HVTN Lab Center Algorithm for Clinical Trial Evaluation

	Antibodies	Cellular	Innate
Primary			
Validated (except *)	Env IgG and IgA magnitude by Binding Ab Multiplex Assay (BAMA)	T cell magnitude based on IL-2/IFN-γ expression 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 *in vivo*	Antigen- and epitope-specific B cell phenotyping by flow cytometry	
		Memory B-cell magnitude by ELISpot	
Secondary			
Qualified or Standardized	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 plasma/serum proteins (e.g. cytokines, antimicrobials) (*Qualified)
	Anti-drug antibody detection		
	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 and myeloid cell phenotypes by flow cytometry (FcR, KIR, C-type lectins, maturation and activation markers)
	FcR effector function: ADCC/ADCP/ADNP	T cell polyfunctionality and phenotype including memory, Tfh, Treg, exhaustion, NKT & γδT cells	
Exploratory			
Standardized	HIV Target recognition: Virion capture (infectious), Infected Cell Binding (ICABA)	CD8+ 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	Transcriptional profiling of bulk populations or single cells (incl. analysis of alternative transcription, miRNA, etc.)	Transcriptional profiling of bulk populations or single cells (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 *ex vivo* mucosal infection in human explants	T and B cell receptor sequence analysis	
Mucosal tissue histopathology for cell types, architecture, HIV infection, inflammation, mAb distribution			
Host genetics *(HLA class I & II, KIR, FcR)*			