October 27, 2021

Elsa Eleco
Section Chief, On-Site Licensing Inspections
California Department of Public Health - Laboratory Field Services
320 W. 4th Street, Suite 890
Los Angeles, CA 90013

Dear Ms. Eleco,

Thank you for your letter dated October 21, 2021, "State Routine Inspection: Notice of Intent to Impose Sanctions upon CDPH Branch Laboratory CPH889339." The CDPH Branch Laboratory's (the "Lab") response is as follows:

D5400 - 42 C.F.R section 493.1250 Condition: Analytic systems

The Lab's August 20, 2021 (the "August 20 Response"), response to your June 8, 2021, letter addresses this provision and provides data fulfilling all the requirements of 42CFR493.1250 and 42CFR493.1253. A summary table of documents included as Exhibit B to the August 20 Response is included here as Table I. This includes the original validation performed and provided to LFS on October 24, 2020 as well as supplemental validation studies performed in July 2021.

Table I: Studies satisfying all parts of 42CFR493 (2) i-vii, and sent to LFS on 8/20/2021 as VAL-RPT-LAB-003 and VAL-RPT-LAB-018.

Validation Requirement	Date complete	Validation Report	Report Accepted Lab Director of Record	Report Accepted by Current Lab Director
LOD Finding	10/19/2020	CA-VALRPT-LAB-003	10/24/2020	2/19/2021
LOD Confirmation	10/20/2020	CA-VALRPT-LAB-003	10/24/2020	2/19/2021
Accuracy (Clinical Evaluation) {CFR 484.1253 (2)(i)}	10/20-21/2020	CA-VALRPT-LAB-003	10/24/2020	2/19/2021
Precision (Intra-run and Inter-run reproducibility) {CFR 484.1253 (2)(ii)}	10/20-21/2020	CA-VALRPT-LAB-003	10/24/2020	2/19/2021
Reportable Range {CFR 484.1253 (2)(v)}	10/20/2020	CA-VALRPT-LAB-003	10/24/2020	2/19/2021
Reference Intervals {CFR 484.1253 (2)(vi)}	N/A	N/A	N/A	N/A
Analyitical Sensitivity (Inclusivity) {CFR 484.1253 (2)(iii)}	7/15/2021	CA-VALRPT-LAB-018	7/15/2021	7/15/2021
Analytical Specificity (Cross-Reactivity) {CFR 484.1253 (2)(iv)}	7/13/2021	CA-VALRPT-LAB-018	7/15/2021	7/15/2021
Analytical Specificity (Interfering Substances) {CFR 484.1253 (2)(iv)}	7/14/2021	CA-VALRPT-LAB-018	7/15/2021	7/15/2021

A list of studies proposed in the Lab's email of June 18, 2021 ("validation plan," Section 9.0, pg 14), the results of which are included in the August 20 Response, are shown below in Table II. This includes pre-validation limit of detection studies, supplemental studies for analytical sensitivity, inclusivity and specificity/interfering substances, and additional studies completed by the laboratory not requested by LFS.

Table II: Studies proposed in the validation plan sent to LFS on June 18, 2021:

Section	Study	Subsection	Sample type	Sample treatment	PCR Targets	Comments	Sent to LFS
9.1	LoD Finding and Confirmation (media collection)	9.1.1	VTM	No heat	Viral + EC*	Completed 10/19/2020 ; CA-VALRPT-LAB-017 (pre-testing)	8/20/2021
				Heat	Viral + EC	Completed 10/19/2020 ; CA-VALRPT-LAB-017 (pre-testing)	8/20/2021
					Viral + EC+ *RPP30*	Not Complete: Justification - no VTM testing done at VBL	N/A
		9.1.2	MTM**	No Heat	Viral + EC	Completed 10/19/2020 ; CA-VALRPT-LAB-017 (pre-testing)	8/20/2021
				Heat	Viral + EC	**Completed 10/19/2020 ; CA-VALRPT-LAB-003 and CA-VALRPT-LAB-017**	**10/24/2020,** 8/20/2021
				Heat	Viral + EC + *RPP30*	Completed 06/28/2021 ; CA-VALRPT-LAB-012	Not requested
9.2	LoD Finding and Confirmation (dry collection)	9.2	Dry swab	N/A	Viral + EC + *RPP30*	Completed 5/28/2021 ; CA-VALRPT-LAB-015	Not requested
9.3	Accuracy (Clinical Evaluation)	9.3.1	MTM	Heat	Viral + EC	**Completed 10/23/2020 ; CA-VALRPT-LAB-003 and CA-VALRPT-LAB-017**	**10/24/2020,** 8/20/2021
					Viral + EC + *RPP30*	Completed 06/28/2021 ; CA-VALRPT-LAB-012	Not requested
		9.3.2	Dry Swab	N/A	Viral + EC + *RPP30*	Completed 5/28/2021 ; CA-VALRPT-LAB-015	Not requested
9.4	Precision (Intra-run and Inter-run Reproducibility)	9.4.1	MTM	Heat	Viral + EC	**Completed 10/23/2020 ; CA-VALRPT-LAB-003 and CA-VALRPT-LAB-017**	**10/24/2020,** 8/20/2021
					Viral + EC + *RPP30*	Completed 06/28/2021 ; CA-VALRPT-LAB-012	Not requested
		9.4.2	Dry swab	N/A	Viral + EC + *RPP30*	Completed 5/28/2021 ; CA-VALRPT-LAB-015	Not requested
9.5	Analytical Sensitivity (Inclusivity)	9.5.1	Bioinformatic data	N/A	N/A	Completed 7/14/2021; CA-VALRPT-LAB-018	8/20/2021
9.6	Analytical Specificity (Cross-Reactivity)	9.6.1	Bioinformatic data	N/A	N/A	Completed 7/14/2021; CA-VALRPT-LAB-018	8/20/2021
		9.6.2	Virus / pathogen panel in MTM	Heat	Viral + EC + *RPP30*	Completed 7/14/2021; CA-VALRPT-LAB-018	8/20/2021
		9.6.3	Virus / pathogen panel in dry swab	Heat	Viral + EC + *RPP30*	Completed 9/10/2021; CA-VALRPT-LAB-021	Not requested
9.7	Analytical Specificity (Interfering substances)	9.7.1	Various substances in MTM	Heat	Viral + EC + *RPP30*	Completed 7/14/2021; CA-VALRPT-LAB-018	8/20/2021
		NA***	Various substances in dry swab	Heat	Viral + EC + *RPP30*	Completed 9/10/2021; CA-VALRPT-LAB-021	Not requested
9.8	Sample stability	9.8.1	MTM sample	Heat	Viral + EC	Not Complete: Justification - not required per CFR 493.1253; but will complete by 12/15/21	N/A
					Viral + EC + *RPP30*	Not Complete: Justification - not required per CFR 493.1253, but will complete by 12/15/21	N/A
		9.8.2	Dry swab sample	N/A	Viral + EC + *RPP30*	Completed 5/28/2021 ; CA-VALRPT-LAB-015	Not requested
		9.8.3	Extracted RNA	N/A	Viral + EC + *RPP30*	Not Complete: Justification - not required per CFR 493.1253.	N/A

* EC = Extraction Control
** PrimeStore MTM is an FDA-cleared microbial nucleic acid storage and stabilization device (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm?ID=DEN170029)
*** Testing added to Validation in amended plan
CA-VALRPT-LAB-003 - Original MTM validation
CA-VALRPT-LAB-012 - RPP30
CA-VALRPT-LAB-015 - Dry Swab
CA-VALRPT-LAB-017 - Appendices to Original (MTM) #
CA-VALRPT-LAB-018 - Original (MTM) Supplement*
CA-VALRPT-LAB-021 - Dry Swab Supplement*
Appendix contains all raw data, pre-testing data and supporting documents;
*Supplement contains interfering substance, specificity, inclusivity

I recognize that a stability study for dry swabs is included in the validation plan and was not performed as of August 20, 2021. However, stability studies for MTM and dry swabs are not required by CLIA, and MTM and dry swab stability have already been demonstrated elsewhere (see DEN170029.Decision.Summary.READY508.docx (fda.gov) and Polyester Nasal Swabs Collected in a Dry Tube are a Robust and Inexpensive, Minimal Self-Collection Kit for SARS-CoV-2 Testing (medrxiv.org)). I agree that such studies are part of good laboratory practice, and

intend to have the MTM and dry swab stability studies completed and to provide corresponding data by December 15, 2021.

Similarly, while study results for asymptomatic patients from a PerkinElmer, Inc. submission to FDA are not yet available, please note that no specific CLIA requirement has been located addressing this point.

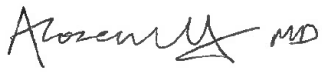
Also note that because all extracted RNA is processed within 24-48 hours, the Lab does not intend to perform extracted RNA stability studies at this time.

Details of the studies and documentation pertinent to the Lab's establishment of Ct cutoff values was provided in Exhibits D-H of the August 20 Response. Ct cutoffs were established after extensive discussion between the Lab's Laboratory Directors at the time and CDPH between October 28, 2020, and January 25, 2021, in response to a rapidly evolving COVID-19 pandemic and non-standardization between available molecular assays. Current Ct cutoffs have remained in place since January 25, 2021. Because the studies reflected in Exhibits D-H of the August 20 Response were conducted after the current Ct cutoffs were established, a policy was written to specifically address requirements for validation of any future changes in Ct cutoffs as provided in Exhibit A of the August 20 response.

Since October 2020, the Lab has undergone multiple inspections by, and provided comprehensive, detailed information in response to three separate agencies: CMS, LFS and CAP. As part of this process and our commitment to continuous quality improvement, the Lab has put significant effort into improving and tightening its quality management processes.

I appreciate and thank you and your team for your diligence in reviewing our completed validation. The staff at the Lab is very proud of the work we have done, and we will continue to cooperate with inspectors. We remain committed to providing high quality SARS-CoV2 testing to the State and citizens of California in compliance with laboratory requirements as set forth in the California Business and Professions Code, CLIA, and CAP checklists.

Sincerely,



Adam Rosendorff, MD
Laboratory Director, CDPH Branch Laboratory, Valencia
Medical Director, PerkinElmer Genomics