Global Influenza Surveillance and Response System
National Influenza Centres
Terms of Reference

I. Introduction

National Influenza Centres (NICs)[1] together with World Health Organization Collaborating Centres for Influenza (WHO CCs),[2] WHO Essential Regulatory Laboratories (ERLs)[3] and H5 Reference Laboratories[4] form the Global Influenza Surveillance and Response System (GISRS) coordinated by the WHO Global Influenza Programme (GIP).[5] Established in 1952, the then Global Influenza Surveillance Network became GISRS following the adoption of resolution WHA64.5 by the Sixty-fourth World Health Assembly in May 2011.[6]

GISRS is the primary network and resource for global influenza surveillance and control, continuously monitoring the evolution of seasonal,[a] pandemic and emerging zoonotic influenza viruses in the interests of public health. NICs and their host countries receive benefits through GISRS to support national and global public health surveillance and response activities (Annex 1). These activities result in the generation of surveillance information, the timely detection of influenza viruses, and the sharing of representative influenza virus isolates and/or influenza virus-positive clinical specimens with GISRS WHO CCs.

NICs are institutions authorized and designated by their national authority and subsequently recognized by WHO for the purpose of participating in the work of GISRS under the WHO NIC Terms of Reference (TOR). An NIC may have additional obligations under the national authority of its host country. WHO recognition of a laboratory as an NIC within GISRS requires that a country accepts and agrees to comply with the following TOR.

II. Membership of GISRS is the result of a stringent, multi-step process that includes:

1. Official request by a national authority to WHO.
2. Collaboration between the national authority and WHO to assess whether the laboratory's capacities, processes and procedures meet the TOR required by WHO.
3. National authority acceptance to participate in GISRS pursuant to the TOR, which includes the sharing of influenza viruses and/or influenza virus-positive clinical specimens with GISRS WHO CCs, and the sharing of relevant surveillance data with the WHO GIP.

[a] Seasonal influenza is an acute respiratory infection caused by influenza viruses which circulate in all parts of the world among humans. Currently circulating in humans are influenza A(H1N1), A(H3N2) and B influenza viruses – https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal).

4. Issuance of an official letter of recognition by WHO.
5. Periodic review by WHO of the laboratory's continued capacities to meet the required standards, as set forth in the NIC TOR, to ensure that influenza surveillance is maintained.

III. General roles and responsibilities

NICs undertake the following general roles and responsibilities:

1. serve as the reference laboratory for influenza in their country;
2. serve as a technical resource on influenza-related matters for their national authority;
3. serve as a key point of contact with WHO on issues related to influenza in their country;
4. share with GISRS WHO CCs, in a timely manner, seasonal influenza virus isolates and/or influenza virus-positive clinical specimens in accordance with national Access and Benefit Sharing (ABS) guidelines;
5. agree to the use and sharing of influenza virus isolates and/or influenza virus-positive clinical specimens by GISRS WHO CCs, ERLs and H5 Reference Laboratories for risk assessment in accordance with their corresponding WHO TOR;
6. share influenza virus sequence data[7] and, where available, accompanying metadata[b, c] through publicly accessible databases;
7. adhere to applicable national and international biosafety standards[8] for working with influenza viruses;
8. adhere to applicable national and international regulations on the transport of dangerous goods (Class/division 6.2)[9] when shipping influenza virus isolates and/or influenza virus-positive clinical specimens;
9. meet the quality requirements of national or international quality standards, as applicable, and participate in the WHO External Quality Assessment Programme (EQAP); and
10. maintain a high level of technical proficiency by participating in training provided by GISRS and other sources.

[b] On the assumption that the sharing of metadata complies with national policy and legislation.
[c] Descriptions of metadata used by databanks are provided in the report of the PIP Advisory Group Technical Working Group on the Sharing of Influenza Genetic Sequence Data. June 2016 (https://cdn.who.int/media/docs/default-source/pip-framework/pip-framework-advisory-group/twg_doced1d1fb3-f99e-4797-82f0-60a357a37aee.pdf?sfvrsn=7efec205_1&download=true).

NICs handle several types of influenza virus isolates and/or influenza virus-positive clinical specimens which are for the purposes of these TOR classified as follows:

1. Human seasonal influenza viruses.
2. Pandemic influenza preparedness (PIP) biological materials (BM), including influenza viruses with human pandemic potential (IVPP).[10]
3. Other influenza viruses from animal or environmental specimens that are not classified as "human seasonal influenza viruses" or PIP BM.[10]

IV. Additional roles and responsibilities

NICs undertake the following additional roles and responsibilities

When working with human seasonal influenza viruses

1. NICs collect respiratory specimens either through an established network of physicians, health care centres or other sentinel sites, and/or through soliciting influenza virus-positive clinical specimens from laboratories providing diagnostic services. Patients included in surveillance should preferably meet the syndromic case definition[11] of influenza-like illness (ILI), acute respiratory infection (ARI) or severe acute respiratory infection (SARI). NICs are encouraged to include specimens representative of all age groups in the surveillance system.
2. Depending on available resources, NICs identify seasonal influenza viruses using molecular detection methods and/or virus culture and/or immunological methods.
3. NICs differentiate between influenza Type A and Type B viruses and attempt to identify the subtype of influenza A viruses and the lineage of influenza B viruses. For assistance with diagnostic testing, NICs can obtain updated reagents and laboratory protocols from GISRS WHO CCs through WHO.
4. NICs report timely[d] defined virological surveillance information to their national authorities, and then either directly to the WHO online FluNet[12] platform of RespiMart[e] or indirectly to a regional platform for uploading to WHO FluNet. Epidemiological information, if available, should be reported

[d] Results for any given week should be reported the following week at a time determined by WHO regional offices and/or headquarters. Already submitted results should be updated when more detailed results (for example, subtype determination) become available. In order to provide global updates on the current situation, reports should be submitted by Thursday 12:00 UTC each week.
[e] RespiMart (developed from FluMart) is a platform to facilitate the exchange, harmonization, consolidation and storage of surveillance data on respiratory viruses with epidemic and pandemic potential, including influenza viruses, RSV and SARS-CoV-2. RespiMart provides a single platform for sharing aggregated and case-based data from different applications and/or data sources thereby allowing for integrated analysis and reporting – https://www.who.int/tools/RespiMart.

to the RespiMart WHO FluID platform[13] – either by the NIC or national focal point as designated by the host country. Reporting should be done weekly during the months when seasonal influenza is commonly observed, but preferably throughout the year.

5. NICs immediately report to their national authorities and to WHO any observation of unusual influenza activity in their country.
6. NICs immediately share with GISRS WHO CCs influenza A virus isolates and/or influenza virus-positive clinical specimens without well-defined results or those that cannot be subtyped using the updated reagents available through GISRS. Such findings should be reported to their national authority according to national and/or international rules and regulations, and where applicable, the International Health Regulations (2005).[14]
7. NICs share representative recent seasonal influenza virus isolates and/or influenza virus-positive clinical specimens in a timely manner with a GISRS WHO CC of their choice for further characterization on the understanding that the sharing of such materials among GISRS WHO CCs and ERLs, in accordance with international ethical guidelines, is essential for: (a) virus characterization and risk assessment; (b) informing WHO influenza virus vaccine composition recommendations; (c) developing reference materials; and (d) implementing the WHO EQAP for GISRS and other influenza laboratories. NICs note the relevant WHO guidance on the frequency and timing of the shipping of influenza virus isolates and/or influenza virus-positive clinical specimens to GISRS WHO CCs.[15]
8. NICs provide relevant virological, clinical and epidemiological information on the representative virus isolates and/or influenza-positive clinical specimens shipped to GISRS WHO CCs.
9. NICs agree, in accordance with national regulations and protocols, that if a seasonal virus shared with a GISRS WHO CC is recommended for development as a candidate vaccine virus (CVV) such a virus may be developed by a GISRS WHO CC as a CVV,[f] and that such a CVV may be shared with vaccine manufacturers, upon their request, for consideration as a component in the development and production of a seasonal influenza vaccine.
10. As members of GISRS, NICs have access to the benefits available and provided by GISRS as outlined in Annex 1.[g]

[f] Candidate vaccine viruses are developed by GISRS WHO CCs with the support of GISRS partner laboratories.

[g] Benefits include contributions acquired from industry under the Pandemic Influenza Preparedness (PIP) Framework, under section 6.14.3, which are used to improve pandemic influenza preparedness and response, strengthen protection against pandemic influenza by improving and strengthening WHO GISRS, conduct disease burden studies, and strengthen laboratory and surveillance capacity, particularly in developing countries (Article 3).

When working with influenza viruses that are classified as PIP BM

TOR are described in Annex 5 of the Pandemic Influenza Preparedness (PIP) Framework (reproduced in Annex 1). NICs share IVPP according to relevant WHO guidance materials.[16]

When working with other influenza viruses from animal or environmental specimens that are not classified as human seasonal influenza viruses or PIP BM

Occasionally, NICs may receive influenza viruses that do not fall into the categories of human seasonal influenza viruses or PIP BM – for example, viruses from animal or environmental specimens.

1. NICs must follow applicable national and/or international biosafety requirements and good microbiology laboratory practice to avoid cross-contamination with viruses of human origin. Such material should preferably be handled in facilities away from those where human specimens and viruses are investigated.
2. NICs share virus samples with GISRS WHO CCs of their choice to support GISRS risk assessment following national and international rules and regulations. It is the responsibility of the NICs to ensure that appropriate permits and other national/international documents and approvals are in place to facilitate virus sharing.

V. References

[1] National Influenza Centres. 28 August 2023. Geneva: World Health Organization (https://www.who.int/initiatives/global-influenza-surveillance-and-response-system/national-influenza-centres).
[2] WHO Collaborating Centres and their Terms of Reference. Geneva: World Health Organization (https://www.who.int/initiatives/global-influenza-surveillance-and-response-system/who-collaboration-center-erl).
[3] WHO Essential Regulatory Laboratories (ERLs) list of laboratories. Geneva: World Health Organization (https://www.who.int/initiatives/global-influenza-surveillance-and-response-system/who-erls).
[4] WHO H5 Reference Laboratories and the Terms of Reference (TOR). Geneva: World Health Organization (https://www.who.int/initiatives/global-influenza-surveillance-and-response-system/h5-reference-laboratories).
[5] Global Influenza Programme [website]. Geneva: World Health Organization (https://www.who.int/teams/global-influenza-programme).
[6] Sixty-fourth World Health Assembly: Geneva, 16–24 May 2011: Resolutions and decisions. Annexes. Geneva: World Health Organization; 2011. Resolution WHA64.5 (https://iris.who.int/handle/10665/106547?locale-attribute=ru&locale=es&mode=full).
[7] Next-generation sequencing of influenza viruses. General information for national influenza centres. Geneva: World Health Organization; 2020 (https://cdn.who.int/media/docs/default-source/influenza/global-influenza-surveillance-and-response-system/related-documents/ngs_guidance_for_nics.pdf).
[8] Laboratory biosafety manual. Fourth edition and associated monographs. Geneva: World Health Organization; 2020 (https://iris.who.int/handle/10665/337956).
[9] Recommendations on the transport of dangerous goods: model regulations, 23rd revised edition. New York, Geneva: United Nations; 2023 (https://unece.org/transport/dangerous-goods/un-model-regulations-rev-23).
[10] Pandemic Influenza Preparedness (PIP) Framework for the sharing of influenza viruses and access to vaccines and other benefits. Second edition. Geneva: World Health Organization; 2021 (https://www.who.int/publications/i/item/9789240024854).
[11] End-to-end integration of SARS-CoV-2 and influenza sentinel surveillance: revised interim guidance, 31 January 2022. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/351409).
[12] FluNet Summary [website]. Geneva: World Health Organization (https://www.who.int/tools/flunet/flunet-summary).
[13] FluID [website]. Geneva: World Health Organization (https://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/fluid).
[14] International Health Regulations (2005). Third edition. Geneva: World Health Organization; 2016 (https://www.who.int/publications/i/item/9789241580496).
[15] Operational guidance for sharing seasonal influenza viruses with WHO Collaborating Centres (CCs) under the Global Influenza Surveillance and Response System (GISRS). Geneva: World Health Organization; 2017 (WHO/WHE/IHM/GIP/2017.6; https://apps.who.int/iris/handle/10665/259400).
[16] Operational guidance on sharing influenza viruses with human pandemic potential (IVPP) under the Pandemic Influenza Preparedness (PIP) Framework. Geneva: World Health Organization; 2017 (WHO/WHE/IHM/GIP/2017.3; https://iris.who.int/handle/10665/259402).

World Health Organization

Global Influenza Surveillance and Response System
National Influenza Centres
Terms of Reference

Annex 1

List of material and non-material benefits of GISRS[h]

As a member of the Global Influenza Surveillance and Response System (GISRS) and in accordance with the National Influenza Centres Terms of Reference, National Influenza Centres (NICs) are provided with, and have access to, a range of benefits, some of which are provided on request.[i] Such benefits support seasonal and zoonotic influenza surveillance, capacity strengthening, and other influenza prevention and control activities in countries, and facilitate collective GISRS actions to mitigate the public health risks associated with influenza outbreaks.

Material benefits include

1. Reagents and viruses[j, k]

    a. Annually updated laboratory reagents for the following influenza virus assays: polymerase chain reaction (PCR) singleplex and multiplex assays; haemagglutination inhibition assays (HIA); indirect fluorescent antibody (IFA) test; and sequencing reagents for Sanger or next-generation sequencing assays.
    b. Primers/probes for the molecular detection of non-influenza respiratory viruses of public health importance, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and respiratory syncytial virus (RSV)[l] for countries implementing epidemiological and virological surveillance of such viruses as recommended for GISRS integrated surveillance.
    c. Updated diagnostic reference control viruses.
    d. Annually updated vaccine antigens for developing potency test reagents.
    e. Tissue culture media for influenza virus isolation.

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[h] This document is intended to be a “living document” and may be updated as appropriate.
[i] For the detailed list of benefits and currently available reagents contact the WHO Global Influenza Programme (GIP) at: gisrs-whohq@who.int.
[j] GISRS diagnostic reagents and viruses are provided by the International Reagent Resources (IRR) initiative developed and supported by the WHO Collaborating Center on for the Surveillance, Epidemiology and Control of Influenza at the U.S. Centers for Disease Control and Prevention (CDC). In order to receive these materials, NICs must register with IRR. Diagnostic reagents and viruses are provided free of charge for the purposes of GISRS activities but there may be some limit restrictions depending upon the TOR of the GISRS activity in which an NIC participates. Information regarding IRR registration is available at: https://www.internationalreagentresource.org/Register.aspx
[k] For information on these, contact WHO GIP at: gisrs-whohq@who.int.
[l] RSV reagents are available to GISRS member countries enrolled in global RSV surveillance.

f. High-growth reassortant viruses developed by reassorting laboratories, and prototype influenza candidate vaccine viruses (CVVs) developed by GISRS WHO Collaborating Centres (WHO CCs).[m]
g. Annual proficiency panels for participation in the WHO External Quality Assessment Programme (EQAP) for the molecular detection of seasonal and zoonotic influenza viruses, and where applicable:
    - proficiency panels for participation in the WHO EQAP for the molecular detection of non-influenza respiratory viruses of public health importance such as SARS-CoV-2 and RSV;
    - proficiency panels for participation in external quality assessments of virus isolation in cell culture and embryonated chicken eggs, and identification of the haemagglutinin subtype of viral isolates by haemagglutination inhibition testing and/or microneutralization assay;
    - proficiency panels for participation in external quality assessments of antiviral susceptibility testing; and/or
    - proficiency panels for participation in external quality assessments of influenza virus gene sequencing.
h. Materials required as described in WHO Guidance on regulations for the transport of infectious substances for shipping of influenza virus isolates and/or influenza virus-positive clinical specimens through the WHO Shipping Fund Project to facilitate the sharing of influenza viruses within GISRS.[n, o, p]

Non-material benefits include

1. Epidemiological and virological public health information and tools, including
    a. Global, regional and national epidemiological and virological information sharing[q] by geographical groupings of countries, areas and territories on influenza, SARS-CoV-2, and RSV (where available) through the reporting by national sentinel and non-sentinel surveillance systems to the WHO surveillance data platform RespiMart. This will include information on the geographical areas most affected, the level of activity according to epidemiological week and severity of cases.
    b. Access to epidemiological and virological surveillance technical updates and to situation reports for: (a) seasonal influenza;[r] (b) influenza at the animal-human interface; (c) influenza viruses with human pandemic potential (IVPP); (d) SARS-CoV-2; (e) RSV; and (f) as applicable, other emerging respiratory

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[m] The development of high-growth CVVs is a complex process, involving collaboration between laboratories involved in developing reassortants and GISRS WHO CCs. Two technologies are currently used: classical reassortment and reverse genetics.
[n] Shipping & logistics: https://www.who.int/initiatives/global-influenza-surveillance-and-response-system/virus-sharing/shipping-and-logistics-activities.
[o] Operational guidance on sharing influenza viruses with human pandemic potential (IVPP) under the Pandemic Influenza Preparedness (PIP) Framework. Geneva: World Health Organization; 2017 (https://www.who.int/publications/i/item/operational-guidance-on-sharing-influenza-viruses).
[p] Operational guidance on sharing seasonal influenza viruses with WHO Collaborating Centres (CCs) under the Global Influenza Surveillance and Response System (GISRS). Geneva: World Health Organization; 2017 (https://www.who.int/publications/i/item/WHO-WHE-IHM-GIP-2017.6).
[q] For respiratory virus updates see: https://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/influenza-updates.
[r] FluNet [website]. Geneva: World Health Organization (https://www.who.int/tools/flunet).

viruses of public health significance. Such technical updates better equip countries to prepare for and respond to future respiratory virus epidemics and pandemics.

c. Analyses and reports from GISRS WHO CCs coordinated by WHO Global Influenza Programme (GIP) and detailing the genetic, antigenic and antiviral-susceptibility characteristics of viruses circulating in the country and shared with GISRS WHO CCs.
d. Updated laboratory protocols for the surveillance, detection and characterization of seasonal and pandemic influenza viruses for:
    i. molecular detection of seasonal and pandemic influenza viruses
    ii. antiviral-susceptibility testing
    iii. genetic characterization (sequencing)
    iv. antigenic characterization
    v. serological detection of influenza viruses
    vi. virus isolation procedures.
e. Tools and other resources to help countries monitor their epidemiological and virological influenza situation, perform risk assessments, and promptly exchange information with GISRS, including:
    i. global epidemiological surveillance standards for influenza;[s]
    ii. data analysis tools provided through the RespiMart platform – such as FluNet[t] and FluID;[u]
    iii. the WHO Epidemic and Pandemic Influenza Severity Assessment (PISA) tool;[v]
    iv. the WHO Tool for Influenza Pandemic Risk Assessment (*TIPRA*);[w]
    v. the WHO Influenza Virus Traceability Mechanism (IVTM);[x]
    vi. the WHO document *A manual for estimating disease burden associated with seasonal influenza*;[y]
    vii. protocols for investigating non-seasonal influenza and other emerging acute respiratory diseases;[z] and

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[s] See: Global epidemiological surveillance standards for influenza. Geneva: World Health Organization; 2013 (https://www.who.int/publications/i/item/9789241506601).
[t] FluNet [website]. Geneva: World Health Organization (https://www.who.int/tools/flunet).
[u] FluID [online platform]. Geneva: World Health Organization (https://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/fluid).
[v] Pandemic influenza severity assessment (PISA). A WHO Guide to assess the severity of influenza in seasonal epidemics and pandemics. Geneva: World Health Organization; 2017 (https://www.who.int/publications/i/item/pandemic-influenza-severity-assessment-(-pisa)-a-who-guide-to-assess-the-severity-of-influenza-in-seasonal-epidemics-and-pandemics).
[w] Tool for influenza pandemic risk assessment (TIPRA). Version 2 Release. Geneva: World Health Organization; 2020 (https://www.who.int/publications/i/item/tool-for-influenza-pandemic-risk-assessment-(tipra)-2nd-edition).
[x] Influenza Virus Traceability Mechanism (IVTM 2.0) [website]. Geneva: World Health Organization (https://extranet.who.int/ivtm2/).
[y] A manual for estimating disease burden associated with seasonal influenza. Geneva: World Health Organization; 2015 (https://www.who.int/publications/i/item/9789241549301).
[z] Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases. Geneva: World Health Organization; 2018 (https://www.who.int/publications/i/item/WHO-WHE-IHM-GIP-2018.2).

viii. Influenza Investigations & Studies (Unity Studies) standardized template protocols.[aa]

f. Assessments of the public health risks posed by evolving and emerging influenza virus strains through the use of standardized and consistent approaches to outbreak investigations, in partnership with GISRS collaborators.
g. Recommendations on risk management measures, including those related to influenza vaccines and antiviral drugs.
h. Access to established GISRS online and, when possible, in-person platforms to share experiences and information, and to interact with other GISRS laboratories.[bb]

2. Training, mentoring, and capacity strengthening (both epidemiological and laboratory) through institutional capacity-building based on participation, collaboration and cooperation with WHO headquarters, regional/country offices, GISRS WHO CCs and other GISRS-associated entities and partners. This includes networking, participation in GISRS meetings, twinning projects and/or joint tasks, and the provision of technical support for troubleshooting, implementing diagnostic procedures and surveillance protocols.[cc]

3. Access to technical support for genomic sequencing and/or bioinformatics from GISRS WHO CCs and GISRS-associated entities and partners for countries without established sequencing capacities, or for the validation of sequencing results obtained by NICs.

4. Access to technical support for inputting data and the analysis of genetic sequence data through appropriate publicly accessible databases such as the EpiFlu™ database of the GISAID Global Data Science Initiative[dd] and databases in the International Nucleotide Sequence Database Collaboration (INSDC).

5. Access to outputs, including estimations of health care burden, pooled vaccine effectiveness data, PISA summaries for countries and TIPRA reports.

6. Direct and free-of-charge real-time access to advanced expertise and support in GISRS WHO CCs, WHO Essential Regulatory Laboratories (ERLs) and H5 Reference Laboratories for seasonal and pandemic viruses.

[aa] Influenza investigations & studies (Unity Studies) [website]. Geneva: World Health Organization (https://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/influenza-investigations-studies-unity).

[bb] These include the EZcollab platform (https://ezcollab.who.int/), the GISRS Information Centre and the GISRS Discussion Forum.

[cc] Some contributions for the support of GISRS are made through the PIP Framework. Countries benefit additionally from distinct contributions from GISRS industry partners for specific activities/projects including the Global influenza hospital surveillance network (GIHSN) and the Partnership for Influenza Vaccine Introduction (PIVI).

[dd] GISRS industry partners provide some contributions towards the functioning and updating of the global and publicly accessible genetic sequence database platforms for seasonal and zoonotic influenza, SARS-CoV-2, and RSV.

7. Collaborative research initiatives with other GISRS members[ee] with acknowledgement made of the research contributions of national scientific presentations and publications.[ff]

8. Inclusion of the name of the institution, its Director and contact details in the list of NICs formally recognized by WHO and available at: https://www.who.int/initiatives/global-influenza-surveillance-and-response-system/national-influenza-centres

For questions on GISRS benefits please contact**:** gisrs-whohq@who.int

[ee] Support for research activities is received from GISRS partners including vaccine manufacturers. Areas of research include clinical trials, evaluation of new manufacturing platforms, use of adjuvants, improved vaccine formulations and knowledge-based studies to support improved vaccine coverage in all age cohorts. For additional information contact GISRS at gisrs-whohq@who.int.

[ff] WHO actively seeks the participation of scientists from GISRS laboratories and GISRS member countries in scientific research on clinical specimens and/or influenza and other respiratory viruses and invites active engagement in the preparation of manuscripts for presentation and publication. Contributors will be appropriately acknowledged in line with guidance such as that published by the International Committee of Medical Journal Editors.

Annex 2

Extract (pp 49–52) from Annex 5 of the Pandemic Influenza Preparedness Framework for the sharing of influenza viruses and access to vaccines and other benefits: National Influenza Centres. Terms of Reference related to work with Pandemic Influenza Preparedness biological materials.[gg]

National Influenza Centres

Terms of Reference related to work with Pandemic Influenza Preparedness biological materials

Background

The WHO global influenza surveillance and response system (GISRS) serves as a global alert mechanism for the emergence of influenza viruses with important features, including those with pandemic potential. For activities related to pandemic influenza, the WHO GISRS includes four complementary categories of institutions and laboratories: National Influenza Centres, WHO Collaborating Centres, WHO H5 Reference Laboratories and Essential Regulatory Laboratories. The WHO GISRS is coordinated by the WHO Global Influenza Programme. Within each category all institutions and laboratories perform functions defined by core terms of reference. Each laboratory or institution that is formally recognized or designated as a part of the WHO GISRS by WHO has accepted to be bound by the core terms of reference applicable to its category. The following are the core terms of reference applicable to the National Influenza Centres.

National Influenza Centres play a key role in pandemic influenza risk assessment by alerting WHO immediately to outbreaks of H5N1 or other influenza viruses with pandemic potential. National Influenza Centres collect specimens from suspected cases of H5N1 or other unusual influenza viral infection, perform laboratory diagnosis and analysis, and ship in a timely manner, such specimens or viruses isolated from them, to a WHO Collaborating Centre or H5 Reference Laboratory for advanced virological analysis. Efficient pandemic influenza risk assessment and risk response are based on collective efforts from all WHO GISRS members through rapid exchange of biological materials, reference reagents, epidemiologic data and other information.

It is understood that the Guiding Principles, as agreed by the Intergovernmental Meeting and reproduced below, will guide all activities, specific terms of reference or associated functions of the WHO GISRS laboratories when they act in their capacity as a WHO GISRS laboratory. The terms of reference for all WHO GISRS laboratories have been developed under the following overarching Guiding Principles:

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[gg] https://iris.who.int/bitstream/handle/10665/341850/9789240024854-eng.pdf?sequence=1

Guiding Principles for the development of terms of reference for current and potential future WHO global influenza surveillance and response system (GISRS) laboratories for H5N1 and other human pandemic influenza viruses

1. All activities conducted by WHO GISRS laboratories under their WHO terms of reference will be consistent with the Framework and the Standard Material Transfer Agreement.*
2. The WHO GISRS laboratories will be coordinated by, and provide support to, WHO.
3. The WHO GISRS laboratories will provide a timely summary report of laboratory analyses and on request any other available information on tests conducted, test results and associated risk assessment and risk response as is specified in their terms of reference.
4. The WHO GISRS laboratories will share experience and provide capacity strengthening support to WHO Member States within their resources where necessary.
5. The WHO GISRS laboratories will provide support as specified in their terms of reference for the development of potential pandemic vaccine, pandemic vaccine, diagnostic test materials and pharmaceuticals.
6. If WHO GISRS laboratories conduct research on influenza viruses received for public health surveillance purposes, they will do so in a manner that includes participation of scientists, to the fullest extent possible, from the submitting National Influenza Centre or other authorized laboratory, especially those from developing countries, including through the publication process.
7. The WHO GISRS laboratories will support global public health preparedness and response, especially for urgent situations including international outbreaks and epidemics.
8. The WHO GISRS laboratories will share in a rapid, systematic and timely manner PIP biological materials, using the Influenza Virus Traceability Mechanism as appropriate, including distribution to other qualified laboratories, to facilitate public health risk assessment, risk response activities and scientific research in accordance with the Standard Material Transfer Agreement.*
9. The WHO GISRS laboratories will submit genetic sequences data to GISAID and Genbank or similar databases in a timely manner consistent with the Standard Material Transfer Agreement.*
10. The originating laboratories which provide the PIP biological materials received by the WHO GISRS laboratories will be given due credit and recognition.

* Editor's note: the reference to "Standard Material Transfer Agreement" is understood to mean "Standard Material Transfer Agreement 1".

Core terms of reference

National Influenza Centres are laboratories that fulfil the terms of reference listed below. A National Influenza Centre is formally designated by the health ministry of the country concerned and is recognized by WHO. A National Influenza Centre may have additional obligations under the authority of its ministry of health.

A. General conditions and activities

National Influenza Centres:

1. work under the coordination of the WHO Global Influenza Programme and provide support to WHO (Guiding Principles 2, 7);
2. use the WHO Influenza Virus Traceability Mechanism to record the receipt and transfer of PIP biological materials (Guiding Principle 8);
3. comply with the Standard Material Transfer Agreement* of the Pandemic Influenza Preparedness Framework for sharing of influenza viruses and access to vaccines and other benefits (Guiding Principle 1);
4. serve as a key point of contact between WHO and the country of the National Influenza Centre on issues related to surveillance, laboratory diagnosis, and sharing of clinical specimens and/or influenza viruses with pandemic potential, as well as sharing of important related clinical or epidemiological information, when available, with WHO (Guiding Principles 2, 3, 4, 7, 8);
5. participate actively in WHO pandemic influenza surveillance activities and maintain active communication and collaboration with other members of the WHO GISRS (Guiding Principles 4, 7, 8).

B. Laboratory and related activities

National Influenza Centres:

1. collect or process as appropriate clinical specimens from patients suspected to be infected with H5N1 and other influenza viruses with pandemic potential (Guiding Principle 7);
2. act as a collection point for virus isolates of suspected pandemic influenza from laboratories within the country;
3. conduct testing of clinical specimens for influenza viruses and detect influenza viruses that cannot be readily identified with diagnostic reagents provided through the WHO GISRS;
4. ship, within one week, clinical specimens and/or viruses that cannot be readily identified with diagnostic reagents provided through the WHO GISRS to

* Editor's note: the reference to "Standard Material Transfer Agreement" is understood to mean "Standard Material Transfer Agreement 1".

a WHO Collaborating Centre or H5 Reference Laboratory of their choice and include the date the specimen was collected and relevant geographical, epidemiological and clinical information (Guiding Principles 2, 3, 5, 7, 8);

5. attend laboratory training courses provided by the WHO Collaborating Centres in an effort to establish and maintain capacity to recognize influenza viruses that cannot be readily identified (Guiding Principle 4);

6. review, maintain and strengthen influenza surveillance in the country (Guiding Principle 2);

7. provide technical advice and support to other influenza laboratories in the country on specimen collection and shipment logistics, laboratory biosafety and other operational procedures related to influenza surveillance (Guiding Principles 2, 7).

C. Information and communication

National Influenza Centres:

1. alert WHO immediately when influenza viruses are detected that cannot be readily identified with diagnostic reagents provided through the WHO GISRS or when unusual outbreaks of nonseasonal influenza or influenza-like illness emerge;

2. provide national authorities and the general public with information on H5N1 and other influenza viruses with pandemic potential circulating in the country in a timely manner.

D. Research, scientific presentations and publications

National Influenza Centres:

1. actively seek the participation of scientists from originating laboratories/countries in scientific projects associated with research on clinical specimens and/or influenza viruses from their countries and actively engage them in preparation of manuscripts for presentation and publication (Guiding Principle 6);

2. appropriately acknowledge in presentations and publications, the contributions of collaborators, including laboratories/countries providing clinical specimens or influenza viruses with pandemic potential or reagents, using guidelines such as those outlined by the International Committee of Medical Journal Editors[1] (Guiding Principle 6).

[1] See http://www.icmje.org/