Title: Variants of Concern Cases and Processes in Ireland, including an update on Global Epidemiology for NPHET

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Action required:

☐ For noting

X **For discussion**

☐For decision

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Contents

Of Note:

The issue of incomplete Passenger Locator Forms is problematic. This repeatedly results in an inability to fully contact trace all passengers on incoming flights of concern, thus creating a significant risk of the introduction and spread of variants of concern.

Updates:

- The UK have designated the B.1.1.7 variant with an additional E484K mutation as a fourth Variant of Concern. It has 28 confirmed cases of this variant to date, in clusters in the South West and the North of England.

- There are no estimates of transmissibility or severity available for B.1.1.7 with the E484K mutation. It is likely that this variant has almost identical properties as B.1.1.7 without E484K, but there may be a decrease in neutralisation by monoclonal antibodies

- It is now mandatory for travellers arriving by air into England from any of the 33 countries listed as "high-risk" to self-isolate in a government-sanctioned hotel for 10 days, at a cost of £1,175 per person.

- Scotland have extended this requirement to travellers from all countries outside the Common Travel Area

- A large number of cases (295) of the B.1.351 variant has recently been reported in Austria, mostly concentrated in the region of Tyrol

- Although some cases of the B.1.351 variant reported in EU/EEA are linked to travel, several EU/EEA countries have reported community transmission of the variant

- Transmissibility of B.1.1.7 is estimated to be up to 56% higher than the previously circulating strains of SARS-CoV2. Preliminary results for B.1.351 indicate that the variant has 50% higher transmissibility. There is no transmissibility estimate for P.1 yet

- There is evidence that B.1.351 and P.1 might have antigenic properties that may give them a selective advantage over B.1.1.7 in populations with high levels of immunity derived from infection or vaccination.

- There is a realistic possibility that B.1.1.7 is associated with increased risk of death compared to non-B.1.1.7 cases. There is substantial uncertainty regarding severity estimates for B.1.351 and P.1

- Ireland updated its list of high risk 'category 2' countries to include: Angola, Austria, Botswana, Brazil, Burundi, Cape Verde, Democratic Republic of the Congo, Lesotho, Malawi, Eswatini, Mauritius, Mozambique, Namibia, Republic of South Africa, Rwanda, Seychelles, Tanzania, United Arab Emirates, Zambia, or Zimbabwe

- Passengers travelling from, or transiting through, these countries are required to self-isolate for 14 days upon arrival and to be tested at day 5 and/or upon onset of symptoms. Enhanced contact tracing measures will be implemented for any cases identified

- Transit through one of these countries is defined as:

A transit stop is a stop where passengers can get on or off. It can apply to coaches, ferries, trains or flights. The ticket should show if a stop is a transit stop.

If the journey involves a transit stop in one of the category 2 countries, enhanced public health measures will apply when they arrive in Ireland if:

- new passengers get on
- the traveller or other passengers get off the transport they are on and then get on again

These measure will not apply, if during the transit stop in one of the category 2 countries:

- no new passengers get on
- no-one on-board gets off
- passengers get off but do not get back on

- Following assessment of several independent studies, UK NERVTAG stated on 11 February 2021 that 'it is likely that infection with VOC B.1.1.7 is associated with an increased risk of hospitalisation and death compared to infection with non-VOC viruses'. Studies assessed included:
  - LSHTM: reported that the relative hazard of death within 28 days of test for VOC-infected individuals compared to non-VOC was 1.58 (95%CI 1.40–1.79), or 1.71 (95% CI 1.48- 1.97) if adjustment is made for misclassification of SGTF and missing data.
  - Imperial College London: mean ratio of case fatality ratio (CFR) for VOC infected individuals compared to non-VOC was 1.36 (95% CI 1.18-1.56).
  - University of Exeter: an updated analysis estimated the mortality hazard ratio for VOC-infected individuals compared to non-VOC was 1.7 (95% CI 1.3 – 2.2)
  - Public Health England: an updated matched cohort analysis has reported a death risk ratio for VOC-infected individuals compared to non-VOC of 1.65 (95% CI 1.21-2.25)
  - The Hospital Onset Covid Infection (HOCI) study: found the overall HR for inhospital mortality of B.1.1.7 was 1.09 (95% CI 0.86-1.36, P=0.48). Increased mortality was only observed with the VOC in women over 65 years. The overall HR for ITU admission for B.1.1.7 was 1.15 (95% CI 0.86-1.53, P=0.35)

Section 1: International epidemiology of Variant of Concern

1.1 Variant identified in South Africa (B.1.351)

As of 11 February 2021, according to media and official sources, the variant B.1.351 has been identified in 40 countries and approximately 1 400 cases have been reported globally. More than 90% of cases sequenced in South Africa since late November have been due to this variant and there is evidence that the variant has been circulating since at least November in Mozambique as well, indicating that it may be widespread in other countries in the region where sequencing is not performed or publicly reported.

Table 1 presents the international detected cases of the South African variant (to 14/02/21):

Country	Total cases reported in media or via IHR/EWRS	Confirmed sequences in GISAID	Cases imported or evidence of local community transmission
Australia	12	17	Imported cases
Austria	304	3	Community transmission
Bangladesh	1	1	Unknown
Belgium	99	76	Unknown
Botswana	1	38	Unknown
Brazil	1		Unknown
Canada	15	2	Community transmission
China	1		Imported cases
Cuba	1		Imported cases
Democratic Republic of the Congo		1	
Denmark	5	7	Unknown
Finland	18	2	Unknown
France	40	50	Unknown
Gambia	1	0	Unknown
Germany	15	8	Unknown
Ghana	Not specified		Unknown
Greece	1		Unknown
Ireland	9	10	Unknown

Israel	80	7	Unknown
Italy	1		Imported cases
Japan	3	5	Unknown**
Kenya	2	6	Unknown
Luxembourg	3	2	Unknown
Malawi	-		Exported cases*
Mayotte	78	23	Unknown
Mozambique	Not specified	42	Unknown
Netherlands	23	31	Unknown
New Zealand	10	7	Local transmission
Norway	2	1	Imported cases
Panama	1	1	Imported cases
Portugal	1	1	Unknown
Singapore		1	
South Korea	7	1	Unknown
Spain	2	2	Unknown
Sweden	7	1	Imported cases
Switzerland	69	43	Unknown
Taiwan	1		Imported cases
Thailand		1	
Turkey	2	2	Unknown
UAE		5	
USA	9	7	Community transmission
Vietnam	1		Imported cases
Zambia	22	31	Unknown
Total	**848**	**435**	

Table 1: International cases S. African variant ***(Data source – UK Variant and Mutation Taskforce slides 15/02/21)***

There have been 202 confirmed or probable cases of B.1.351 in the UK; England = 182 (data updated to 10/02/21); Scotland = 7 (to 10/02/21); Wales = 13 (to 05/02/21); Northern Ireland = 0 (to 28/01/21)

1.2 Variant identified in Brazil

International epidemiology of the Brazilian variants (P.1 – variant of concern; P.2 – variant of interest)

As of 11 February 2021, P.1 has been identified in 17 countries and approximately 200 cases have been reported globally. In the EU/EEA, around 30 cases have been identified in 5 countries and areas (France, including La Reunion, Germany, Italy, the Netherlands and Spain).

Table 2 presents the international detected cases of the Brazilian P.1 variant of concern:

Country	Total cases reported in media or via IHR/EWRS	Confirmed sequences in GISAID	Cases imported or evidence of local/community transmission
Argentina	2**		Community transmission
Belgium		1	
Canada	1**		Imported case
Colombia	2	9	Unknown
Faroe Islands	1	1	Imported case
France	3	4	
Germany	3		Imported cases
Italy	12*	3	Unknown
Japan	4	7	Imported cases
Netherlands	2	2	Unknown
Peru	1	1	Unknown
South Korea	1 (4*)	1	Unknown
Spain	1*		Imported case
Switzerland	1	9	
Turkey	1*		Unknown
USA	3	3	Community transmission
Total	40	41	

Table 2: International cases Brazilian P.1 variant of concern (Data source – *UK Variant and Mutation Taskforce slides 15/02/21)*

***Information not available for whether this is P.1 or P.2**

Section 2: Variant of Concern processes and Covid-19 cases in Ireland

2.1: Variant of Concern Processes

1. Nationally agreed processes have been established to identify Persons Under Investigation (those with confirmed Covid-19 infection and relevant travel history) to ensure appropriate isolation advice is given and all contacts appropriately traced and tested, as per national guidance for VOC. Weekly data reports have been agreed.
2. A National Variants of Concern Operational group has been established across Departments of Public Health, CMP, CTC, HPSC and HSE data processing to ensure clear processes are in place for actions required from probable and confirmed cases, and for monitoring of processes within and between Departments of Public Health and the CMP / CTC. Updates and interlinking with NVRL for this group are established and used as required.
3. A National Oversight Group for Variants of Concern has been established, with a broad appropriate multi-disciplinary membership, to ensure the challenges identified with new VOC are discussed and addressed, and the situation across the island of Ireland is monitored and discussed. This group includes membership from colleagues in Northern Ireland.
4. The National Clinical Director of Health Protection will meet once a fortnight with the clinical lead in Public Health England on VOC – first meeting scheduled for Friday Feb 19th.

2.2: South African Variant Covid-19 cases in Ireland

(Based on NVRL results up to 15th February 2021. Definitions in Appendix One)

Confirmed 501Y.V2 cases (new in the last week): 11 (0)

Probable cases (new in the last week): 5 (0)

Prior to the week commencing 15th February 2021, all **confirmed** and **probable** cases had been identified and followed up through CTCs initially or Departments of Public health and appropriate public health actions undertaken.

The Biomnis laboratory had contacted both the DPHs in the East and in the West, with regards to “potential VOCs”. Work is currently ongoing to elucidate the testing performed on these samples and the definition used for “potential VOCs”, as well as the means by which such results are notified to the HSE and DPHs, in order to align with the process agreed with the NVRL, DPHs and CMP.

- In the East region, a “potential VOC” was identified in a positive sample from a mother of a child attending a childcare facility. All appropriate measures were undertaken by the DPH and the sample was subsequently identified as being not a

VOC upon re-testing at NVRL. WGS of the samples of all close contacts has been requested.

- "Potential VOC" cases were identified in samples from two different families (with no epi link and no travel history) in the West. In the first family, all 4 members were deemed "potential VOCs" and in the second, 2 of 4 positive family members were "potential VOCs". Further analysis of the other 2 family cases' samples has been requested. All necessary Public Health measures have been taken while WGS results are awaited.

2.3: Brazilian variant of concern cases in Ireland

No confirmed cases of Brazilian P.1 (variant of concern)

Probable cases (new in the last week): 2 (2)

With regards to the new **probable** cases:

- Two cases travelled together from Brazil, via Lisbon, arriving in Ireland on 26th January 2021. They moved immediately to self-isolation accommodation in a hotel, organised by their employer (meat processing plant). No close contacts were identified in Ireland (apart from 3rd member of travelling party, who is in self-isolation and tested positive on 11/02/21 – for WGS). 66 of 91 people on board the flight were traced and tested, resulting in 3 additional cases being identified (1 of whom was probably infected by a housemate upon return to his home in Ireland – managed by PHD South East). 1 has been self-isolating since arrival, with no close contacts; the remaining case had 6 close household contacts, all of whom have been tested and managed by the PHD in the East.

- An outbreak control meeting was held on 15th February. All persons on the flight from Lisbon to Dublin had been designated as close contacts. An attempt to contact and follow up every passenger on the flight from Lisbon will be made, to check for results of any tests taken and to organise day 10 tests (ASAP as past day 10) for those not having previously tested positive. Portuguese authorities will also be notified of the travellers flying during their infectious period. The investigation is ongoing.

- **The issue of incomplete Passenger Locator Forms was raised. This repeatedly results in an inability to fully contact trace all passengers on incoming flights of concern, thus creating a significant risk of the introduction and spread of variants of concern.**

Section 3: CTC / CMP update Brazil / South Africa Travel-related Cases / Close Contacts

Updated to 9:00am on 15th February 2021.

Potential cases of the VOCs identified are through a combination of referrals through Healthlink and notification of cases from the Routine Queue of the CCT System to the Specialised Queue managed by UCD CTC on behalf of Departments of Public Health. These processes are outlined in detail in Appendix 2.

Table 3 presents the number of potential cases of VOC among those who had a history of travel from Brazil or South Africa, or close contact with a person with a history of travel from Brazil or South Africa, within 14 days of the onset of Covid-19. Also presented are the number of VOCs confirmed by Whole Genome Sequencing (WGS) for Brazil and South Africa among those cases.

	Brazil	South Africa
Travel-related Referrals for Testing identified through Healthlink	1645	336
Travel-related Positive Results (Cases) identified through Healthlink	60	12
Travel-related Positivity Rate for cases identified through Healthlink	*3.65%*	*3.57%*
Additional Cases identified through CMP Contact Tracing	27	9
Total Brazil & South Africa Travel-Related Cases	**87**	**21**
VOC (Variant of Concern) Detected by WGS, NVRL	**0**	**11**

Table 3: Cases with a history of travel from Brazil and South Africa and Variant Testing outcome to 09:00am 15th February 2021

Of note is that two-thirds of all cases (72/108) were identified through Healthlink. The remaining one-third (36/108) relies on identification of such cases through the CTCs of Contact Management Programme.

Figure 1 (below) presents the numbers of Brazil and South Africa travel-related referrals through Healthlink only by week to date. The number of referrals through Healthlink with a history of travel from Brazil has decreased steadily over the period. There is some variation in referrals with a history of travel from South Africa.

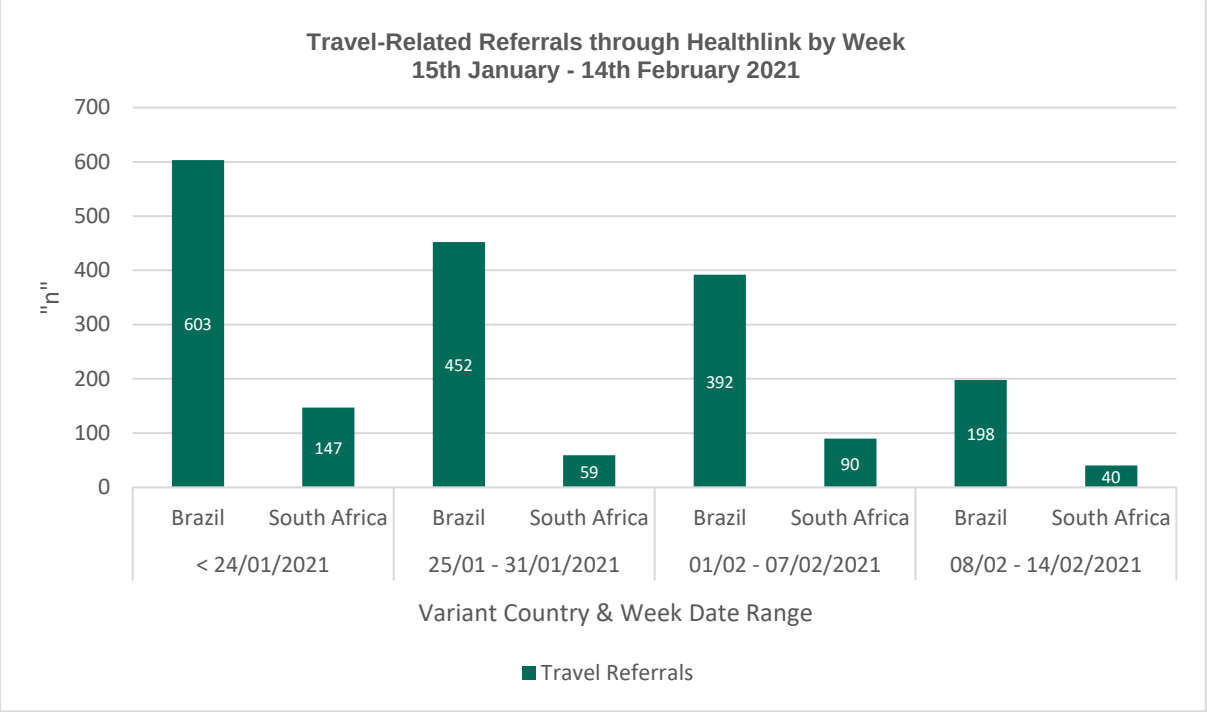

Figure 1: Travel Related Referrals through HealthLink by week to 09:00am 15th February 2021

Figure 2 presents the number cases with a history of travel from Brazil and South Africa identified through Healthlink and CMP combined by week to date.

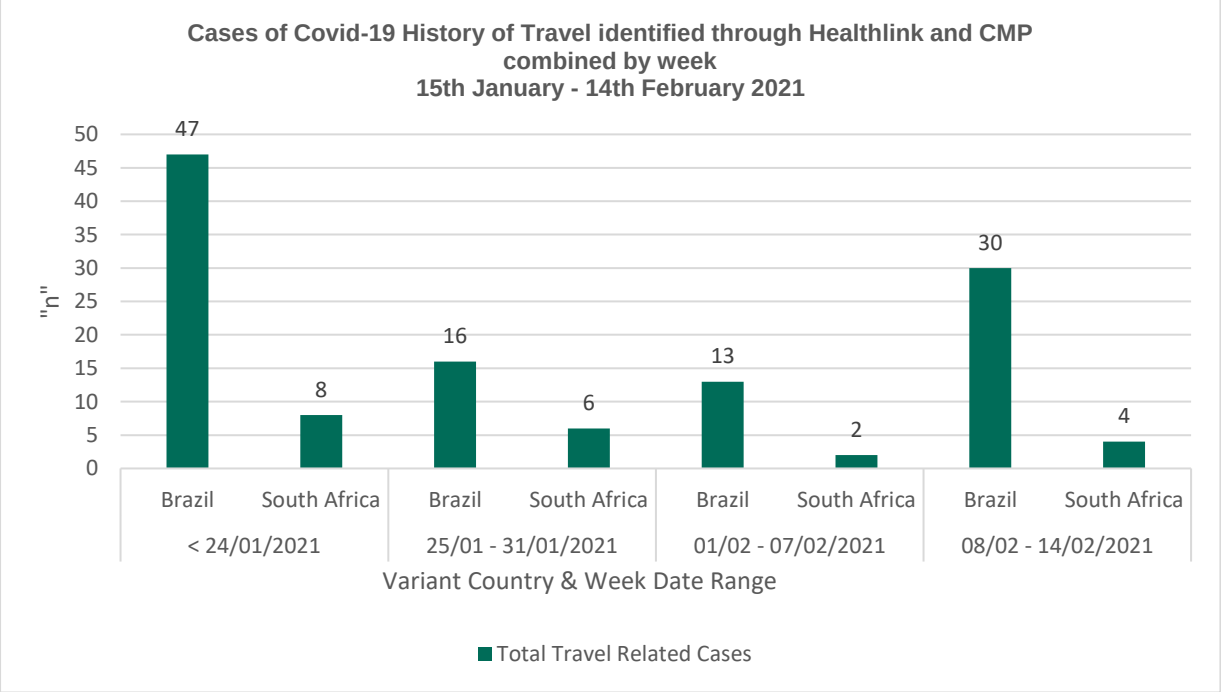

Figure 2: Cases of Covid-19 with History of Travel identified through Healthlink and CMP combined, by Week

Contact Tracing

Enhanced Contact Tracing has been completed for all cases to date with a travel history of concern.

Of cases for whom Contact Tracing complete:

- Detailed travel history has been established in so far as possible (dates, route, flight numbers, seat numbers). Further details may be required for some cases if identified as having a VOC.
- Close contacts of cases have been identified and scheduled for testing; self-isolation advice has been provided, and contacts have been asked to advise their household members to restrict their movements for 14 days.
- Exposure Investigations have been created for flights undertaken during infectious period (n=15)
- Passenger details from flight manifests are sourced by the Data Processing Team (DPT). The passenger details for 6 flights have been provided so far. Details of Contact Tracing of passengers on these six flights are given in Table 4.

Date Received	Flight Number	Route	Flight Date	Total Passengers	Uncontactable (No number or not answered)	Successfully Contacted
25.01.21	**EI2595**	Madrid-Dublin	14.01.21	114	38	76 (67%)
26.01.21	**LH980**	Frankfurt-Dublin	15.01.21	96	24	72 (75%)
26.01.21	**TP1324**	Lisbon-Dublin	18.01.21	134	41	93 (74%)
02.02.21	**TP1324**	Lisbon-Dublin	26.01.21	91	32	59 (65%)
11.02.21	**LH980**	Frankfurt-Dublin	02.02.21	99	21	78 (79%)
13.02.21	**IB3454**	Madrid-Dublin	03.02.21	126	48	74 (61%)

Table 4: Exposure Investigation of Eligible Flights

Contact tracing is completed for all passengers who could be contacted. Reasons for being uncontactable include: no number given; wrong number; international number provided not answered; or occasionally number provided for booking agent.

Of note are the lengthy time intervals from flight arrival date to enhanced contact tracing.

- Time interval from date of flight to date of contact tracing (past 3 weeks):
    - Week 25.01 (11 days)
    - Week 01.02 (8 days)
    - Week 08.02 (9 days) & (10 days)

These are a combination of:

- the interval to case identification – usually identified on a Day 5 post-arrival test if asymptomatic;

- the interval for result reporting, creation of the case in the CCT, contact tracing and creation of an Exposure Investigation for the flight;
- the request by PH Data Processing Team to the airline for flight manifest;
- time taken for an airline to provide the flight manifest.
- Cross-checking of flight manifest with e-PLFs.

Contacts who remain uncontactable following multiple call attempts are forwarded to Public Health Data Processing (PH DP). These contacts are emailed (if email addresses are available) in order to ascertain updated contact information, and any new contact information is subsequently provided to UCD CTC for further call attempts. Consideration also given to arrange testing for those with valid phone numbers who have not been reached supported by Public Health.

Appendix One

How are SARS-CoV-2 variants identified?

Following initial confirmation that SARS-CoV-2 RNA is detected using PCR assay, specimens are currently screened using either a 501 allele-specific PCR assay or the ThermoFisher TaqPath assay.

The 501 allele-specific PCR identifies the N501Y amino acid (AA) change in the spike protein: this AA change (or mutation) is present in B117, 501Y.V2, and P1

➢ 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 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, but none of these has been detected in Ireland to date.

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

These samples (N501Y Detected, S gene Detected on TaqPath) require further testing. 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 P1 and 501Y.V2 variants.

Testing Timescales

The 501 allele-specific PCR and the TaqPath can be completed within 24-48 hours, depending on when samples arrive at the laboratory; these tests are undertaken when the NVRL receives samples of interest. Sanger sequencing of the relevant portion of the S gene takes approximately 36 hours and is done on an as required basis. Whole Genome Sequencing takes 3-4 days and is currently being done weekly.

Appendix Two

Identification of Cases by the Contact Management Programme

Covid-19 positive cases who have travelled from Brazil or South Africa are identified by the following means:

1) Referral of individuals for Covid-19 testing through the HSE GP Healthlink: Two new options, which can be selected at the point of referral, have been added to the options listed for testing in Healthlink. These are: 'Travel from Brazil', and 'Travel from South Africa'. Anyone referred for testing for whom these fields have been chosen, and who tests positive, can be identified by the Integrated Information System (IIS). These cases are extracted on a daily basis for onward referral to the National Virus Reference Laboratory (NVRL) for WGS;

2) Cases of Covid-19 in persons who have travelled from Brazil or South Africa are identified through the Contact Management Programme's contact tracing process. The Contact Tracing Centre (CTC) at UCD collates this information from all CTCs through a Work Instruction (WI) issued on 15th January 2021. The cases identified include those identified through 1) above, as well as cases identified by CTCs through other routes.

Consolidation and Distribution of Information

The HSE IIS Team circulates a data extract from Healthlink of cases of Covid-19 linked to the Brazil and South Africa travel testing categories. This is sent on a daily basis to Public Health leads, UCD CTC, NVRL, Laboratory Operations Team and HSE Test and Trace Project Management representatives. Additional cases identified by the UCD CTC are manually added to the list and re-circulated to the above group. This allows for cases identified by both the Healthlink referral categories and Contact Tracing to be consolidated.

Samples are sourced by the Laboratory Teams and delivered to NVRL laboratory for WGS to test for the Variants of Concern (VOC). All samples for which WGS for the Brazil and South Africa variants is warranted are either currently at the NVRL or are en route to the NVRL for this analysis.

Contact Tracing

The Contact Tracing Team in UCD undertakes enhanced contact tracing of Brazil and South Africa travel-related cases and their close contacts. In addition, an exposure investigation is carried out on any eligible flights relating to Brazil and South Africa. An update on these activities is provided below:

Contact Tracing of Cases and Close Contacts

All cases of Covid-19 are entered into the Routine Queue (RQ) of CovidCare Tracker (CCT) system. Cases with a travel history from Brazil or South Africa within 14 days prior to testing positive for Covid-19 (or 14 days prior to symptom onset, if symptomatic) are routed to the Specialised Queue (SQ) for enhanced Contact Tracing and routing to NVRL for WGS by UCD. Callers in all CTCs are appraised of, and reminded, to follow the WIs on establishing travel history in Brazil and South Africa cases and the appropriate routing of cases to the SQ without undertaking contact tracing in these cases.

Enhanced Contact Tracing is undertaken by a specialised team of callers at UCD CTC.

Variant Detection & Public Health Response

All detected positive samples identified by GP Healthlink referrals and UCD Contact Tracing Centre are routed to NVRL for whole genome sequencing to detect the Variant of Concern.

On conclusion of NVRL genome sequencing, all results are communicated to Public Health who contact the individual in question.

- If the VoC is present in the sample, Public Health will communicate with the individual and initiate a Stand Up Process which will involve increasing the individual's isolation restrictions.
- If the VoC is not present in the sample, Public Health will communicate with the individual and initiate a Stand Down Process which will involve decreasing the individual's isolation restrictions.