

COVID-19 Diagnostic Testing

NAT Technical Screening

Name of the device	PRECISION BIOMONITORING INC.
Manufacturer	PRECISION BIOMONITORING INC.
Application #	313602
DED Screener	Catherine Milley

	Guidance	Acceptable	Comment
Device Description	<p>Intended use Testing setting Extraction methods Targeted sequence Probes and primers Sequences</p>	Deficient	<p>Appears to be a rRT-PCR kit, fluorescence based, using "primers and probes targeting the E gene and UTR regions of the SARS-CoV-2-virus"</p> <p>Inadequate description – information also references a different test, and that this one is a lyophilised version</p> <p>See questions below</p>
Limit of Detection	<p>Spiking RNA / inactivated virus into clinical (preferred) or artificial matrix. The matrix should represent the most challenging clinical matrix.</p> <p>Initial study Dilution series including 3 replicates for each concentration.</p> <p>Confirmatory study 20 replicates of the final concentration. Acceptance criteria: 19/20 positive</p>	Deficient	<p>See questions below</p>
Inclusivity	<ul style="list-style-type: none"> Provide results of in silico analysis including the % identity to published COVID19 sequences. 100% of the published sequences should be detectable. 	Deficient	<p>See questions below</p>
Cross-Reactivity	<ul style="list-style-type: none"> Provide results of in silico analysis of primers and probes against: common respiratory flora, other viral infections Wet testing is recommended Cross-reactivity is defined as greater than 80% homology Matrix-specific cross-reactivity should be assessed 	Deficient	<p>See questions below</p>
Precision (This is not an essential requirement)	<p>Conduct internal precision testing (i.e., at the manufacturer's site) in accordance with CLSI, EP5-A2. In the context of SAP, the 3x5x5 (3 instruments x 5 days x 5 replicates) design is acceptable to provide preliminary estimates of the repeatability (within run) and reproducibility of the assay. Full assessment of repeatability using the 20x2x2 (20 days x 2 run per day x 2 replicates) is expected at time of licensing.</p>	Deficient	<p>See questions below</p>
Stability	<ul style="list-style-type: none"> Briefly describe stability test plan reagent stability studies do not need to be completed at the time of IO issuance, however the study design should be agreed upon during review and the stability studies started immediately following authorization 	Deficient	<p>Label states 1 year. See questions below</p>
Clinical Evaluation	<p>Known positive samples or contrived clinical samples Minimum of 30 reactive and 30 non-reactive specimens</p> <ul style="list-style-type: none"> 20 samples at 1x-2x LoD (95% agreement) Other concentrations and non-reactive (100% agreement) <p><i>Serological assay</i> Positive samples should include infection times of 4-10 days and 11-24 days</p>	Deficient	<p>See questions below</p>
Point of Care	<p>Near patient studies performed in clinical setting by intended users. Minimum of 9 operators and questionnaire to assess IFU clarity.</p>	n/a	
Labeling	<p>Instructions for use Reagent labels</p>	Y	<p>Text provided for IFU, but not actual document (DSL D deficiency)</p> <p>Labels provided.</p>

Note to DSLD: The device name needs to be corrected in MDS to "TripleLock SARS-COV-2 Test Strips".

Questions:

Please provide the following information and scientific evidence. As a guide, the expected format for study summaries has been provided below the questions.

1. Provide a complete device description, with details on each component, and rationale for its design, and for your selection of reagents and buffers. Describe the extraction methods and materials, and PCR equipment that have been validated to work with your kit.
2. Provide a description of all controls used with the kit (e.g. negative control, positive control, internal control), including a rationale for their selection, and their source. Describe the the results expected and acceptance criteria. Ensure you identify the concentration of the positive control relative to the LoD
3. Provide a clear description outlining the specimen types that can be used with the device, and the extraction methods that are to be used for each. Note that the evidence you provide in support of your device must include all labelled sample types, or you must provide evidence that these sample types are equivalent.
4. Describe the targeted sequences of the SARS-CoV-2 genome. Provide a list of all primers and probe sets and briefly describe what they detect, and include their nucleic acid sequences. Indicate if biotin-streptavidin/avidin chemistry is used in any steps of the test. You may include relevant supporting literature.
5. Provide the intended use, intended users, and the intended testing setting to be used with your device (lab, Point of Care).
6. Provide a study report, or a detailed summary of methods and results, to support the claimed Limit of Detection (LoD)/analytical sensitivity. LoD can be determined by spiking RNA or inactivated virus into clinical (preferred) or artificial matrix. The matrix should represent the most challenging clinical matrix. The initial study requires a dilution series including 3 replicates for each concentration. The confirmatory study with 20 replicates of the final concentration is needed. A precise description (with the source and sequence) of the samples used in these studies are needed.
7. Provide the results of your *in silico* analysis of inclusivity, including the % identity to published COVID19 sequences..
8. Provide results of Matrix-specific cross reactivity studies demonstrating that the following pathogens are not cross-reacting with the assay. *In silico* analysis and all currently available results of wet testing should be submitted.
Note: For wet testing, concentrations of 10⁶ CFU/ml or higher for bacteria and 10⁵ pfu/ml or higher for viruses is recommended.
Note: If *in silico* analysis reveals ≥ 80% homology between the cross-reactivity microorganisms and your test primers/ probe(s), we recommend that you perform a microbial interference study with SARS-CoV-2 and the microorganisms that your test primers/ probe(s) have homology to, or, provide an appropriate scientific rationale which supports the clinical utility of your test given your results.

High priority pathogens from the same genetic family	High priority organisms likely in the circulating area
Human coronavirus 229E	Adenovirus (e.g. C1 Ad. 71)
Human coronavirus OC43	Human Metapneumovirus (hMPV)
Human coronavirus HKU1	Parainfluenza virus 1-4
Human coronavirus NL63	Influenza A & B
SARS-coronavirus	Enterovirus (e.g. EV68)
MERS-coronavirus	Respiratory syncytial virus
	Rhinovirus
	<i>Chlamydia pneumoniae</i>
	<i>Haemophilus influenzae</i>
	<i>Legionella pneumophila</i>
	<i>Mycobacterium tuberculosis</i>
	<i>Streptococcus pneumoniae</i>
	<i>Streptococcus pyogenes</i>
	<i>Bordetella pertussis</i>
	<i>Mycoplasma pneumoniae</i>
	<i>Pneumocystis jirovecii</i> (PJP)
	Pooled human nasal wash - to represent diverse microbial flora in the human respiratory tract
	<i>Candida albicans</i>
	<i>Pseudomonas aeruginosa</i>

	<i>Staphylococcus epidermis</i>
	<i>Staphylococcus salivarius</i>

9. Provide the study reports for interference testing of endogenous substances (Hb, bilirubin, Proteins, TG, HAMA, RF, Total IgG, Total IgM), and of exogenous substances (common medications).
10. Provide the study reports for precision testing. Conduct internal precision testing (i.e., at the manufacturer's site) in accordance with CLSI EP5-A2. In the context of the Interim Order, the 3x5x5 (3 instruments x 5 days x 5 replicates) design is acceptable to provide preliminary estimates of the repeatability (within run) and reproducibility of the assay. Full assessment of repeatability using the 20x2x2 (20 days x 2 run per day x 2 replicates) is expected at time of authorization.
11. Provide the reports for any Clinical Performance Studies using known positive samples or contrived clinical samples. A minimum of **30 reactive and 30 non-reactive specimens** is needed. Validation of the reactive and non-reactive samples using a reference standard is needed. For reactive samples, 20 samples at 1x-2x LoD demonstrating 95% agreement is needed. Other concentrations and non-reactive samples should demonstrate 100% agreement. A statistical rationale for the sample size of the study should also be provided.
12. Stability (Shelf life and Shipping/transport stability)
Provide all evidence currently available supporting the stability of test kit, including sample stability. Alternatively, submit a plan for stability studies. Note that reagent stability studies do not need to be completed at the time of IO issuance, however the study design will be assessed during review of your submission, and we will require that the stability studies be started no later than immediately following authorization. Provide the claim you are making for stability of your device and how you arrived to this claim.
13. Provide the Instructions for Use that will accompany the kit.

Study format guide

- a) Study Title
- b) Objectives
 - Provide a short description of the objective
- c) Methodology
 - Sample type: description of the matrix
 - Number of samples tested (pos & neg)
 - Sample characterization: Name of assay or method used to characterize the samples
 - Testing algorithm: time-point, replicates, run, days, site, etc
- d) Results
 - Tabular format whenever possible
 - Statistical analysis
 - Discrepant results (explanation and resolution)
 - Results for each setting and/or sample type
- e) Conclusion
 - Clear conclusion supporting the performance claim
 - Rationale for method deviation