



The role of National Influenza Centres (NICs) during Interpandemic, Pandemic Alert and Pandemic Periods

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INTRODUCTION

National Influenza Centres (NICs) are the backbone of the WHO Global Influenza Surveillance Network (GISN). Since its establishment in 1948, the GISN has worked to protect global public health by updating seasonal influenza vaccine compositions, and by functioning as a global alert mechanism for the emergence of influenza viruses with pandemic potential. As a result, the GISN has contributed greatly to the understanding of influenza epidemiology.

Within individual countries, the NIC is likely to represent the primary source of expertise in surveillance and response to epidemics and pandemics of influenza. Consequently, the triggering of many of the well-planned interventions described in national influenza pandemic preparedness plans will depend upon its effective functioning. At present there are 118 NICs in 89 countries officially designated by national authorities and recognized by WHO.

The role of NICs in conducting seasonal influenza surveillance and supporting WHO recommendations on annual vaccine composition during the **Interpandemic period** have already been clearly outlined in the WHO Terms of Reference (TORs) for NICs. During this period, NICs collect specimens or virus isolates from subnational laboratories and conduct preliminary analysis. Representative virus isolates are then selected and shipped to the WHO collaborating centres (WHOCCs) for reference and research on influenza for advanced antigenic and genetic analysis. Based on the results of this, WHO makes an annual recommendation on influenza vaccine composition. NICs also alert WHO to unusual outbreaks of influenza or influenza-like illness, and to the detection of non-subtypable or low-reacting virus isolates using WHO diagnostic reagents provided through the GISN. These clearly outlined functions during the Interpandemic period serve to link together individual NIC activities under the umbrella of global influenza surveillance.

However, since the early 2004 avian influenza A/H5N1 outbreak in Asia, awareness of the threat of an influenza pandemic has significantly increased. In order to assist Member States in the development of comprehensive national pandemic preparedness

plans, WHO published its revised influenza preparedness plan in early 2005¹ along with a number of other important documents.^{2,3,4,5} As a result, the different phases of influenza pandemic preparedness have been redefined and recommendations made on the national measures required. However, the current WHO TORs do not explicitly deal with the specific roles of NICs during all the different periods of pandemic preparedness. Although many NICs have made significant progress in preparing for a pandemic, most do not have sufficient experience of the steps required to deal with influenza outside its seasonal context. To address this, the WHO Global Influenza Programme, jointly with NICs and WHOCCs, has developed the current document to:

- provide guidance to national authorities on how to properly integrate the key component of laboratory-related activities into the national influenza pandemic preparedness plan and other national plans; and
- define the role of NICs and the recommended actions they should take during the different periods of influenza pandemic preparedness.

This document is not intended to replace the existing TORs. Instead it provides complementary recommendations to NICs as the main technical resource and reference point for national authorities on all issues related to virological surveillance and laboratory diagnosis of human influenza infection. Because the objectives and actions of the NIC at different pandemic preparedness phases are closely linked to the same periods defined in the WHO influenza preparedness plan, the recommendations in this document are divided as follows:

- During the **INTERPANDEMIC PERIOD** as part of routine seasonal influenza surveillance, NICs should always be alert to non-subtypable or low-reacting virus isolates using the WHO diagnostic reagents provided through the GISN. NICs should assist national authorities in properly integrating laboratory-related components into the framework of national pandemic preparedness plans; strengthen NIC capacity to prepare for the Pandemic Alert period; and establish intersectoral collaboration.
- During the **PANDEMIC ALERT PERIOD** NICs should be able to detect new subtype influenza infection in humans as early as possible, and assist national authorities in the development, amendment and implementation of the national preparedness plan. NICs should also take responsibility for assisting WHO in related public health activities, including prototype pandemic vaccine strain selection, review

¹ WHO global influenza preparedness plan. *The role of WHO and recommendations for national measures before and during pandemics*. Geneva, World Health Organization, 2005 (WHO/CDS/CSR/GIP/2005.5).

² WHO checklist for influenza pandemic preparedness planning. Geneva, World Health Organization, 2005 (WHO/CDS/CSR/GIP/2005.4).

³ World Health Assembly resolution (WHA59.2) on application of the International Health Regulations (2005) to strengthen pandemic preparedness and response.

⁴ WHO pandemic influenza draft protocol for rapid response and containment. May 2006 (under revision). Updated version will be available at:
http://www.who.int/csr/disease/avian_influenza/guidelines/draftprotocol/en/index.html

⁵ WHO strategic action plan for pandemic influenza 2006–2007. Geneva, World Health Organization, 2006 (WHO/CDS/EPR/GIP/2006.2).

and update; pandemic risk assessment; diagnostic reagents and protocols development, validation and update; and antiviral susceptibility monitoring. NICs should also build in surge capacity to meet challenges such as inputting large numbers of specimens for diagnosis under time pressure during this period.

- During the **PANDEMIC PERIOD** NICs in countries not yet affected should maximize surveillance to detect the start of the pandemic as early as possible in order to trigger relevant and timely national interventions. In affected countries, NICs should review and adjust the objectives of virological surveillance from early detection of each case to monitoring the progression of the pandemic, while maintaining adequate surveillance to ensure the monitoring of antigenic drift, antiviral susceptibility, and virulence in the pandemic virus. In countries with subsided epidemic waves, NICs should review and rebuild capacity for the early detection of any subsequent waves.

In order to further match individual NIC *objectives* and *actions* with the WHO recommended national measures, the above sections have also been divided into the same five categories as the WHO plan, namely:

- planning and coordination;
- situation monitoring and assessment;
- prevention and containment;
- health system response; and
- communications.

In practice there is likely to be great variation from country to country in the capabilities of NICs and the roles they undertake. Ultimately, the fulfilment of the WHO TORs and the implementation of the recommendations made in each of these areas will depend largely upon the commitment of national authorities and upon available resources.

The recommended actions are intended to continue after up-scaling to a higher phase unless they are superseded by actions in the higher phase. If up-scaling skips a phase, actions in the skipped phase should also be implemented, unless they too are superseded by actions in the higher phase.

INTERPANDEMIC PERIOD

- Phase 1** – Risk of human infection with new influenza subtypes considered to be none or low
- Phase 2** – A circulating animal influenza subtype virus poses a substantial risk of human disease

OVERARCHING GOALS

- Phase 1** – Strengthen influenza pandemic preparedness at the global, regional, national and subnational levels.
- Phase 2** – Minimize the risk of transmission to humans; detect and report such transmission rapidly if it occurs.

PLANNING AND COORDINATION

NIC OBJECTIVES

1. To ensure proper integration of laboratory-related components into the framework of national pandemic preparedness.
2. To build NIC capacity to ensure the early detection of human cases of new subtype influenza infection.
3. To establish mechanisms for intersectoral collaboration, including the sharing of specimens/virus isolates and information.

NIC ACTIONS

1. Participate in national pandemic planning, with representation on relevant national committees.
2. Provide national authorities with technical guidance on influenza virological surveillance and information on the GISN to ensure that national efforts are part of the global agenda.
3. Develop standard procedures for the rapid sharing of specimens/virus isolates and relevant information among national authorities, the NIC, subnational influenza laboratories and laboratories within health-care facilities.
4. Develop standard procedures for fast information exchange and technical collaboration with other sectors, including veterinary laboratories.
5. Provide regular guidance and training to subnational laboratories involved in influenza surveillance and diagnosis to ensure that basic laboratory capacity is in place.
6. Develop surge-capacity plans in response to possible needs during the Pandemic Alert period.

7. Participate in table-top exercises and other national pandemic preparedness activities whenever relevant.
8. Wherever possible, develop the capability to work with influenza viruses under BSL3 containment.

SITUATION MONITORING AND ASSESSMENT

NIC OBJECTIVES

1. To monitor circulating influenza strains in the country, and remain alert to non-subtypable or low-reacting virus isolates using WHO diagnostic reagents provided through the GISN.
2. To detect human cases of new subtype influenza infection as early as possible.
3. To contribute to ongoing pandemic risk assessment in affected countries.

NIC ACTIONS

All countries

1. Develop and strengthen the national laboratory network for influenza surveillance in humans.
2. Conduct seasonal influenza virus isolation and preliminary analysis of the virus isolates, and send representative isolates to the WHOCCs.
3. Serve as a key point of contact between WHO and the national authority, and report routine surveillance findings to national authorities and WHO.
4. Immediately alert national authorities and WHO to unusual outbreaks of influenza or influenza-like illness, and to non-subtypable or low-reacting virus isolates using reagents provided by WHO. Immediately forward such virus isolates to a WHOCC.
5. Establish and maintain collaboration with other sectors, including veterinary laboratories, to ensure regular information exchange.
6. Conduct joint research, wherever possible, with animal health experts on influenza at the human-animal interface.

PREVENTION AND CONTAINMENT

NIC OBJECTIVES

1. To contribute to the WHO annual recommendations on seasonal influenza vaccine composition.
2. To assist in monitoring the antiviral susceptibility of emerging influenza strains.
3. To contribute to the development of national seasonal and pandemic influenza vaccination policy.

NIC ACTIONS

1. Ship timely representative seasonal influenza virus isolates to WHOCCs.
2. Develop and integrate the laboratory-related components of public health interventions in line with WHO recommendations.
3. Provide recommendations to national authorities on the timing of vaccination and choice of vaccines (for southern or northern hemisphere) to assist the national seasonal influenza vaccination campaign.
4. Assess the burden of seasonal influenza in collaboration with national epidemiological institutes.
5. Wherever possible, conduct seasonal influenza vaccine effectiveness studies.
6. Wherever possible, conduct antiviral susceptibility testing of emerging influenza strains.

HEALTH SYSTEM RESPONSE

NIC OBJECTIVES

1. To ensure that laboratory capacity for detecting human infection with non-circulating influenza viruses is in place within health-care facilities, and that levels of awareness are high.
2. To ensure that biosafety requirements for influenza diagnosis – including the safe handling and shipment of specimens – are met in laboratories within health-care facilities.

NIC ACTIONS

All countries

1. Provide guidance and training to laboratories within health-care facilities on specimen collection, storage, transport and diagnosis, and on relevant biosafety measures.
2. Assess overall diagnostic capacity in laboratories within health-care facilities and assist in the development of surge-capacity plans.

Affected countries and countries with extensive travel/trade links with affected countries

1. Alert laboratories within health-care facilities of the need to:
 - a. consider the new subtype influenza infection in patients with travel or epidemiological links to an affected area;
 - b. secure specimens/virus isolates and forward these to the NIC or a national reference laboratory; and
 - c. immediately report diagnostic results of possible public health significance to the national authorities.

COMMUNICATIONS

NIC OBJECTIVES

1. To serve as the key point of contact between WHO and the national authorities in all questions relating to influenza surveillance in humans.
2. To ensure smooth routine and emergency communication with national partners and WHO.

NIC ACTIONS

1. Provide a weekly report during the influenza season to the WHO FluNet giving information on influenza virology and epidemiology surveillance, and details of any shipments.
2. Maintain active communication with national authorities, the WHO Global Influenza Programme, WHOCCs and other members of the GISN.
3. Periodically provide influenza surveillance information to national authorities, public health workers, clinicians and the general public.
4. Develop a phased communication strategy between the NIC, subnational influenza laboratories, laboratories within health-care facilities, national authorities and WHO.

PANDEMIC ALERT PERIOD

- Phase 3** – Human infection with a new subtype, but no (or very rare) human-to-human spread
Phase 4 – Small cluster(s) with limited and localized human-to-human spread
Phase 5 – Larger cluster(s) but human-to-human spread still localized (substantial pandemic risk)

OVERARCHING GOALS

- Phase 3** – Ensure rapid characterization of the new virus subtype and early detection, notification and response to cases.
Phase 4 – Contain the new virus within limited foci or delay spread to gain time to implement preparedness measures, including vaccine development.
Phase 5 – Maximize efforts to contain or delay spread, to possibly avert a pandemic, and to gain time to implement pandemic response measures.

PLANNING AND COORDINATION

NIC OBJECTIVES

1. To ensure laboratory components are properly in place in national mechanisms for detecting and reporting imminent potential human health threats.

NIC ACTIONS

Affected countries and countries with extensive travel/trade links with affected countries

1. Develop, review and implement the laboratory components of national contingency plans and other national plans where appropriate.
2. Review and implement laboratory surge-capacity and sustainability plans when required.
3. Review and finalize laboratory preparations for an imminent pandemic.

SITUATION MONITORING AND ASSESSMENT

NIC OBJECTIVES

1. To detect or exclude as early as possible new subtype influenza infection in humans.
2. To contribute to pandemic risk assessment, cluster detection and risk factor identification.

NIC ACTIONS

All countries

1. Implement enhanced surveillance in humans when appropriate.
2. Learn from the experience and lessons of affected countries and adjust national surveillance as appropriate.

Affected countries and countries with extensive travel/trade links with affected countries

1. Implement enhanced surveillance of humans based on relevant WHO recommendations, and report results rapidly and regularly to national authorities (including public health and animal health sectors) and WHO.
2. Alert local health-care providers and laboratories to the possibility of new subtype influenza infection in patients with travel or epidemiological links to an affected area, and immediately report laboratory findings of possible public health significance to national authorities.
3. Establish, review and strengthen diagnostic capacity for reliable detection of new subtype influenza infection in humans, including algorithms for laboratory confirmation and for exclusion of human cases; incorporate surveillance of the new subtype influenza strain into seasonal influenza surveillance.
4. Provide subnational laboratories with reference services for the diagnosis of new subtype influenza infection in humans, and facilitate the immediate transfer of all positive or suspected human specimens/virus isolates of new subtype influenza to the NIC or a national reference laboratory.
5. Immediately report any results of possible public health significance to national authorities and WHO, and share with WHO specimens/virus isolates of all confirmed human cases and other information contributing to pandemic risk assessment, development or updating of diagnostic reagents and protocols, and other WHO activities of public health significance.
6. Facilitate the intersectoral exchange of information and specimens when required, ensuring that the relevant biosafety requirements are met.
7. Conduct field investigations in affected area(s) and serological surveillance of farmers, animal workers and other possible groups at high risk of new subtype influenza infection to assess the threat to human health.
8. Where possible, conduct collaborative research, for example into the pathogenicity of new subtype influenza viruses in humans, and influenza at the human-animal interface.

PREVENTION AND CONTAINMENT

NIC OBJECTIVES

1. To contribute to the selection, development, review and updating of prototype pandemic vaccine strains.
2. To contribute to the continuous monitoring of antiviral susceptibility among emerging strains.

NIC ACTIONS

Countries with human case(s)

1. Actively share with WHO specimens/virus isolates of all confirmed human cases and other information (including clinical information) for prototype pandemic vaccine strain development, and antiviral susceptibility testing.
2. Where possible, conduct antiviral susceptibility testing on emerging influenza strains.

HEALTH SYSTEM RESPONSE

NIC OBJECTIVES

1. To strengthen diagnostic capacity in health-care facilities.
2. To improve awareness of the importance of laboratory biosafety during influenza diagnosis.

NIC ACTIONS

1. Provide algorithms to laboratories within health-care facilities to confirm or exclude human cases of new subtype influenza infection.
2. Provide guidance on specimen collection, storage and transport to the NIC or a national reference laboratory.
3. Provide continuous guidance and training in laboratory diagnosis of influenza infection in humans.
4. Conduct periodic reviews and training to improve awareness of the importance of laboratory biosafety during influenza diagnosis to ensure specific biosafety requirements are always met in health-care facilities.

COMMUNICATIONS

NIC OBJECTIVES

All countries

1. To provide a smooth and efficient communication channel for laboratory diagnostic information, linking national authorities, WHO and other partners.

NIC ACTIONS

All countries

1. Rapidly report laboratory diagnostic results, especially those of possible public health significance, to national authorities and WHO.
2. Actively forward the results of the analysis of specimens/virus isolates from the country by WHO designated reference laboratories – and explain the relevant implications – to national authorities.

3. Immediately inform national authorities and WHO of laboratory findings with potential direct and indirect public health significance.
4. Develop and implement standard procedures for laboratory information sharing with different partners in the country.

PANDEMIC PERIOD

Phase 6 – Increased and sustained transmission in the general population

- The intensity of activities in a country will depend largely upon whether there are cases in the country. The eventual appearance of cases in all countries is considered virtually inevitable.
- Affected countries should follow the recommendations below. Countries not yet affected should prepare to implement these recommendations rapidly, especially if they have extensive trade/travel links with affected countries.

OVERARCHING GOALS

Phase 6 – Minimize the impact of the pandemic.

SITUATION MONITORING AND ASSESSMENT

NIC OBJECTIVES

1. To contribute to the monitoring of the epidemiological, virological and clinical features, course and impact of the pandemic.

NIC ACTIONS

Countries not yet affected

1. Conduct enhanced and sustainable virological surveillance at maximum intensity to rapidly detect the appearance of cases of pandemic influenza infection.

Affected countries and countries with extensive travel/trade links with affected countries

1. Provide laboratory diagnosis for monitoring the geographical spread of the pandemic in the country.
2. As the pandemic intensifies and becomes widespread, adjust virological surveillance (for example, by using near-patient-tests together with clinical diagnosis, or clinical diagnosis alone, and discontinuing the case-management database) in order to monitor the progress of the pandemic in the country.
3. Maintain adequate virological surveillance to assist WHO in monitoring for example antigenic and genetic changes in the pandemic virus, pathogenicity, and antiviral susceptibility.

Subsided (end of pandemic or between waves)

1. Maintain/reinstate enhanced virological surveillance for the early detection of a possible subsequent rise in pandemic influenza activity.
2. Evaluate resource needs and fill the possible gaps in effective virological surveillance for subsequent waves, if any.
3. Where possible, conduct serological studies to understand the spread and other features of the pandemic.