

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

Author: Dr Abigail Collins, Dr Matt Robinson following engagement with Depts of Public Health, CMP and members of the National Oversight Group for Mutations of Concern.

Organisation: Office of the National Clinical Director Health Protection, HSE HPSC

Date: 3rd February 2021

Action required:

For noting

For discussion

For decision

Approved for future publication: NO

Contents

Title: Variants of Concern Cases and Processes: Update for NPHET	1
Section 1: International epidemiology of Variant of Concern	3
1.1 South African Variant	3
1.2 Brazilian Variant	4
Sections 2: Variant of Concern Covid-19 cases in Ireland	6
2.1: South African Variant Covid-19 cases in Ireland	6
2.2: Brazilian variant of concern cases in Ireland	7
Section 3: CTC / CMP update Brazil / South Africa Travel-related Cases / Close contacts.....	7
Section 4: Public Health Process document	8
Pathway One	8
Pathway Two.....	10
Appendix 1	11
Appendix 2	12

News:

- Public Health England published a document where they report the detection of an E484K mutation in eleven B.1.1.7 VOC 202012/01 sequences. This mutation was previously found in VOC 202012/02 B1.351 and VOC 202101/02 P1. Studies have shown that this mutation is known to cause reduced neutralisation by natural and vaccine-induced immunity (from ECDC Round Table report 02/02/2021).
- Preliminary data from clinical trials report reduced efficacy of the Novavax vaccine against the South African variant (BMJ 2021;372:n296)

Section 1: International epidemiology of Variant of Concern

1.1 South African Variant

(Data source – PHE Variant and Mutations Taskforce (VAMT) presentation slides 2/2/2021)

A total of 143 confirmed or probable cases of the South African variant have been detected in the UK. England = 125; Scotland = 5; Wales = 13; N.Ireland = 0

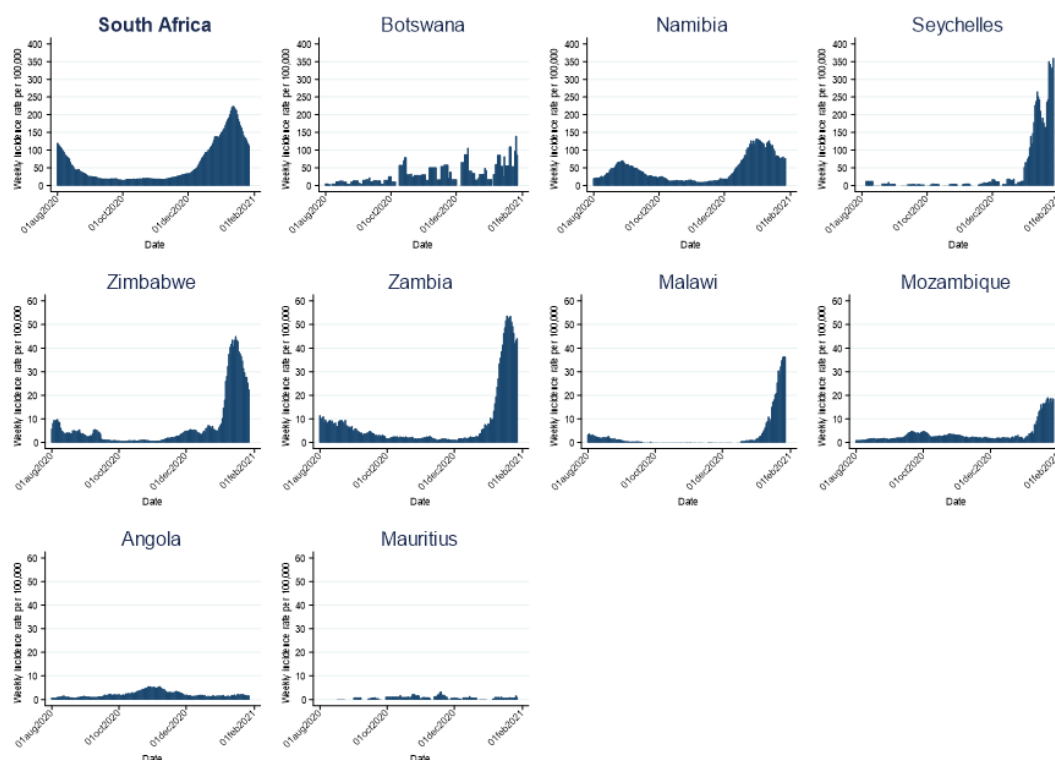
Table 1 presents the international detected cases of the South African variant:

Table 1: International cases S. African variant

Country	Total cases reported in media or via IHR/EWRS	Confirmed sequences in GISAID	Cases imported or evidence of local community transmission
Australia	12	9	Imported cases
Austria	1	1	Imported cases
Belgium	16	8	Unknown
Botswana	1	7	Unknown
Brazil	1		Unknown
Canada	11		Unknown
China	1		Imported cases
Cuba	1		Imported cases
Denmark	4	3	Imported cases
Finland	11	2	Unknown
France	40	12	Unknown
Gambia	1		Unknown
Germany	27	8	Unknown
Ghana	Not specified		Unknown
Greece	1		Unknown
Ireland	9	9	Imported
Israel	22		Unknown
Japan	2	5	Unknown**
Kenya	2	2	Unknown
Luxembourg	3		Unknown
Malawi	-		Exported cases*
Mayotte	50	6	Unknown
Mozambique	Not specified	20	Unknown
Netherlands	14	22	Unknown

Country	Total cases reported in media or via IHR/EWRS	Confirmed sequences in GISAID	Cases imported or evidence of local community transmission
New Zealand	10	7	Local transmission
Norway	2	1	Imported cases
Panama	1	1	Imported cases
Portugal	1	1	Unknown
South Korea	4	1	Imported cases
Spain	1	1	Imported cases
Sweden	2	1	Imported cases
Switzerland	26	11	Unknown
Taiwan	1		Imported cases
UAE		5	
USA	3	2	Community transmission
Vietnam	1		Imported cases
Zambia	22		Unknown
Total	305	145	

Genome sequencing capacity is limited in many countries neighbouring South Africa; however many have experienced a significant increase in overall COVID-19 incidence recently:



1.2 Brazilian Variant

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

No cases of the P.1 Brazilian variant of concern have been detected in the UK.

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

Table 2: International cases 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
Colombia	2	2	Unknown
Germany	3		Imported
Italy	4	3	Imported
Japan	4	6	Imported
Netherlands	2		Unknown
Peru	1		Unknown
South Korea	1	1	Unknown
USA	Not specified	1	Community transmission
Faroe islands	1	1	Imported
Total	18+	14	

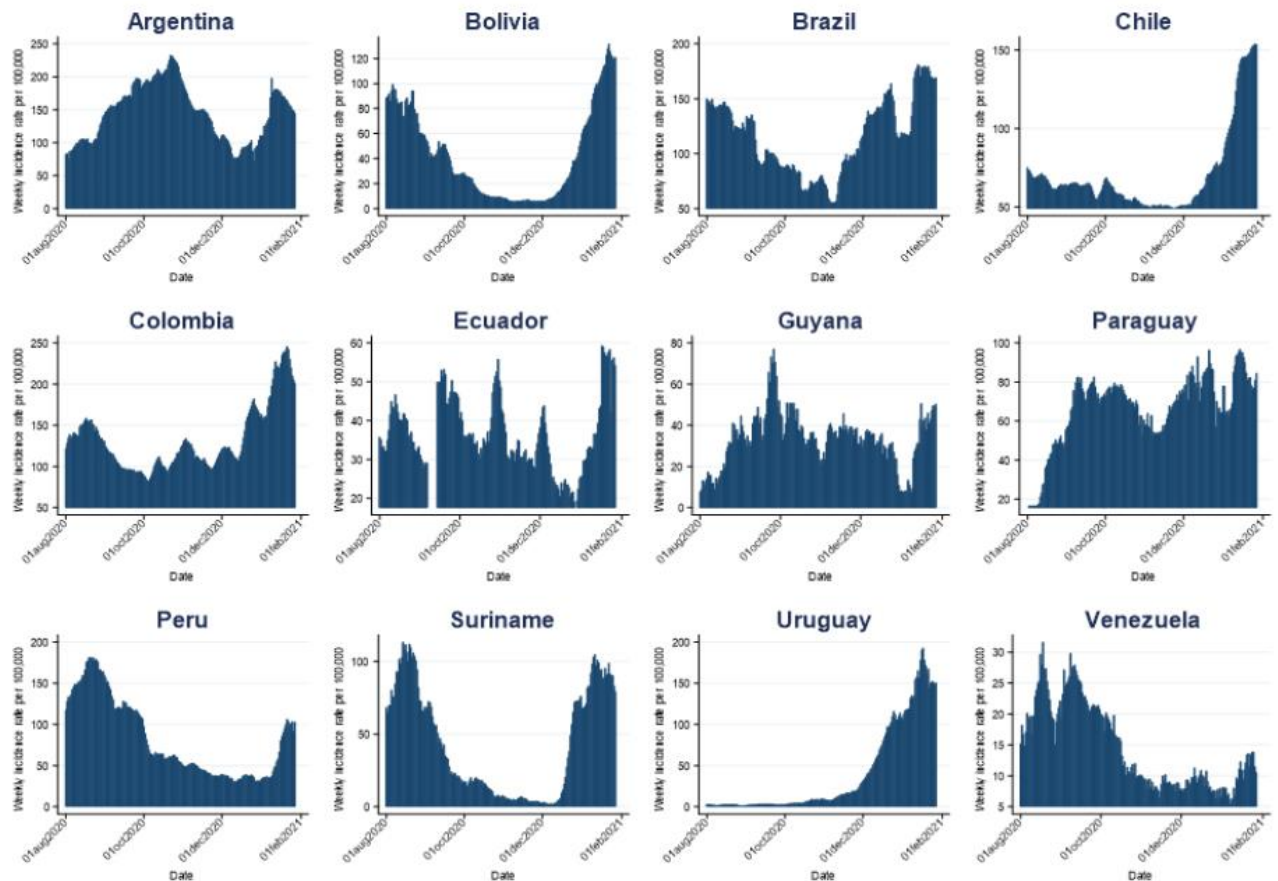
Eighteen cases of the P.2 Brazilian variant of interest have been detected in England. None in other UK countries.

Table 3 presents the international detected cases of the Brazilian P.2 variant of Interest

Table 3: International cases Brazilian P.2 variant of interest

Country	Total cases reported in media or via IHR/EWRS	Confirmed sequences in GISAID	Cases imported or evidence of local/community transmission
Argentina	5	5	Community transmission
Australia		1	
Canada	1	13	Unknown
Denmark		4	Imported
French Guiana		2	
Ireland		4	
Italy		1	Imported
Japan		3	Imported
Netherlands	2	2	Unknown
Norway		3	
Singapore		1	
Switzerland		3	
South Korea	1		Unknown
USA		24	
Total	9	66	

Genome sequencing capacity is limited in many countries neighbouring Brazil. Many have also experienced a significant increase in overall COVID-19 incidence recently:



Sections 2: Variant of Concern Covid-19 cases in Ireland

2.1: South African Variant Covid-19 cases in Ireland

Based on NVRL results up to 2nd February 2021

Confirmed 501Y.V2 cases (based on Sequencing):	9
Probable cases (501Y Detected <i>and</i> S gene target failure (SGTF) not detected <i>and</i> relevant travel history. Unable to generate sequence or WGS pending):	4
Possible cases	1

To date, nine **confirmed** variants identified and followed up through CTCs initially or Departments of Public health. All followed up and appropriate public health actions undertaken.

- Three are part of a family cluster. This family has no outward further contacts and has been isolating as per guidelines. Probable source of infection was another family member who had flown in from South Africa on 22/12. Became symptomatic on 24th and tested Covid-19 detected. Sample wasn't suitable for WGS. This likely index case has also had no onward contacts of concern.
- One case flew from SA on 08/01/21, became symptomatic on 12th. No contacts outside family unit. All isolation and restrictions undertaken.
- One case tested after re-entering Ireland from South Africa. Was notified as close contact of cases in South Africa. Departed South Africa 31/12/21, arriving in Dublin 01/01/21. Tested positive 03/01/21. Four household members have tested 'not detected'. Flight was traced, no other symptomatic people were identified out of those contactable, no other confirmed cases were identified out of those tested outside of the family unit.
- Two were part of a family outbreak, with recent travel to South Africa. All public health measures in place.
- One case became unwell 4.1.21 and tested positive through hospital visit on 14.1.21. Probable source of case was collecting friend and 2 children from Dublin airport and transporting them to their family home. They arrived in Ireland on 29.12.20 flying from Zambia. The friend became unwell 30th/31st December and tested positive for Covid-19 with a swab on 8.1.21 undertaken by NAS as no transport. No sequencing done. Both families involved have been sent for testing. No-one else symptomatic. No outward contacts from two families. All public health measures in place.
- One case arrived from South Africa with family and was sent to self-isolation facility. Family members have tested negative. Public Health measures in place.

The four **probable** variant cases have been dealt with by the contact tracing centres, in order to prevent onward transmission:

- One case travelled from South Africa, via Dubai, on the 22nd December 2020, having tested positive on the 21st December. He became symptomatic on the 23rd December and subsequently returned positive tests on the 1st and 11th of January 2021. Four close contacts contacted by CTC and given advice as per the guidelines at the time. None was tested.

Partner became symptomatic but not tested. Followed up by Public Health, all complied with restriction, no onward contacts.

- One case is an aid worker in Zambia. Returned to Ireland on 11th January 2021. She was contacted by PH England on 17/01/21 to say she was a contact on the plane. Became symptomatic on 17th January and tested positive. She has been self-isolating since arrival and has no close contacts. Followed up by Public Health.
- Two cases are housemates who travelled from South Africa. First became symptomatic on 26th December 2020 and tested positive. Completed isolation before travelling to Ireland on 8th January. Second tested “not detected” prior to departure but (erroneously) informed that she was a close contact on a flight. Tested on 1st January – positive. Both have been self-isolating for the appropriate periods of time. No other close contacts.

There is one possible case of variant of concern. This is in an elderly resident in a residential care facility. Active investigation of this is underway and a precautionary approach is being taken, whilst further laboratory results are awaited.

2.2: Brazilian variant of concern cases in Ireland

- No confirmed cases of Brazilian P.1 (variant of concern)
- Two possible cases in returned travellers living in the same household (sample date 18/01/2021 – 501Y Detected; unable to generate result for S gene; unable to generate sequence). Followed up by CTC
- Three confirmed cases of Brazilian P.2 (variant of interest) in Ireland. Followed up by CTC

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

Updated to 20.00 on Tuesday, 02 February 2021. Thanks to Dr Sarah Doyle, May Codd and UCD CTC team

	<u>Brazil</u>	<u>SA</u>
Total cases identified across all CTCs (Fri, 15/01/21 –Tues 02/02/21 incl.)		
<u>with</u> a history of recent travel from Brazil or South Africa	68	12*
Cases identified within the past 7 days (Wed, 27/01/21 – Tues 02/02/21 incl.)		
<u>with</u> a history of recent travel from Brazil or South Africa	20	2

*(*revised following travel history validation)*

Contact Tracing has been completed for all identified cases with a travel history of concern (n=80)

- Need for ongoing reminder to callers to follow WIs re establishing travel history in Brazil and South Africa cases, route appropriately to SQ and not undertake contact tracing in these cases

Of cases for whom CT complete:

- Travel history established in so far as possible (dates, route, flight numbers, seat numbers). Further detail required for some cases if identified as having variant.
- Close contacts identified and scheduled for testing, self-isolation advice provided, and household members of close contacts advised to restrict movements for 14 days.
- Exposure Investigations created for flights undertaken during infectious period (n=12), of which (n=4) have been identified within the past 7 days (on or after 27/01/2021).
- Exposure Investigation Flights: Passenger manifests received for four flights:

Date Received	Flight Number	Route	Flight Date	Total Passengers	Uncontactable (No number or unanswered)	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	51	83 (62%)
02.02.21	TP1324	Lisbon-Dublin	26.01.21	91	41	50 (55%)

- Contact tracing complete for all passengers who could be contacted, tests arranged, self-isolation advice and household contact advice provided.
- Request to email non-responders / those uncontactable if email address available.
- Request re arranging test for those with valid phone numbers who have not been reached
- Significant work on end-to-end-process for case identification and notification undertaken in conjunction with IIS, Track & Trace (Bill Cotter), PH Data Processing (Dr Paul Deignan), Public Health (Dr Jennifer Martin, Matt Robinson), Scripts and Scenarios (Dr Natasha Rafter) and Niall Hayden (Chair). Progress towards a unified approach to reporting is ongoing and an update to be provided on 05.02.2021

Section 4: Public Health Process document

Pathway One

- 1) CMP/CTC end
 - Confirmed cases Covid-19

Enter call 1 queue – CMP

Travel hx asked - have you, or a contact, travelled from SA / Brazil?

- If yes this goes in the specialised queue for CTC UCD to undertake enhanced CT and WGS request made to NVRL .

OF NOTE: this goes in to the specialised queue but is picked up by UCD – not required for the Departments of Public Health to pick up this.

- If no travel history - usual CMP processes

2) NVRL identifies a confirmed or probable variant subsequently – Both Actionable within Departments of Public Health

- **Confirmed** is based on sequencing
- **Probable** (for both Brazil & South Africa) means 501Y Detected **and** S gene target failure (SGTF) not detected **and** relevant travel history. Unable to generate sequence or WGS pending. (See **appendix 2** for lab explanation, thanks to Cillian de Gascun)

3) Transfer of confirmed / probable results to Departments of Public Health

- Email sent from NVRL Surveillance nvrl.surveillance@healthmail.ie
- Subject title will be ‘**Urgent Confirmed New Variant Of Concern for PH action**’
- File will be password protected with the password **NVRLVOC**.
- First line of text in email will clarify the Public Health Department result pertains to for action
- First sheet of excel sheet will have VOC for action ie variants from Brazil / South Africa. Second sheet will have UK variants – no longer for enhanced PH actions
- CMP / CTC will be included in this email

4) Within Departments of Public Health

4.1 - Declare an individual case as an outbreak

4.2 - Outbreak code combination - **EVOC7**COVID01 e.g. E (east or region) VOC (Variant of Concern) **7 (CHO area)**. This OB code can be used when sharing information back to CMP leads and National Health protection so instantly recognisable that the OB pertains to a VOC.

4.3 - PH Departments follow up as per [HPSC updated guidance](#)

1. **Look at CTC information**; link with CTC as required for story/actions as they have. CMP will look to make more easily visible actions taken as per HPSC guidance
2. **Ring case** and inform they are confirmed variant. Basic information points **Appendix 1**. Check and itg further details as required (e.g. check right contacts, re-enforce isolation and restricted movements, identify any links you are concerned with eg MPP)
3. **Identify further** if contacts / flights etc which require usual follow up. Departments of Public Health to contact the on-call CMP clinical lead to discuss (contact details for CMP clinical leads circulated routinely) and they will assist with getting these work pieces undertaken.
4. **Household contacts of the close contacts** should be informed that they need to restrict movements for same duration as close contact is isolating. No need for test unless symptomatic . *AC to check with CMP that this group will then be contacted directly by CTC*

4.4 - Email brief copy of ‘story’ to Abigail.collins@cancercontrol.ie and Matt.Robinson@hpsc.ie with information on these cases for national collation and reporting (Hopefully only required until CIDR processes in place)..

Pathway Two

1. Confirmed as variant from SA / Brazil through NVRL 'random' sequencing but no travel hx elucidated at CMP
2. Referred to Departments of PH through usual email format as per above **3) Transfer of confirmed / probable results to Departments of Public Health**
3. Declared as OB and OB code generated as above in **4.2**
4. None of enhanced contact tracing or actions will have been undertaken by CTC as there was no declared travel hx. Usual CMP only recommendations would have been given.
5. Departments follow up as per HPSC guidance and as outlined above.
6. Clear reconfirmation of travel hx / place of work etc to elucidate travel or connection to travel e.g. Midlands case linked to Zambia
7. Work pieces identified that need doing e.g. close contacts ringing and testing organising; flights to be CT etc – contact on-call CMP clinical lead to discuss further supports required
8. Email brief copy of 'story' to Abigail.collins@cancercontrol.ie and Matt.Robinson@hpsc.ie with information on these cases for national collation and reporting (Hopefully only required until CIDR processes in place)..

Appendix One

Information for cases and close contacts identified as having, or suspected as having, one of the Covid-19 Variants of Concern

- South African variant is associated with an increased risk of transmission
- Brazilian variant suspected to be associated with an increased risk of transmission
- No association with increased disease severity
- The impact of these new variants on the effectiveness of the vaccine is still under investigation – it is too early to have a definitive answer
- For this reason, enhanced measures are taken in order to prevent their spread in Ireland
- Stress the importance of:
 - self-isolation of (suspected) cases and their close contacts;
 - testing of close contacts;
 - restricted movements of contacts' household members
 - if these household members become symptomatic – self-isolate and test
- Stress continued importance of all simple mitigation measures (masks, hand washing, avoiding contacts)

Appendix Two

How are SARS-CoV-2 variants identified? *(Courtesy of Dr Cillian De Gascun)*

Following initial confirmation that SARS-CoV-2 RNA is detected using PCR assay

Specimens can be screened using either the 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 ('South African' Variant), and P1 ('Brazil' variant)

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 this is the UK variant

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

Timescales for testing:

The 501 allele-specific PCR and the TaqPath assay are simple PCRs that can be turned around in a day, and are being done when NVRL has samples of interest. Sanger sequencing takes about 36 hours and again is done on an as required basis. WGS takes 3-4 days and is currently being done weekly.