European variant detection and variant assessment

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SARS-CoV-2 genomic monitoring approaches

National and EU-level SARS-CoV-2 genomic monitoring should be based on complementary

1. Representative sampling of COVID-19 cases from existing, population-based surveillance systems
2. Targeted sampling of COVID-19 cases occurring in special settings or populations

Representative sequencing of SARS-CoV-2 cases from routine surveillance

Rare/novel variant event detection
Detection of emergence of a new variant in humans among SARS-CoV-2 positive surveillance specimens

Situation awareness
Monitoring the prevalence and spread of known variants

Targeted sampling of SARS-CoV-2 cases

Signal of possible emergence of a variant
Epidemiological and virological characterisation

- Vaccine breakthrough infections
- Reinfections
- Outbreaks and clusters
- Confirmed cases with travel history in areas of concern
- Unusual events

SARS-CoV-2 genomic monitoring approaches

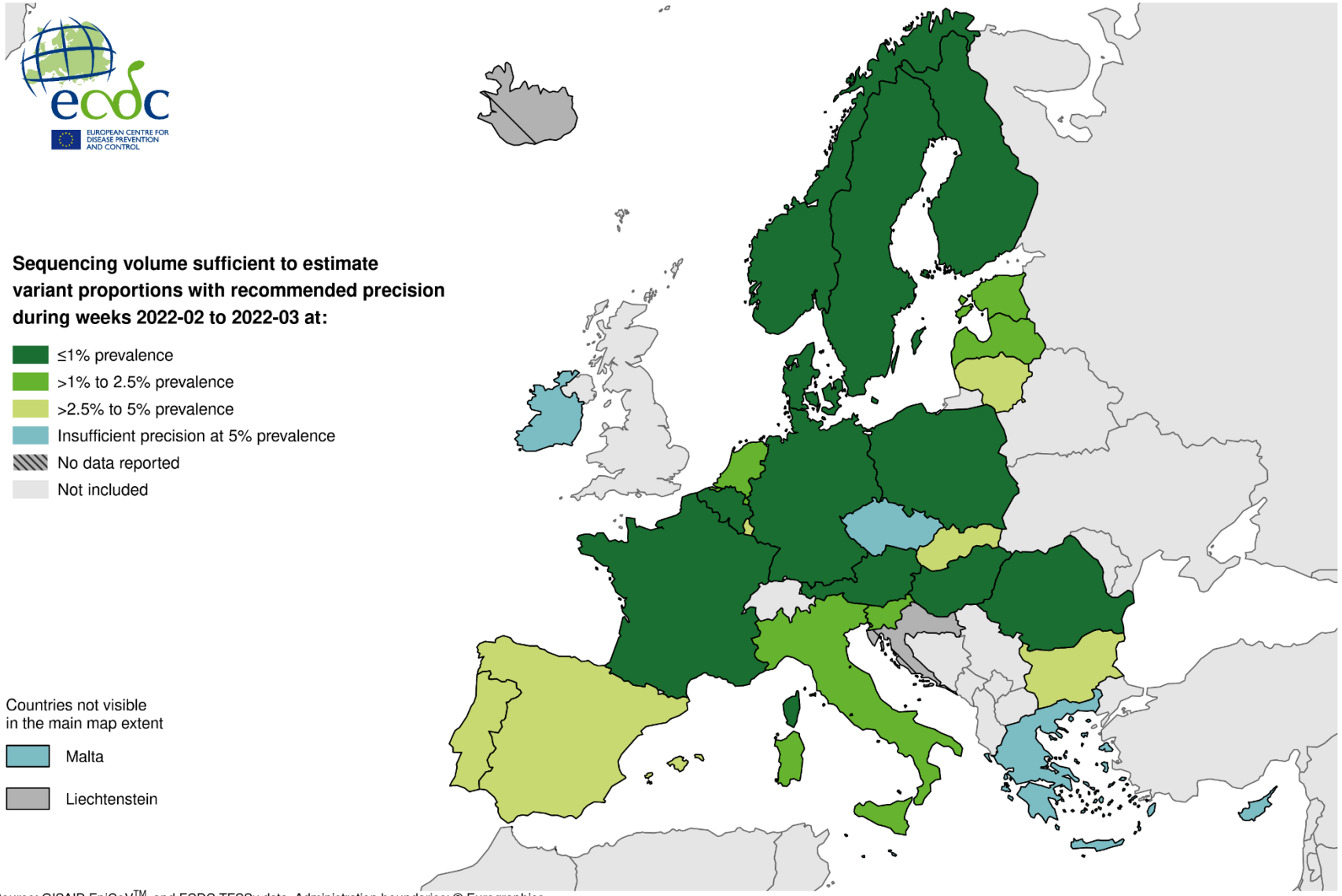
Representative sampling of SARS-CoV-2 RT-PCR positive cases

- ECDC recommends sequencing of a number of samples that allows quantification of variants at **1-2.5%** prevalence per country

	Sample size* based on the minimum prevalence of a variant to be detected		
Number of positive SARS-CoV-2 cases	**1%**	**2.5%**	**5%**
> 100 000	1 522	600	292
50 001–100 000	1 500	597	292
25 001–50 000	1 478	593	291
10 001–25 000	1 435	586	289
5 001–10 000	1 321	567	284
2 501–5 000	1 167	536	276
1 001–2 500	947	484	262
501–1 000	604	375	227
< 500	377	273	185

** Green shade marks the recommended minimum threshold.*

Current EU/EEA sequence reporting volume (weeks)



Source: GISAID EpiCoV™ and ECDC TESSy data. Administration boundaries: © Eurographics
The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on 2 February 2022

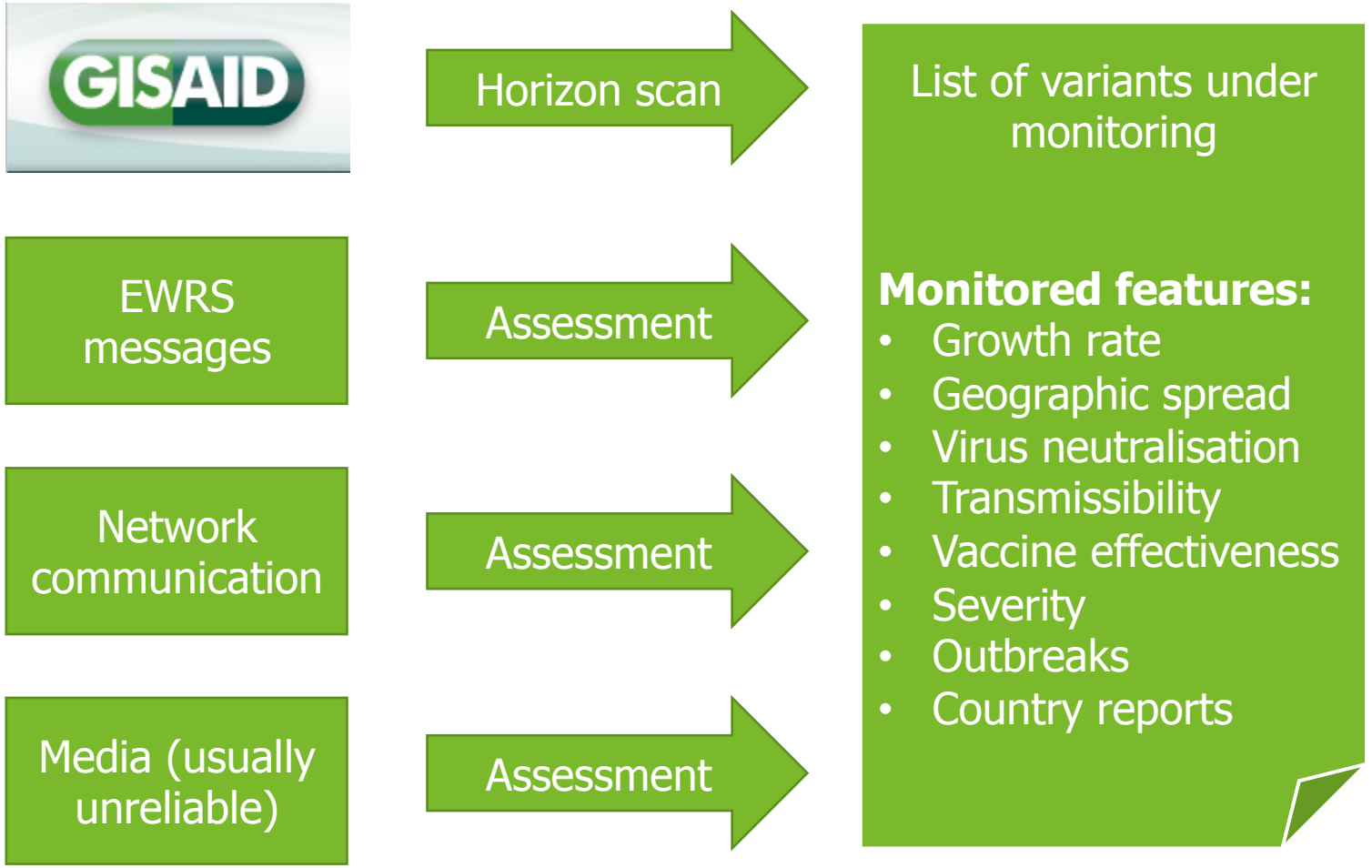
We use GISAID and TESSy as two complementary reporting platforms, we recommend reporting to both

Reporting to the COVID-19 data portal is also recommended to make the data available to the research community

The target timeliness is reporting maximum 2-3 weeks after the sample is taken

The reporting in this time-window is not always representative for the actual sequencing volume, please refer to the respective Public Health Institute for more detailed information

ECDC variant detection workflow



- Algorithm* used for horizon scan takes into account:
  - Mutation profile
  - Number of viruses detected
  - Geographic spread
  - Temporal spread
- Assessment of written variant reports are often challenging, especially media reports
- Weekly teleconferences are arranged by WHO EURO where countries present variant-related situation updates

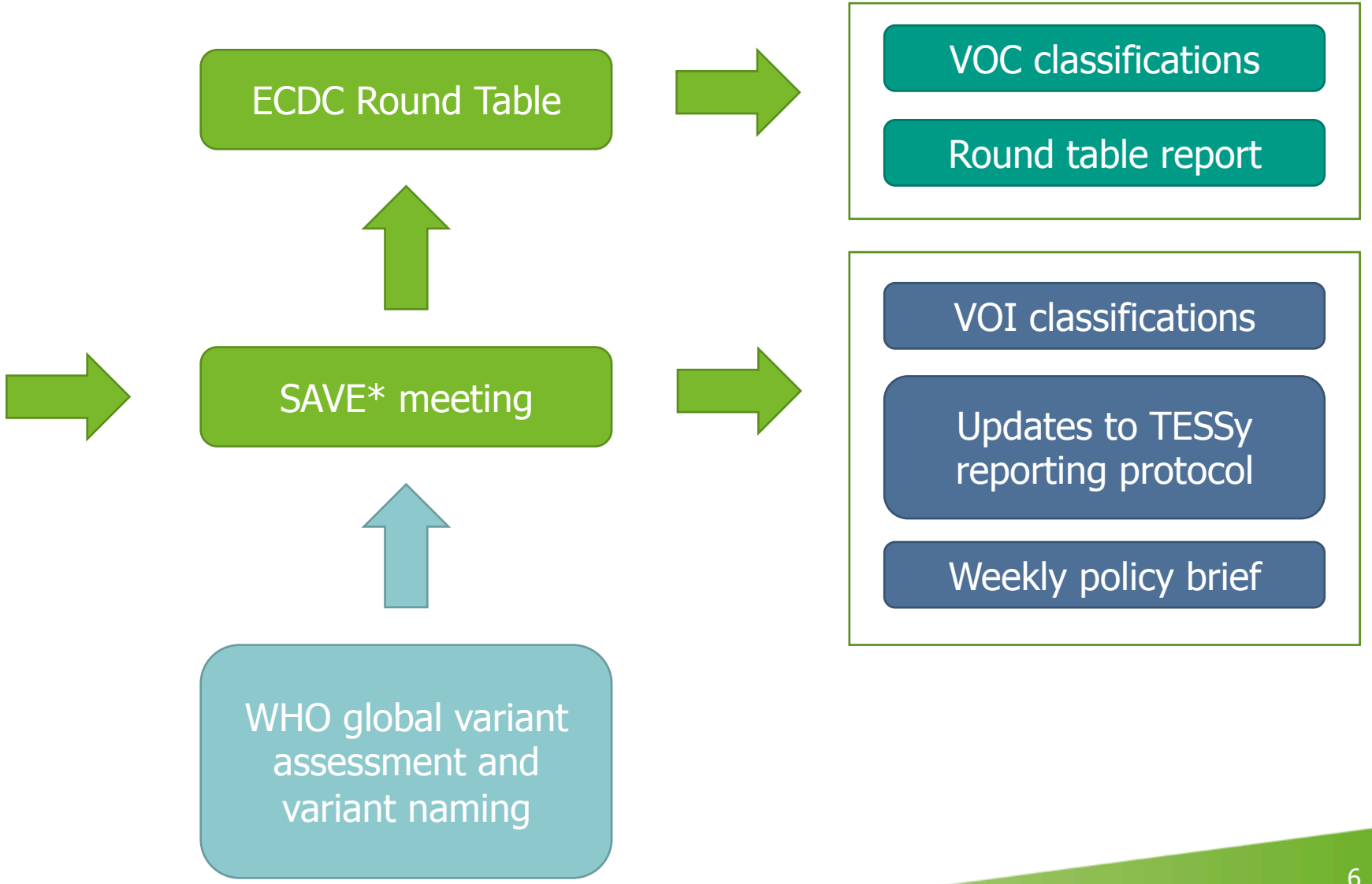
* https://github.com/erikalmecdc/ecdc_virology

ECDC weekly variant assessment workflow

List of variants under monitoring

Monitored features:

- Growth rate
- Geographic spread
- Virus neutralisation
- Transmissibility
- Vaccine effectiveness
- Severity
- Outbreak reports
- Country reports



*Strategic Analysis of Variants in Europe

ECDC variant criteria

- The main difference at the VOC level compared to the WHO working definitions is the criterion about *impact on the epidemiological situation in the EU/EEA*, where WHO instead uses the wording *global public health significance*.

- ECDC assesses variants against a background of previously circulating variants, assessing the hypothetical impact of a variant replacing the variants that were there before

Variants of concern

- For these variants, clear evidence is available indicating a significant impact on transmissibility, severity and/or immunity that is likely to have an impact on the epidemiological situation in the EU/EEA. The combined genomic, epidemiological, and in-vitro evidence for these properties invokes at least moderate confidence. In addition, all the criteria for variants of interest and under monitoring outlined below apply.

Variants of interest

- For these variants, evidence is available on genomic properties, epidemiological evidence or in-vitro evidence that could imply a significant impact on transmissibility, severity and/or immunity, realistically having an impact on the epidemiological situation in the EU/EEA. However, the evidence is still preliminary or is associated with major uncertainty. In addition, all the criteria for variants under monitoring outlined below apply.

Variants under monitoring

- These additional variants of SARS-CoV-2 have been detected as signals through epidemic intelligence, rules-based genomic variant screening, or preliminary scientific evidence. There is some indication that they could have properties similar to those of a VOC, but the evidence is weak or has not yet been assessed by ECDC. Variants listed here must be present in at least one outbreak, detected in a community within the EU/EEA, or there must be evidence that there is community transmission of the variant elsewhere in the world.

Current ECDC variants of concern

WHO label	Lineage + additional mutations	Country first detected (community)	Spike mutations of interest	Year and month first detected	Impact on transmissibility	Impact on immunity	Impact on severity	Transmission in EU/EEA
Beta	B.1.351	South Africa	K417N, E484K, N501Y, D614G, A701V	September 2020	Increased (v) (1)	Increased (v) (2, 3)	Increased (v) (4, 5)	Community
Gamma	P.1	Brazil	K417T, E484K, N501Y, D614G, H655Y	December 2020	Increased (v) (6)	Increased (v) (7)	Increased (v) (5)	Community
Delta	B.1.617.2	India	L452R, T478K, D614G, P681R	December 2020	Increased (v) (8)	Increased (v) (9-11)	Increased (v) (10, 12)	Community
Omicron	B.1.1.529	South Africa and Botswana	(x)	November 2021	Unclear (v) (13-15) a	Increased (v) (16)	Reduced (v) (17-23) b	Dominant

x: A67V, Δ69-70, T95I, G142D, Δ143-145, N211I, Δ212, ins215EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F

a: The observed increased growth rate may be due to increased inherent biological transmissibility, contextual factors such as transmitting in population groups with increased contact rates, or escape from immunity which increases the size of the susceptible population.

b: Preliminary studies show reduced risk of hospitalisation, but more data from EU/EEA countries is required to determine if this effect is observed across population groups (e.g. by age, vaccination and prior infection status). Conclusive evidence on mortality risk is not yet available.

All sub-lineages of the listed lineages are also included in the variant, e.g., C.37.1 is included in Lambda as it is a sub-lineage of C.37.

Selected challenges associated with variant detection and response

- Sequencing efforts globally are spread very unevenly – delays variant detection in some regions
- Current estimates of virus properties from genome sequences are very crude
- Delay before supporting data for transmissibility, immunity and severity becomes available
- VOC emergence so far happens in sudden evolutionary jumps in unpredictable ways – no way to anticipate antigenic change and adapt vaccines in time
- Travel measures can at best delay introduction of a variant by up to 4-6 weeks