Indicator	Red, amber, or green status*	Confidence level	Assessment and rationale The risk assessment is presented in comparison to the current predominant variant (BA.2). Red indicates the assessed variant as worse than BA.2 in a characteristic, amber equivalent, green improved. The laboratory data is supplied by VTG members (Oxford University, Genotype to Phenotype Consortium) and has been reviewed by VTG but is unpublished.
Overall growth advantage	**Red**	**Low**	**Evidence of a growth advantage compared to BA.2, in the context of South Africa** Available data from South Africa suggests that BA.4 and BA.5 are increasing as a proportion of sequenced cases and based on SGTF may already be predominant. As of 26 April, the reported weekly incidence in South Africa has more than doubled compared to the previous week and test positivity has increased. The provinces with the greatest increases in BA.4 or BA.5 based on sequence data are also those showing the greatest rise in incidence. This data suggests BA.4 and BA.5 are showing a growth advantage over BA.2 in South Africa. However, it should be noted that South Africa has different background population immunity to the UK and has not experienced a large BA.2 wave. The conditions favouring BA.4 and BA.5 growth in South Africa may not be replicated elsewhere. There is evidence of international spread including small numbers of cases in the UK and Europe (note differences in testing and sequencing across countries). There is no other country where BA.4 and BA.5 are showing a clear growth advantage as yet.
Growth advantage 1: Transmissibility			**Insufficient data** There is no epidemiological data available.
Growth advantage 2: Immune evasion	**Red**	**Moderate**	**There is evidence of some antigenic change compared to BA.2 based on structural modelling and pseudovirus neutralisation data** BA.4 and BA.5 are most closely related to BA.2. Structural modelling indicates there is likely to be antigenic change related to L452R (found in Delta) and F486V (a more radical version of the F486L found in some mink adapted viruses), both of which may affect the binding of neutralising antibodies. In addition, the differences between BA.2 and BA.4 and BA.5 at position 493 may have some effect, as well as the 2-residue deletion in the N-terminal domain in BA.4 and BA.5 compared to BA.2. In preliminary unpublished pseudovirus data from one laboratory there is a reduction in neutralising activity of vaccinee sera (including vaccinees who have also had BA.1) for BA.4 compared to BA.2. In a second laboratory, sera from BA.1 infected animals neutralised BA.4 poorly but sera from BA.2 infected animals did not show the same reduction in neutralisation. These findings support the modelled predictions of a degree of antigenic change. There is no data for vaccinees who have also had Delta or BA.2, both of which profiles are relevant in the UK context and require additional assessment.
Infection severity			**Insufficient data** There is no comparative data available. A slight increase in people admitted to hospital is noted in South Africa in the past week.

* Refer to scale and confidence grading slide.