WHO consultation to adapt influenza sentinel surveillance systems to include COVID-19 virological surveillance

Virtual meeting

6 – 8 October 2020
WHO consultation to adapt influenza sentinel surveillance systems to include COVID-19 virological surveillance: virtual meeting, 6 – 8 October 2020

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## Abbreviations and acronyms

<table>
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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ARI</td>
<td>Acute respiratory infection</td>
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<tr>
<td>COVID-19</td>
<td>Coronavirus disease 2019</td>
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<tr>
<td>EQAP</td>
<td>External quality assessment project</td>
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<td>GIP</td>
<td>Global Influenza Programme</td>
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<td>GISRS</td>
<td>Global Influenza Surveillance and Response System</td>
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<tr>
<td>GISAID</td>
<td>Global Initiative on Sharing All Influenza Data</td>
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<tr>
<td>ICD</td>
<td>International Statistical Classification of Diseases and Related Health Problems</td>
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<tr>
<td>ILI</td>
<td>Influenza-like illness</td>
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<tr>
<td>IRR</td>
<td>International reagent resource</td>
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<tr>
<td>PCR</td>
<td>Polymerase chain reaction</td>
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<td>NIC</td>
<td>National Influenza Centres</td>
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<td>SARI</td>
<td>Severe acute respiratory infection</td>
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<tr>
<td>SARS-CoV-2</td>
<td>Severe acute respiratory syndrome coronavirus 2</td>
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<tr>
<td>US CDC</td>
<td>United States Centers for Disease Control and Prevention</td>
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<td>WHO</td>
<td>World Health Organization</td>
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<td>WHO CC</td>
<td>WHO Collaborating Centre for reference and research on influenza</td>
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Executive summary

Sentinel surveillance for influenza and COVID-19 is a resource-effective approach to gathering critical information about both viral infections in patients seeking medical attention and meeting influenza surveillance case definitions. The COVID-19 pandemic has reinforced the value of sentinel surveillance systems for providing timely information on epidemiologic and virus trends, detecting co-circulation of influenza and COVID-19 and evaluating the impact of these two diseases on health systems. Adaptation of influenza sentinel surveillance systems to include COVID-19 can guide national, regional and global responses to the COVID-19 pandemic and has important public health value for influenza and COVID-19 preparedness and response.

To provide guidance to countries on using existing influenza sentinel surveillance systems, WHO initiated the development of interim guidance on maintaining influenza surveillance and adapting these systems for monitoring COVID-19 in August 2020. WHO and external experts in three workstreams developed the guidance, a draft of which was then reviewed and discussed during the virtual consultation that is the subject of this report. The interim guidance, *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*, was finalized with input from the consultation, and published on WHO’s website in November 2020. It is hereafter referred to as ‘the interim guidance’ in this report. It is intended to be piloted during the coming northern hemisphere influenza season to address the system disruptions caused by repurposing of resources, changes in health seeking behaviour and other factors that may impede timely and high-quality testing and reporting. Experiences garnered during the next six to twelve months will improve global understanding of how countries can reduce disruptions and adapt existing systems to conduct robust sentinel surveillance for influenza and COVID-19 simultaneously.

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Introduction

The Global Influenza Surveillance and Response System (GISRS) and its associated disease and virological surveillance systems constitute a well-established network for surveillance of influenza and other respiratory viruses. Since the beginning of the COVID-19 pandemic, the GISRS network has been engaged in the COVID-19 response.

- More than 90% of National Influenza Centres (NICs), WHO H5 reference laboratories and other public health laboratories under the GISRS network are testing for SARS-CoV-2.
- Syndromic and virologic information from existing influenza sentinel surveillance systems have been used in many countries to understand COVID-19 community transmission trends and inform national responses to the pandemic.
- Existing influenza reporting systems have become the primary platforms for sharing COVID-19 data to regional and global levels.
- A rapid global external quality assessment programme (EQAP) for COVID-19, conducted in mid-2020, was based on the influenza EQAP of GISRS with 164 countries (233 labs) participating in the project.
- Sharing of genetic sequence data continues to be facilitated through publicly accessible databases (such as GISAID).
- The GISRS mechanism has been used for shipping SARS-CoV-2 virus materials to WHO COVID-19 reference laboratories.

Although pairing influenza surveillance with that of SARS-CoV-2 has had indisputable benefits, it has caused a range of disruptions to influenza sentinel surveillance systems as staff, supplies, sites, and laboratories were repurposed for the COVID-19 response. A decrease in reporting of data to FLUNET and FLUID in 2020 compared to previous years has been observed. WHO, at various levels, has continued to stress the importance of continued surveillance and monitoring for the continuing influenza threat.

The virtual consultation from 6-8 October provided an opportunity for GISRS members, national influenza surveillance focal points, WHO and partners to review and discuss:

- countries’ challenges in maintaining routine influenza sentinel syndromic and virologic surveillance
- countries’ experiences using influenza sentinel surveillance systems for COVID-19
- opportunities and potential limitations for influenza and COVID-19 sentinel surveillance in the coming 6-12 months
- the draft interim guidance, developed in the several months before the consultation, for adapting national sentinel surveillance systems to maintain high quality influenza sentinel surveillance and incorporate COVID-19 surveillance, where possible.

The expected outcome of the consultation was to finalize and publish the interim guidance.

Preparatory activities before the meeting

Preparations started two months before the consultation. Three teams, each with between eight and 15 members, were tasked with drafting the interim guidance sections on 1) case
definitions for sentinel surveillance, 2) epidemiological considerations and 3) laboratory considerations. A planning group oversaw the progress of the three workstreams and the development of the meeting agenda. The work on case definitions and laboratory considerations was informed by evidence reviews. An online survey for national surveillance focal points conducted before the consultation provided information on how national influenza surveillance systems have been affected by the COVID-19 pandemic response. The information gathered from the survey contributed to the teams’ discussions and the draft interim guidance. Finally, country representatives attending the consultation were invited to share their experiences, including challenges, successes and future plans by developing slide decks made available to all participants ahead of the consultation.

Considerations for the interim guidance

The consultation focused on the scope of the draft interim guidance, considerations for maintaining routine sentinel surveillance for influenza and for meeting selected COVID-19 surveillance objectives. General and specific epidemiological and laboratory considerations for the interim draft guidance were highlighted and discussed through presentations, panel sessions, and small breakout group discussions.

Scope of the interim guidance

Participants agreed that the interim guidance should cover no more than the next twelve months, considering that the COVID-19 pandemic will continue to evolve. It was agreed that the focus of this interim guidance should be on sentinel surveillance only, while acknowledging that epidemiological and virological information from non-sentinel sources often contributes significantly to influenza surveillance. With careful adaptations, influenza sentinel surveillance systems can continue to contribute to the COVID-19 response while retaining their core functions of influenza preparedness and response.

It was agreed that the final interim guidance should emphasize that the existing influenza epidemiological and virological surveillance system – and the comprehensive COVID-19 surveillance many countries are currently heavily engaged in – have different objectives; and that testing of sentinel samples for surveillance objectives is different from the testing of samples for clinical management and diagnostic purposes.

Maintaining routine sentinel surveillance for influenza

Assessing and addressing disruptions to routine sentinel surveillance for influenza were agreed to be priorities for GISRS and associated surveillance systems. There was positive feedback on these topics within the draft interim guidance with some suggested revisions for WHO to consider, such as:

- providing guidance on a rapid assessment of the surveillance system rather than a thorough evaluation, considering time and resource limitations
- refining the table of example disruptions and solutions to address the most commonly encountered issues
- highlighting opportunities from the COVID-19 response that can be leveraged for influenza surveillance, such as the digitalization of health information registries (e.g.
the increased use of ICD codes for surveillance) and the development of additional non-sentinel data sources such as real-time mortality monitoring.

COVID-19 surveillance objectives
Some of the surveillance objectives for influenza and COVID-19 are aligned. It was proposed that using existing sentinel surveillance systems would be likely to achieve or contribute to certain objectives common to influenza and COVID-19 surveillance. There was general agreement on the proposed categorization of objectives for COVID-19 surveillance, with some suggestions:

- provide additional clarity on what sentinel ARI/ILI/SARI syndromic surveillance can and cannot achieve for COVID-19 surveillance
- provide additional clarity on which COVID-19 surveillance objectives the existing sentinel systems can likely achieve and which objectives the data from sentinel surveillance (as one of several data sources) can help achieve
- include the caveat that the likelihood of meeting COVID-19 surveillance objectives depends on the COVID-19 transmission scenario in the country
- include the caveat that sentinel surveillance for COVID-19 could likely be used for early detection of community transmission but not outbreaks.

Epidemiological considerations for maintaining influenza surveillance and meeting COVID-19 surveillance objectives
During the consultation, many countries shared their experiences on adaptations made to maintain routine influenza sentinel surveillance and incorporate the virological surveillance of COVID-19. Actions included expanding sentinel surveillance systems through the addition of new sites and changing the case definitions to include ARI surveillance during the COVID-19 pandemic period.

It was generally agreed that summarizing and presenting these important experiences in the interim guidance would be useful and practical. Additionally, countries expressed a need for guidance on how to pilot adaptation of their influenza sentinel surveillance systems to ensure high quality data and timely reporting. In particular, WHO can reinforce the importance on data quality over quantity to ensure that sentinel surveillance can capture useful information on virus trends.

Regarding case definitions for sentinel syndromic surveillance, the evidence review done prior to the consultation and presented to the wider group during the consultation, indicated that the ILI and SARI case definitions have reasonable specificity and sensitivity for sentinel surveillance conducted to monitor trends in COVID-19.

There was general agreement during the consultation that the minimum sample size considerations in the interim guidance (test a minimum of 50 sentinel samples per week but up to 150 per week if resources allow) were achievable.
Laboratory considerations

The laboratory considerations discussed during the consultation highlighted the value of GISRS for the COVID-19 response. Countries’ regular use of real-time PCR for influenza surveillance has led to tremendous national, regional and global growth in testing experience and capacity. NICs’ and other laboratories’ experiences with seasonal and pandemic influenza has provided countries with a robust platform for COVID-19 national and subnational testing. This capacity is demonstrated by the fact that 96% of participating GISRS laboratories scored 100% on the first global COVID-19 EQAP conducted early in the COVID-19 pandemic.

The draft interim guidance emphasizes that real-time PCR remains the gold standard testing approach for all GISRS laboratories. Prior to the consultation, the laboratory group also reviewed current evidence on the following:

- types of specimens
- storage and transport of clinical specimens to the laboratory
- handling of clinical specimens in the laboratory.

An additional important topic during the consultation was the laboratory testing algorithm for samples obtained from syndromic sentinel surveillance. In March 2020, WHO provided countries with algorithms for influenza and SARS-CoV-2 testing to use based on their national context. Up until the consultation, the majority of countries were testing samples sequentially, first for SARS-CoV-2 and then for influenza. In mid-2020, the United States Centers for Disease Control and Prevention (CDC) published information about a multiplex PCR assay for the simultaneous detection of influenza viruses and SARS-CoV-2. This test was developed and thoroughly validated by the CDC. While influenza and SARS-CoV-2 multiplex tests will streamline testing processes, they were not widely available for many countries to use for their surveillance systems at the time of the consultation.

Shortly before the consultation, the International Reagent Resource (IRR) anticipated making a limited number of the CDC-designed multiplex tests available to countries. They would include primers, probes, and controls but not enzymes and other ancillary reagents. Thus, the laboratory group included in the interim guidance considerations on testing sentinel specimens either in parallel for influenza and SARS-CoV-2 by performing multiplex (preferred) or in single-plex assays using the tests provided through GISRS or in-house or commercial assays. Regarding the implementation of a new assay, it was agreed that laboratories should conduct proper validation of the assay.

Participation in EQA programmes for influenza and SARS-CoV-2 was discussed as an important opportunity for countries to validate their laboratories’ successful identification of both of these viruses. Laboratories need to maintain high quality standards for their

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supplies and testing practices even though the COVID-19 pandemic has led to shortages of resources for testing, limited staff capacity and shipping challenges.

The participants recommended that the final interim guidance clearly include the potential for the monitoring of co-infections of influenza and SARS-CoV-2 in testing algorithms and reporting processes. This information could be useful to report to WHO for an improved global understanding of co-infection rates.

It was also agreed that the interim guidance should emphasize the importance of confirmatory tests for SARS-CoV-2 when possible using different PCR gene targets or a second sample from the patient, especially when circulation of SARS-CoV-2 is low.

Weekly reporting of influenza and SARS-CoV-2 results supports national, regional, and global preparedness and response, and participants agreed it is an important aspect of virological surveillance that should be clearly addressed in the interim guidance. Influenza reporting, virus sub-typing and lineage determination are key to understanding the landscape of circulating viruses and for maintaining vigilance in the identification of influenza viruses with pandemic potential.

Other considerations
Engagement with policy makers was considered critical for successful adaptation of sentinel surveillance systems. It was agreed that the interim guidance has the potential to enhance policy makers’ appreciation for the value of influenza sentinel surveillance systems for the COVID-19 pandemic as well as for influenza epidemic and pandemic preparedness.

Supplementary activities
The participants recommended that WHO offer additional support to countries through the following approaches.

- WHO should collect country experiences and lessons learned from sentinel surveillance system challenges and successes during the COVID-19 pandemic. The collated best practices could be summarized and shared as case studies for countries and the global community. These examples would be useful in illustrating how case definitions have been adapted, how countries have made their system more flexible and how they have approached the expansion of case definitions, if applicable. This pooling of experiences will also provide WHO with an understanding of the impact these disruptions have had and the types of support that are needed at national, regional and global levels.

- WHO should develop a brief list of the most common causes and solutions for disruptions to national influenza sentinel surveillance systems. This list could be developed from the above-mentioned collection of country experiences and would be used by countries for timely and resource-effective assessments and rebuilding of their national influenza sentinel surveillance system.
Conclusions

Additional comments on the draft interim guidance from GISRS members, national influenza surveillance focal points, WHO colleagues across the global, regional and country levels, and partners were provided shortly after the consultation. The interim guidance was finalized, based on discussions during the consultation and during the post-consultation review, and was published on 8 November 2020.

The interim guidance is intended to be a resource for countries looking for practical and globally standardized approaches to maintaining, strengthening and adapting high-quality influenza sentinel syndromic and virological surveillance systems that meet existing and emerging public health needs for both influenza and COVID-19.

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<td>Maya Allan</td>
<td>HQ/WRE/HIM</td>
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<td>Lora Alsawalha</td>
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<td>Amal Barakat</td>
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<td>Amgad Elkholy</td>
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<td>Christian Fuster</td>
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<td>Shoshanna Goldin</td>
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<td>23</td>
<td>Aspen Hammond</td>
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<td>24</td>
<td>Belinda Herring</td>
<td>AF/RGO/EPR/EMP</td>
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<td>25</td>
<td>Siddhi Hirve</td>
<td>HQ/WPE/GIH/GIP</td>
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<td>26</td>
<td>Francis Inbanathan</td>
<td>SE/RGO/WHE/IHM</td>
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</table>
27  Sandra Jackson  HQ/WPE/GIH/GIP
28  Kazunobu Kojima  HQ/WPE/GIH/BSI
29  Franciscus Konings  EM/RGO/DCD
30  H. Laurenson-Schaffer  HQ/WPE/GIH/GIP
31  Juliana Leite  AM/PAHO
32  Maja Lievre  HQ/WPE/GIH/GIP
33  Bikram Maharjan  HQ/WPE/GIH/GIP
34  Jaouad Mahjour  HQ/WPE/EPA
35  Awandha Mamahit  HQ/WPE/GIH/GIP
36  Marie-jo Medina  HQ/WPE/GIH/GIP
37  Ann Moen  HQ/WPE/GIH/IPR
38  Piers Mook  EU/RGO/WHE
39  Pamela Mrad  EM/ACO/LEB
40  Karen Nahapetyan  WP/RGO/WHE
41  Boris Pavlin  HQ/WRE/HIM
42  Richard Pebody  EU/RGO/WHE
43  Dmitriy Pereyaslov  HQ/WPE/GIH/GIP
44  Anne Perrocheau  HQ/WRE/HIM
45  Angel Rodriguez  AM/PAHO
46  Mohammad Sahak  EM/ACO/AFG
47  Magdi Samaan  HQ/WPE/GIH/GIP
48  Ahmed Thabit  EM/ACO/YEM
49  Soumia Triki  EM/ACO/MOR
50  Katelijn Vandemaele  HQ/WPE/GIH/GIP
51  Andrea Vicari  AM/PAHO
52  Pushpa Wijesinghe  SE/RGO/WHE
53  Wenqing Zhang  HQ/WPE/GIH/GIP
Annex 2: Declarations of interest

The WHO consultation to adapt influenza sentinel surveillance systems for including COVID-19 was held on 6-8 October 2020 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.
WHO consultation to adapt influenza sentinel surveillance systems for including COVID-19

(final virtual meeting)

FINAL AGENDA

Chair: Mahmudur Rahman; Session chairs: Ian Barr, Cheryl Cohen

(Meeting room will open at 10:45 on each day for to allow participants to join in and for sound-check)

Day 1: 6 October 2020, 11h00 – 14h00 CET

11:00 – 11:10 Opening

Jaouad Mahjour
Assistant Director-General,
WHO Emergence Preparedness

11:10–11:20 Objectives and expected outcomes

Disclosure of interests declared by experts
Selection of chair and co-chairs

Wenqing Zhang

11:20 – 11:35 GISRS surveillance and response since day 1 of the identification of SARS-CoV-2

Wenqing Zhang

11:35 – 11:40 Q&A

11:40 – 11:55 Surveillance objectives for COVID-19 in the upcoming influenza season

Aspen Hammond


Siddhi Hirve

12:15 – 12:35 Q&A

12:35 – 12:45 Health break
# Session 2: Maintain Influenza Surveillance and add Value to COVID-19

Meeting the challenge during the COVID-19 pandemic:

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Speaker(s)</th>
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<tbody>
<tr>
<td>12:45 – 12:55</td>
<td>- experiences from South Africa</td>
<td>Sibongile Walaza</td>
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<tr>
<td>12:55 – 13:05</td>
<td>- regional response from WHO European Region</td>
<td>Richard Pebody</td>
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<tr>
<td>13:05 - 13:20</td>
<td>Q&amp;A</td>
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14:00 Close of day 1
### Day 2: 7 October 2020, 11h00 – 14h15 CET

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
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<tbody>
<tr>
<td>11:00 – 11:15</td>
<td>Recap of Day 1</td>
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<tr>
<td>11:15 – 11:20</td>
<td>Introduction to breakout sessions</td>
<td>Aspen Hammond</td>
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</table>

#### Parallel session 3A: Epi surveillance aspects

Co-chair: Cheryl Cohen

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker</th>
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<tbody>
<tr>
<td>11:30 – 11:55</td>
<td>Sentinel surveillance practices - disruptions and considerations</td>
<td>Cornelia Adlhoch</td>
</tr>
<tr>
<td>11:55 – 12:10</td>
<td>Data analysis and interpretation</td>
<td>Angel Rodriguez</td>
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<tr>
<td>12:10 – 12:50</td>
<td>Plenary discussion</td>
<td>Cheryl Cohen</td>
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<tr>
<td>12:50 – 13:00</td>
<td>Introduction to break-out sessions</td>
<td>Aspen Hammond</td>
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</tbody>
</table>

#### Parallel session 3B: Laboratory aspects

Co-chair: Ian Barr

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker</th>
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<tbody>
<tr>
<td>11:30 – 11:45</td>
<td>Laboratory considerations for quality influenza and SARS-CoV-2 surveillance testing – practical aspects</td>
<td>Erik Karlsson</td>
</tr>
<tr>
<td>11:45 – 11:55</td>
<td>Needs, availabilities, and expectations from single and multiplex influenza+SARS-CoV-2 RT-PCR assays</td>
<td>Becky Kondor</td>
</tr>
<tr>
<td>11:55 – 12:05</td>
<td>Laboratory recommendation highlights including algorithm</td>
<td>Ian Barr</td>
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<tr>
<td>12:05 – 12:50</td>
<td>Plenary discussion</td>
<td>Sylvie Van der Werf</td>
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<tr>
<td>12:50 – 13:00</td>
<td>Introduction to break-out sessions</td>
<td>Marie-Jo Medina</td>
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13:00 – 13:20  Health Break
<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Lead</th>
<th>Rapporteur</th>
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<tbody>
<tr>
<td>13:20–14:15</td>
<td>Break-out group epi-1</td>
<td>Silke Buda &amp; Kaat Vandemaele</td>
<td>Henry Laurenson-Schafer</td>
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<tr>
<td>Break-out group epi-3</td>
<td>Lead: Weigong Zhou &amp; Julia Fitzner</td>
<td>Rapporteur: Vanessa Cozza</td>
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<tr>
<td>13:20–14:15</td>
<td>Break-out discussion lab-1</td>
<td>Lead: Xiyan Xu &amp; Karen Nahapetyan</td>
<td>Rapporteur: Sandra Jackson</td>
</tr>
<tr>
<td>Break-out discussion lab-2</td>
<td>Lead: Erik Karlsson &amp; Marie-jo Medina;</td>
<td>Rapporteur: Thedi Ziegler</td>
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</tr>
<tr>
<td>Break-out discussion lab-3</td>
<td>Lead: Angeliki Melidou &amp; Dmitriy Pereyaslov</td>
<td>Rapporteur: Catherine Thompson</td>
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<tr>
<td>14:15</td>
<td>Close of day 2</td>
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</table>
### Day 3: 08 October 2020, 11h00 – 14h00

<table>
<thead>
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<th>Time</th>
<th>Session</th>
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<tbody>
<tr>
<td>11:00 – 11:05</td>
<td>Chair’s remarks</td>
<td>Mahmudur Rahman</td>
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</table>

#### Session 4: Going forward

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Presenter(s)</th>
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<tr>
<td>11:05 - 11:30</td>
<td>Summarizing the discussions and outputs from the epidemiology session of day 2</td>
<td>Cheryl Cohen</td>
</tr>
<tr>
<td>11:30 – 11:55</td>
<td>Summarizing the discussions and outputs from the laboratory session of day 2</td>
<td>Ian Barr</td>
</tr>
<tr>
<td>11:55 – 12:35</td>
<td>Plenary discussion: feasibility, practical challenges for implementing considerations to sustain sentinel surveillance systems for influenza and COVID-19</td>
<td>Abdinasir Abubakar</td>
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<tr>
<td>12:35 – 12:45</td>
<td>Health break</td>
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<tr>
<td>13:10 – 13:45</td>
<td>Plenary discussion: Way forward of GISRS influenza surveillance in the next 6-12 months</td>
<td>Moderator: Ann Moen</td>
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<tr>
<td>13:45 – 14:00</td>
<td>Summary and closing remarks</td>
<td>Mahmudur Rahman Wenqing Zhang</td>
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<tr>
<td>14:00</td>
<td>Close of meeting</td>
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Annex 4: Post-consultation feedback

The results of a feedback survey shared with all participants after the consultation showed that most responders attended all three days of the meeting. Overall, the feedback was very positive. Survey responders agreed that the meeting program was logical and effective, delivered the information they expected and that the panellists’ responses were thorough and helpful. Particularly helpful to the responders was hearing about other country experiences, the relevance and timeliness of the topics discussed and the high quality of session chairing and facilitation. Most agreed that the interim guidance document is very likely to help maintain sentinel syndromic surveillance for influenza and other respiratory disease in the next 6-12 months. Responders commented that there was not enough time for better quality discussions because of the virtual method used for the consultation.