of life.

Figure 1 Example Global Pandemic Curve and Pandemic phases



Phase 4	Human to human transmission of an animal or human-animal influenza reassortant virus able to sustain community-level outbreaks has been verified.
Phase 5	The virus has caused sustained community level outbreaks in two or more countries in one WHO Region.
Phase 6	The virus has caused sustained community level outbreaks in at least another country in another WHO Region in addition to the criteria defined in Phase 5.

2. Scope of the document

In December 2007, A global consultation was held to discuss the objectives, critical data elements, feasibility, and outputs of global pandemic influenza surveillance. The outcomes of the consultation were taken forward and further developed by an expert working group to produce the current document . Each surveillance component will be field tested in several countries during seasonal influenza and simulation exercises during 2009. The test results will help to refine this document, whereupon it will be distributed widely.

Purpose of the guidance document

To enable all countries to participate in the global surveillance effort this document outlines the critical information that should be collected during different time periods in the course of an influenza pandemic. This information should be submitted from all Member States beginning with the first recognition of human-to-human transmission of an influenza virus with pandemic potential. WHO will facilitate the construction of a global picture of pandemic activity and will be the primary clearing house for sharing information internationally. Specifically, this document:

- identifies specific information to be collected and reported at different phases of the pandemic;
- gives guidance for reporting information to WHO;
- describes the processes that WHO will use to disseminate critical information and to ensure that it is available to the relevant audience.

Underlying principles

The working group of experts selected the information required for global surveillance. The aim was to identify a minimum set of data which will be feasible to collect and useful to guide countries in managing the pandemic.

An influenza pandemic is an extraordinary event and requires preparation especially for surveillance activities. To the extent possible, the manual does not prescribe new surveillance activities. Rather it attempts to build upon existing or developing surveillance systems and to standardize data collection at global level. This in turn will help ensure that surveillance information will be readily available and useful to public health planners nationally.

Target audience

This document is for use primarily by policy makers and public health professionals at national level who are involved in disease surveillance, outbreak investigation, and information management, specifically dealing with influenza.

3. International Health Regulations (2005)

The International Health Regulations 2005 (IHR) is the international legal framework for public health actions of WHO and all of its Member States[4] to prevent, control and respond to the international spread of disease. The IHR includes a number of rights and obligations of Member States relevant to pandemic influenza, such as: notification, reporting and verification of public health events to WHO (including all cases of new subtype human influenza); measures at international borders, ports and airports, protections for international travellers, required capacities for domestic surveillance and response in all States, and coordinated response to public health emergencies of international concern.

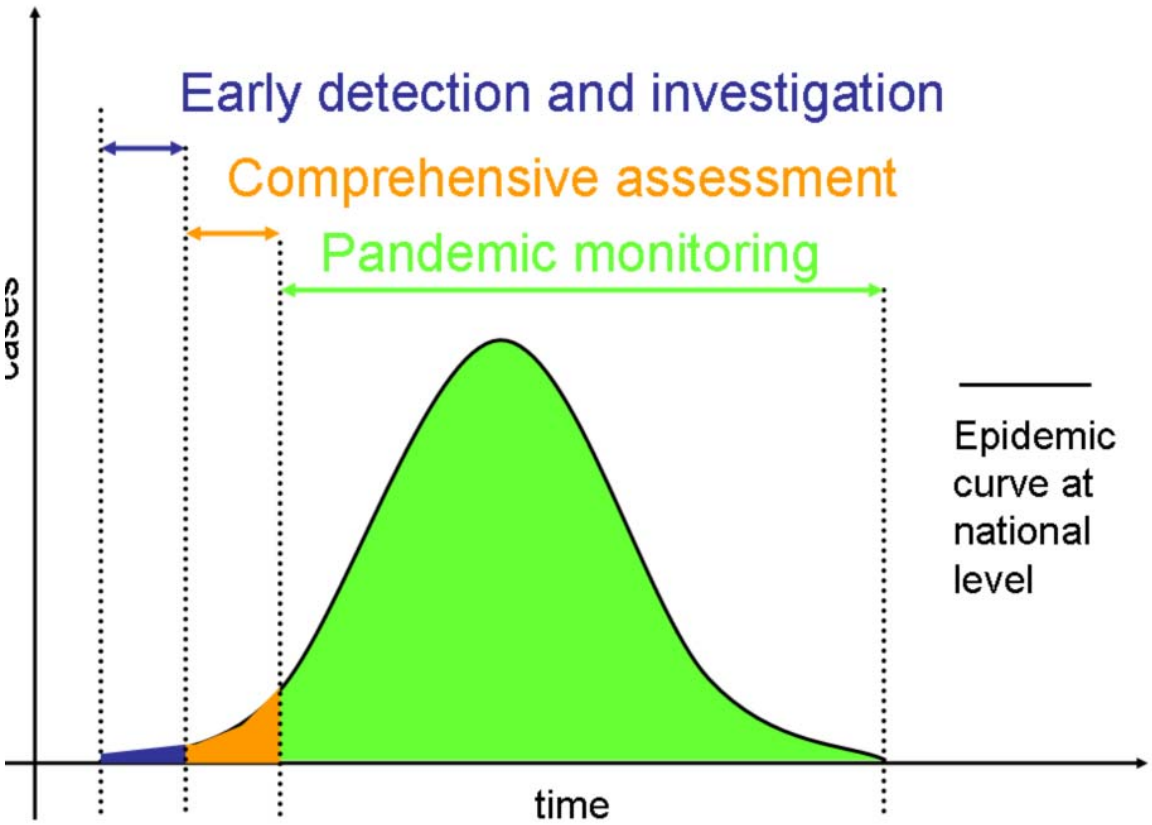
The IHR (2005) also contain functions for WHO concerning international surveillance, assessment and public health response. Once there is credible reason to believe that an animal or human-animal influenza virus has evolved that is capable of sustained human transmission in a community, the IHR (2005) gives the Director-General of WHO the authority to determine that the event constitutes a Public Health Emergency of International Concern (PHEIC). On such occasions, an IHR Emergency Committee will provide its views to the Director-General on Temporary Recommendations for the most appropriate and necessary public health measures to prevent or reduce the international spread of disease and avoid unnecessary interference with international traffic. These Recommendations may include the activation of national pandemic surveillance systems (1) to rapidly detect, characterize and notify additional human clusters, (2) to assess the virological, clinical and epidemiological features of infection by the new virus, and (3) to monitor disease spread and the impact of response measures. Relevant provisions in the International Health Regulations (2005) can be found under Article 5 to 14 and Annex 1 and 2 of the International Health Regulations at http://www.who.int/csr/ihr/IHR_2005_en.pdf.

[4] The States who are parties to the IHR include all 193 WHO Member States, as well as the Holy See. While these are referred to as "States Parties" in the IHR, for ease of reference, this document generally uses the terms States or Member States.

4. Overview of the surveillance components

The critical information needed during the course of the pandemic will vary at different points in time and will be generated by different types of surveillance activities. This document describes three (3) types of surveillance activities or components of pandemic surveillance (Figure 2).

Figure 2 Overview of the three (3) surveillance components at national level



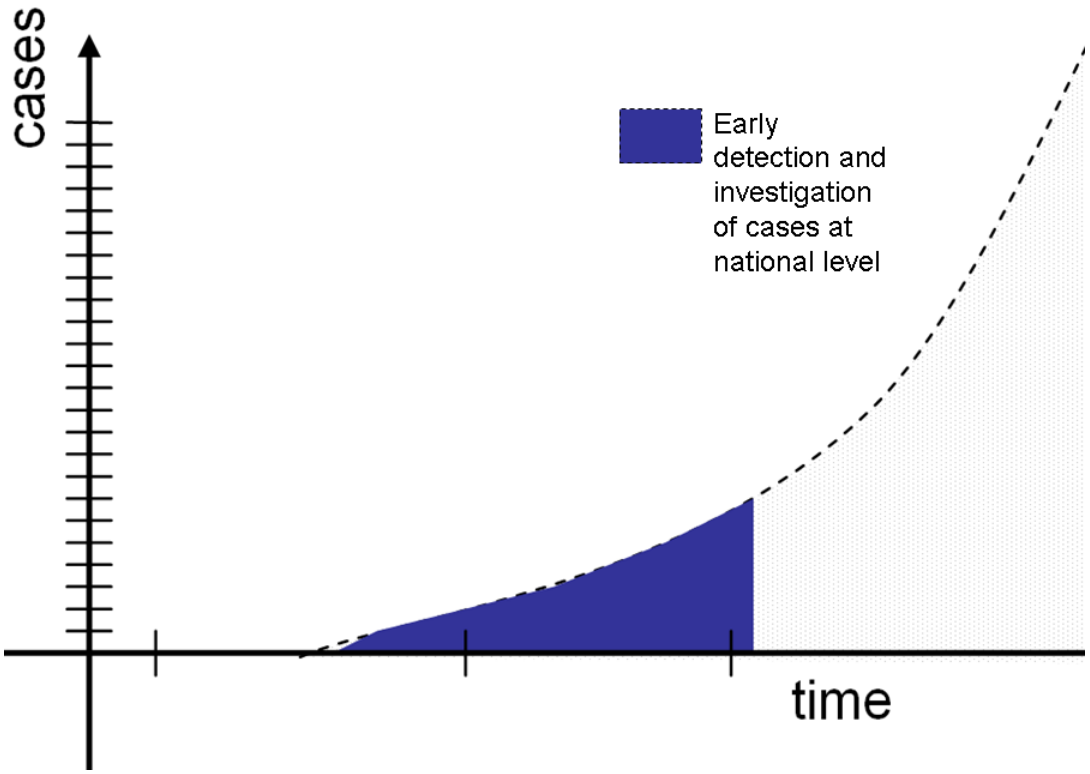
- ***Component 1: Early detection and investigation (*Figure 3*)***

Objective: The objective of this component is to detect and investigate the first evidence of sustained human-to-human transmission of an influenza virus with pandemic potential.

Preparedness: Under the IHR 2005, each country must have, or develop within a limited time period, the public health capacities to detect, investigate, assess, control and report domestically all events involving disease or death above expected levels for the time and place, throughout the country's territory. In addition, countries must have the capacities to do the assessments and notify, report and verify to WHO as required under the IHR.

Benefits: At *global level,* this information will guide decisions about a change in pandemic phase. At *national level* in the affected country: this information will be used to assess the feasibility of rapid containment, and will help to inform recommendations about control activities if containment is unsuccessful. For the non-affected countries, this notification enables government authorities to take necessary and appropriate health measures to get prepared.

Figure 3 Component 1 of global surveillance during a pandemic: "Early detection and investigation"



- ***Component 2: Comprehensive assessment (*Figure 4*)***

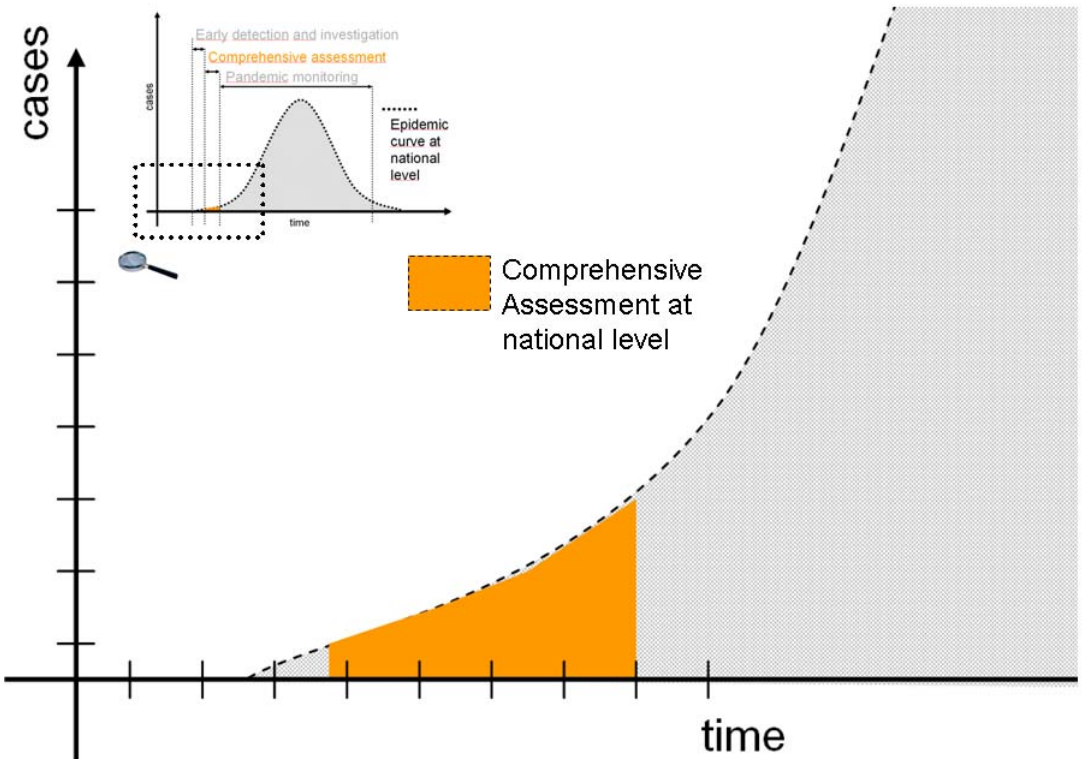
Objective: Once the initial investigation indicates that sustained human-to-human transmission is occurring, comprehensive assessment of 100 of the earliest cases of pandemic influenza will be needed. This information will more accurately characterize the new disease including its clinical characteristics, risk factor information, and epidemiological and virological features.

Preparedness: Collecting these detailed data will require intensive effort on the part of Member States. Trained and equipped teams will be needed. All Member States must include a plan for these investigations in their pandemic plans.

Benefits: At *global level* this information will help determine the composition of a pandemic vaccine. It will also allow WHO to provide initial and updated assessments of the severity of the pandemic. The severity assessment will be helpful to all countries (i) for updating their plans before the arrival of the pandemic, (ii) for benchmarking and indirect measurement of the effectiveness of control measures, and (iii) for communicating with the general public and the media.

At national level this information will be useful to prioritize and scale the interventions, according to the severity of disease and predict evolution of the epidemic.

Figure 4 Component 2 of global surveillance during a pandemic: "Comprehensive Assessment"



- ***Component 3: Pandemic monitoring*** **(Figure 5)**

Objective: This component aims to gather information regularly to monitor the course of the pandemic at global level and answer critical questions such as is the pandemic increasing or decreasing; are new countries or regions affected; is the pandemic over; is a new wave beginning.

Preparedness: Monitoring the course of the pandemic will use existing indicators that are, or soon will be, routinely reported for seasonal influenza. The type of data available for monitoring influenza currently varies widely from country to country. As more countries institute routine respiratory disease surveillance monitoring data will become more complete and standardized, and thus more useful.

Benefits: Regular reporting from countries will make monitoring of the pandemic at *global level* possible. It will also provide reliable information on the evolution of the crisis. At *national level* these data will be important to track the spread of the virus, monitor its rise and fall, and watch for changes. Although not described in this document monitoring could be done at sub-national level using the same indicators.

Figure 5 Component 3 of global surveillance during a pandemic: "Pandemic monitoring"

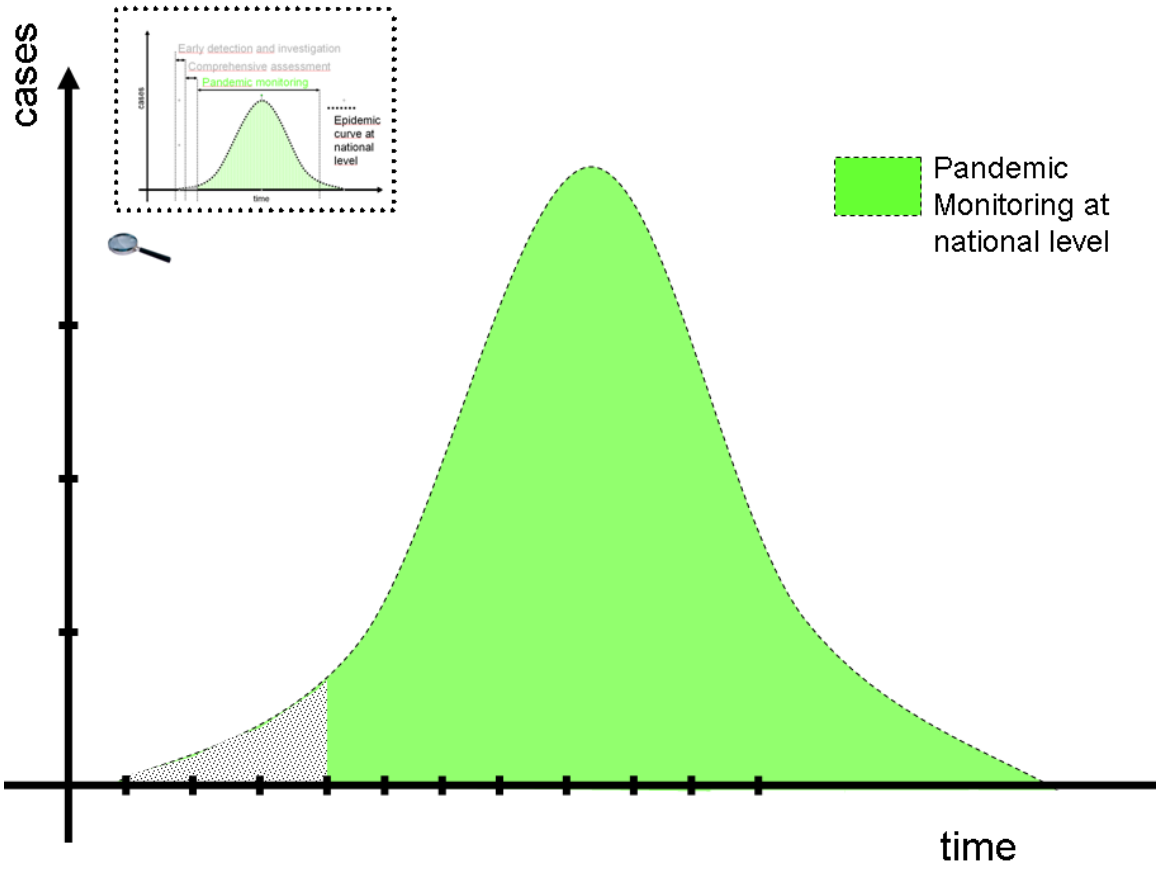


Table 1 Summary of the three components of pandemic surveillance

	Component 1	*Component 2*	*Component 3*
	Early detection and investigation	**Comprehensive assessment**	**Monitoring**
Objective	Detect sustained human-to- human transmission of influenza virus with pandemic potential	Characterize the features of the new disease • virological • epidemiological • clinical	Monitor the disease • geographical spread • trend • intensity • impact
Time frame	Early	Early	Throughout pandemic
Using existing system	Yes: event based system	Probably no: will require preparation	Yes: seasonal influenza system with modifications
Action at national level	• Rapid containment for the first affected country • Alert phase for all other of countries	• Review and revise pandemic plan • Define high risk groups to prioritize interventions	Monitor the situation
Action at global level	• Change the pandemic phase • Deploy support to affected countries	• Change vaccine composition • Provide early assessment of severity and subsequent updates	• Monitor the pandemic • Change the pandemic phase (e.g. end of first wave, end of pandemic)

5. Essential Capacities

The essential capacities for each component will vary and will not all be present in every Member State. The capacity to detect, assess, respond to, and report public health emergencies of international concern, which relates to the first component of pandemic surveillance, is mandated by International Health Regulations for all Member States. In addition, the ability to do adequate case investigations and routine monitoring of respiratory disease activity is a capacity that has value beyond the evaluation and monitoring of influenza virus with pandemic potential. Specific capacities for each component of surveillance include:

Early Detection and Investigation

- A system able to detect and report events that are a potential risk to public health.
- Laboratory capacity to identify influenza viruses with pandemic potential or rapid access to outside laboratory facilities with this capacity.
- Epidemiological expertise to carry out the initial investigation of signal events.
- A national IHR focal point to report public health emergencies of international concern to WHO.
- Outbreak response and pandemic preparedness plans.
- Materials and personnel for rapid containment of outbreaks of influenza with pandemic potential.

Comprehensive Assessment

- Laboratory capacity or access to laboratory capacity for virus culture, polymerase chain reaction (PCR), and serological testing.
- Epidemiological capacity for extended field investigation and detailed analysis of case data.
- Supplies and personnel for a large field investigation involving hundreds of potential cases and contact tracing.
- Communications and data transfer capability.

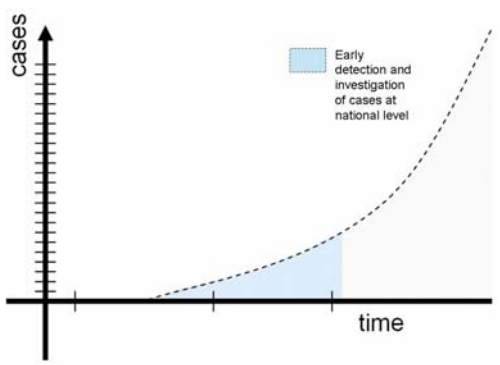
Monitoring

- Routine surveillance for influenza-like illness (ILI) and/or severe acute respiratory illness (SARI).
- Epidemiological capacity for data analysis and interpretation.
- Communication systems for regular reporting of surveillance data internationally.

B Surveillance Components

1. Early Detection and Investigation

1.a. Objectives



The primary goals of early detection and investigation are to document that sustained human-to-human transmission of an influenza virus with pandemic potential is occurring and to provide information for initial risk assessment. Detailed recommendations for outbreak investigation, response, and rapid containment activities are available elsewhere.[5,6]

Specific objectives of the surveillance activity include:

- detection and identification of an influenza virus with pandemic potential;
- confirmation that an influenza virus with pandemic potential has acquired the ability to transmit from person-to-person and to initiate and sustain community level outbreaks;
- description of the early epidemiological, virological, and clinical characteristics of the outbreak;
- estimation of the geographical extent of virus spread to inform containment and control efforts;
- alert other member states of a public health event of international concern or PHEIC.

The first episode of human-to-human transmission resulting in sustained community level transmission is the most crucial. Detailed information both from individual cases and from the investigation itself will be important for making critical decisions about the phase of the pandemic and the extent of containment efforts, and will provide information important for preparations by other Member States that have not yet been affected.

[5] WHO guidelines for investigation of human cases of avian influenza A(H5N1) WHO/CDS/EPR/GIP/2006.4r1. Available at: http://www.who.int/csr/resources/publications/influenza/WHO_CDS_EPR_GIP_2006_4r1.pdf Accessed 23 June 2008.
[6] WHO Interim Protocol: Rapid operations to contain the initial emergence of pandemic influenza. Available at: http://www.who.int/csr/disease/avian_influenza/guidelines/RapidContProtOct15.pdf

This component of pandemic influenza surveillance is closely allied to the notification reporting and verification requirements under the International Health Regulations (IHR), which provide a legal framework to support the technical description specified in the guidance. Using the decision instrument in Annex Two of the IHR, all cases of human influenza caused by a new subtype are to be notified to WHO. WHO has published the case definition to assist such notification (the definition is available at http://www.who.int/csr/ihr/Case_Definitions.pdf).

Equally important in terms of surveillance, Annex Two of IHR requires that all events are notified, even before laboratory confirmation of any new influenza subtype, when they meet at least two of four public health criteria: (1) potential serious public health impact, (2) unusual or unexpected, (3) significant risk of international spread, and (4) significant risk of international restrictions. The characteristics of such notifiable events are described more specifically as they relate to influenza in this section of the manual.

The Global Outbreak Alert and Response Network (GOARN) can be deployed to assist in the initial investigation if requested by the affected country. In addition, WHO has stockpiled antiviral medications that are propositioned for a pandemic response and can be deployed once the presence of sustained human-to-human transmission has been identified and notified.

1.b. Description of surveillance activities

Effective response to an emerging pandemic requires detection in the very earliest stages of the outbreak when the number of cases is small and geographical extent of spread limited.

A sensitive surveillance system capable of detecting small scale, unusual events is necessary to achieve this. In many settings, existing event-based surveillance systems are the primary means for early detection of unusual events, including the emergence of influenza virus with pandemic potential influenza strains.[7] These systems include a broad range of activities such as rumour surveillance, monitoring of media sources, informal community-based reporting networks, the immediate reporting of signal/trigger events by health care workers.[4] The occurrence of certain events or signals/triggers should prompt immediate investigation to inform a risk assessment. Potential outcomes of such an assessment are the decision to notify the event to WHO under Annex Two of the IHR or the consultation with WHO regarding the status of event.

[7] WPRO "A Guide to Establishing Event-based Surveillance" available at: http://www.wpro.who.int/NR/rdonlyres/92E766DB-DF19-4F4F-90FD-C80597C0F34F/0/eventbasedsurv.pdf

Triggers/signals for investigation of possible human-to-human transmission.

The primary focus of early detection is to detect events that may signal human-to-human transmission of an influenza virus with pandemic potential. As new pandemic strains are thought to arise from viruses circulating in animal populations, events related to human infection with animal influenza viruses should also trigger and initial investigation. Specific triggers include:

- clusters[8] of cases of unexplained acute lower respiratory illness;
- severe, unexplained lower respiratory illness occurring in a health care worker who provides care for patients with respiratory disease;
- changes in the epidemiology or mortality associated with the occurrence of ILI or lower respiratory illness in a community, for example, a change in the age distribution of severe lower respiratory illness, an increase in deaths observed from respiratory illness or an increase in the occurrence of severe respiratory illness in previously healthy adults or adolescents;
- persistent changes noted in treatment response or outcome of severe lower respiratory illness;
- a laboratory finding of a strain of influenza with pandemic potential from routine surveillance or other investigation (Note that such a finding will automatically require notification to WHO under Annex 2 of the IHR);
- outbreaks of death or illness in fowl (e.g. poultry or ducks) or other animals (e.g. swine, cats);
- any suspect human case of infection with an influenza virus with pandemic potential.

Data requirements

Following the initial notification of suspected pandemic influenza, Article Six of the IHR requires the affected country to communicate to WHO further information to enable risk assessment, especially to determine if sustained human-to-human transmission is occurring. It is likely that not all the data required for an accurate risk assessment will be immediately available, especially virological data. Early reporting of incomplete data will be more helpful in assessing the likelihood of human-to-human transmission and associated public health risks than late reporting of complete data.

The specific necessary data are summarized below:

- Summary description of the initial outbreak investigation findings including:
    - case finding activities, nature and extent of enhanced surveillance activities;
    - case definition used for case finding and classification, and algorithm for screening;
    - timeline of suspect, probable, and confirmed cases with dates of illness onset within clusters and dates of exposures;
    - best estimates for case fatality ratio and incubation period;
    - testing criteria for cases;
    - results of investigation for related animal outbreaks if any;
    - evidence for human-to-human transmission;
    - geographic extent of investigation and estimation of spread of virus.

[8] A cluster is defined as two or more persons presenting with manifestations of unexplained acute lower respiratory illness with fever (>38ºC) (or who died of an unexplained respiratory illness) are detected with onset of illness in a two-week period and in the same geographical area and/or are epidemiologically linked.

- Copies of all data collection forms for each case containing the following:

  - a unique identifier that links epidemiological information with clinical specimens
  - patient demographic and exposure information
  - pre existing conditions
  - clinical presentation and course (requires follow up of patients)
  - outcome: death, recovery, hospitalization, convalescent, lost for follow up
  - date clinical samples taken and results
  - final status: discarded, suspected, probable, confirmed, lost for follow up.

- Virological characteristics (may come from both national laboratory and WHO Collaborating Centre)

  - name of laboratory and contact details
  - antigenic characterization of the virus
  - antiviral sensitivity.

- Summary description of control measures taken

  - isolation and quarantine measures used;
  - contact tracing and management, including the number of contacts under observation, their clinical status, and the date the last known contact;
  - infection control measures implemented in health care facilities;
  - extent of animal culling, if any;
  - use of antivirals for treatment or prophylaxis;
  - border controls and travel restrictions, if any;
  - risk communication activities;
  - estimates or indicators of effectiveness of containment;
  - lessons learned.

1.c. Reporting to WHO

In line with Article Six (6) of the IHR, countries should notify WHO by the most efficient means of communication available through the WHO IHR focal point and within 24 hours of assessment of the public health information all events which constitute a public health emergency of international concern. Such notifications should include the Office of the WHO Country Representative where one is present. On receipt of such a notification the WHO IHR Contact Points at the Regional Office level will initiate the necessary joint assessment of risk involving the appropriate technical units and levels of the Organization, and, with the WHO Country Office, will continue to be the main channel of communication with the affected state.

Immediately report

- an influenza virus with pandemic potential;
- all acute respiratory events with severe and unusual characteristics even if unsure of agent;
- all acute respiratory events with severe or unusual characteristics and potential for international spread.

WHO will follow the principles of confidentiality as required in the IHR document; note that WHO has greater confidentiality obligations regarding officially reported information than for

unofficial or media reports. This is a strong incentive for States to provide official information to the organization.

Data obtained from the ongoing investigation should be reported as it is being collected to update the initial risk assessment.

If containment is unsuccessful or if the pandemic virus is discovered late and containment is no longer feasible, countries will be asked to report the *first appearance of pandemic influenza* within their borders and to submit data from their comprehensive assessments as described below.

Verification requests

In addition to country-initiated notifications and reports, WHO IHR Contact Points will request that States verify reports WHO has received from non-official sources. Following such a request, the Member State is required to respond within 24 hours and to provide further information as it becomes available in accordance with the section above on data requirements.

Virus sample submission

All virus isolates from human infections obtained as part of the initial assessment should be submitted for further characterization to a WHO Collaborating Centre. For countries without the capacity for virus isolation, clinical specimens from all suspect human cases should be submitted to a WHO Collaborating Centre for virus isolation and characterization. Each sample should be labelled with the same identifying information or number from the case epidemiological and clinical data forms so that virological data can be linked with the other data.

Component 1. Early Detection and Investigation:

KEY POINTS

- *Goal:* detect and confirm sustained human-to-human transmission of an influenza virus with pandemic potential or start of the pandemic.
- *Reporting:* through the National IHR Focal Point to the WHO IHR Contact Point and including the WHO Country Office where applicable
  - First affected country: complete Case Summary Forms and report of investigation.
  - Subsequently infected countries: report first appearance of pandemic virus.
- *Benefits for affected Member State:* joint risk assessment with WHO, data will inform containment efforts, WHO support in risk communications.
- *Benefit at global level:* other Members States are alerted on basis of official information.

2. Comprehensive Assessment

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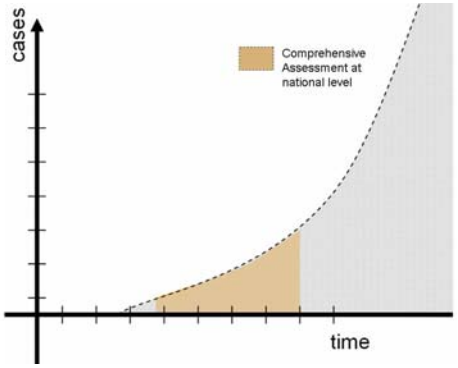
2.a. Objectives



The primary goal of the comprehensive assessment is to characterize the new pandemic at an early stage to facilitate more effective response both nationally and internationally. This information will allow WHO to provide an **early assessment of the severity of the pandemic**. The information from the comprehensive assessment will be critical to policy makers in the affected country for making decisions about pandemic mitigation strategies, to health care providers for treating ill persons and to the general public for reducing their risk of infection and minimizing damaging rumors.

Specific objectives include:

Characterize the epidemiological features

- Characterize the **epidemiological features** of the outbreak that distinguish it from seasonal influenza (e.g. epidemiological curve, age specific attack rates, age specific mortality rates, attack rates in health care workers).
- Describe the **impact** of the illness on the community compared to mild seasonal influenza (e.g., attack rates for symptomatic illness and severe disease).
- Describe **transmission** characteristics (e.g. epidemiological curve, incubation period, generation time, reproductive number, R_0).

Characterize the clinical features of the illness to inform clinical management, surveillance and control.

- Describe the clinical presentation and spectrum of the illness to facilitate development of effective treatment protocols.
- Refine the case definition for use in surveillance and early detection in subsequently infected countries.
- Define the population at highest risk for severe outcome to enable efficient resource targeting (e.g. pregnant women).

Characterize the virological features of the new strain.

- Characterize the antigenicity of the virus to guide the development of vaccines and diagnostic tests.
- Assess the antiviral susceptibility of the virus to direct treatment decisions.

The emergence of a new virus capable of sustained human-to-human transmission is a continuous threat. The precise characteristics of neither the virus nor the location and timing of its emergence will be known in advance. Experience with past pandemics has shown that not all viruses capable of pandemic spread have the same degree of virulence and that the associated health impact may vary significantly (**Table 2**). In addition, key characteristics used to describe transmission dynamics such as the reproductive number (R_0) and measures of severity such as the case fatality ratio may also vary depending on the country and season of the year in which they are studied. Therefore, data will be required from multiple places over time as the pandemic emerges and spreads in order to fully understand its epidemiological and clinical characteristics. The data collected as part of comprehensive assessments must be carefully interpreted in the context in which they were gathered. This will require reporting of detailed information on how assessments were carried out, including methods for case finding and selection.

Table 2: 20th Century pandemics: comparison of main characteristics[9]

Pandemic (date)	**Virus type**	**Estimated reproductive number (R_0)**	**Estimated case fatality ratio**	**Estimated attributable excess mortality worldwide**	**Age groups most affected** (simulated attack rates)
1918–1919	H1N1	1.54–1.83	2–3%	20–50 million	Young adults
1957–1958	H2N2	1.5	<0.2%	1–4 million	Children most affected
1968–1969	H3N2	1.28–1.56	<0.2%	1–4 million	Across all age groups

Planning resource requirements and defining strategies for pandemic control are based on data from previous pandemics or seasonal influenza outbreaks. The first affected countries will play an important role by providing crucial information on the new disease that will enable the rest of the world to better prepare.

[9] Source: ECDC website accessed on 18th March 2008: http://www.ecdc.europa.eu/Health_topics/Pandemic_Influenza/stats.html

Some of the observed characteristics of the pandemic disease will vary from country to country (e.g. age specific mortality rates). In addition, it is possible that the virus will evolve as it spreads. Therefore, the comprehensive assessment should not be limited only to the first affected countries during the first wave. Comprehensive assessments should be carried out by all countries to improve our understanding of the pandemic and refine interventions during its course.

2.b. Description of surveillance activities

The comprehensive assessment is an intensive data gathering activity which may coincide with other pandemic response and control activities. Carrying out both activities at the same time has the potential of seriously straining already overstretched resources. Member States are urged to do advance planning and resource allocation, to train teams in investigation techniques, and to designate individuals responsible for the comprehensive assessment. Member States should assess how best to collect the information described in this document. at country level.

The comprehensive assessment will require a combination of different approaches (case based data collection, community and cluster investigations) to collect clinical data on at least 100 confirmed cases, to obtain epidemiological information on the affected community and to collect virological samples.

Member States will have varying capacity to carry out the comprehensive assessment; however, data gathered on the early cases even with limited field investigation will still be useful for guiding subsequent control, management, and mitigation activities. The earliest affected countries are encouraged to request support from the WHO GOARN for human resources and technical expertise.

Member States also will have varying capacity for testing clinical specimens and antigenic characterization of influenza viruses. All countries, including those with capacity for testing, should submit virus isolates and/or clinical specimens for further evaluation and confirmatory testing to a WHO Collaborating Centre.

Data requirements

Countries are requested to provide **four types of information:**

- epidemiological characteristics
- clinical characteristics
- virological characteristics
- methods used for investigation, case finding, and specimen and data collection (e.g. case definition, sampling methods, selection of sites).

The specific data is described below:

1. Epidemiological characteristics:

Epidemiological features that distinguish this outbreak from seasonal Influenza or another epidemic that recently affected the country (e.g. dengue, cholera):

- total number of cases (suspect, confirmed) and deaths;
- distribution of cases and deaths by age group
- attack rate by age group;
- case fatality ratio;
- epidemic curve for the first 4 weeks of the pandemic;
- number of cases in health care.

Impact of the illness in the community:

- qualitative assessment of severity by comparing the pandemic situation with a typical influenza season or another epidemic that recently affected the country ;
- rate of symptomatic illness;
- proportion of cases with severe illness;
- attack rates by geographic location and/or mapping of most affected geographic locations.

Transmission characteristics:

- incubation period
- period of infectiousness (viral shedding)
- reproduction number (R_0), generation time, serial interval.

2. Clinical characteristics: Database of information for 100 cases

Member States will be requested to provide information for 100 laboratory confirmed cases, similar to data outlined in Component 1 (Early Detection and Investigation) using the WHO Pandemic Influenza Case Summary Form.. For each person, clinical information and samples will be collected initially and two weeks later..

It is likely some clinically ill persons will have other respiratory infections and not pandemic influenza. Therefore, countries are encouraged to collect data for more than 100 persons if possible. This will increase the likelihood of achieving the goal of 100 laboratory-confirmed cases of pandemic influenza and the ability to analyse information in a meaningful way.

The WHO Pandemic Influenza Case Summary Form will include the following elements:

- a unique identifier that links epidemiological information with clinical specimens
- patient demographic and exposure information
- pre existing conditions
- clinical presentation and course (requires follow up of patients)
- outcome: death, recovery, hospitalization, convalescent, lost to follow up
- clinical samples obtained and results
- final case classification: discarded, suspected, probable, confirmed.

For the first comprehensive assessment in each country, all viruses isolated from these 100 cases should be submitted to a WHO Collaborating Centre for further characterization.

If virus isolation facilities are not available, clinical specimens should be submitted from probable cases. Submission should occur continuously as specimens are collected and viruses are isolated and not wait until completion of the comprehensive assessment component. All specimens should be labelled with an identifier that links it to the epidemiological and clinical data for the case.

3. Virological characteristics: Virological Summary Form

This form is being developed by a working group of national influenza centres and will be made available to laboratories after field testing is completed.

4. Methods used for data collection

A report should be prepared describing the investigation methods used to collect information for the comprehensive assessment including:

- case definitions for suspect and probable cases;
- sources of information;
- demographic data;
- methods for information gathering, e.g. cluster based survey or community based approaches;
- potential difficulties or bias.

Although a written report is required, qualitative information sharing and direct discussions between countries and WHO are encouraged. This will help ensure that the interpretation of data includes the country's perspective and facilitate sharing of non quantifiable information.

2.c. Reporting to WHO

There will be a critical need for these data at the start of the pandemic from the first affected countries.. Data (even if incomplete) should be reported by the quickest means possible. Reports should be made on a **weekly** basis during the **first four weeks** after initiation of the comprehensive assessment. An online data entry tool is under development.

Countries that continue to collect detailed epidemiological and clinical information after the first four weeks or after the first 100 cases are requested to send additional updates to WHO as they become available.

Depending on the course of events, WHO at some point during the pandemic may announce that detailed case based data reports are no longer needed from newly affected countries if the information available is sufficient to enable an effective response in all settings.

Component 2: Comprehensive Assessment

KEY POINTS

- *Goal:* Provide accurate description of epidemiological, clinical and virological characteristics of the emerging pandemic.
- *Reporting:*
  - epidemiological data
  - clinical data
  - virological characteristics
  - investigation methods.
- *Benefit for Member States:* assess the severity of the event and guide national control activities.
- *Benefit at global level:* inform pandemic vaccine composition; provide early assessment of severity; - update response plans and tailor control measures to the severity of the event.

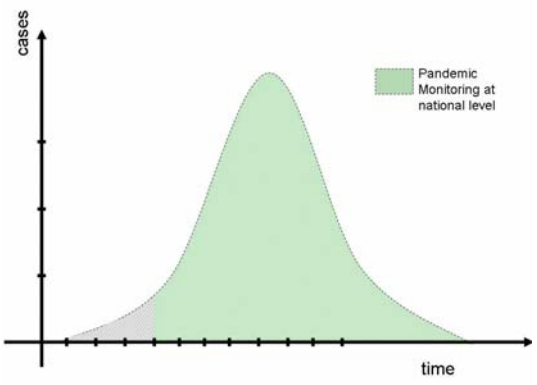
3. Monitoring

3.a. Objectives

The primary goal of the monitoring component is to track the course of the pandemic.

Specific objectives include:

- track the geographical spread of the virus globally
- track the trend of disease occurrence as it rises and falls
- track the intensity of transmission (e.g. how is the population affected; how many cases and deaths)
- track the impact of the pandemic on health care infrastructure
- monitor for changes in the antigenicity and antiviral sensitivity of the virus.



Complete reporting from all Member States will greatly improve the value of these data. This in turn will lead to as accurate a picture of the progress of the pandemic as possible. In addition, some changes in the epidemiological characteristics of the pandemic may only be detectable with large data sets derived from a global perspective. Complete and timely data from all Member States will facilitate early detection and characterization of these changes.

3.b. Description of surveillance

Monitoring the progress the pandemic is similar to the monitoring of seasonal influenza activity with some slight modification. Monitoring of the pandemic must take into account (i) the difficulty of gathering reliable numbers of cases and deaths during a crisis situation; this difficulty has been noted by many countries including those confronted by the 2003 SARS outbreak and (ii) the wide variation in the types of data currently being collected by Member States.

Therefore, the monitoring component will include two types of data reporting:

- The first is required of all Member States. A general interpretation of a variety of information sources will be made by the Ministry of Health. It is a subjective estimate of the geographical spread, the trend of cases, the intensity of disease, and the impact on the health care system.
- The second type will be requested of countries with established surveillance systems. These data will be numerical in nature and will be derived from existing respiratory disease, influenza, or mortality surveillance systems.

Currently, surveillance for seasonal influenza is not standardized from country to country, although efforts are under way to accomplish this. Nor is the capacity to do routine surveillance the same everywhere. Standard manuals for influenza surveillance are available or being drafted by all WHO Regional Offices. Member States are urged to follow the guidelines to improve their respiratory disease surveillance capacity. This in turn will lead to a better understanding of the epidemiology of seasonal influenza in their countries and assist pandemic preparedness efforts. Member States that currently do not do influenza or

respiratory disease surveillance are encouraged to consult their respective WHO Regional Offices for guidance and assistance in developing such surveillance. Respiratory disease is a major source of morbidity and mortality globally and data from routine surveillance can be used to describe country specific patterns of transmission, disease burden, seasonality, risk groups, and will ultimately be a useful tool for tracking pandemic influenza.

Data requirements

Data to be reported by all countries on a weekly basis

The following reports are intended to be within the capacity of all Member States. They are based upon the interpretation of a wide variety of information sources as described below.

- **Activity**

  Activity can be indicated by any of the following: laboratory confirmed case(s) of influenza, or evidence[10] of increased or unusual respiratory disease activity
  - *yes*
  - *no*
  - *no information available* for this week.

- **Geographic spread**

  Geographic spread refers to how many areas are reporting the disease activity.
  - *localized: limited to one area of the country only*
  - *regional: appearing in multiple areas representing less than half of the area of the country (or reporting site)*
  - *widespread: appearing in multiple areas representing more than half of the area of the country (or reporting site)*
  - *no information available: no information available for the previous 1 week period.*

- **Trend**

  Trend refers to changes in the level of respiratory disease activity compared to the previous week.

  - *increasing:* evidence that the level of respiratory disease activity is increasing compared to the previous week;
  - *unchanged:* evidence that the level of respiratory disease activity is unchanged compared to the previous week;
  - *decreasing:* evidence that the level of respiratory disease activity is decreasing compared to the previous week;
  - *no information available.*

- **Intensity**

  The intensity indicator is an estimate of the overall level of respiratory disease activity in the population.

  - *low or moderate :* normal or slightly increased proportion of the population is currently affected by respiratory illness;

[10] *Evidence can be based on any or all of the following: data from sentinel sites, data on school or work absenteeism related to respiratory disease, data regarding use of pharmaceuticals for symptomatic relief of respiratory disease, data from outpatient or emergency department visits for respiratory complaints, data from registrations on death due to respiratory disease, informal reports from district health authorities or health care providers, or other similar information sources.*

- *high:* a large proportion of the population is currently affected by respiratory illness;
- *very high:* a very large proportion of the population is currently affected by respiratory illness;
- *no information available.*

- **Impact**

  Impact refers to the degree of disruption of the health care infrastructure due to influenza.

  - *low:* demands on health care infrastructure are not above usual levels;
  - *moderate:* demands on health care infrastructure are causing some stress to system above usual levels, but still below maximum capacity;
  - *severe:* demands on health care infrastructure exceeding capacity to provide care;
  - *no information available.*

Data to be reported by countries with formal surveillance systems:

- data from Influenza Like Illness (ILI) -sentinel sites or outpatients visits

  - number of ILI cases reported in the last 1 week period by age group
  - number of total outpatient visits for all causes
  - number of reporting sites.

- data from Severe Acute Respiratory Illness (SARI) - sentinel surveillance sites or inpatient facilities

  - number of new SARI cases admitted in the last 1 week period by age group
  - number of total admissions (from same facilities as number of SARI cases reported)
  - number of SARI-related deaths by age
  - number of SARI sentinel sites reporting.

- data on mortality

  - number of deaths related to acute respiratory disease by age group
  - population covered.

Data from National Influenza Centres (NICs) or reporting laboratories:

- number of specimens collected for influenza testing
- number of specimens tested that are positive for influenza by subtype.

3.c. Reporting to WHO

Epidemiological data will be entered online in FluID. Virological data will be entered online through the FLUNET. Data entry forms are provided by WHO. For further information please contact WHOinfluenza@who.int

Virus sample submission

Virus sample submission during pandemic phase 6 will be similar to seasonal influenza surveillance procedures. On a routine basis, each NIC will submit at least 10 specimens per week. In addition, clinical specimens or viruses from an outbreak investigation should be submitted from the beginning, middle, and end of the outbreak. Any virus isolates which

cannot be sub-typed or which are associated with unusual epidemiological/clinical observations should be submitted.

Time frame

Monitoring of influenza activity during the pandemic is an extension of routine monitoring for seasonal influenza. Monitoring data will be reported on **a weekly basis**. During the pandemic, the display of information on the WHO Global Influenza Monitoring (GIM) web site will be modified to reflect the presence of pandemic influenza in a country so that the progress of the pandemic can be tracked. This website will be available after field testing of the components of the global surveillance system is completed.

Component 3: Monitoring

Key Points

- *Goal:* track the course of the pandemic.

- *Reporting:*
  - activity
  - geographic spread
  - trend
  - intensity
  - impact on health care system
  - quantitative data on cases and deaths of ILI and/or SARI if possible.

- *Benefit for Member States:* modify mitigation and management strategies in response to changes in the course of the pandemic.

- *Benefit at global level: d*ecide on changes in pandemic phase; anticipate second wave.

Table 3 Information for action: summary of the objectives and associated actions for the pandemic surveillance components

Objective:	*Action:*
Early Detection and Investigation	
Detect influenza virus with pandemic potential	Launch investigation for evidence of sustained human-to-human transmission
Document human-to-human transmission	Determine if influenza virus with pandemic potential the cause; if so conduct assessment and decide if rapid containment appropriate.
Describe early pandemic characteristics	Refine case management and control measures; Provide vaccine strain candidate.
Estimate geographic extent	Plan and adjust extent of rapid containment measures
Alert Member States	Notify IHR focal point, Request assistance and support if needed
Comprehensive Assessment	
Describe epidemiological characteristics	Assess severity and initiate appropriate community mitigation measures
Describe clinical characteristics	Refine definitions for case finding, target treatment and control measures to high-risk groups
Describe virological characteristics	Adapt recommendations for use of antiviral drugs. Submit samples and isolates to WHO Collaborating Centre for confirmation and characterization.
Monitoring	
Track activity	Adjust mitigation and control measures as milestone events are reached
Track geographical spread	
Track trend of pandemic	
Track impact of pandemic	Adjust allocation of health care resources, initiate additional management strategies as indicated
Track intensity of transmission	
Monitor changes in antigenicity and antiviral sensitivity	Adjust use of pharmaceutical interventions

C Additional considerations related to global surveillance during an Influenza pandemic

1. Surveillance data from rapid containment activities

The rapid containment strategy aims to stop the development of pandemic influenza when it is initially detected and before the virus has been able to spread more widely. The geographically-based strategy includes 1) creation of a Containment Zone around the initial cluster of cases where widespread antiviral medications and public health measures such as movement restriction and social distancing are used and 2) creation of one or more Buffer Zones outside of the Containment Zone that are "at increased risk" for new cases of pandemic influenza to occur.

Surveillance will be an integral part of rapid containment to monitor disease activity and the evolution of the outbreak, evaluate the effectiveness of the containment measures, guide decisions to continue, modify or end the containment operation, and understand the key parameters of the pandemic virus. At a minimum, aggregated data should be collected and reported daily during the containment operation for the Containment and Buffer Zones including:

- number of hospitalized cases
- number of outpatient cases
- number of pneumonia or other severe cases
- number of influenza-related deaths
- geographic map of cases.

The concentration of cases in the Containment Zone provides an important opportunity to determine more detailed information about the epidemiological, clinical and virological characteristics of the emerging pandemic virus. However, collection of these data cannot compromise the primary goal of stopping the spread of the emerging pandemic and monitoring that effort. If resources are available then the approach outlined in the Comprehensive Assessment component should be used.

2. Additional Investigations

If rapid containment efforts prove ineffective and circulation of the pandemic influenza virus becomes established, it will be important to continue to monitor the behaviour of the virus in the population. Certain events noted during any of the ongoing surveillance activities described in this document should trigger an investigation. Results of these investigations will be of great value to both the local and global management of the pandemic and should be shared with WHO in a timely manner.

Examples of potentially important signal events that should be investigated include:

- changes in the age distribution of cases or age-specific mortality rates;
- changes in the response to clinical management, including a change in response to antiviral treatment or prophylaxis;
- changes in the clinical presentation;
- changes in the antigenicity of the virus either in the laboratory or suggested by increasing numbers of cases occurring in vaccinated individuals;

- changes in laboratory markers of antiviral sensitivity.

Clinical or virological samples from these investigations should be submitted to a WHO Collaborating Centre along with reports of investigation findings.

In addition, countries and organizations with greater capacity for scientific investigation will be expected to assess and report their findings regarding other important pandemic related issues such as:

- optimum case management
- age specific mortality rates
- risk factors for severe disease and poor outcome
- incubation period
- carefully designed studies of transmission characteristics including R_0, period of infectiousness, etc
- mode of transmission
- antiviral sensitivity
- viral antigenicity
- effectiveness of mitigation measures
- development and evaluation of tests for the pandemic virus
- duration of survival of the pandemic virus in the environment
- evaluation of infection control methods
- defining the primary mode of transmission
- models of transmission dynamics.

Results of these studies will help refine appropriate and effective management and control strategies. While WHO respects the rights of investigators to publish their results in peer reviewed journals, investigators are strongly encouraged to report findings to WHO prior to publication so that all Member States can be given appropriate guidance.

3. Data analysis

In addition to the data analysis done in country, WHO will convene a special Virtual Network of experts to evaluate, analyse, and interpret submitted data. This network will convene on a regular basis with additional special sessions as needed during the pandemic. The findings of this network will be made available to Ministries of Health of Member States through the GIM web site.

4. Information Dissemination

Reported information, interpretations, and summaries of the current knowledge about the pandemic will be displayed or linked through the GIM web site. The GIM will be updated with new information regularly and will graphically display information reported by Member States. It will contain links to other important sites that contain specific information and advice regarding the pandemic including:

- IHR Event Information site for National IHR Focal Points
- Disease Outbreak News
- Travel Advice web site
- World Epidemiological Report (WER)
- WHO regional office web sites
- National reporting web sites.

WHO will also publish frequent press releases with updated information.

5. Ethical issues - confidentiality and data ownership

Ethical obligations

Accurate, timely, and complete sharing of data are indispensable for public health action essential for containment, control and mitigation of a pandemic. Knowledge gained from countries affected early in the course of the pandemic will guide response in countries affected later in the pandemic. The experience of SARS demonstrated that international response and open communication can lead to effective disease control. The timely and transparent reporting from countries with limited resources will also facilitate the international response and support to those countries and will ultimately provide the best opportunity for containment and control of an emerging pandemic.

Countries not only have a moral obligation to share such information and lessons learned but are required under international law to report events of international concern to the international community. Governments also have a responsibility to disseminate information to their own people. Part of effective pandemic preparedness is an effective communications strategy. Communications plans need to include strategies for notifying the international community, reporting data to national policy makers, and providing data and health promotion messages to the health care community and population at large.

Confidentiality

All patients have a right to privacy and confidentiality. Health information collected or received by WHO that refers to an identified or identifiable person will be kept confidential except to the extent necessary to disclose or transmit it for public health purposes. Country specific summary data will be displayed on public websites as reported by the member states.

Data ownership at international level

It is understood that the data collected by WHO during pandemic is primarily for public health purposes for the benefit of all Member States. A review of different potential uses of this data will be organized by WHO to further discuss data handling at international level, during and after the pandemic.

Useful References:

- WHO guidelines for investigation of human cases of avian influenza A(H5N1) WHO/CDS/EPR/GIP/2006.4r1. Available at: http://www.who.int/csr/resources/publications/influenza/WHO_CDS_EPR_GIP_2006_4r1.pdf Accessed 23 June 2008.

- Ethical considerations in developing a public health response to pandemic influenza. WHO/CDS/EPR/GIP/2007.2. Available at: http://www.who.int/csr/resources/publications/WHO_CDS_EPR_GIP_2007_2c.pdf

- Collecting, preserving and shipping specimens for the diagnosis of avian influenza A(H5N1) virus infection. WHO/CDS/EPR/ARO/2006.1. Available at: http://www.who.int/csr/resources/publications/surveillance/CDS_EPR_ARO_2006_1.pdf

- WHO Interim Protocol: Rapid operations to contain the initial emergence of pandemic influenza. Available at: http://www.who.int/csr/disease/avian_influenza/guidelines/RapidContProtOct15.pdf

- Recommendations and laboratory procedures for detection of avian influenza A(H5N1) virus in specimens from suspected human cases. Available at: http://www.who.int/csr/disease/avian_influenza/guidelines/RecAIlabtestsAug07.pdf

- The role of National Influenza Centres (NICs) during Interpandemic, Pandemic Alert and Pandemic Periods. Available at: http://www.who.int/csr/disease/avian_influenza/guidelines/RoleNICsMayf.pdf