

GISRS

INFLUENZA

SURVEILLANCE  
COVID-19



## Operational considerations to expedite genomic sequencing component of GISRS surveillance of SARS-CoV-2

16 FEBRUARY 2021



World Health  
Organization

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## WHO/2019-nCoV/genomic\_sequencing/GISRS/2021.1

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## KEY POINTS

- Representative, quality, timely and continuous genetic surveillance of SARS-CoV-2 is critical to the COVID-19 outbreak response to monitor genetic variants.
- GISRS sentinel surveillance sites provide specimens for systematic and standardized sampling to conduct sequencing to monitor genetic variants of SARS-CoV-2.
- Countries are encouraged to expedite genomic sequencing of SARS-CoV-2 of a minimum of 15 samples per week from sentinel surveillance systems and share the genetic sequence data through a publicly accessible database.



## Introduction

This document provides practical guidance to Global Influenza Surveillance and Response System (GISRS) laboratories (1) and other relevant national laboratories to move beyond virus detection to genomic sequencing of SARS-CoV-2 PCR positive materials obtained from sentinel surveillance of influenza-like illness (ILI), acute respiratory infection (ARI) and severe acute respiratory infection (SARI). Operational aspects addressed include sample selection for sequencing, numbers of viruses to be sequenced, metadata and timeliness for sharing genetic sequence data (GSD) and opportunities for technical support.

The goal is for GISRS and other relevant national laboratories to contribute to the evidence base essential for an effective COVID-19 pandemic responses by achieving the following objectives:

- improve the geographic and demographic representativeness and timeliness of SARS-CoV-2 genetic sequence data in publicly accessible databases, such as the Global Initiative on Sharing All Influenza Data (GISAID) (2)
- monitor the trend and prevalence (proportions) of existing and emerging (co-) circulating genetic variants (clades) among samples from sentinel sites
- wherever possible, contribute to a better understanding of associations between genetic characteristics of SARS-CoV-2 and transmission scenarios and severity of COVID-19 disease.

In addition to sentinel surveillance, special studies (3) or convenience sampling should be considered for sourcing virus samples for sequencing (4) to achieve other important public health objectives of SARS-CoV-2 genomic sequencing, such as the early detection and outbreak investigations.

This document will be of use mainly for National Influenza Centres (NICs) of GISRS and other national laboratories, especially those performing SARS-CoV-2 surveillance using ILI/ARI/SARI sentinel surveillance systems. It should also be of interest to national influenza programme managers and national managers responsible for the laboratory component of COVID-19 response and other public health professionals involved in disease and laboratory surveillance at a national level.

## Background

Genomic sequencing of SARS-CoV-2 viruses by laboratories in the GISRS network from samples obtained through systematic and standardized sampling of cases meeting ILI, ARI and SARI case definitions enables continuous monitoring of the trend and proportions of existing and emerging genetic variants and improved geographic and demographic representativeness. GISRS, currently comprising laboratories in 126 countries with more than 90 laboratories sharing SARS-CoV-2 genetic sequences, is uniquely placed to efficiently bridge the critical gap in systematic genomic surveillance.

Since March 2020 (5), GISRS has incorporated testing for SARS-CoV-2 into laboratory algorithms for testing of specimens from sentinel surveillance to monitor relative trends in co-circulation of influenza and SARS-CoV-2 viruses (6). On 15 January 2021, the 6th International Health Regulations (2005) (IHR) Emergency Committee for COVID-19 recommended increasing global genomic sequencing capacities and encouraged rapid sharing of sequence data and meta-data; and for WHO to actively support countries to strengthen systematic genomic surveillance by leveraging GISRS and other relevant networks (7). A week earlier, WHO had published interim guidance on SARS-CoV-2 genomic sequencing for public health goals (4).

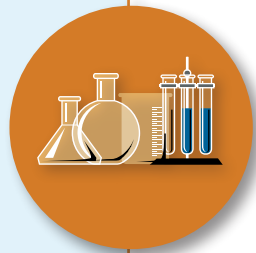
This operational guidance, which was developed in response to recommendations by the Emergency Committee, builds on the abovementioned WHO interim guidance to leverage the existing GISRS influenza capacities and mechanisms for SARS-CoV-2 surveillance through ILI/ARI/SARI sentinel surveillance systems (6). The document was developed based on evidence generated from the WHO Consultation to Adapt Influenza Sentinel Surveillance Systems for Including COVID-19 in October 2020, the review of SARS-CoV-2 sentinel surveillance functions and data reporting to the WHO FluMart (8) by the NICs and other national officers. Sizes of sampling for sequencing are based on earlier guidance for SARS-CoV-2 sentinel surveillance through the GISRS; SARS-CoV-2 positivity rates among sentinel specimens; sequencing capacity in GISRS; experience from the field; and extensive consultations with national and international experts, WHO Regional Offices and partner organizations.

# Operational considerations for GISRS laboratories with established sequencing capacity

Key considerations for GISRS laboratories are:

- **systematic nature** of sample collection
- **representativeness** of sampled patients (i.e., geographical origin, age and sex, disease severity, timepoint during the outbreak)
- **quality** of the genetic sequencing data (GSD)
- **timeliness** including time from sample collection to sequencing and GSD sharing in a publicly accessible database
- **continuity and sustainability** of the sequencing activity as part of ongoing national surveillance

*For pandemic response, the above considerations are far more important than the absolute numbers of viruses sequenced from a country.*



## 1. Sample Selection

### A. For countries performing sentinel surveillance of ILI/ARI/SARI

In general, specimens with a real-time reverse transcription polymerase chain reaction (rRT-PCR) cycle-threshold (Ct) value of  $\leq 30$  will likely allow for generating good quality genetic sequence of whole genomes.

Unless laboratories conduct genomic sequencing of **all** SARS-CoV-2 PCR-positive sentinel specimens, selection should take the quality of the specimens and representativeness of the sampled patients into utmost consideration.

***Selection of SARS-CoV-2 PCR-positive sentinel samples should reflect the representativeness of:***

- different age groups (e.g. 0 to <2 years, 2 to <5 years, 5 to <15 years, 15 to <50 years, 50 to <65 years,  $\geq 65$  years)
- different geographic locations (sentinel sites) within the country
- different time points
- patients representing the spectrum of disease meeting case definitions in use for ILI, ARI or SARI
- clinically significant cases from sentinel surveillance (e.g. fatal cases, vaccinated individuals, immunocompromised individuals, patients receiving treatment such as antivirals, plasma therapy or monoclonal antibodies), re-infected cases.

### B. For countries not performing sentinel surveillance of ILI/ARI/SARI

Sampling strategy should follow Chapter 6.1 of the WHO technical document on Genomic sequencing of SARS-CoV-2: a guide to implementation for maximum impact on public health (9).

## 2. Number of viruses to be sequenced

For GISRS *sentinel* surveillance of SARS-CoV-2, WHO recommends at least 50 to 100 clinical specimens and ideally 150 specimens *per week* to be collected from sentinel systems and tested for SARS-CoV-2 (6).

- For countries collecting **150 or less specimens per week** from ILI/ARI/SARI *sentinel surveillance* systems:
  - ◆ Wherever resources allow, laboratories should consider genomic sequencing of **all** SARS-CoV-2 PCR-positive sentinel specimens with a RT-PCR Ct value of  $\leq 30$ .
  - ◆ Otherwise, try to maintain a **minimum of 15** SARS-CoV-2 PCR-positive sentinel specimens per week for sequencing. If there are not enough good quality specimens from sentinel surveillance systems, random selection of samples from non-sentinel surveillance sources can be considered.
- For countries collecting **more than 150 specimens per week** from ILI/ARI/SARI *sentinel surveillance* systems:
  - ◆ Depending on resources available, consider sequencing **all or a subset** (ideally  $\geq 10\%$  as an indication), but at least a **minimum** of 15 SARS-CoV-2 PCR-positive *sentinel specimens* with a RT-PCR Ct value of  $\leq 30$  *per week*.

## Operational considerations for countries without established sequencing capacity

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