NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
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FREQUENTLY ASKED QUESTIONS: C.1.2 COVID-19 LINEAGE

1. What is C.1.2?

C.1.2 is a new lineage (or version) of the SARS-CoV-2 virus.

2. How did it come about?

SARS-CoV-2 like all viruses mutates/changes continually and randomly. When a mutation offers some benefit, for example, enabling the virus to replicate better or evade immune responses in humans, the mutation is passed on as the virus multiplies. This mutated virus is then transmitted to another person. The C.1 lineage was detected during our first wave of infections in South Africa and now in the third wave has accumulated additional mutations and evolved into the C.1.2 lineage.

3. What is a VOI and a VOC?

A VOI is a variant of interest and a VOC is a variant of concern. These are classifications for different variants of SARS-CoV-2. A variant of interest is one that has spread significantly within a region or globally and has some mutations that might alter transmissibility, pathogenesis, immune resistance or the epidemiology of the virus. A variant of interest becomes a variant of concern when it has been proven to have changes in transmissibility, pathogenesis, immune resistance or epidemiology. To date, the C.1.2 lineage is neither a VOI nor a VOC.

4. How did we find it?

The Network for Genomic Surveillance in South Africa routinely collects samples from people that have tested positive for SARS-CoV-2 throughout the country and sequences the virus within these samples to monitor viral mutations. We then compare these sequences to ones we have seen before, like a game of spot the difference. If we see differences, we take note of where these differences are and whether they are likely to alter the function of the virus or our immune responses to the virus.

5. Which places in the world has C.1.2 been detected in and where was it first detected?

C.1.2 was first detected in South Africa in May 2021 but has been seen sporadically in nine other countries (Botswana, Zimbabwe, the Democratic Republic of the Congo, Mauritius, New Zealand, Portugal, China, Switzerland and England).

6. Is there any evidence to suggest that C.1.2 is more transmissible?

It is not yet clear whether C.1.2 is more transmissible. The variant shares mutations with other variants and some mutations have been linked to increased transmission. Although the variant was detected in May, the levels remain low and the NICD continues to monitor the variant and its spread.

7. **Why is there no Greek name yet?**
   Variants are assigned a Greek name when it is classified as a variant of concern (VOC) or a variant of interest (VOI). Variants with mutations that are predicted to impact function are classified as a VOI once that variant has spread either significantly in an area or globally. A VOI becomes a VOC when the effect of the mutations on function has been proven to be detrimental. Due to the low frequency of C.1.2 and lack of data to explain the effect of the mutations in this lineage, it does not meet the criteria to be classified as a VOI or VOC.

8. **As of 01 September 2021, how many genomes in SA have been identified as the C.1.2 variant?**
   There are 114 C.1.2 genomes from South Africa in GISAID (the global reference database for SARS-CoV-2 viruses, www.gisaid.org). However, these only account for ~2.5% of the viruses circulating in South Africa right now, with the majority being Delta.

9. **Some of the press released on this variant describe it as a "potential" variant but the "potential" is later dropped. Is it a "potential" variant or a variant proper?**
   It is a variant, meaning a different "version" of the virus; however, the "potential" refers to its potential to eventually either be classified as a VOC/VOI. It shares mutations with VOCs that have a functional impact as well as additional mutations that we are currently studying. So although it is a variant, it is not yet a VOC/VOI, but it has the potential to become one.

10. **If there are so many new mutations on this variant, how can we be so confident that vaccines are working?**
    Viruses randomly mutate all the time; mostly these do not have a great effect on function, but sometimes these mutations give the virus an added benefit. Therefore, the identification of many mutations does not necessarily mean a "worse" virus.
    One reason we expect that the vaccines will work, despite the mutations in C.1.2, is because we are familiar with several of these mutations. We have extensive data from the other variants, like Beta and Delta, showing the effect of these mutations. Because of this, we can to some extent predict the effect of those mutations, even in the context of C.1.2.
    Another reason is that the T cell arm of the immune system in part mediates protection from severe disease, which is separate from the antibodies. T cells are much more tolerant of mutations and there is data from laboratories across the world that although there might be a reduction in the ability of antibodies to bind to these viruses, T cells (which are the cells that protect you from severe disease) maintain their activity against the currently circulating variants

11. **The C.1.2 lineage preprint suggests that frequency is low but that it is gaining traction at the same rate as delta did in the early days. So from this can we assume it will grow exponentially?**
    C.1.2 is present at a low frequency and is gaining traction slightly, which is why we are tracking and watching it carefully. It is to some extent doing what Delta did at the beginning of the second wave. However, at this stage, it is impossible to predict what variants are going to do.

12. **Which provinces in South Africa have the C.1.2 lineage been dominant in?**
    We cannot conclusively say that the C.1.2 lineage is dominant in any of the provinces, purely because our sequencing efforts are not equal across all the provinces. The most number of C.1.2

sequences are from Gauteng, but we also have the most number of sequences from Gauteng province.

13. **Scientists have referred to the lineage to have mutations similar to previous variants - why is this significant? Is this a precursor to it being classified as a variant of concern?**
We have defined the impact of mutations in current VOIs or VOCs because they have been in circulation for some time and have infected a significant number of individuals. We have been able to pinpoint the detrimental impact of individual and combined mutations in these VOIs or VOCs. Therefore, when we see emerging lineages with similar mutations, we take notice because we expect a detrimental impact.

14. **Scientists also emphasised that C.1.2 has been identified at low frequency - at which point does it become a problem?**
The C.1.2 lineage has to be present in a significant amount of sequences for a sustained period in order for it to be recognised as a VOI by the World Health Organization. If it is classified as a VOI, further studies showing that the lineage alters viral pathogenesis, immune resistance, transmissibility and epidemiology are needed before it can be classified as a VOC.

15. **Is there any need at this point to review lockdown restrictions in South Africa in anticipation of what will come from this variant?**
There is no need to review lockdown restrictions at this time. All the regulations that are required in terms of managing this current third wave/resurgence are in place, regardless of the variant. Adherence to non-pharmaceutical interventions remain critical and individuals who qualify for vaccination are encouraged to do so.

16. **How do you decide when to announce a new variant as you are doing with this one, or not - especially given the risk of impact on sentiment and tourism and travel restriction?**
The Network for Genomic Surveillance in South Africa continuously and rigorously monitors the emergence of new SARS-CoV-2 variants in South Africa and globally. This continual monitoring we hope will enable us as a country to be better prepared to respond if further public health action is warranted. Because C.1.2 has been detected throughout South Africa as well as other countries we intended to inform other scientists and authorities including the WHO and South African NDoH to enable others to be on the lookout as well. However, it is important to note that we will likely continue to identify different variants and the public should really only be concerned when these variants are classified as either a VOI or VOC.

17. **Would it be fair to describe the C.1.2 as the most mutated variant in the world?**
It certainly has more mutations than the currently described VOI/VOCs we have seen circulating globally. C.1.2 has on average 30 mutations across its entire genome, which is quite mutated when you compare it to other VOC/VOIs, which have on average 18 mutations.

18. **Why do you say it is mostly in SA - when it has been found in Switzerland, China, England and Mauritius? Is it just being better-detected here- or is it common in SA?**
Out of the 127 C.1.2 sequences currently on GISAID, 114 are from South Africa. C.1.2 has generally only been detected in one or two sequences from other countries. We have been sequencing genomes extensively throughout South Africa. Additionally, in comparison to the UK for example, we

are doing relatively light genomic surveillance, yet we have detected many more C.1.2 sequences than any other country. Further to this, the genomic data shows that C.1.2 evolved from a precursor lineage (called C.1) that was predominant in South Africa in the first wave.

19. **Based on modelling, what can we expect?**
Based on the types of mutations we have seen in C.1.2 that are also seen in other VOI/VOCs we can expect some level of increased transmissibility similar to Delta and reduced antibody sensitivity. Data from laboratory tests should be able to inform modelling scenarios in the coming weeks.

20. **Given C.1.2 is not yet a VOI, what is it about this variant that has raised your concern more than other variants and made you decide to announce this a one to watch/a potential threat?**
We have raised awareness of this particular variant because of its mutation profile and its sustained spread throughout South Africa. It has many mutations that are shared with other VOI/VOCs as well as additional mutations within regions that might affect its function.

21. **What would it mean for South Africa and the world if C.1.2 actually turns out to be a "Breakthrough"? What has to happen for you as a scientist to ring the alarm bells?**
Many variants are circulating globally and will continue to circulate unless we can get a high enough coverage of vaccination in South Africa and globally. Our raising the awareness of C.1.2 has been to inform others to be on the lookout for this lineage. However, right now there is no reason to expect that it would be any different to any other VOC/VOI currently circulating.

22. **You are doing such important science but stories like this keep SA from being seen as an unsafe destination for tourists and keeps SA on the UK red list - This has an impact on the entire travel industry. How do we balance important genomic surveillance with the fact that this excellent science is leading to irreparable damage to SA's travel industry?**
This is indeed a very difficult balancing act. It is imperative for us to do this type of monitoring so that we would be able to detect new variants that might pose a threat very early on to get ahead of the virus in some ways. It is important to note that new variants are not unique to South Africa. Of the nine VOC/VOIs that are listed by the WHO, only one was first detected in South Africa. This is a global phenomenon and is crucial for everyone to continue to monitor. Since we and others across the globe will continually detect these variants one should only be concerned when they reach the status of VOC. Right now C.1.2 is only a variant under investigation (VUI) which means it is being monitored but does not meet the criteria for either VOI/VOC.

23. **It has been found in other countries too but do we have the most samples of it?**
Yes, the majority of the sequences assigned to C.1.2 come from South Africa. We think it originated here having evolved from C.1, which was one of the viruses that predominated our first wave of infections with limited spread globally.