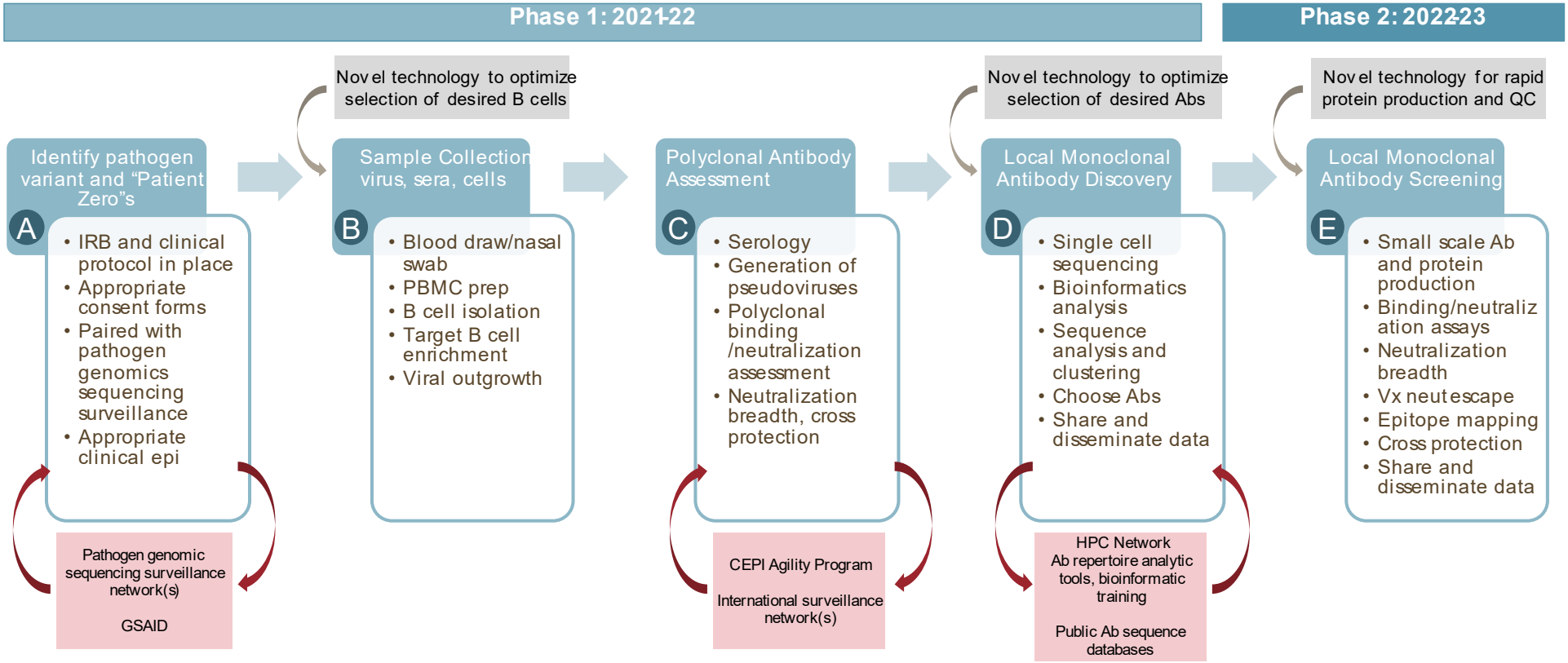
DRAFT

GIISER FOR SARS-COV-2 VARIANTS OF CONCERN



Outline of Existing Capacity, Needs, and Gaps

The table below show the actual capacities and the needs in funding, training/capacity building, technological transfer, etc. to be effective GIISER sites.

	Existing Capacity	Needs & Gaps
A- Identify SARS-CoV-2 pathogen variants and appropriate cases		
a. Ethics approvals and clinical protocols in place with appropriate consent forms that allow for the connection of pathogen sequencing, longitudinal/contextual clinical data and subsequent immunological analysis.		
b. Pathogen sequencing and analytical infrastructure in place that meets international quality standards and shares sequence data on GISAID in a timely manner.		
B- Sample Collection		
a. Laboratory capacity for virus sampling for sequencing and virus outgrowth (nasal swabs or other), including BSL3 capacity.		
b. Laboratory capacity for blood draws, including serum, plasma, PBMCs, B cell and/or plasmablast enrichment.		
c. Antigen specific B cell sorting via flow cytometry with tagged protein baits (generated locally or provided by collaborators).		

C- Polyclonal Antibody Assessment		
a. Quantitative assays measuring polyclonal antisera binding against both prior and VOC spike proteins (ELISA, MSD or other), calibrated against international standards or reference panels.		
b. Surrogate neutralization assays measuring inhibition of binding to ACE2 by polyclonal sera/plasma.	.	
c. Generation and use of VSV or lentivirus pseudoviruses containing novel spike protein sequences to quantitatively measure pseudovirus neutralization activity in sera/plasma, calibrated against international standards or reference panels.		
d. Implementation of live virus neutralization assays in BSL3 facilities to measure neutralization activity in polyclonal sera/plasma, calibrated against international standards or reference panels.		
e. Assessment of neutralization activity in sera/plasma from prior infections with sequence-confirmed viral infections and vaccinated individuals to determine magnitude and breadth of natural and vaccine-induced cross neutralization.		
f. Coordinate with other GIISER sites, international networks (WHO, CEPI, etc.) to share high quality binding and neutralization results. Establish appropriate MTAs between sites to share materials.		

D- Local Monoclonal Antibody Discovery		
a. Single cell immunoglobulin heavy and light chain sequencing from B cells enriched for binding to VoC spike proteins. This can be accomplished by a number of different technologies, including 10X, Seqwell, or others. Multiple specific baits and labels could be used for enrichment, targeting VOC specific mAbs (unique epitopes) or broadly neutralizing mAbs (conserved epitopes), or both.		
b. Proficiency in immunoglobulin sequence bioinformatics and clustering algorithms to assess somatic hypermutation, assign clonal lineages and evaluate Ab repertoire. Leverage opportunities via H3Bionet, Human Cell Atlas and GH-VAP to assist.		
c. Choose representative heavy + light chain pairs for subsequent expression and in vitro screening assays.		
d. Engage with international antibody sequencing databases and consortia to share mAb repertoire information and sequences as appropriate, with future-use data sharing terms clearly outlined.		
E- Local Monoclonal Antibody Screening		
a. Small scale production of selected high quality mAbs from cDNA sequence.		
b. Systematic screening of mAbs for binding to a variety of spike proteins, including epitope mapping.		

c. Evaluation of neutralizing activity of selected mAbs against VOCs using the live virus and pseudovirus assays from step C above. Evaluate neutralization breadth and cross protection.		
d. Disseminate findings and engage with additional partners to share mAbs that have utility as either research tools or potential developability as therapeutics. Participate in international consortia such as COVIC when sufficient data supports such a move.		