Title: Variants of Concern (VOC): Interim public health guidance

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DRAFT FOR REVIEW

The situation with regard to variants of concern can change rapidly and the guidance may therefore change relatively frequently. Please make sure to check the website for the latest version.

Version	Date	Changes from previous version
1.8	6/4/2021	Structure and organisation altered to reflect new arrangements Included WHO definitions of VOC Added reference to the Health (amendment) Act 2021 and requirements for mandatory hotel quarantine for incoming travellers from designated states Release from hotel quarantine on receipt of a "not detected" PCR test at Day 10 (rather than after 14 days) Removal of advice relating to the public health response to incoming travellers from category 2 countries, as this has been replaced by updated guidance for designated states Added reference to national testing capacity for WGS and strategy development group Removal of the requirement for contacts of contacts of PUI and VOC to restrict movements Governance arrangements for management of PUI and probable and confirmed VOC included More detail provided on international contact tracing arrangements for VOC and PUI Key points section added Added in more details on the public health response to non-travel associated VOC including surge testing
1.7	5/3/2021	Change to frequency and timing of tests for incoming travellers from category 2 countries from one test at Day 5 to 2 tests at Day 0 and Day 10 Added clarification that enhanced public health measures apply to incoming travellers from category 2 countries who have documented history of prior infection, or vaccination

1.6	17/02/2021	Added clarification that enhanced public health measures apply to those who transited through the category 2 countries. Definition of transit included in the guidance, and a link to the cases definitions of VOC has been included.
1.5	15/02/2021	Title of guidance on page 4 updated to say "Guidance for those who have recently arrived in Ireland from South Africa, Brazil or a category 2 country.
1.4	12/02/2021	This guidance now also applies to all travellers coming to Ireland on the list of Category 2 countries, published by the Department of Health at https://www.gov.ie/en/publication/be1be-list-of-high-risk-countries-as-of-12th-february-2021/ as well as to those travelling to Ireland from Brazil and South Africa
1.3	10/02/2021	Removal of enhanced contact tracing measures for those who have travelled to Ireland from Great Britain
1.2	29/01/2021	Addition of requirement for incoming travellers from Great Britain to self-isolate for 14 days, with test at day 5.
1.1	26/01/2021	Removal of enhanced contact tracing measures for those who have travelled to Ireland from Great Britain Updated threshold for initiation of enhanced contact tracing: for cases with COVID-19 it also includes those who have household and workplace contacts with a travel history from South Africa or Brazil (in addition to personal history of travel)

Key points

- Variants of concern (VOC) are caused by mutations in SARS-CoV-2 viruses which have adverse public health consequences. These consequences include an increase in transmissibility, or virulence, or a decrease in the effectiveness of vaccines, treatments, diagnostic assays or other public health measures. The World Health Organization (WHO) currently defines three VOC: B.1.17, B.1.353 and P.1
- The Health Amendment Act, 2021 is the legal framework to prevent the importation and spread of VOC from other countries into Ireland. The Act provides for mandatory quarantine in designated facilities for people travelling into the State from high risk countries with high levels of transmission of COVID-19 or VOC. These travellers are required to quarantine for 14 days, with early exit if they receive a "not detected" test result on the Day 10 test.
- A Whole Genome Sequencing (WGS) surveillance programme is being developed, with plans to sequence up to 1,500 samples per week, sampling both reactively, i.e. incoming travellers, complex clusters, potential vaccine escape etc., and proactively, i.e. to sequence randomly-selected samples, that are representative of the population.
- The public health management of incoming travellers from "designated states", also known as high risk countries, who have SARS-CoV-2, known as persons under investigation comprises:
    - Mandatory hotel quarantine,
    - PCR testing
    - Comprehensive flight contact tracing

  A designated state is a state where there is known to be sustained human transmission of COVID-19, or any VOC, or from which there is a high risk of importation of COVID-19 or any VOC, by travel from that state. The list of designated states is set out by the Government on this website.

- The public health management of persons with a probable or confirmed VOC associated with travel comprises:
    - Establishment of an outbreak control team
    - Epidemiological investigation of the case, and identification of exposures in the 14 days prior to diagnosis.
    - International notification to other countries by the HPSC National IHR Focal Point and EWRS Contact Point, and further local or flight contact tracing if required
    - Cases who, within the 14 days prior to onset of COVID-19, have had exposure to someone in their household, workplace or with another close contact who has travelled from or through any high risk designated states (or former category two countries) in the last month are managed in the same way as travel associated cases.
- The Public Health Management of persons with a probable or confirmed VOC not associated with travel is as follows.

- Establishment of an outbreak control team,
- Identification of exposures in the 14 days prior to diagnosis
- Wider testing of workplace or other epidemiologically linked community, with use of diagnostic screening using PCR-based assays for positive cases and sequencing of screening assay positive cases
- Wider diagnostic screening using PCR-based assays as indicated by initial epidemiological investigation, including surge testing where indicated

Variants of concern

Viruses constantly change and mutate due to evolution and adaptation processes. As a consequence, the emergence of new variants is to be expected. Mutation refers to the actual change in the virus genetic sequence. A changed virus is called a variant of the original virus. Variants can differ by one mutation or many. Mutations may result in the virus being more transmissible, and/or may increase disease severity, and/or may influence efficacy of diagnostics, therapeutics or vaccines. Most of these emerging mutations will not have a significant impact on the spread of the virus. Some mutations or combinations of mutations may provide the virus with a selective advantage and when these variants increase the risk to human health, they are considered to be variants of concern (VOC).

Three virus variants have caused initial concern, because of mutations which have led to increased transmissibility and deteriorating epidemiological situations in the areas where they have recently become established. These variants were B.1.1.7, B.1. 351 (501Y.V2) and variant P.1 (B.1.1.28.1).

On 25th February 2021, WHO issued working definitions of variants of interest (VOI) and VOC as follows:

Working Definition of "SARS-CoV-2 Variant of Interest"

A SARS-CoV-2 isolate is a variant of interest (VOI) if it is phenotypically changed compared to a reference isolate or has a genome with mutations that lead to amino acid changes associated with established or suspected phenotypic implications;

AND

has been identified to cause community transmission/multiple COVID-19 cases/clusters, or has been detected in multiple countries;

OR

is otherwise assessed to be a VOI by WHO in consultation with the WHO SARS-CoV-2 Virus Evolution Working Group.

WHO Working Definition of "SARS-CoV-2 Variant of Concern"

A variant of interest is a variant of concern (VOC) if, through a comparative assessment, it has been demonstrated to be associated with

- Increase in transmissibility or detrimental change in COVID-19 epidemiology;
- Increase in virulence or change in clinical disease presentation; or
- Decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics.

OR

assessed to be a VOC by WHO in consultation with the WHO SARS-CoV-2 Virus Evolution Working Group.

WHO recognises that their definitions are focused on global risk and that countries may designate variants of local concern. In time, new variants of concern may continue to be identified.

In its updated rapid risk assessment "SARS-CoV-2 increased circulation of variants of concern and vaccine rollout in the EU/EEA, 14th update, 15th February " the European Centre for Disease Prevention and Control has stated that "the risk associated with further spread of the SARS-CoV-2 VOCs in the EU/EEA is currently assessed as high to very high for the overall population and very high for vulnerable individuals.

VOC 202012/01 (B.1.1.7) was identified first in southern England, United Kingdom in December 2020, though the earliest sample in which it was detected was in September 2020. Since then it has become the predominant variant circulating in the UK.

- It is characterised by an increased transmissibility (studies showing that it is 56-75% more transmissible than previously circulating variants), and has led to increased pressures on the healthcare system.
- In February 2021, a large UK study had detailed information on 2,245,263 positive SARS-CoV-2 community tests in whom there were 17,452 COVID-19 deaths in England from 1 September 2020 to 14 February 2021. In the analysis investigating the link between the variant type and the risk of mortality, the team controlled for the age, sex, ethnicity, deprivation level and living arrangement (residential, care home, or other) of each test-taker, and compared rates of death among individuals testing positive with and without B.1.1.7 who live in the same local authority and took their test on the same day. They estimated that B.1.1.7 infection was associated with a 55% (95% confidence interval 39–72%) higher mortality compared to other strains of SARS-CoV-2 over this time period.
- In an observational cohort study in Denmark, all SARS-CoV-2 RT PCR test-positive individuals sampled between the 1st January and 9th February, 2021, identified in the national COVID-19 surveillance system, which includes national individual RT PCR test results and viral WGS analyses and data from national health registers including COVID-19 related hospitalisations, were analysed. They controlled for sex, age, period, follow-up time less than 14 days, region, and comorbidities. The adjusted odds ratio for hospitalisation for B.1.1.7 was 1.64 times that of other lineages.
- There is no evidence that it disproportionally affects certain age groups. In Ireland, latest data indicates that this variant accounts for the majority of cases (>90%) sequenced in Ireland. It has been seen in all age groups and in all areas of the

country. **It is therefore too late to prevent introduction of this variant of concern into Ireland.**

B.1.351 (501Y.V2) was first identified in South Africa. The earliest detection was in October 2020. In South Africa, it is now the most prevalent variant. Preliminary results indicate that this variant may also have an increased transmissibility (50% more than other variants in South Africa). At this stage it is uncertain whether B.1.351 is associated with more severe infection. It has been reported that a small study with 2000 participants in South Africa found that the AstraZeneca vaccine had significantly reduced efficacy against mild disease due to the South African variant. The study was not able to ascertain its effect against severe disease and hospitalisation as those in the study were predominantly young healthy adults. B.1.351 has been found in some cases in Ireland.

The P.1. variant (B.1.1.28.1) has been reported in 41 countries across all six WHO regions (as at March 23rd). The capital of Amazonas, Manaus, is currently experiencing an upsurge in COVID-19 cases and significant pressure to the healthcare system. A recent study that analysed the national health surveillance data of hospitalisations and frequency of variant P.1 in Manaus city, found that P.1 is 2.5 times more transmissible (95% CI:2.3-2.8) compared to the previously circulating variant while the reinfection probability was found to be low i.e. 6.4% (CI:5.7–7.1%). However, these are preliminary findings and more studies are required to fully understand the transmissibility and severity of P.1 variant. It has been found in a small number of cases in Ireland.

WHO maintains a summary table of emerging information on key VOCs, in its Weekly Epidemiological update available at https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports

A similar useful summary table is maintained and updated by the New South Wales Critical Intelligence Unit, and is available at https://aci.health.nsw.gov.au/covid-19/critical-intelligence-unit/sars-cov-2-variants

The UK government also publishes regular updates at https://www.gov.uk/government/publications/covid-19-variants-genomically-confirmed-case-numbers/variants-distribution-of-cases-data

A report on confirmed VOC in Ireland will be available on the HPSC website (www.hpsc.ie) in the coming weeks.

Control of importation and spread of VOC

Legislative framework

On 5th February 2021 new Regulations (S.I. No. 44 of 2021) came into effect. They placed obligations on passengers arriving into Ireland who had travelled from overseas. Travellers were required to provide evidence that they had been tested for COVID-19 (using RT-PCR

within 72 hours before their arrival). Relevant travellers were also obligated under these Regulations to self-quarantine. Where a traveller had been in South Africa, Brazil or any other Category 2 country (a list of 33 countries deemed to be at high risk) in the period of 14 days prior the date of arrival in the State, he or she was obligated to self-quarantine for 14 days beginning on the date of arrival.

The legislation covering quarantine changed with the passing of the Health Amendment Act 2021, which came into effect on the 26th March. For reference, the Library and Research services of the Oireachtas has produced a user-friendly digest of the Bill (prepared prior to it being passed).

The primary aim of the Act is to amend the *Health Act 1947* to provide for mandatory quarantine in designated facilities for people travelling into the State, particularly from areas where there is sustained human transmission of COVID-19 or VOC. Travellers, apart from certain exempted travellers, arriving from 'designated states', which are high risk countries with high levels of transmission of COVID-19 or variants of concern, are required to quarantine for 14 days. They can leave quarantine earlier if they receive a "not detected" test result on the Day 10 test.

The Act gives the Minister for Health the power to designate states (high risk countries) in writing. The current list of designated states is available at https://www.gov.ie/en/publication/b4020-travelling-to-ireland-during-the-covid-19-pandemic/#designated-high-risk-countries-mandatory-hotel-quarantine

Travellers are required to pre-book their place at a designated facility and to pay for the cost of it themselves. However, the Minister can make regulations providing that certain classes of people will be exempt from the requirement to pay due to their financial circumstances.

Unaccompanied minors (i.e. those under 18 years of age) can be quarantined at home if their guardian (parent or approved representative e.g. school) can supervise their quarantine. They quarantine at home in a similar way to the conditions in the hotel and they are subject to the Day 0 and 10 tests. They can exit from quarantine if both tests are not detected. In these circumstances, testing is undertaken in the home by the National Ambulance Service.

Where a person arrives into the State wishing to apply for international protection or requests not to be returned to their country of origin due to fear of persecution, serious harm etc., they self-isolate in accommodation arranged by the Minister for Children, Equality, Disability, Integration and Youth.

The Act allows the Minister, or the HSE at the direction of the Minister, to enter into agreements for the provision of services related to quarantine including accommodation, maintenance, medical treatment, and security services.

These requirements apply to any passenger who has been in any of these designated states/countries in the previous 14 days prior to their arrival in Ireland, even if only transiting through one of these countries, and even if they had remained airside.

Incoming travellers from designated states are required to take an RT-PCR test at the time(s) that are designated in writing by the Minister in line with the recommendations of the Health Protection Surveillance Centre. The testing requirements apply to all children over three years of age.

These testing requirements are required to be published on a website maintained by the Minister or the Government. Current advice is that PCR testing is required at Day 0 and Day 10. If the result of the Day 10 PCR test is "not detected" then they can exit from hotel quarantine.

For those who test positive for COVID-19, the period of self-isolation required is 14 days from the date of onset of symptoms, or the date of the test, if asymptomatic, the last 5 of which must be fever-free. This is different to the requirement for 10 days self-isolation for other community cases of COVID-19.

For travellers coming from countries that are not designated states, this legislation doesn't apply. For incoming travellers from these states, they have to quarantine at home for 14 days, but can be released following a day 5 test that is "not detected".

Laboratory surveillance and increasing capacity to detect mutations and variants of concern.

A European Commission Recommendation from 19 January 2021 stated that "all EU Member States should reach a capacity of sequencing at least 5% and preferably 10% of positive test results. To reach this target, there needs to be a significant increase in sequencing capacity in Member States".

Within the EU, the capacity for sequencing is limited, as outlined in its document "Detection and characterisation capacity for SARS-CoV-2 variants-EU". Although most countries were below the level recommended by the European Commission, most are planning to increase capacity.

In Ireland in January 2021, a proposal for a national SARS-CoV-2 surveillance and whole genome sequencing (WGS) programme was approved by the National Public Health Emergency Team (NPHET). Over the next 2-3 months, sequencing capacity will aim to increase to around 1,500 samples per week, by leveraging existing publicly funded capacity as well as contracting with commercial providers. Two parallel streams of sequencing are planned: reactive and proactive.

Reactive sequencing of samples will occur when SARS-CoV-2 has been detected in travellers who have been in a designated state within the 14 days of arrival into Ireland, or at the request of Departments of Public Health when investigating complex outbreaks, potential episodes of vaccine escape, cases of reinfection, in cases of unusual clusters of respiratory infection or if there are unexpected changes in epidemiology, transmissibility or virulence. The numbers of samples sequenced each week will vary according to demand.

The remaining national sequencing capacity will be used to proactively sequence randomly-selected samples, using a structured sampling framework, which is representative of the population. This will enable the surveillance of all variants circulating within the country, as well as the detection of new variants and the tracking of VOC. The National SARS-CoV-2 Surveillance & Whole Genome Sequencing Programme Steering Group was established in March 2021. The group is a multi-disciplinary expert group tasked with overseeing the design and development of a comprehensive and sustainable national WGS surveillance programme.

A national North South VOC oversight group has also been established, to maintain regular oversight of the emergence of new and existing mutations of concern of SARS-CoV-2 globally, to advise on their implications for the island of Ireland, to undertake ongoing review of surveillance data, to advise on investigation, and control and to report its findings to the HSE and the Chief Medical Officer, Department of Health.

Public Health Response to VOC

The aim of the public health response is to delay the importation and spread of VOCs in an area where they are not widely circulating. This is achieved by a combination of testing before arrival in Ireland, and quarantine and testing of incoming travellers from states where there is a risk of importation of VOC, due either to high levels of virus in the community and/or known circulation of VOC. As VOC can arise in any country, systematic random surveillance of the population in Ireland is an essential component and may detect VOC.

Enhanced contact tracing for cases suspected to be infected with VOC should be undertaken. It is expected that most cases will arise in incoming travellers from designated states who will be in mandatory hotel quarantine. It is also possible that cases may be detected in Ireland via systematic surveillance for VOC in those who do not have a travel history. See here for case definitions of (1) persons under investigation for VOC, (2) probable and (3) confirmed cases, and here for a description of the laboratory methods used to diagnose VOCs.

Management of persons under investigation (PUI) for VOC

The threshold for initial public health action is a COVID-19 case with a personal history of having been in a **designated state** within 14 days of arrival in Ireland. This person is called a person under investigation (PUI) for VOC, and is defined as

A person who is SARS-CoV-2 positive and has a history of travel from or transit through one of the designated states within 14 days of arrival into Ireland*

Or

A person who is SARS-CoV-2 positive and is a close household workplace or other close contact of a person with a history of travel from or transit through one of the designated states within 14 days of arrival into Ireland*

*transit through includes those who have transited through a port or airport in a designated State, even if they stay airside or portside, in the 14 days prior to their arrival in Ireland

- Comprehensive contact tracing should be undertaken of any flight taken into Ireland by a PUI during their infectious period. The whole flight should be contact traced.
- The Contact Management Programme (UCD CTC) is coordinating the contact tracing of persons under investigation (PUI) for VOC.

- Passengers on a direct flight from the designated country may still be in hotel quarantine if ten days have not elapsed; co-passengers on a connecting flight may have dispersed.
- Flight contacts who have not recently been in a designated state should be told to go into home quarantine for 14 days and be tested at Day 0 and Day 10, with exit from home quarantine if the 10-day test is “not detected”.
- All children are included for testing if they are close contacts, but whether testing is required will be determined by Public Health risk assessment in individual cases.
- The airline is advised of the seat number where the passenger was sitting and if known to be a PUI or VOC. They are asked to return a short crew survey for risk assessment by Public Health. In most instances the airline occupational health team, rather than public health, deals with the contact tracing of the crew.
- This work requires international contact tracing, which is carried out by HPSC, Ireland’s IHR National Focal Point and EWRS National Contact point.
- All those coming in from designated states will be in hotel quarantine and will not have Irish close contacts outside the mandatory hotel quarantine location. However, in the unusual circumstance where a PUI is identified who is a close household, workplace or other contact of a person with recent relevant travel from a designated country, the following measures are required:
    - All close contacts of these PUI cases are advised to be tested at Day 0 and Day 10 and asked to self-isolate for 14 days, with exit possible if a “not detected” test result is obtained on Day 10.
    - For one week after this 14-day period (10 days post Day 10 “not detected” test result) of self-isolation, contacts are asked to be vigilant in observing physical distance measures and to wear a cloth face covering or mask. They should self -isolate and report to their GP immediately if any symptoms develop.

Following initial confirmation that SARS-CoV-2 RNA is detected using PCR assay, specimens are further characterised using variant screening assays.

Variant screening assays for VOC

The ThermoFisher TaqPath assay is a PCR assay that detects three distinct SARS-CoV-2 targets: orf1-ab, N gene, and S gene. Due to a deletion (at position 69-70) in the Spike protein of the UK variant (lineage B.1.1.7) the TaqPath assay S gene component yields a Not Detected result when testing the UK variant (but the two other targets are Detected). This is referred to as S gene target failure (SGTF) or 'S dropout'.

➢ If S drop out/S gene target failure is seen, then in the Irish setting, this is most probably the UK variant. Of note, SGTF has been reported in other (non-B.1.1.7) lineages, including B.1.525

➢ If all three targets are detected in the TaqPath assay, then the specimen does not contain B.1.1.7.

The 501 allele-specific PCR identifies the N501Y amino acid (AA) change in the spike protein: this AA change (or mutation) is present in B.1.1.7, B.1.351, and P.1

➢ If the N501Y AA change is not detected, then no further testing is required. The virus can be reported as wild-type SARS-CoV-2.

➢ If the N501Y is present, then further testing is required to distinguish between the three variants.

The Eurofins ViroBOAR assay combines SNP detection assays to identify the N501Y and A570D AA changes, both of which are present in B.1.1.7, but only N501Y is present in B.1.351 and P.1

➢ If neither AA change is detected, then no further testing is required. The virus can be reported as wild-type SARS-CoV-2.

➢ If both AA changes are detected, then the virus can be reported as B.1.1.7.

➢ If any other combination of 501Y and A570D is detected, the virus can be provisionally considered as a variant of concern, with further testing required to distinguish between the variants.

The 484 allele-specific PCR identifies the E484K amino acid (AA) change in the spike protein: this AA change (or mutation) is present in B.1.351 and P.1, but NOT in B.1.1.7.

➢ If the E484K AA change is not detected, the virus can be reported as wild-type SARS-CoV-2, or B.1.1.7, depending on the other results available.

➢ If the E484K AA change is detected, the virus can be provisionally considered as a variant of concern, with further testing required to distinguish between the variants.

Samples provisionally characterised as VOC samples require further testing to confirm whether they are VOC or not. They are deemed probable cases for public health action. They may go for Sanger sequencing of the S gene alone (or a portion thereof) or for whole genome sequencing (WGS); either of these sequencing methods can identify the B.1.351 or P.1 variants.

Testing Timescales

The allele-specific PCRs, TaqPath, and ViroBOAR assays can be completed within 48-72 hours, depending on when samples arrive at the laboratory; these tests are undertaken when the NVRL receives samples of interest and are currently scheduled to be performed twice weekly. Sanger sequencing of the relevant portion of the S gene takes approximately 36-48 hours and is done on an "as required" basis. Whole Genome Sequencing takes 4-5 days and is currently being done weekly.

Specimens of particular concern or interest should be brought to the attention of the laboratory in advance, and will be prioritised insofar as is possible.

If PCR testing indicates that the PUI is not a probable or confirmed case of VOC, then arrangements are in place to enable these enhanced measures as described above, i.e. flight contact tracing with self-isolation for flight contacts to be stood down and revert to usual contact tracing practices. When HPSC is notified, they will provide this follow up information to the relevant countries.

Comprehensive public health outbreak investigation and response for all probable and confirmed cases of VOC

Clinical governance PUI

People traveling into Ireland who are considered to be at risk of having a VOC are required to stay in mandatory hotel quarantine (MHQ) for a period of 14 days during which time they are given a COVID-19 test on day 0 and day 10. Individuals who are "not detected" on the Day 10 test can leave the quarantine centre and return to their area of residence. Weekly serial testing is also undertaken for staff members associated with the quarantine facilities.

Test results are electronically labelled and queued for management by a purpose-built team based at the UCD Contact Tracing Centre (CTC). When a person tested in MHQ is identified as SARS-CoV-2(PUI) by UCD CTC, the Department of Public Health in the region that the person is usually resident or had intended to travel to, is informed. The public health management of the PUI case is under the governance of the MOH of the region.

The clinical team in the MHQ facility are automatically alerted to the positive result and arrange that the case is moved into a separate section of the hotel designated for positive cases.

The Regional Department liaises with the CHO 9 Medical Officer of Health who will ensure that all appropriate public health measures are in place in the hotel. CHO9 (where the MHQ hotels are located) will act as a liaison between the regional departments and the hotel and

give advice to the hotel. CHO9 will advise on management of the case and their close contacts (who are with them in the hotel) until the definitive result is available.

The Regional Department of Public Health in collaboration with UCD undertake any needed Public Health Risk Assessment concerning, for example, flight contacts and countries outside Ireland*.*

Clinical governance probable and confirmed cases

If a travel-associated case is a probable or confirmed VOC, the MOH in that department takes overall responsibility for the case and the UCD team works on behalf of that MOH. UCD CTC undertakes any additional contact tracing required, and attends the outbreak response team.

If the probable or confirmed VOC is not travel related, then the management and governance remains with the local MOH. UCD CTC supports the work of the local MOH, undertakes the contact tracing on behalf of the local MOH, and attends the outbreak response team.

Notification of non-travel associated cases will come from the NVRL or Eurofins Biomnis via secure email labelled as “urgent, requiring action2.

A single case is managed as an outbreak. The outbreak code flags that it is a probable or confirmed VOC.

Management of travel-associated probable or confirmed VOC

- The MOH will contact the case and inform them of their variant diagnosis and what this means, and will reinforce public health messages including 14-day isolation period.
- It is likely that the majority of travel-associated probable and confirmed VOC will be at the hotel where they are undergoing mandatory hotel quarantine.
- An outbreak should be declared and an outbreak control team established. An epidemiological investigation should be undertaken in relation to exposures and contacts abroad and in Ireland from 14 days before arrival to date of diagnosis. Further contact tracing should then be undertaken based on this investigation.
- All efforts should be made so that contact tracing of the full flight is completed.
- Information on exposures abroad should be notified to HPSC on call support team who will provide this information to the relevant countries via IHR or EWRS for follow up. Notifications to HPSC and international jurisdictions should clearly state that the exposures are related to a probable VOC.
- When results of WGS are obtained and a case is confirmed, the NVRL will notify HPSC on call support team who will provide this follow up information to the relevant countries.

- For probable cases of VOC, if WGS results do not confirm the presence of VOC, the enhanced public health measures will cease and further investigation will not be required. The NVRL will notify HPSC who will provide this follow up information to the relevant countries.
- If for any reason it is not possible to sequence the VOC (insufficient sample or insufficient viral load), enhanced public health measures will need to continue.

Management of non-travel associated probable or confirmed VOC

Routine WGS is being undertaken as part of the WGS strategy, and as a result confirmed cases can be detected via this testing. In addition, some laboratories (e.g. Biomnis) are undertaking diagnostic PCR screening assays which may indicate a probable VOC.

If this happens, NVRL or Eurofins Biomnis notifies the Department of Public Health, who will manage the case. Notification of these cases will come from the relevant laboratory via secure email labelled as urgent, requiring action. A single case is managed as an outbreak. The outbreak code flags that it is a probable or confirmed VOC.

An outbreak should be declared and an outbreak control team established as appropriate. An epidemiological investigation should be undertaken in relation to exposures and contacts in the previous 14 days in Ireland. This will include checking if any contacts have a relevant travel history (designated state or former category 2 country) in the preceding month. Further contact tracing should then be undertaken based on this investigation. For cases that are not linked to travel, extensive efforts are required to identify any epidemiological links with other cases.

For non-travel associated probable and confirmed VOC cases, the following applies:

a) Case to self-isolate for 14 days, the last 5 days of which must be fever-free.

b) Contacts of the case will be asked to self-isolate, and to be tested for COVID-19 at day 0 and day 10, with exit following a “not detected” test at day 10.

c) For one week after this 14-day period of self-isolation, contacts are to be vigilant in observing physical distance measures at all times and to wear a cloth face covering or mask. These contacts should self-isolate and report to their GP immediately if any symptoms develop.

For probable and confirmed VOC cases that are not linked to travel and where there is evidence of community transmission of VOC, extensive efforts are required to identify any epidemiological links with other cases. This may include having a low threshold for wider testing of those with any potential epidemiological links. If links are not found, there may be the need to then use diagnostic screening assays and fast-track sequencing, as well as considering surge testing in geographically defined affected area(s).

The nature of the epidemiological investigation will be decided by the MOH in the regional Department of Public Health. This will be informed by local Public Health Risk Assessment and overseen by the local outbreak control team working with key partners including the Laboratory Operations team, and the Contact Management Programme supported by the National Health Protection Operations team.

It may include

a. testing (and sequencing) of all associates in a workplace, or other potentially epidemiologically linked setting

b. sequencing of historical SARS-CoV-2 samples of interest (limited benefit, as samples are not retained for long periods)

c. retro/proactive diagnostic PCR screening for VOC, and sequencing of all SARS-CoV-2 positive samples from a chosen geographical region over a chosen time period to detect potential hidden chains of infection

d. Surge testing of the population in affected areas, with those who are SARS-CoV-2 positive undergoing screening assays for VOC, and WGS as indicated. This is done in order to detect potential hidden chains of infection.

The aim is to rapidly detect any additional cases and identify and implement actions to contain spread of the VOC. These actions were informed by the approach taken by NHS Test and Trace in England, see here, although this is a bespoke response for Ireland, given our circumstances, capacities and resources.

Options a, b and c have already been undertaken in Ireland in response to non-travel related clusters. In the response to one non-travel related cluster, Public Health agreed with the HSE Laboratory Operations Team and Eurofins Biomnis laboratory operational procedures to enable identification of all SARS-CoV-2 samples in a defined area from local laboratories and for them to be screened using PCR screening assays with the results provided to the MOH for response. This is set out in more detail in Appendix A.

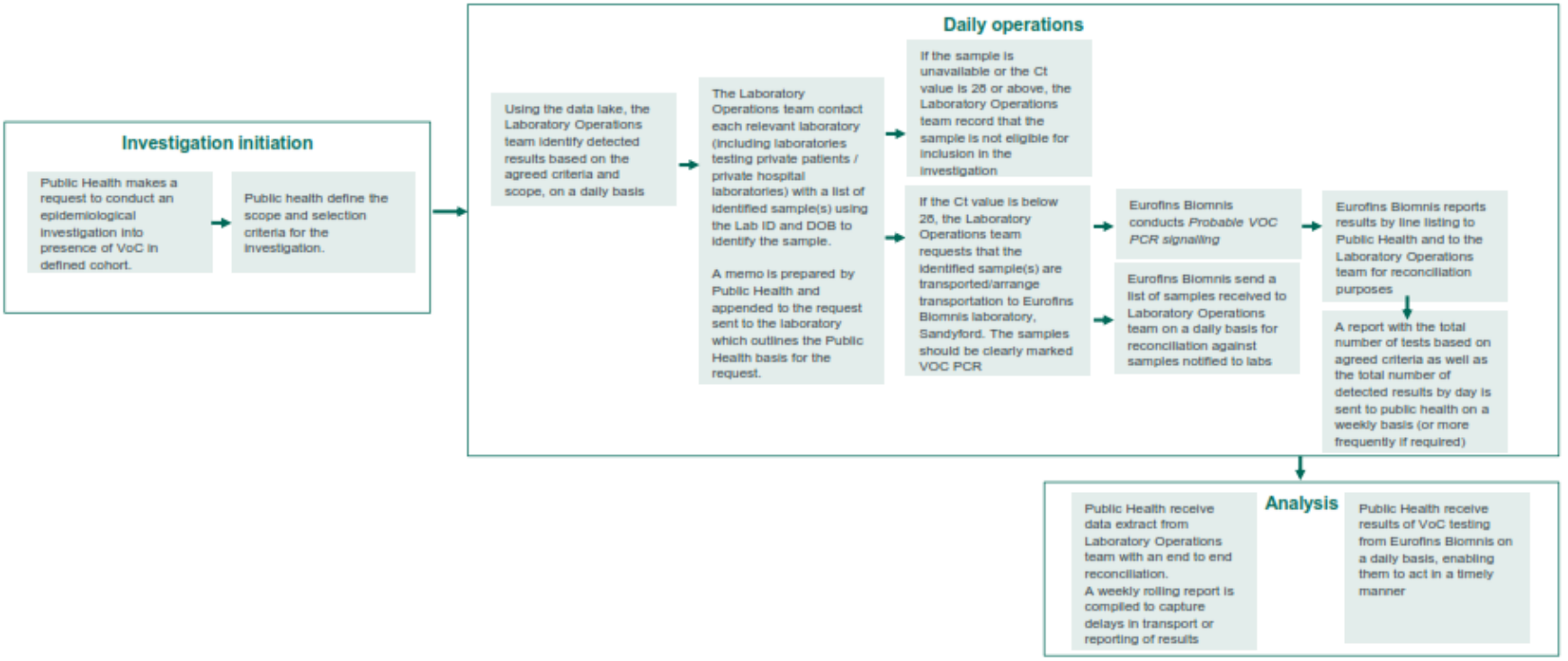
In order to implement option d, this requires alignment of the new 'walk-in, no appointment necessary' COVID-19 testing centres with these agreed procedures. Testing centres can be established in the area where there is concern about community transmission of VOC, and any SARS-CoV-2 positive results would follow the pathway established for c above. This is being planned now in response to a second cluster and further learning about the practicalities in implementing this approach will emerge from this work. A walk-in clinic in this area will encourage the local population to undertake testing, working with local affected communities using local publicity and social media channels. If, as is planned, these samples go directly to Biomnis laboratories this will simplify the reporting process. As well as providing the results of those positive on screening assays, the laboratory operations team will need to be in a position to monitor and report to the MOH on the total numbers

of tests undertaken during the defined time period, and the test positivity rate in the affected area of concern. **This requires further discussion and agreement and guidance may be amended based on the learning from this first implementation of surge testing.**

The MOH, and outbreak control team will decide on any additional actions required based on the results of the surge testing. As well as responding to any new VOC cases identified, the local MOH through the results of surge testing may find that other unrelated clusters or outbreaks that are not VOC related are also identified. Sufficient surge capacity to deal with non-VOC related clusters should be planned for the local MOH. The CMP should work with the local MOH to support this work.

Epidemiological investigation within a specific geographic region

Pathway for VOC PCR testing with ViroBOAR assay



Epidemiological investigation within a specific geographic region

Dataflows for VOC PCR testing with ViroBOAR assay