

HVTN Lab Center Algorithm for Clinical Trial Evaluation

	Antibodies	Cellular	Innate
Validated (except *)	<b>Primary</b>		
	Env IgG and IgA magnitude by Binding Ab Multiplex Assay (BAMA)	T cell magnitude based on cytokine expression (and polyfunctionality*) by intracellular cytokine staining (ICS)	No validated assays
	Tier 1 and Tier 2 neutralization by TZM-bl	T cell magnitude based on IFN-γ expression by ELISpot	
mAb PK levels <i>in vivo</i>			
Qualified or Standardized	<b>Secondary</b>		
	Cross-clade breadth specificity, linear and conformational epitope mapping	Proliferative capacity of T cells	Cell population frequencies by Trucount (*Qualified)
	FcR array (FcγRI, FcγRII, FcγRIII)	Antigen-specific cytokine expression profile: Multiplex Protein Detection Assay (MPDA) on MSD platform	
	Expanded neutralization panel for breadth, epitope mapping, precursor detection	T cell specificity by epitope mapping and MHC restriction analysis	Concentration of serum cytokines (and additional factors e.g. antimicrobials) by Multiplex Protein Detection Assay (MPDA) on the Meso Scale Discovery (MSD) platform (*Qualified)
	Anti-drug antibody detection	Antigen-specific B cell phenotyping by flow cytometry	
	Avidity (avidity index, off-rate, avidity score)	Interferon Gamma Release Assay (IGRA): QuantiFERON for TB sensitization	
	IgG subclass (IgG1, 2, 3, 4), IgA subclass and form (IgA1, IgA2, SIgA)	AIM assay	NK cell, monocyte, DC phenotypes by flow cytometry (FcR, KIR, C-type lectins, activation markers)
	FcR effector function: ADCC/ADCP/ADNP	T cell phenotype including memory, Tfh, Treg, exhaustion, NKT & γδT cells Memory B-cell magnitude by ELISpot	
Standardized	<b>Exploratory</b>		
	HIV Target recognition: Virion capture (infectious), Infected Cell Binding (ICABA)	CD8 <sup>+</sup> T cell mediated HIV suppression, cytotoxicity and avidity	NK cell cytotoxicity assay by flow cytometry
			Innate Effector cell function (cytokine, degranulation)
	Fc functions: Complement binding / activation, glycan profiling; epitope mapping for ADCC/ADCP/ADNP	Single-cell RNAseq of PBMC, cell subpopulations, non-specific and Ag specific	Transcriptional profiling of bulk/sorted cell populations (incl. analysis of alternative transcription, miRNA, etc.)
	Mucosal Ab functions: mucin binding, aggregation, FcαR binding	Lymph node germinal center cell phenotypes by flow cytometry	
Ab-mediated inhibition of <i>ex vivo</i> mucosal infection in human explants	T and B cell receptor sequence analysis		
<b>Mucosal tissue histopathology</b> for cell types, architecture, HIV infection, inflammation, mAb distribution			
<b>Host genetics</b> ( <i>HLA class I &amp; II, KIR, FcR</i> )			