

Integrated sentinel surveillance of influenza and SARS-CoV-2 and the development of the Global Influenza Surveillance and Response System Plus

Virtual meeting
12 – 14 October 2021



Integrated sentinel surveillance of influenza and SARS-CoV-2 and the development of the Global Influenza Surveillance and Response System Plus: virtual meeting, 12–14 October 2021

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Acknowledgements

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Acronyms

ARI	Acute respiratory infection
COVID-19	Coronavirus disease 2019
EQAP	External quality assessment project
GISRS	Global Influenza Surveillance and Response System
GISAID	Global Initiative on Sharing All Influenza Data
ILI	Influenza-like illness
PCR	Polymerase chain reaction
NIC	National Influenza Centre
PISA	Pandemic influenza severity assessment
SARI	Severe acute respiratory infection
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WHO	World Health Organization

Background

The first WHO consultation from 6-8 October 2020 developed interim guidance¹ for the integrated epidemiological and laboratory surveillance of influenza and SARS-CoV-2 using the Global Influenza Surveillance and Response System (GISRS) and associated systems. Since the implementation of the interim guidance, including expediting GISRS genomic surveillance² as part of global efforts, extensive experience has been gained at national, regional and global levels. Meanwhile, the approach of integrated surveillance of influenza and SARS-CoV-2 to simultaneously address critical public health needs of both influenza and SARS-CoV-2 using existing systems has been welcomed by countries and supported by international agencies.

A year and a half into the coronavirus disease 2019 (COVID-19) pandemic, countries and the world have started building longer-term health emergency preparedness. The low seasonal influenza activity and frequent detections of zoonotic influenza infections are an ominous sign of an impending threat of influenza. It was critical to have a follow up global consultation one year after the first consultation to review and address immediate needs and discuss strategy for the mid- to long-term development of GISRS. A virtual consultation was, therefore, held on 12-14 October 2021. An agenda and list of participants is provided in the meeting report annex.

Objectives of the meeting

The overall aim was to update the interim guidance on the integrated surveillance of influenza and SARS-CoV-2 and chart a roadmap for the development of GISRS towards GISRS Plus for influenza and other respiratory viruses including SARS-CoV-2, respiratory syncytial virus and other future respiratory viruses of pandemic and epidemic potential. Specific meeting objectives were to:

- take stock of experience and lessons learned from countries in using influenza sentinel systems in sampling, testing, sequencing, reporting SARS-CoV-2 surveillance data and sharing of SARS-CoV-2 genetic sequence data
- review and update the interim guidance on integrating influenza and SARS-CoV-2 surveillance
- assess and update existing surveillance tools for influenza as learned from the COVID-19 pandemic to date, and potentially for SARS-CoV-2
- review and enhance readiness of the GISRS pandemic response
- develop a roadmap for GISRS development towards GISRS Plus.

Expected meeting outcomes were updated practical guidance on integrated surveillance of influenza and SARS-CoV-2; a compendium of country best practices for integrating influenza and SARS-CoV-2 sentinel surveillance; and a GISRS Pandemic Response Plan and a GISRS Plus roadmap.

Meeting overview

The meeting reviewed recent evidence on severe acute respiratory infection (SARI), influenza-like illness (ILI) and acute respiratory infection (ARI) case definition performance for SARS-CoV-2 surveillance; best practices for integrated surveillance from participating countries; interim standards for and current gaps in SARS-CoV-2 epidemiologic, laboratory and genomic sentinel surveillance; the Pandemic influenza severity assessment (PISA) and GISRS pandemic response plan; and the GISRS Plus strategy and roadmap. A full agenda is given in Annex 1.

Participants included national laboratory and epidemiology national focal points for influenza; experts from WHO Collaborating Centers and other laboratories of GISRS; international experts in surveillance of influenza, SARS-CoV-2 and other respiratory viruses; global and regional partners; and other interested bodies. A list of participants and their affiliations is provided in Annex 2.

Impact of the COVID-19 pandemic on influenza sentinel surveillance

The pandemic has caused disruptions to many elements of influenza surveillance systems, especially at the start of the pandemic. Surveillance was restarted integrating SARS-CoV-2 into influenza surveillance. Significant progress has been made by all countries taking part in integrated surveillance, including uploading data in a timely manner to FluNet and with at least 79% of GISRS laboratories having submitted data to the Global Initiative on Sharing All Influenza Data (GISAID).

The need for integrated respiratory sentinel surveillance

Meeting participants shared information on best practices for integrated influenza and SARS-CoV-2 surveillance, recognizing that these can be used to assist countries to overcome challenges in establishing and sustaining effective integrated surveillance. It was noted that there is increased national interest in respiratory surveillance at this time and an opportunity to work with new partners to build a resilient and effective surveillance system for the future. Participants agreed that we need to tackle the joint challenge of influenza [low circulation during the past year and thus low levels of immunity] and COVID-19 [continuing SARS-CoV-2 circulation and the threat of new variants] and to address co-circulation of these viruses; and we need to learn from the COVID-19 pandemic and to build integrated respiratory surveillance for the future that can rapidly integrate the surveillance of a new virus.

General lessons learned based on experience reported by participants include the need for:

- greater clarity on the definition of “integrated surveillance” and its core and expanded objectives [these could be collection of data for vaccine effectiveness studies]

- support and practical guidance from WHO on:
 - how to disaggregate sentinel and non-sentinel data from all surveillance data
 - how to source samples from COVID-19 test centres (where necessary) so that representative samples meeting agreed case definitions are selected and essential meta-data are collected
 - how to ensure a focus on higher quality data (that meet the agreed case definition and are therefore interpretable) is achieved
 - what to do if core data are not available for the expanded sample set for samples meeting the agreed case definition
 - clear recommendations on case definitions to be adopted, including addressing implications for comparisons with historical data
 - guidance on actions required to report sentinel SARS-CoV-2 results separately to FluNet.

The main principles that should guide adaptation of sentinel surveillance were the need for them to:

- be agile / adaptable - timely revisions to the system may be needed in future
- accommodate expansion – whilst maintaining feasibility, data quality and representativeness in a way that is sustainable
- maximize representativeness – essential for data extrapolation more widely beyond the surveillance population.
- facilitate future digitalisation – to promote real time access to data for decision making and timely intervention and to facilitate data management and data sharing; with the understanding that this would require detailed system specification and preparation [with in depth planning and piloting] and new electronic systems accessible to all stakeholders.

Integrated surveillance guidelines

It was noted that the systematic review of published studies and surveillance data from the 7 countries studies assessing ILI and SARI in different age groups against laboratory confirmed SARS-CoV-2 infection supported the recommendations that countries could continue to use ILI and SARI for influenza and SARS-CoV-2 surveillance and collect essential metadata. It was noted that countries with high testing capacities can continue with an ARI case definition.

Suggested revisions to the guidance document included:

A. Epidemiology

- ARI case definition to be recommended for case detection
- specification of a core minimum data set, aligned with core objectives
- more background on the rationale for 50-150 specimens / week
 - 50 per week is the minimum number per National Influenza Centre (NIC) to achieve core objectives
 - 150 per week is the ideal number per NIC, where possible
 - additional specimens needed to achieve additional objectives

- more detail on sourcing of specimens from non-sentinel sites or SARS-CoV-2 testing laboratories needed
- recommendation to operate year-round surveillance in temperate climates to determine seasonality post-pandemic.

It was noted that the use of non-sentinel systems will require attention to:

- ensuring cases meet a recognized WHO case definition
- need for country-specific algorithms for selecting SARS-CoV-2 test samples
- sending metadata together with samples to the laboratory
- identifying data as from a sentinel or non-sentinel site
- support for consumables and for transport and other additional logistics
- need for guidelines / new authorisations for sharing samples with NICs
- need for staff feedback on problems to identify and solve problems
- staff training needs and human resources, with care not to over-burden staff
- consideration of what needs to be put in place to ensure sustainability.

It was noted that NICs may be able to secure additional samples from non-sentinel sites or COVID-19 testing laboratories to meet sample size requirements. However, priority should be given to samples from patients with symptoms consistent with the ILI/SARI/ARI case definitions, who represent the wider population seeking healthcare. Data recording and reporting should distinguish sentinel from non-sentinel sites, and data should be reported appropriately to global and/or regional platforms.

B. Laboratory

The meeting highlighted the need for clear guidance on sample size for testing and sequencing and on how to maintain representativeness of samples [if testing more than 150 such as during epidemics]. It was noted that there was a need for robust genomic surveillance to assess the impact of emerging variants; and for contingency plans for accumulating mutations in terms of re-manufacture, re-qualification, and quality control processes. It was suggested that the use of variant-specific polymerase chain reaction (PCR) for surveillance may be useful when there is no dominant variant [but is not useful for clinical decision-making]. It was considered important to:

- maximize representativeness, timeliness, continuity and quality [rather than quantity]
- upload sequences to GISAID or other publicly accessible databases weekly or fortnightly, together with essential minimum metadata including sampling strategy variable
- develop more concrete guidance on the use of sequencing, including guidance on sample size
- link the guidance on technical quality of sequencing to WHO COVID-19 laboratory network guidance on sequencing
- build a sustainable laboratory infrastructure for different viruses as an essential element of GISRS Plus.

GISRS Plus

GISRS has gained extensive experience over many years and is a secure platform and strong foundation from which to build integrated surveillance. GISRS Plus adds in other respiratory viruses with epidemic and pandemic potential; integrates laboratory and epidemiological capabilities and built upon the success of the existing GISRS infrastructure [whilst not creating parallel systems]. It was agreed that there is a need to prepare GISRS Plus to meet both influenza and SARS-CoV-2 future surveillance needs, and it was noted that there is the potential for GISRS Plus to track future COVID-19 activity globally. Consequently, there is a need to prepare GISRS to meet future SARS-CoV-2 (as well as influenza) needs.

It was proposed that the core objectives of GISRS integrated surveillance should be achievable with ILI and SARI case definitions and proposed sample sizes and include:

- signalling the start and end of influenza and SARS-CoV-2 epidemic periods and describing the seasonality
- establishing baseline levels of activity for illness and severe disease [to evaluate the impact and severity of each epidemic period and of future pandemic events]
- identifying locally circulating virus types and subtypes and their relationship to global and regional patterns
- providing candidate viruses for vaccine production.

Additional objectives included identifying high risk groups; understanding the relationship between virus strains and disease severity; generating data for focused studies on health and economic burden and to help decision-makers prioritize resources and plan public health interventions; providing a platform for vaccine effectiveness studies; monitoring antiviral sensitivity; describing the antigenic character and genetic makeup of circulating viruses; and detecting unusual and unexpected events or clusters that may herald a change in virus characteristics. It was noted that in deciding whether to adopt additional (non-core) objectives, sustainability should be carefully considered.

GISRS Plus roadmap

A broader respiratory pathogen preparedness and response approach aligns with the vision in the Global Influenza Strategy 2019-2030, and GISRS will continue to be the backbone for pandemic preparedness and response. Whilst the development of GISRS Plus is a logical next step, this needs to be done in a measured and scientific manner, working together with countries and with resources made available to countries. It was agreed that GISRS Plus gives the opportunity to expand cooperation and should help ensure sustainability. It was noted that for countries that cannot add new pathogens, consideration should be given to how support can be given to help them engage in GISRS Plus. It was recommended that, based on experience in WHO PISA, a core set of parameters for seasonal and pandemic situations; more emphasis on health care capacity measurements; more work on the threshold setting in pandemic situations; and inclusion of dynamic parameters are all needed.

The GISRS Pandemic Response Plan [PRPi] has been developed to describe the overall GISRS operational response to an influenza pandemic; synergize national and wider GISRS

responses; guide preparedness and readiness of all GISRS partners; and serve as a foundation for future development of GISRS PRPx for other viruses.

Conclusions and next steps

A summary list of priority actions included:

- finalization of revised guidance and a compendium of best practices as soon as possible
- definition of the objectives and development of operational plans for integrated surveillance at the country level, following the revised guidance and with WHO support [in providing training, logistics support and additional guidance]
- review the use of and secure supplies of multiplex PCR kits and ancillary reagents
- review laboratory procedures, focusing on those laboratories with a reduced performance in the external quality assessment project (EQAP) 2021 and with support from WHO on reagents [jointly with International Reagent Resource], tailored training, on-site problem-shooting on virus detection; and guidance and support to achieve a sustainable laboratory infrastructure
- review of the timeliness and completeness of current reporting of data in regional platforms or directly to FluNet and FluID and of subsequent analysis and feedback to sentinel sites and relevant stakeholders with WHO support in training, developing online training modules and one-on-one mentoring; and communicating results
- working at the country level to achieve representative, systematically sampled viruses from sentinel surveillance systems for sequencing and with uploading of sequence and meta data according to the GISRS guidance; with support from this WHO, which will monitor the development of sequencing capacity in GISRS and the completeness and timeliness of uploaded genetic sequence data; continue to support sequencing capacity building in GISRS (including with reagents, logistics arrangements and sequencing and bioinformatics collaborations with GISAID and other agencies); develop and implement strategic plans and guidance for GISRS genomic surveillance; and help build sustainable capacity at national, regional and global levels.
- completion of a landscape analysis of GISRS capacities.

The meeting closed with a reminder for countries to be vigilant about influenza threats and to get ready for situations of co-circulating of influenza and SARS-CoV-2 viruses; to be alert to unusual clusters of non-COVID-19 respiratory cases; to raise awareness among policy makers of the threat of influenza; and to resume influenza surveillance and monitoring activities, including the reporting of PISA indicators.

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1. World Health Organization. (2020). Maintaining surveillance of influenza and monitoring SARS-CoV-2: adapting Global Influenza Surveillance and Response System (GISRS) and sentinel systems during the COVID-19 pandemic: interim guidance, 8

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2. World Health Organization. (2021). Operational considerations to expedite genomic sequencing component of GISRS surveillance of SARS-CoV-2, 16 February 2021.

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Annex 1. Meeting agenda



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2nd WHO Global Consultation on the Integrated Sentinel Surveillance of Influenza and SARS-CoV-2 and the Development of GISRS Plus

(virtual meeting)

FINAL AGENDA

Chair: *Dr. Mahmudur Rahman*
(Meeting room will open at 10:45AM CET each day)

Day 1: 12 October 2021, 11h00 – 14h15 CET

11:00 – 11:15	Opening	<i>Sylvie Briand</i>
	Objectives, expected outcomes Disclosure of interests declared by experts Selection of chair and co-chairs	<i>Wenqing Zhang</i>
11:15 – 11:20	Housekeeping rules	<i>Aspen Hammond</i>

Session 1: Best practice models of integrated surveillance of influenza and SARS-CoV-2

11:20-11:35	Integrated surveillance of influenza and SARS-CoV-2 – progress overview	<i>Siddhi Hirve</i>
11:35 – 11:55	Best practices of end-to-end integration of influenza and SARS-CoV-2 – key considerations	<i>Durga Kulkarni</i> <i>Madhurima Nundy</i>
11:55 – 12:05	<i>Health break – instructions for group discussions</i>	
12:05 – 13:30	Breakout group discussions: From field experiences to best practice models of integrated surveillance of influenza and SARS-CoV-2	<i>Group leads:</i> <i>Room #1- Angel Rodriguez</i> <i>Room #2 - Francis Inbanathan</i> <i>Room #3 – Karen Nahapetyan</i> <i>Room #4 - Amal Barakat</i>
13:30 – 14:15	Panel discussion: what surveillance practices worked and in what context?	<i>Moderator: Belinda Herring</i>

14:15

Close of day 1

Day 2: 13 October 2021, 11h00 – 14h00 CET

11:00 – 11:05 Recap of day 1

Mahmudur Rahman

Session 2: Reviewing interim guidance

11:05 – 11:35 Overview – Objectives of GISRS integrated surveillance
- Panel discussion

Joshua Mott
Moderator: Richard Pebody
Panelists: Sheena Sullivan, Lynette Brammer,
Harline Razanajatovo Norosoa

11:35 – 11:50 Influenza case definitions for SARS-CoV-2 surveillance
- Discussion

Christina Bancej

11:50 – 12:00 *Health break / Break into parallel sessions*

Parallel session 2A: Reviewing interim guidance - Surveillance

Co-chair: Cheryl Cohen; Rapporteur: Harry Campbell

12:00 – 12:40 Sentinel systems – revisions in the guidance
- Panel discussion

Silvia Bino
Moderator: Pushpa Wijesinghe
Panelists: Carla Voto, Ivy Asante,
Mayan Lumandas, Silvia Bino

12:40 – 13:20 Sourcing specimens
- Panel discussion

Sibongile Walaza
Moderator: Andrea Vicari
Panelists: Talat Mokhtari, Flavia
Riccardo, Sikuru Badaru, Chinthana
Perera

Parallel session 2B: Reviewing interim guidance - Laboratory

Co-chair: Maria Zambon; Rapporteur: Marie-jo Medina

12:00 – 12:30 Laboratory recommendation highlights
including algorithm

Ian Barr

12:30 – 12:55 rRT-PCR multiplex PCR assays for the
simultaneous detection of influenza and
SARS-CoV-2 viruses

John Barnes

12:55 – 13:20 Expediting Genomic surveillance

Dmitriy Pereyaslov

13:20 *Re-group to plenary*

13:20 – 13:35 Reporting SARS-CoV-2 to FluNet

Aspen Hammond

13:35 – 14:00 Panel Discussion: Sentinel surveillance to inform public health decisions

Moderator: Julia Fitzner
Panelists: Jean-Michel Heraud, Varsha Potdar, Silke Buda, Jim McMenamin

14:00 *Close of day 2*

Day 3: 14 October 2021, 11h00 – 14h00 CET

11:00 – 11:05 Chair's remarks *Mahmudur Rahman*

Session 3: Interim recommendations

11:05 – 11:30 Summarizing the discussions and outputs from the surveillance session of day 2
- Discussion *Harry Campbell*

11:30 – 11:55 Summarizing the discussions and outputs from the laboratory session of day 2
- Discussion *Marie-jo Medina*

11:55 – 12:05 *Health break*

Session 4: GISRS development and pandemic preparedness

12:05 – 12:45 GISRS Plus roadmap *Ann Moen*
- Panel discussion
Moderator: Ann Moen
Panelists:
Sonam Wangchuk,
Stefano Tempia,
Erik Karlsson,
John McCauley,
Sylvie van der Werf

12:45 – 13:05 WHO Pandemic Influenza Severity Assessment
- an update *Holly Sadler*
Kaat Vandemaele

13:05 – 13:25 GISRS Pandemic Response Plan development
- an update *Xiyan Xu*

Session 5: Next steps

13:25 – 13:45 Priority actions – for countries, WHO
- Discussion *Wenqing Zhang*

13:45 – 13:55 Chair summary remarks *Mahmudur Rahman*

13:55 – 14:00 Closing remarks *WHO*

14:00 *Close of consultation*

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Annex 3. Declarations of interest

The WHO consultation on integrated sentinel surveillance of influenza and SARS-CoV-2 and the development of Global Influenza Surveillance and Response System Plus was held on 12–14 October 2021 as a virtual meeting.

In accordance with WHO policy, all WHO external participants completed the WHO form for Declaration of Interests for WHO experts before being invited to the consultation. At the start of the consultation, the interests declared were disclosed to all participants.

The interests declared by the participants were reviewed by WHO and determined not to present a conflict of interest with the objectives of the WHO consultation.

