24 April 2020

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Coronavirus Standards Working Group

What should a Coronavirus Standards Working Group do?

Assure development and availability of standards, controls, interlab testing, knowledge to support successful rollout & scaling of 2019-nCoV testing

Identify and develop critical infrastructure to support…

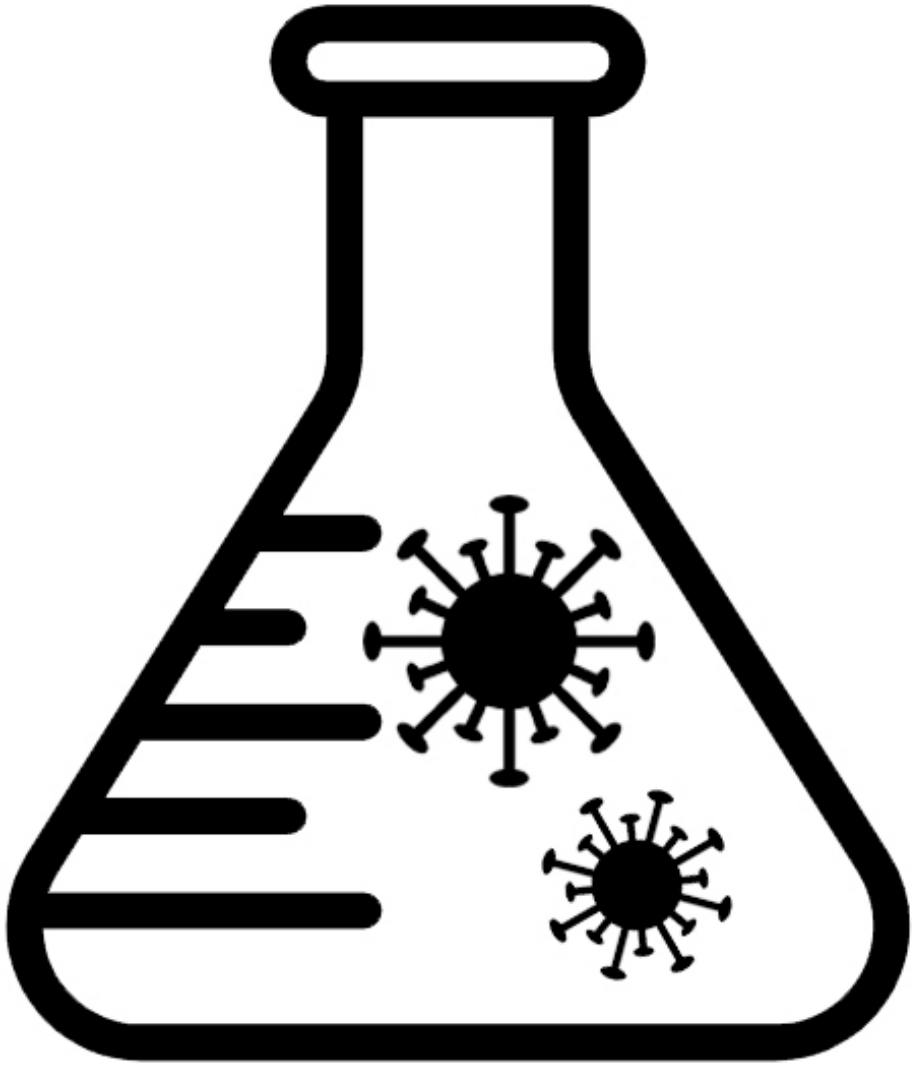
- confidence in test results
- interoperability
- scale-up
- long-term capacity

Identify best practices that should be institutionalized

Learn what we need to so next time we have a global network in place ready to make standards.

24 April Agenda

- Manuscript Overview
- Structure
- Figures
- Table(s)
- Draft Minimum Information Standard
- 1st Complete Database of Controls



Story

Our paper describes the technical and operational needs for a coordinated global project assuring the availability of standards (documentary and control materials) and standardization efforts for coronavirus testing.

- Process analysis to identify sources of bias and variability
- Role of standards to mitigate
- Minimum Information About…
  - Standards
  - Assays
- Inventory of available control materials/standards

Outline

- Abstract
- Introduction
- Testing as a Measurement Process and roles of standards, validation studies and Standardization practices (interlab and proficiency testing)
  - Molecular testing (virus)
  - Serological testing (host response)
- Analysis and Interpretation of test results for SARS-CoV2 (what are we doing well, and what are we missing?)
  - Molecular testing (virus)
  - Serological testing (host response)
- Minimum Information Standards to report attributes
  - Standards/Controls
  - Assays
- Immediate gaps and Recommendations to fill them
- Resources
  - dynamic, web-hosted standards inventory
  - Assay surveys
- Roadmap
  - Resource maintenance
  - Maintain gap analysis
  - Standards development

Figure 1 - Emergence of diagnostic signal though clinical course of SARS-CoV-2.

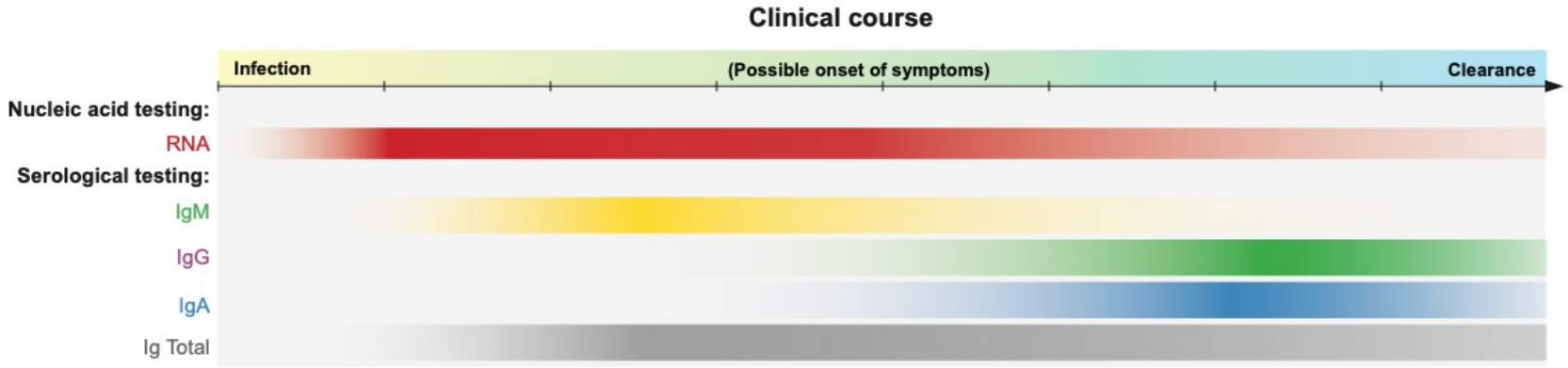


Figure 1 – Clinical Course of Biomarkers

- This Figure is intended to support the narrative of what testing is appropriate for what clinical purpose, and consideration for interpretation

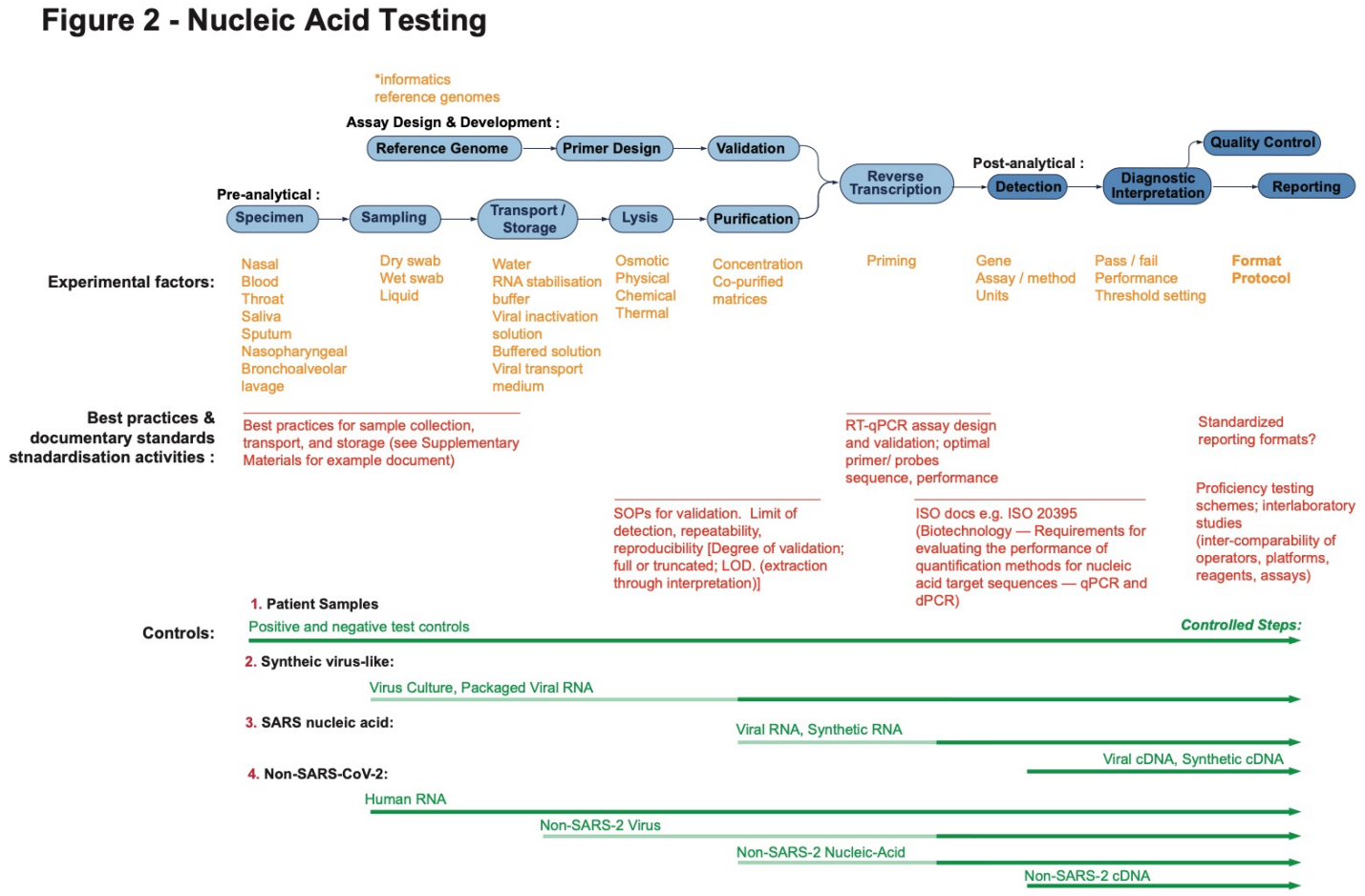


Fig 2– Molecular Test Measurement Process

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- Assay Design & Development, Pre-analytical, Analytical, Post-analytical

Figure 2 - Nucleic Acid Testing

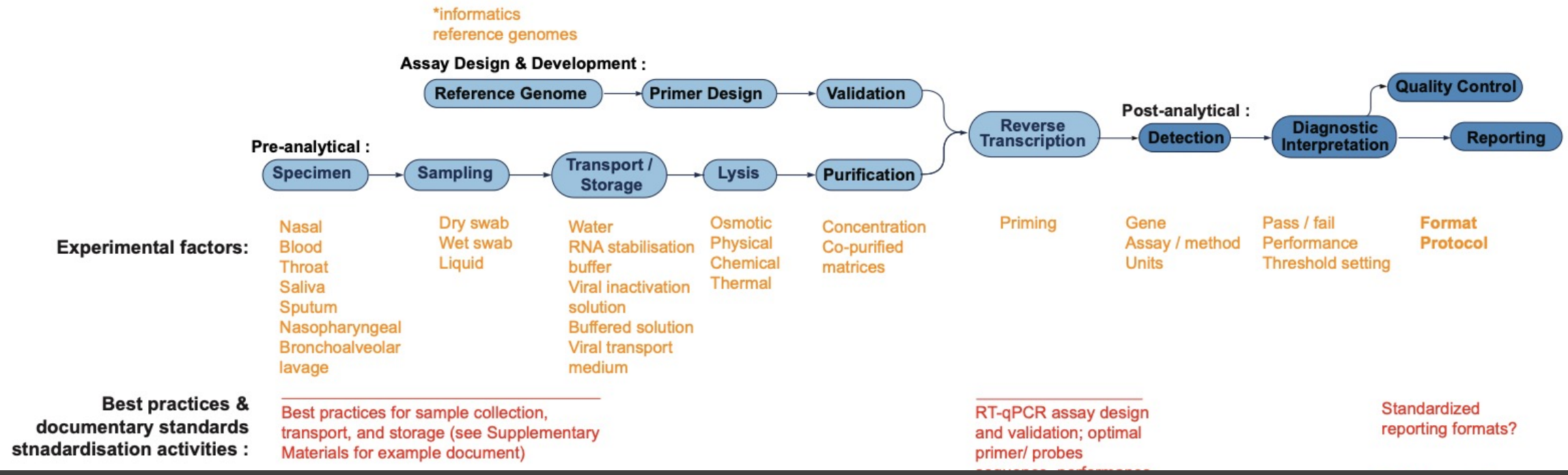
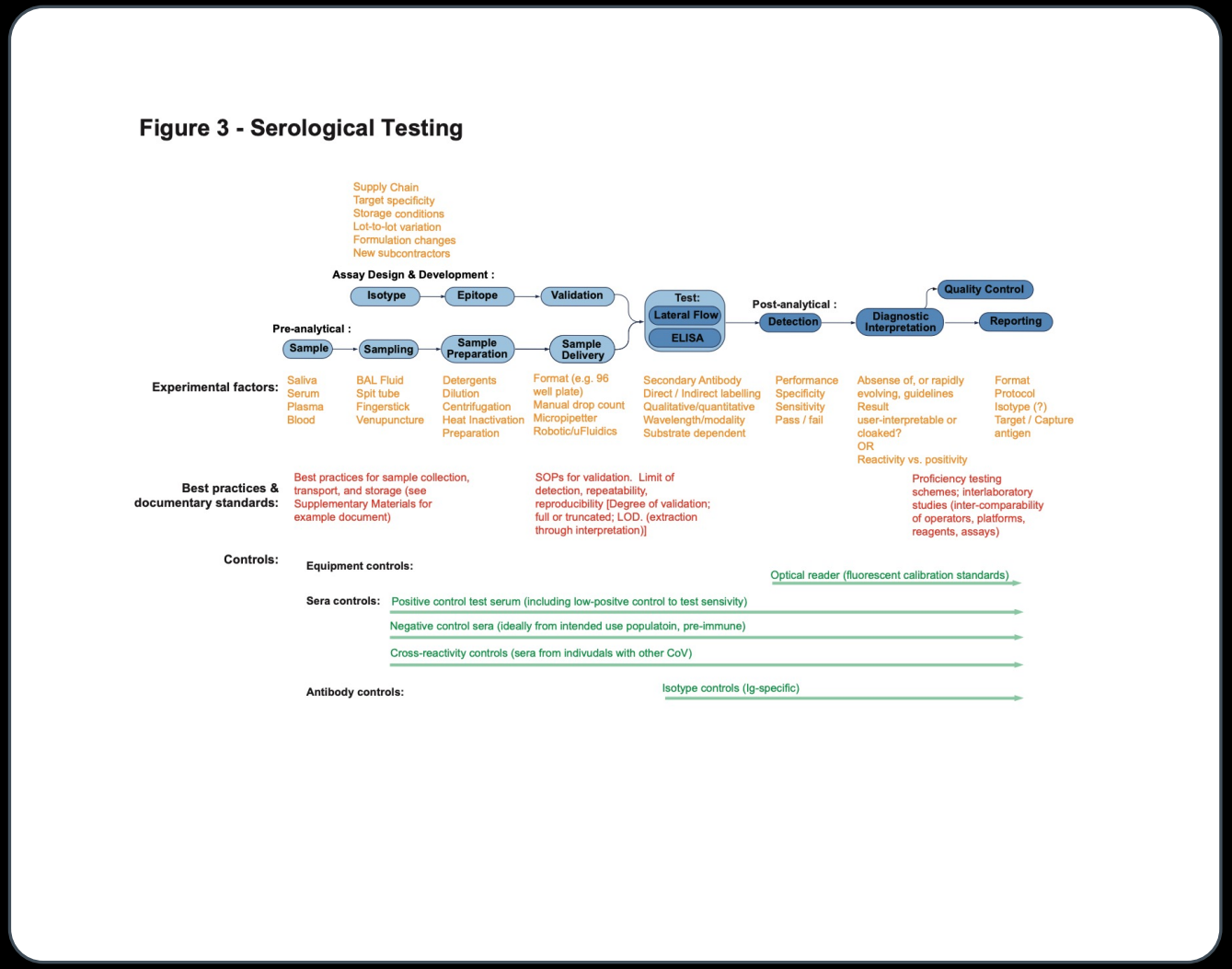


Fig 3 – Serological Test Measurement Process



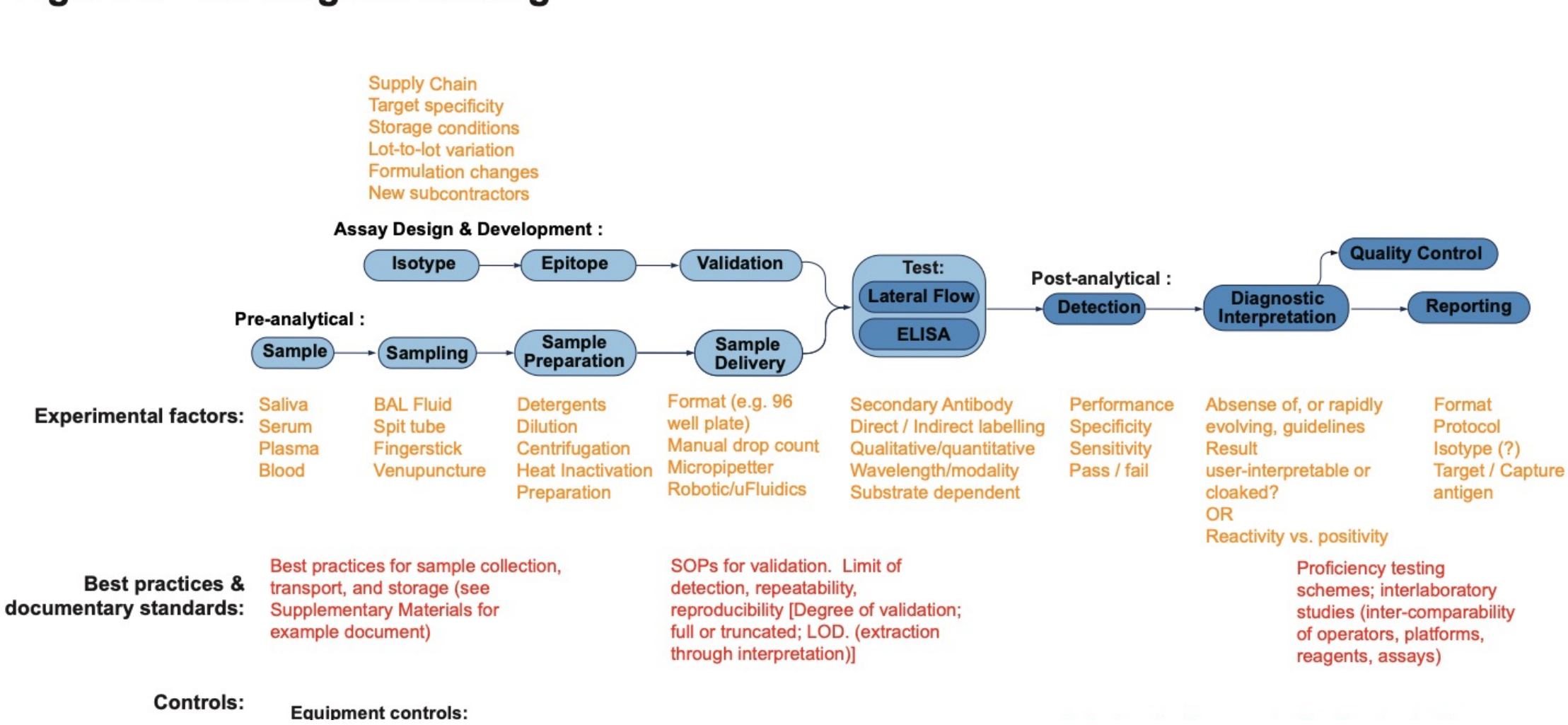


Fig 3 – Serological Test Measurement Process

Phase	Element	Action	Experimental Factors	Effect of poor performance	Standards & Validation Approaches (how does std help?)	Gaps	Influence of Element on diagnostic performance
Pre-analytical	Specimen Type	Specify patient sample to collect		Significant uncertainty in diagnostic comparability and performance	Mock sample to evaluate whole process	No authoritative knowledge of viral distribution in different fluids Imperfect understanding of sampling biases from different fluids/locations	+++
	Sampling	Specify sample collection device			Spike-in positive and negative controls	Performance differences between sampling devices in efficiency and RNA degradation	++
	Sampling	To obtain an accurate sampling from the patient/subject that represents their current health status	Sample collection method Substrate used for collection Interim storage (time/temp)	False negatives Underestimation of viral load Perceived variability in NA assay performance		Variability in collection substrate (collect and release) PCR inhibitors in collection substrate	

Table I – Molecular Process Annotation

- Deeper annotation of measurement process figures: including element description, effect on performance, gaps, relative influence

Table I – Molecular Process Annotation

- Phase
  - Assay Design, Pre-analytical, Analysis, Post-analytical
- Element
  - Specimen type, Sampling, Transport/Storage, Processing, Assay, Interpretation
- Action
  - functional description
- Experimental Factors
  - influential factors (swab type…)
- Effect of poor performance
  - what breaks
- Standards & Validation Approaches
  - what standardization can bring confidence
- Gaps
  - what don’t we have
- Influence on diagnostic performance
  - +, ++, +++

Controls for Specimen taking	Type of material
Controls for Storage-transport	Matrix
Controls for Lysis	Volume
Controls for Purification	Concentration
Controls for Reverse transcription	Stabilizer
Controls for PCR	Storage
Genes	Cost
Catalog #	Regional availability
Vendor or Origin	Web links
Safety level	Further Info

Minimum Information Standard: Standards and Controls

Standards Inventory

- Compiled by Alexandra Whale, Megan Cleveland, Jim Huggett, Pete Vallone
- Uses the Minimum Information About a Control Material draft standard
- Will be web-hosted, searchable
- 41 materials in current inventory

Item name	Sampling: specimen taking	Sampling: storage-transport	Extraction: lysis	Extraction: purification	Assay: reverse transcription	Assay: PCR	Genes	Catalog #	Vendor or Origin	Safety level	Type of material	Matrix	Volum
Quantitative Synthetic SARS-CoV-2 RNA: ORF1ab, N (ATCC® VR-3276SD™)	No	No	No	No	Yes	Yes	Fragments of: ORF1ab, nsp14, RdRp, Full gene: E and N	ATCC® VR-3276SD™	ATCC	BSL 1	Synthetic RNA	molecular grade water	100 µL
Quantitative Synthetic SARS-CoV-2 RNA: Spike S (ATCC® VR-3277SD™)	No	No	No	No	Yes	Yes	S (partial-5' end gene)	ATCC® VR-3277SD™	ATCC	BSL 1	Synthetic RNA	molecular grade water	100 µL
Quantitative Synthetic SARS-CoV-2 RNA: Spike S (ATCC® VR-3278SD™)	No	No	No	No	Yes	Yes	S (partial-3' end gene)	ATCC® VR-3278SD™	ATCC	BSL 1	Synthetic RNA	molecular grade water	100 µL
Quantitative Synthetic SARS-CoV-2 RNA: nsp9, nsp12 (ATCC® VR-3279SD™)	No	No	No	No	Yes	Yes	RdRp	ATCC® VR-3279SD™	ATCC	BSL 1	Synthetic RNA	molecular grade water	100 µL
Genomic RNA from SARS-CoV-2 strain USA-WA1/2020 (ATCC® VR-1986D™)	No	No	No	No	Yes	Yes	Whole genome	ATCC® VR-1986D™	ATCC (Deposited by the Centers for Disease Control and Prevention and obtained through BEI Resources, Isolate USA-WA1/2020, NR-52285)	BSL 2	Genomic RNA	10 mM Tris-HCl, 1 mM EDTA, pH 7.0	100 µL
Heat-inactivated SARS-CoV-2 strain USA-WA1/2020 (ATCC® VR-1986HK™)	No	No	Yes	Yes	Yes	Yes	Whole genome	ATCC® VR-1986HK™	ATCC (Deposited by the Centers for Disease Control and Prevention, obtained through BEI Resources, Isolate USA-WA1/2020, NR-52286)	BSL 1	Heat-inactivated cell lysate and supernatant	growth medium	0.25 mL
Genomic RNA from SARS-CoV-2 strain Hong Kong/VM20001061/2020 (ATCC® VR-1991D™)	No	No	No	No	Yes	Yes	Whole genome	ATCC® VR-1991D™	ATCC (Deposited by the Centers for Disease Control and Prevention and obtained through BEI Resources, Isolate Hong Kong/VM20001061/2020, NR-52388)	BSL 2	Genomic RNA	10 mM Tris-HCl, 1 mM EDTA, pH 7.0	100 µL

Regional availability contact details												
Vendor or Origin	North America and The Caribbean	Central America	South America	Europe	Middle East and North Africa	Sub-Saharan Africa	Central Asia	South Asia	North East Asia	South East Asia and Pacific	Oceania	Known restrictions or other considerations
ATCC	Cedarlan Corporation (Canada)	Científica Senna, S.A. de CV. (Mexico)	Pensabio Biotechnologia (Brazil)	LGC	LGC	LGC	LGC	Chromachemie Laboratory Private Limited (India)	Summit Pharmaceuticals Intl. Corp. (Japan)	Biomedia Co., Ltd (Thailand)	In Vitro Technologies Pty. Ltd. (New Zealand)	
					Biological Industries Beit Haemek Ltd (Israel)		Beijing Zhongyuan Limited (China)		Funakoshi Co., Ltd. (Japan)	SPD Scientific (M) Sdn Bhd (Malaysia)	In Vitro Technologies Pty. Ltd. (Australia)	
							Genetimes ExCell Technology, Inc (China)		KORAM Biotech Corp. (Korea)	Bio-REV Pte Ltd.		

Notes | ATCC | Asuragen | BEI | Exact Diagnostics | EVAg | INSTAND | JRC | Microbiologics | Seracare | Twist Bioscience

All other business

Mailing list – converting to Google Groups (MailChimp too much work)

Communications, planning, engagement, process, operations?

Discussion