

## SYNTHESIS

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# COVID-19 B.1.351 (501Y.V2) Variant of Concern – What We Know So Far

## Introduction

Public Health Ontario (PHO) is actively monitoring, reviewing and assessing relevant information related to Coronavirus Disease 2019 (COVID-19). “What We Know So Far” documents provide a rapid review of the evidence related to a specific aspect or emerging issue related to COVID-19.

See PHO’s rapid review *COVID-19 UK Variant VOC-202012/01 – What We Know So Far* for information on the the United Kingdom (UK) variant of concern (VOC).<sup>1</sup>

## Key Findings

- The B.1.351 (501Y.V2) variant emerged in late 2020 in Eastern Cape Province, South Africa and subsequently spread throughout South Africa and to over 40 countries worldwide, including Canada. As of February 4, 2021, one B.1.351 case has been detected in Ontario.
- Epidemiological and modelling studies show that the B.1.351 variant is more transmissible compared to lineages circulating during the first wave of the pandemic. Currently, there is uncertainty with respect to the ability of B.1.351 to impact COVID-19 severity.
- B.1.351 does not appear to affect real-time reverse transcription polymerase chain reaction (RT-PCR) assays including those currently used in Ontario, which means they will still detect B.1.351.
- Emerging evidence raises concern for increased risk of reinfection by B.1.351. Preliminary studies found that B.1.351 mutations conferred partial or complete escape from three classes of therapeutically relevant monoclonal antibodies and neutralizing antibodies in COVID-19 convalescent plasma.
- Studies have shown that vaccine-induced neutralizing antibodies had diminished neutralizing ability against B.1.351 mutations; vaccine manufacturers are developing and evaluating updates to mRNA vaccines that incorporate B.1.351 mutations.

## Background

New Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) variants are arising as the virus continues to spread globally. To date, three SARS-CoV-2 variants of public health importance have been identified: lineage B.1.1.7 (501Y.V1, VOC 202012/01; originated in the United Kingdom [UK]); lineage P.1 (previously P.1.1.28; originated in Brazil); and lineage B.1.351 (501Y.V2; originated in South Africa). These variants have been termed variants of concern (VOCs) and have been associated with evidence of increased transmissibility, severity, and/or possible immune evasion with potential implications for reinfection and vaccine effectiveness.

Notably, these VOCs harbour many mutations, including some in the receptor-binding domain (RBD) of the spike (S) protein, encoded by the *S* gene. Mutations in SARS-CoV-2 arise naturally through viral replication. The RBD mutations of interest in the *S* gene include the following amino acid substitutions: N501Y, K417N/T and E484K. The N501Y mutation is found in all three VOCs. The E484K mutation is found in P.1 and B.1.351. In addition, P.1 carries a K417T mutation, while B.1.351 has a K417N mutation.<sup>2</sup>

The emergence of B.1.351 has been attributed to within-host evolution during prolonged infection in COVID-19 patients with immune system compromise, with detection of the E484K and N501Y mutations.<sup>3,4</sup> Tegally et al. (2021) hypothesized that a population with high seroprevalance and immunity led to a strong selection pressure for the evolution of mutations in B.1.351.<sup>5</sup>

When transmissibility is higher for a VOC, this can lead to a rapid increase in cases, putting a strain on health care resources. Monitoring for VOCs and emerging mutations is critical to the early identification and mitigation against potential impacts, as well as quickly identifying new VOCs. Here we synthesize the current literature examining the B.1.351 VOC. For simplicity, we use B.1.351 to refer to B.1.351 VOC, B.1.351 variant, “South African variant”, lineage B.1.351 or 501Y.V2.

## Methods

In considering feasibility, scope, and a need for responsiveness, we chose a rapid review as an appropriate approach to understanding B.1.351. A rapid review is a knowledge synthesis where certain steps of the systematic review process are omitted in order to be timely (e.g., quality assessment).<sup>6</sup>

From January 17 to February 4, 2021, PHO Library Services conducted daily searches of primary literature in several databases (e.g., MEDLINE; search strategies available upon request). Relevant articles were identified daily. In addition, we performed grey literature searches using Google. English-language peer-reviewed and non-peer-reviewed (preprint) records that described B.1.351 were included.

Prior to posting, PHO subject-matter experts review all “What We Know So Far” documents.

As the COVID-19 outbreak continues to evolve and the scientific evidence rapidly expands, the information provided in this document is only current as of the date of respective literature searches.

## Findings

### Epidemiology

B.1.351 emerged in Nelson Mandela Bay (Eastern Cape Province) in early October 2020, and by the end of November 2020 became the dominant virus lineage in the Eastern and Western Cape provinces, replacing the previously circulating B.1.1.54, B.1.1.56 and C.1 lineages.<sup>5</sup> In a spatiotemporal phylogeographic analysis, Xie et al. (2021) suggested that B.1.351 emerged as early as the start of August 2020 (95% highest posterior density: early July to end August 2020).<sup>5</sup>

By December 2020, B.1.351 spread to Botswana, France, Scotland, South Korea, Sweden, Switzerland and the UK.<sup>2</sup> In addition, by January 2021, the variant was detected in at least eight European Union (EU) countries (Austria, Belgium, Denmark, Finland, Germany, Ireland, the Netherlands and Norway) and

eight other countries (Australia, Brazil, Canada, China, Japan, Taiwan, United States [US] and Zambia).<sup>7,8</sup> As of February 2, 2021, the World Health Organization has reported B.1.351 cases in 41 countries.<sup>9</sup>

As of January 19, 2021, there were approximately 570 confirmed B.1.351 cases worldwide (447 in South Africa).<sup>7</sup> Outside of South Africa, confirmed cases in affected countries range from one to six cases, with the UK being a notable exception with 54 cases. In the EU, most cases have been related to travel but not all have a history of travel to South Africa. The number of B.1.351 cases reported worldwide is likely an underestimate as identification is based on each jurisdiction's approach to testing from their pool of all SARS-CoV-2-positive specimens.

In the US, three B.1.351 cases have been reported by two states (South Carolina [n= 2], Maryland [n=1]) as of February 2, 2021.<sup>8</sup> In Canada, seven B.1.351 cases have been reported in Alberta (as of February 1, 2021), four in British Columbia (as of January 23, 2021) and one in Ontario (as of February 4, 2021).<sup>10-12</sup>

## Transmissibility and Disease Severity

As mentioned in the previous section, data from South Africa suggest that B.1.351 quickly displaced other circulating lineages in the country within weeks.<sup>5</sup>

- Preliminary results reported by Mahasse (2021) using a mathematical model estimated that B.1.351 is 50% (95% confidence interval: 20–113) more transmissible than previously circulating variants in South Africa.<sup>13</sup>

Currently there is substantial uncertainty as to whether the South African variant causes a change in disease severity.<sup>7</sup> However, studies are ongoing in the UK and South Africa to describe the epidemiology of B.1.351.<sup>14</sup>

## Diagnostic Assays

Unlike B.1.1.7 (originated in the UK), the mutations in B.1.351 do not appear to affect diagnostic assays, including those currently used in Ontario.

- Peñarrubia et al. (2021) reported that B.1.351 mutations did not impact on the sensitivity of a real-time reverse transcription polymerase chain reaction (RT-PCR) assay targeting *RdRp* and *E* genes, or with an assay targeting *Nsp2* and *N* genes.<sup>15</sup>
- In a review of molecular methods to detect SARS-CoV-2, Arena et al. (2021) reported that mutations in B.1.351 have little to no effect on the sensitivity of RT-PCR assays.<sup>16</sup>

## Immunity and Reinfection

Two preprint studies highlighted a potential for increased risk of reinfection with B.1.351, if initially infected with another SARS-CoV-2 strain.

- Wibmer et al. (2021) (preprint) reported that mutations in B.1.351 conferred complete escape from three classes of therapeutically relevant monoclonal antibodies and showed substantial or complete escape from neutralizing antibodies in COVID-19 convalescent plasma.<sup>17</sup>
- Cele et al. (2021) (preprint) reported a similar escape of B.1.351 from the neutralizing antibody response elicited by natural infection with earlier variants.<sup>18</sup>

## Vaccine Effectiveness

Several preprint articles have tested plasma from recipients of both authorized mRNA vaccines (Moderna and Pfizer-BioNTech) against SARS-CoV-2 viruses with various spike mutations (i.e., VOCs).<sup>19-21</sup> These *in vitro* studies have found that vaccine-induced neutralizing antibodies had diminished neutralizing ability against B.1.351 mutations; however, reduction magnitude varied by study.

- In one study (Wu et al., 2021) that examined neutralizing antibody response to antibodies elicited by the Moderna vaccine, there was reduced neutralization observed for B.1.351 mutations; however, the titres were still above the neutralizing titers found to protect non-human primates from wildtype viral challenge.<sup>21</sup>

The mRNA vaccines prevent infection through both humoral and cell-mediated immunity, so it is difficult to know with certainty whether the diminished neutralizing antibody response to B.1.351 mutations observed in *in vitro* studies will result in reduced protection.

Moderna has publicly announced that it plans to develop and evaluate in preclinical studies a new mRNA vaccine candidate that incorporates B.1.351 mutations.<sup>22</sup> Moderna is also initiating a Phase 1 study to evaluate whether immunological boosting with an additional dose of its current vaccine can improve protection against VOCs. Antibodies induced by the vaccine appeared less potent against B.1.351, compared to the original strain. Pfizer has also issued public statements that it is possible to update their vaccine with a new variant sequence, if needed.<sup>7</sup>

Vaccine effectiveness is potentially decreased in two non-mRNA vaccines not currently authorized for use in Canada.

- Mahase 2021 reported on the results of a phase III trial in the UK and South Africa with the Novavax vaccine.<sup>23</sup> Novavax was 95.6% effective against the original SARS-CoV-2 strain and 60.0% effective against B.1.351.
- Johnson & Johnson announced that their candidate vaccine had 72% efficacy in preventing moderate to severe COVID-19 at 28 days after vaccination in the US, compared to 57% in South Africa.<sup>24</sup>

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