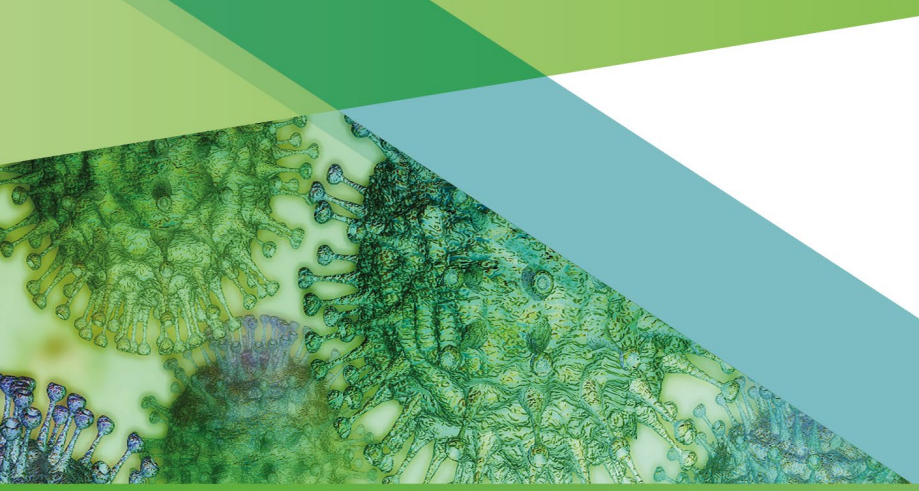

TECHNICAL REPORT

Pilot study outline for targeted genomic surveillance of SARS-CoV-2 in travellers in response to a worsening or unknown epidemiological situation in a third country

13 January 2023

Background and context

On 4 January 2023, European Union (EU) and European Economic Area (EEA) countries agreed on a coordinated precautionary approach in the light of COVID-19 developments in China, especially considering the need for sufficient, reliable data and the easing of travel restrictions by China starting on 8 January 2023. The agreement included the setting up of complementary random testing of passengers travelling from China on arrival in EU Member States and the sequencing of all positive results as part of a surveillance protocol to detect virus variants of concern. This outline aims to provide guidance to Member States willing to set up this surveillance system, through pilot sentinel sites at select travel hubs for the genomic surveillance of incoming travellers from countries with a worsening of the epidemiological situation and insufficient volume of sequencing, starting with China, for a period of eight weeks. After that the results of the study will be reviewed, and the study outline will be revised accordingly.

The timely detection and characterisation of SARS-CoV-2 variants is essential to inform risk assessment and to limit the impact of the virus, e.g. by strengthening vaccination programmes or updating vaccines' composition, and by adjusting or implementing new non-pharmaceutical measures as needed. The basis of variant surveillance in the EU/EEA has been outlined in ECDC's 'Guidance for representative and targeted genomic SARS-CoV-2 monitoring'. Implementing targeted genomic surveillance in travellers should not result in decreasing EU/EEA Member States' national routine respiratory virus surveillance, including sampling, and sequencing for SARS-CoV-2 and other respiratory viruses in the community. In situations of severely limited resources, routine respiratory virus surveillance in the community should take precedence over surveillance at travel hubs. Targeted genomic surveillance activities in travellers are most relevant in situations where the third country under investigation does not perform representative genomic surveillance with international sharing of relevant data.

Targeted genomic surveillance in travellers can support global SARS-CoV-2 variant monitoring through the early detection of new variants that can be further investigated with specific studies and through routine community-based surveillance. This surveillance in travellers will be complementary to wastewater surveillance activities coordinated by the European Aviation Safety Agency and the European Commission's Joint Research Centre, another initiative agreed upon by Member States as part of the coordinated precautionary approach.

There are important limitations associated with such a surveillance system. Firstly, the sampling strategy does not allow for a fully representative (geographically or otherwise) analysis of the third country population from which the samples come. In addition, epidemiological and virological investigations are required to perform risk assessment, some of which may only be possible to perform in a timely manner in the country of origin. Routine population-based representative sampling and sequencing of positive specimens from sentinel systems in primary and secondary care in EU/EEA Member States remain the most effective means of monitoring transmission and virus evolution in a timely manner in the EU/EEA, as described in the joint 'ECDC and WHO Operational considerations for respiratory virus surveillance in Europe'.

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Scope of this document

In response to European Commission request 276 of 29 December 2022, this document provides practical guidance to EU/EEA Member States willing to implement a pilot study for the harmonised and coordinated targeted genomic surveillance of SARS-CoV-2 at selected international points of entry (PoE), to complement national and international genomic surveillance and to trigger more in-depth analysis at community level, such as studies for the characterisation of transmissibility, severity, and immunity evasion properties of a given virus variant.

Target audience

Public health authorities and relevant stakeholders responsible for setting up targeted genomic surveillance in travellers in EU/EEA Member States.

Overall objectives for traveller-based targeted genomic surveillance

- To provide an early warning for new SARS-CoV-2 variants to trigger, if necessary, strengthening of community-based sequencing in EU/EEA countries and to assess new variants' possible growth advantage over already dominant variants, and other characteristics of concern.
- To obtain information on the distribution of SARS-CoV-2 variants in a third country or region based on the distribution of variants detected in travellers, and to contribute to global SARS-CoV-2 variant surveillance.
- To determine if a rapidly deteriorating epidemiological situation outside of the EU/EEA may be variant-driven.
- To evaluate the feasibility, effectiveness, cost, and usefulness of targeted genomic surveillance in travellers to the EU/EEA.

Population under targeted genomic surveillance for the pilot study

For the duration of the pilot study, the population under targeted genomic surveillance will be passengers testing positive for SARS-CoV-2 upon arrival to EU/EEA Member States on flights originating from China. Member States are to decide on the start date of the exercise, the initial pilot phase of which will then last eight weeks.

Based on the review of the data obtained from this pilot, targeted genomic surveillance in travellers could be expanded in future to other areas of the world with rapidly deteriorating epidemiological situations outside of the EU/EEA and uncertainties over the effectiveness of genomic surveillance for SARS-CoV-2. More specific criteria for the selection of areas of the world under this type of surveillance will be defined as result of the evaluation of this pilot.

Recruitment strategy

Member States with airports that constitute a major point of entry from China and have the logistical capacity to host in situ sampling and testing should consider enrolling SARS-CoV-2-positive individuals. For the duration of the investigation, the number of positive isolates sent for genomic sequencing from each site selected will depend on the number of participating travel hubs and the target detection threshold (Table 1). ECDC recommends this threshold be set no higher than 20%. The number of passengers to test to reach the target volume of isolates for sequencing will depend on the prevalence of COVID-19 in country of origin and on additional factors, such as whether reliable pre-departure testing is implemented before travelling to the EU. Pre-departure testing is expected to reduce the number of positive passengers identified at arrival. Any cases identified in such situations are likely to have low viral loads which may also pose difficulties for genomic sequencing. It is likely that the number of passengers initially tested will require periodic calibration based on epidemiological situation in the country of departure and the positivity rate observed in travellers.

Table 1. Weekly number of positive samples per hub needed to be sequenced to detect a new circulating variant with a prevalence of 5%, 10% and 20% in travellers from the country of origin

	Target SARS-CoV-2 variant prevalence in travellers from the country of origin		
#EU airport hubs	**5%**	**10%**	**20%**
2	146	69	31
4	73	35	15
6	49	23	10
8	36	17	8
10	29	14	6

Table 1 assumes infinite population size in the country of origin; for very small countries and countries with a very low number of cases this will overestimate the number of sequences. Formula source: https://www.ecdc.europa.eu/sites/default/files/documents/Guidance-for-representative-and-targeted-genomic-SARS-CoV-2-monitoring-updated-with erratum-20-May-2021.pdf

ECDC will review the results of this study as they are submitted from the countries and will update this outline as needed. In-country coordination between relevant public health authorities and airport stakeholders needs to be the responsibility of the country but aim to have minimal impact on aviation operations. The protocol in each implementing country needs to be cleared by the appropriate ethical review board according to national policies and the participation of passengers must be voluntary. For the calibration of sample sizes during the pilot phase, Member States will be requested to keep a record of the total number of people asked to participate, the number of participants, the number of positive samples, and the number of sequences that were successfully obtained from SARS-CoV-2-positive samples.

Sampling, testing, and data collection

Passengers, over 12 years old should be randomly selected for testing by reverse transcription polymerase chain reaction (RT-PCR) only or with rapid antigen detection tests (RADT) followed by RT-PCR in case of positive RADT. The number of samples required to reach the target number of weekly positive samples for sequencing will guide the number of passengers to test per incoming flight and will need to be calibrated periodically. Passengers should be informed about the purpose of the testing upon arrival. It is up to implementing Member States to decide the random approach to select the targeted number of passengers to be tested, upon informed consent.

- Recruited passengers should be tested for SARS-CoV-2 using RT-PCR or RADT listed in European Commission Common list of COVID-19 rapid antigen tests.
- If RT-PCR is used, one respiratory specimen suitable for RT-PCR is sufficient for both testing and sequencing at nationally appointed laboratories.
- If a RADT is performed first and the result is positive, an additional respiratory sample should be taken for RT-PCR testing at nationally appointed laboratories.
- All positive RT-PCR specimens from the travellers should be processed for whole genome sequencing, provided the Ct value is within the range for successful sequencing.
- The collection of the following metadata is recommended: origin of travel (city, country).

There is no need to collect personal identifying information from the tested passengers. The passenger may remain anonymous, and the test results and sequences may be unlinked to the passenger's identity. If countries choose to collect identifiable data, they must comply with EU regulations/national guidance/GDPR.

Data reporting

Data sharing and reporting are described in the report 'Methods for the detection and identification of SARS-CoV-2 variants-second update' published by ECDC and WHO's Regional Office for Europe on 2 August 2022. The following modes of reporting are recommended:

- **The European Surveillance System (TESSy)** – detections of SARS-CoV-2 among travellers should be reported on a weekly basis by the designated data managers of national public health authorities in the reporting countries, using the most recent version of the COVID-19 reporting protocol. The RESPISURV case-based record type should be used. Minimum variables to report include Pathogen, Place of Infection, SARS-CoV-2 variant type and Sequencing category (= TARGETED). Countries already routinely reporting national data to RESPISURV should use a new TESSy data source (e.g. XX_RESPISURV_travel) to enable distinction between cases identified through this study and routinely reported national cases.
- **EpiPulse** – any suspicious signals related to a SARS-CoV-2 lineage considered of relevance should be reported immediately by nominated users of EU/EEA countries through EpiPulse, and by nominated users of all countries of the region through the Early Warning and Response System (EWRS) and IHR.

- **GISAID** – SARS-CoV-2 consensus sequences should be submitted to GISAID and be clearly identified as pertaining to a travel based genomic surveillance study by indicating 'Airport screening' as the sample strategy and providing the travel history as 'Additional location information'.

Data analysis

Information on sequence methodologies, analysis and suggested applications at the local and national level can be found in ECDC's technical report, 'Guidance for representative and targeted genomic SARS-CoV-2 monitoring', published on 3 May 2021, as well as the joint ECDC/WHO guidance, 'Operational considerations for respiratory virus surveillance in Europe', published on 18 July 2022. ECDC will monitor the data collection regularly and will coordinate the analysis with Member States and international partners.

Dissemination of results

ECDC will assess the quality of the collected data and use them within its routine mechanism for assessing genomic variants to better understand the distribution of virus variants in passengers' country of origin, and to trigger further assessments if a new variant is detected. ECDC will disseminate relevant results in its routine communication on variants when it is appropriate to do so.

Key considerations

- As SARS-CoV-2 variants continue to emerge it is of key importance to strengthen routine population-based representative sampling and sequencing of positive specimens from sentinel systems in primary and secondary care in all countries to monitor variant circulation in the EU/EEA in a reliable manner;
- Travel based targeted genomic surveillance is intended to act as an early warning system to identify new variants and to prompt community-based and laboratory studies for assessing the variants' transmissibility, severity and immune evasion properties. It is, however, not a mechanism to prevent the introduction of novel SARS-CoV-2 variants which is not feasible through these means.
- Individuals testing positive for SARS-CoV-2 should be provided with local COVID-19 case management information and handled according to national guidelines on isolation and case management;
- As COVID-19 is widely circulating in all parts of the world, including EU/EEA countries, public health response efforts have to be objective-driven, coherent, and sustainable;
- Travel-based targeted genomic surveillance should not divert necessary resources from routine national genomic surveillance initiatives which are essential for early detection and for assessing the properties and expected impact of new virus variants and for informing effective mitigation strategies, including changes in vaccination strategies and vaccine composition; in situations of severely limited resources, routine respiratory virus surveillance in the community should take preference over surveillance at travel hubs.

Contributing and consulted experts (in alphabetical order)

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External experts: Operational Contact Points for Influenza and COVID-19, National Focal Points for Viral Respiratory Diseases, and the Advisory Forum.

Disclaimer

All data published in this are correct to the best of our knowledge at the time of publication.