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Detection and characterisation capability and capacity for SARS-CoV-2 variants

Fields marked with * are mandatory.

Detection and characterisation capability and capacity for SARS-CoV-2 variants

Dear Colleagues,
We invite you to take part in a survey on detection and characterisation capability and capacity for SARS-CoV-2 variant viruses in your country. This information has been requested by the Health Security Committee.
The survey focuses on the following areas:

- Purpose of variant screening
- Sampling frame and target isolates Methods for screening
- Characterisation of viruses
- Sequencing capability and capacity
- Self-assessment of capacities

The questionnaire is sent to the Health Security Committee, EWRS Contact Points and Operational Contact Points for COVID-19 (Microbiology) in the EU/EEA countries, respectively, copying National Coordinators and National Focal Points for Viral Respiratory Diseases.
We ask the national level experts to estimate the situation for the whole country including the peripheral laboratories and not to cascade the questionnaire to regional or local level. Please coordinate within your country that there is **only one response per country**.

Please submit your responses by end of business **18 January 2021**.

Privacy statement

Data_Privacy_Statement_2021.pdf

* I hereby confirm that I have read and understood the privacy statement and I give consent to the processing of my data for the purpose of this survey.
  - (•) Yes
  - ( ) If no, feel free to give any comments at the end of the survey

* Name:

5.1.2e 5.1.2e

* Email contact:

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* Country of report:

the Netherlands

* Institute of report:

Centre for Infectious Disease Control - RIVM

* Type of contact point (multiple answers allowed)
  - [ ] HSC Member
  - [ ] EWRS Contact Point
  - [ ] ECDC National Coordinator
  - [ ] ECDC National Focal Point for Viral Respiratory Diseases
  - [x] ECDC Operational Contact Point for COVID-19 (Microbiology)
  - [x] Other, please comment

Comments [free text]

5.1.2e 5.1.2e alternate ECDC NFP for Viral Respiratory Diseases, ECDC OCP for COVID-19 (Microbiology)

* **Question 1.** Is your country actively investigating the emergence of new SARS-CoV-2 virus variants?
  - (•) Yes
  - ( ) No
  - ( ) Don't know

Comments [free text]

Question 2. What is the purpose of pre-screening for variants in your country?
Multiple answers possible.

Definition of pre-screening for variant SARS-CoV-2 viruses: Pre-screening for variant SARS-CoV-2 viruses by using PCR to detect suspected variant virus cases in the population, e.g. screening for infection with viruses with a deletion in position 69-70 (del69-70) of spike protein.

- [x] Reduce importation of cases of variants of concern
- [x] Early detection of community cases of variants of concern
- [x] Investigating outbreaks of variants of concern
- [x] Surveillance of trends for variants of concern
- [x] Detecting emerging variants of concern within your country
- [x] Research
- [ ] Other

Comments [free text]

The spectrum of variants that have emerged and without doubt will emerge in the (near) future is/will be broader than that what can be captured by single/or limited multiplex RT-PCR. Therefore sequencing of random selections of positive cases is the approach to ensure capture of a broad range of variants. Currently we pre-screen for the UK Variant using the Taqpath assay only through labs that use this specific platform (it is not an open PCR Platform and requires dedicated machinery that is not ubiquitously present in the country). We have asked those labs to inform us about S-gene drop-outs and send them in for sequencing. The latter is necessary as we have circulation of other variants with the del69070 that also causes the drop-out. This pre-screening in combination with sequencing supports us in getting an overview of the current situation in addition to the random sequencing plan. However, as the South-Africa variant is also detected in the country, we doubt the benefits of this pre-screening approach because the different variants need different pre-screening protocols. We are currently implementing RT-PCR protocols for the variants at the ref labs and other labs that are interested, currently to be used on a selection of SARS-CoV-2 positive specimens and not as primary diagnostic test. How these subsequently are going to be implemented versus the routine SARS-CoV-2 RT-PCRs that are being performed is under consideration.
However, implementing those protocols across the country in the testing lanes, hospital labs is not being considered at this point.

Question 3. What is your country's sampling strategy for variant viruses?
Multiple answers possible.

- [x] Sampling done only in outbreaks
- [x] Sampling done only in areas where rapid increase in case numbers is detected
- [x] Random samples of SARS-CoV-2 positive specimens are screened for variants on a weekly basis
- [ ] Systematic and convenience sampling of SARS-CoV-2 positive specimens, e.g. first 10 specimens of the week are screened for variants
- [ ] Comprehensive sampling (all SARS-CoV-2 positive specimens are pre-screened by PCR for variants, e.g. using S-gene drop-out, and positive ones subsequently sequenced)
- [ ] Retrospective investigation of SARS-CoV-2 positive specimens

Comments [free text]

It is not clear whether this question refers to pre-screening or to the whole package of monitoring including sequencing. I have included our sequencing strategies in the answers given.

Question 4. Please describe your sampling strategy in short or upload your file below.

1) random sequencing based surveillance. 17 -21 labs send in at a weekly basis 24 randomly selected samples from SARS-CoV-2 positive patients for sequencing.
2) SARS-CoV-2 positive individuals with a recent history of travel from UK, South-Africa, Brazil (dynamic list of countries) that come up in follow-up of cases by Municipal Health Services
3) sampling of approx. 10% of cases in suspicious outbreaks (outbreaks with an unusual signature, e.g. unusual speed of spread in a nursing home)
4) SARS-CoV-2 positive individuals that come up in contact tracing of SARS-CoV-2-specific variant positive individuals by municipal health services
5) special SARS-CoV-2 cases (e.g. unusual disease, re-infection cases/vaccine break thru's, linked to animals)

Please upload your file here

Question 5. What methods do you use for SARS-CoV-2 variant virus pre-screening?
Multiple answers possible.

- [x] S-gene target failure PCR test (e.g. Thermo Fisher TaqPath or Yale university)
- [x] Specific RT-PCR with melting curve analysis to detect del 69-70 (TibMolBio – VirSNiP SARS-CoV-2 Spike N501Y)
- [ ] In-house PCR (please comment if you have a protocol available for sharing within the ECOVID-LabNet)
- [x] No pre-screening by PCR, but direct sequencing (please comment if you have a protocol available for sharing within the ECOVID-LabNet)
- [ ] Other method, please describe below

Comments/description of method [free text]

TibMolBiol is currently being implemented.

Several labs in the network in the Netherlands are developing single or multiplex assays for variant determination of which the protocols are shared with the ref labs. In addition, we are in contact with several other manufacturers developing or having available single or multiplex assays for variant determination. It is a rapidly moving field.

Sequencing protocols can be shared.

Question 6. What is your current pre-screening capacity for variant viruses (e.g. del 69-70 viruses), per week by number of processed specimens? Please comment also on any possible plans for changing your capacity.

It is not being done systematically country-wide. There are currently 3 laboratories that use the TaqPath assay as primary assay in diagnosing SARS-CoV-2 cases. The number of specimens being processed per week is estimated between 10,000 and 20,000. One laboratory has recently started to test specimens coming from more regions and one laboratory has just started with a new facility using the TaqPath assay. So, numbers can increase in the coming weeks. A country-wide strategy is being developed whether more laboratories should start using a variant pre-screen assay on top of their primary diagnostic test. However, this will decrease the primary diagnostic capacity and puts an extra burden on personnel capacity and usage of plastics, e.g. pipetting tips, for which there are still shortages.

Question 7. What is the turn-around time of PCR pre-screening results shared with public health authorities?

- ○ within 48 hours
- ○ within 5 days
- ○ within 7 days
- ○ more than 7 days
- ◉ Other, please provide comments

Comments [free text]

We have asked the 3 labs for weekly reports, however LIMS are not suited to extract this type of information easily because Ct values are not stored in LIMS. In addition, we ask to submit a subset of S-gene drop-outs for sequencing to determine the variant.

Question 8. What is the current proportion of SARS-CoV-2 positive specimens characterised by sequencing in your country? (number of sequenced specimens / number of total positive specimens)

- ○ < 0.1%
- ◉ 0.1- 0.5%
- ○ 0.5-1%
- ○ 1-2%
- ○ 2-5%
- ○ 5-10%
- ○ > 10%

Comments [free text]

The number of positive cases on a weekly basis is not fixed. We don't believe this is the correct parameter to monitor.
We have calculated the minimum resolution that we need for the different goals we have for sequencing. Right now we are targeting sequencing 1600 RANDOM samples per week which gives the minimal required precision needed for modelling and monitoring (0.5 - 1.5% proportion of variant among all circulating viruses)

Question 9. What is your current sequencing capacity per week by number of processed specimens?

Indeed the CURRENT situation (will increase): 700 together at both ref labs (RIVM and Erasmus MC), this is done with approx. 300 per week from random sampling across the country. we are in process of looking into scaling up towards the 1600 per week at RIVM and support monitoring with sewage water surveillance data. A total of 250 in other institutes that do not have (yet) a systematic approach but sequence mainly outbreaks in their hospitals.

Question 10. What proportion of your SARS-CoV-2 positive specimens are you characterising by antigenic characterisation i.e. neutralisation assay? (Number of antigenically characterised / number of positive specimens)

- None
- We characterise the following number of our positive specimens antigenically (please give the number of characterised / number of positive specimens) in the comment field.

Comments [free text]

This is being developedon research basis depending on what variants we detect and wish to include. This is not being done at a routine basis. There are plans to incorporate such a work flow (like the flu model). However, standardized reagents for antigenic characterization like available for flu, i.e. reference viruses with accompanying variant specific antibodies, are lacking.

Comments [free text]

Question 20. How do you plan to implement surveillance of variant viruses?

It has been implemented, see above.
In addition to that we have calculated what we believe is the minimal amount of sequences that we need to determine at a weekly basis in relation to the questions asked. More important than the number is the sampling strategy.
We are not interested in all variants that circulate but those that have a significant phenotypic change and that are prone to become dominant. One could argue that a certain threshold of circulation needs to be in place for a variant to have an epidemiological influence and that sequencing for finding variants that circulate below this threshold is not efficient.
We have full support of our ministry to implement needed capacities.

Any other comment you would like to forward to ECDC?

-clear direction WITH ARGUMENTS about the number of random sampling/sequencing at a weekly basis to answer the questions asked.
-address the effects of the use of different sequencing platforms and pipelines for retrieving consensus sequences in across border comparisons; address also whether within patient minority variant analysis should have a place in sequence analysis and interpretation, within country and across border
-address the fact that countries that are going to scale up sequencing need to keep in mind that a good bio-informatics pipeline needs to be in place and that sequencing also asked for expert interpretation of the observations (in other words it is more than generating sequences and deposit them in databases).
-address the fact (with GISAID) that this is not an open data source like GenBank is (there are restrictions to use)

Thank you for participating in this survey!

The results of this survey will be used for informing the European Commission and the European COVID-19 Surveillance Network. We aim also to make the summary of the results publicly available acknowledging the contributions of the responders.

If you have any questions, please do not hesitate to contact [redacted] @ecdc.europa.eu

Best wishes,
ECDC PHE Microbiology team

Contact

Contact Form