Agility Program Biweekly Progress

CEPI

Agility Program: To enable the rapid assessment of the biological impacts of new variants of SARS-CoV-2

Partners:
Public Health England (PHE)
National Institute for Biological Standards and Control (NIBSC)

Slideset provided on a biweekly basis to update latest in vitro neutralization activity and in vivo pathogenesis and cross protection data against SARS-CoV-2 virus variants

Find this slide set posted at:

https://epi.tghn.org/covax-overview/enabling-sciences/agility_epi/#ref1

WHO Variants of Concern and Interest Monitored by the Agility Project

WHO Variants of Interest (VOIs)	Status*		WHO Variants of Concern (VOCs)	Status*
Epsilon - B.1.427/B.1.429	Sourced		Alpha - B.1.1.7	Assessed
Zeta – P.2	Assessed		Beta - B.1.351	Assessed
Eta - B.1.525	Seeking		Gamma - P.1	Assessed
Theta - P.3	Seeking		Delta - B.1.617.2	Assessed
Iota - B.1.526+E484K or S477N	Seeking			
Kappa-B.1.617.1	Sourced			
Lamba – C.37	Seeking			

Link to the WHO weekly Epi report website, where new VOIs and VOCs are updated for the public: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports

*From; Not selected/Seeking/Sourced/Assessed

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Questions? Reach us at agility@cepi.net

Table updated as of July 12, 2021

Agility Project: Variant Growth/Testing for Neutralization Phenotype

	Variant	Sourcing or Propagation Seeking/In progress/Complete	Characterisation In progress/Complete/No longer required	In vitro (neutralisation) In progress/Complete/No longer required	In vivo Not selected/Planning/In progress/In-life complete
WHO VOCs	**Alpha (B.1.1.7)**	Complete	Complete	Complete	In-life complete
	Beta (B.1.351)	Complete	Complete	Complete	
	Gamma (P.1)	Complete	Complete	Complete	
	Delta (B.1.617.2)	Complete	In progress	In progress	Planning
WHO VOIs	**Eta (B.1.525)**	Seeking			
	Epsilon (B.1.427/B.1.429)	In progress			
	Zeta (P.2)	Complete	In progress	Complete	
	Theta (P.3)	Seeking			
	Iota (B.1.526+E484K)	Seeking			
	Kappa (B.1.617.1)	Complete	In progress		
UK	**Alpha+E484K**	Complete	In progress		
n/a	**Cluster V (Denmark) and N439K**	Complete	No longer required	No longer required	*n/a*

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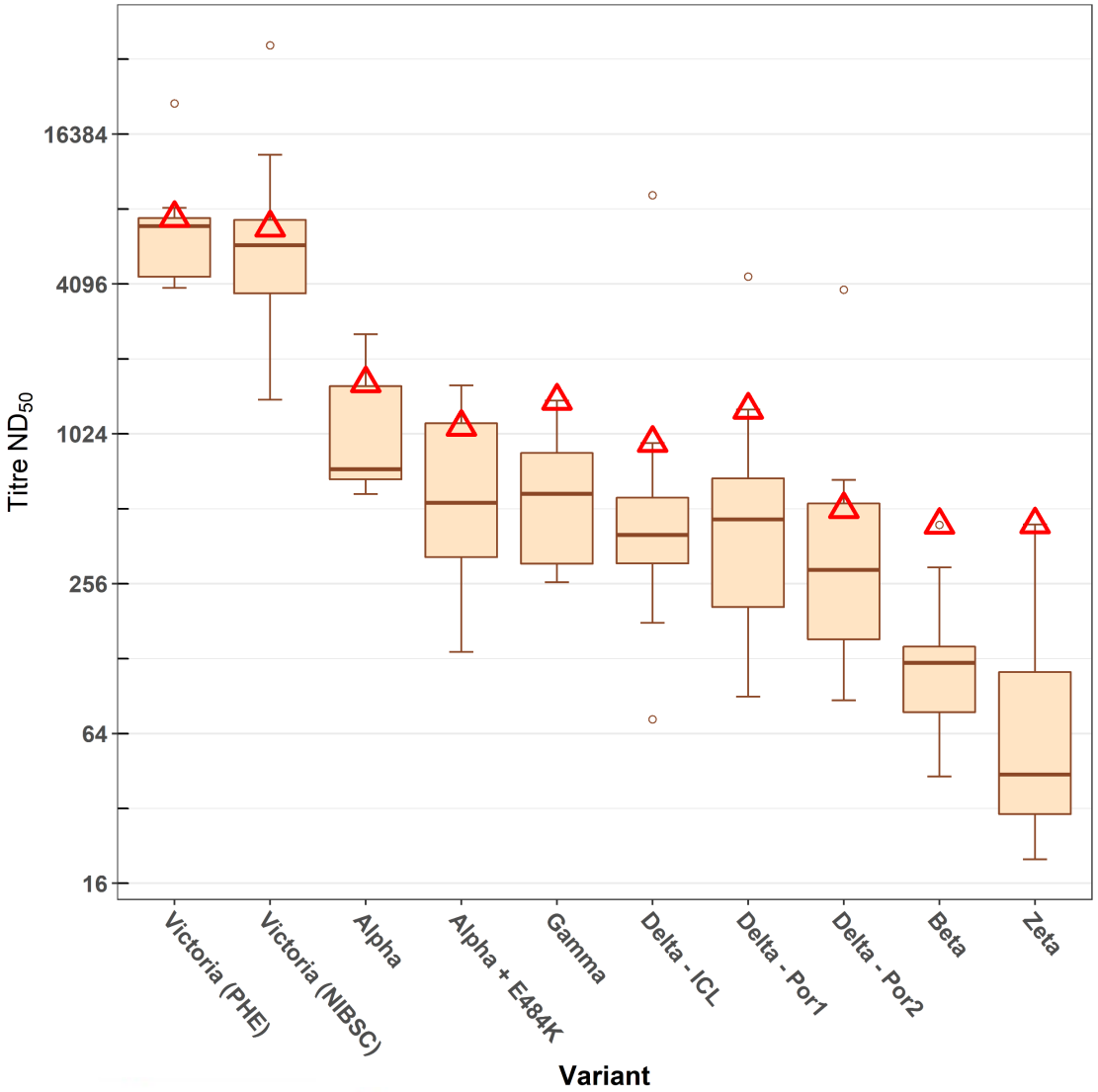
Live-virus *in vitro* antibody neutralization assay progress



- Variants assessed to date against a "pre-Alpha" serum panel
- WHO International Standard for anti-SARS CoV-2 (NIBSC code: 20/136) shown as red triangles
- Most serum in panel neutralise all tested variants
- Lowest neutralisation has been seen for Beta and Zeta
- Delta resistance is similar to Gamma

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Updated as of July 12, 2021

The broader scientific community is currently collecting biological infection data to understand disease severity and immune reponse to variants of concern in the following ways, plus many others:

- Human clinical studies assessing vaccine effectiveness against variant infections
- Animal studies in various laboratory model species to evaluate effectiveness of original vaccines against variants, and new vaccines, need for boosters, etc.

The Agility Program is leveraging CEPI Preclinical Laboratory Network Partners to perform hamster modeling studies under high ethical standards

- CEPI Network of Partners was established in 2019 via a call for proposals to engage laboratories with high animal ethics standards, biocontainment laboratory capabilities and high-quality research methods that meet regulatory requirements
- All animal studies are performed in accordance with UK NC3Rs guidelines (https://www.nc3rs.org.uk/the-3rs)
- All research is done in compliance with CEPI's Animals in Research Policy

Primary infection studies confirmed typical coronavirus disease; and Re-Infection Studies showed solid protection from disease in hamsters, even across variants

1st Infection Variant virus	Weight loss over 7 days after infection	Clinical signs over 7 days after infection	2nd Infection Variant virus	Weight loss over 7 days after 2nd infection	Clinical signs over 7 days after 2nd infection
Gamma (Brazil P.1.)	>10%	+++	None	-	-
Beta (South Africa B.1.351)	>10%	+++	None	-	-
Gamma (Brazil P.1.)	>10%	+++	Gamma (Brazil P.1.)	None	None
Beta (South Africa B.1.351)	>10%	+++	Beta (South Africa B.1.351)	None	None
Gamma (Brazil P.1.)	>10%	+++	Beta (South Africa B.1.351)	None	None
Beta (South Africa B.1.351)	>10%	+++	Gamma (Brazil P.1.)	None	None

All studies were conducted in compliance to all UK government regulatory requirements. Study complete: full data analysis is underway. Alpha and Delta variants will be evaluated similarly in upcoming studies.

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Important considerations for laboratory methods

- Serial propagation of SARS-CoV-2 variants in Vero E6 or other cell types may lead to furin cleavage site mutations that affect how the virus grows and behaves in vitro or in vivo. Propagation of unwanted mutations can be mitigated by growth in cells such as Vero/hSLAM and by frequent sequence confirmation (deep sequence methods preferred). link
- WHO International Antibody Standard should be used for neutralization assays, but it performs differently for each variant. Any data presented comparing the WHO IS should always identify the variant under test.

Recent relevant publications

- Quantification of SARS-CoV-2 neutralizing antibody by wild-type plaque reduction neutralization, microneutralization and pseudotyped virus neutralization assays Nature Protocols **16**, 3114-3140 (2021)
- A cautionary perspective regarding the isolation and serial propagation of SARS-CoV-2 in Vero cells NPJ Vaccines **6**:83 (2021)

Recent online conference presentations

- 19 May 2021: WHO SARS-CoV-2 Assays Working Group
- 19 April 2021 ECDC/WHO Euro laboratory network
- 16 April 2021 COVAX ES-SWAT Workshop 'Global and Local Efforts to Detect and Interpret SARS-CoV-2 Variant'