COVID-19 Diagnostic Testing

Technical Screening Serological Assays (ELISA, antigen and antibody tests)

Name of the device	Dimension Vista SARS-CoV-2 Total Antibody (COV2T) Assay Dimension Vista/Dimension EXL SARS-CoV-2 Total Antibody Calibrator (COV2T CAL/CV2T CAL) Dimension Vista/Dimension EXL SARS-CoV-2 Total Antibody Quality Control (COV2T/CV2T Pos/Neg)
Manufacturer	Siemens Healthcare Diagnostics Inc
Application #	**316782**
Technology	**Antibody**
Test Setting	**Lab**
DED Screener	**Elana Cherry**
Date	**July 8, 2020**

Notes to reviewer	Device quality and performance appear good

Interim order respecting the importation and sale of medical devices for use in relation to COVID-19

STEP 1: Screen for MEETING SENSITIVITY and SPECIFICITY REQUIREMENTS:

Initial Screen for Serology Tests:

	Guidance	Acceptable	Comment
Sensitivity and Specificity COVID-19 serological testing devices: Notice on sensitivity and specificity values	Health Canada considers the following to be unacceptable for authorization: • sensitivity below 90% for IgG antibodies or total antibodies in samples collected 2 weeks or more after onset of symptoms, or • specificity below 95% Tests with sensitivity and specificity values below these minimums do not meet the criteria of 5(c) and (d) of the Interim order respecting the importation and sale of medical devices for use in relation to COVID-19, and will not be authorized. If minimum values are not met, proceed to completing the Refusal Recommendation Memo If the timing of the samples is not clear, ask Questions below.	Yes	As described in Sub-section 4 – Clinical Agreement of Section 12.0 – PERFORMANCE EVALUATION of our application (page 22), the sensitivity of COV2T is demonstrated to be 100% in samples > 14 days post PCR positive and the specificity is demonstrated to be 99.8%. Furthermore, information on the timing of collection for each positive sample, including the date of symptom onset was provided in the line data provided as Appendix 3 of the application (under tab "Sensitivity").
Clinical Evaluation Requirements for serological antibody tests submitted under the COVID-19 Interim Order: guidance	• A minimum of 50 positive clinical samples and 200 negative clinical samples is required for clinical evaluation. • **Comparator assay (RT-PCR) should be authorised**, either by HC, or EUA from US, or WHO EUL. • **ELISA:** reference range study with a minimum of 500 samples • **POC intended use**: Performance data required for each sample type. • **Timing of the collection of positive** samples (infection time)	Yes	

Sensitivity and Specificity Performance Screening Question:

You are asked to reply to this email within 10 calendar days. Please provide the requested information within this time. If you will require an extension, please provide a date by which you will reply. If you do not reply to this email request within 10 calendar days, we will consider the non-response as a formal withdrawal of your application. In

such an instance, Health Canada will not follow-up with any additional communication regarding your application and will mark the application as withdrawn in our database.

You are asked to respond to all the questions in a single, comprehensive package, using a Question and Answer format with references to attachments, as needed. Your response should be submitted in a single e-mail communication; attachments can be included in a compressed zip file format. Please ensure that the actual study reports are provided when requested; it is not considered sufficient to simply state performance characteristics without providing the scientific results. Failure to provide a complete and comprehensive response may result in refusal of the application.

The clinical performance data submitted in the application do not meet Health Canada's requirements under the Interim Order Respecting the Importation and Sale of Medical Devices for Use in Relation to COVID-19 and as described in the Requirements for serological antibody tests submitted under the COVID-19 Interim Order: guidance and in the COVID-19 serological testing devices: Notice on sensitivity and specificity values. Please address the following questions

1. As stated in Health Canada's COVID-19 serological testing devices: Notice on sensitivity and specificity values, sensitivity below 90% for IgG antibodies or total antibodies in samples collected 2 weeks or more after onset of symptoms, or specificity below 95% are considered to be unacceptable for authorization, regardless of other factors. Please clearly identify the timing of the collection of positive samples (infection time) in your clinical study.

2. Provide a statistical rationale for the sample size of the study. A minimum of **50 positive samples** and **200 negative samples** should be tested. The positive sample set should include relevant samples from the targeted population to support the claimed intended use, for example:
    - Samples in early onset stage of the disease
    - Samples in intermediate onset stage of the disease
    - Samples in convalescence stage of the disease
    - Samples from patients with severe symptoms
    - Samples from patients with mild symptoms

    Include patient demographic information, such as sex and age.

3. Clinical accuracy should be established using human specimens from patients with confirmed COVID -19 infection. Include the name and manufacturer of the RT-PCR test used to characterize the samples. Comparator RT-PCR assays should be authorized under the Interim Order. In the absence of Health Canada authorization, Emergency Use Authorization from the United States Food and Drug Administration, or declaration of eligibility for procurement by the World Health Organization under the Emergency Use Listing Procedure, will be accepted.

    Verify the associated links to determine if the comparator RT-PCR assay is eligible for use as a comparison for the clinical study:
    Health Canada COVID-19 Authorization
    Emergency Use Authorization from the United States Food and Drug Administration
    World Health Organization under the Emergency Use Listing Procedure

4. Show the clinical agreement to establish the diagnostic sensitivity (PPA) and specificity (NPA) of the test; 95% confidence intervals should be provided.

5. Provide a breakdown of the assay sensitivity and specificity for each sample type. Alternatively, a sample equivalency study may be submitted.

	Guidance	Acceptable	Comment
Device Description	**Type of technology:** - ELISA, Lateral-Flow, antigen detection, antibody detection. - qualitative, quantitative - instrumentation required **Sample type / collection methods**: Fingerstick samples require additional validation for POC use (see below) **Testing setting:** Laboratory / Point of Care **Calibrator and controls** (value assignment) **Antigen source:** what it is and what is the source. **Intended use statement assessed during review**	Yes	The Dimension Vista COV2T assay is a homogeneous, sandwich chemiluminescent immunoassay based on LOCI technology.
Analytical Sensitivity	**There is no requirement for LoD for serological assay**. Diagnostic Sensitivity demonstrated in clinical studies is more relevant. **For antigen tests, LoD is required.** Relative analytical sensitivity of ELISA can be assessed by end-point dilution analysis which indicates the dilution of serum in which antibody is no longer detected. Should be requested at screening only if nothing is provided (quality of information assessed during review)		Note: Not relevant until there is a standardised testing panel available. Until then, do not need to screen on this attribute.
Cut Off	How the cutoff was established	Yes	
Hook effect	Applicable for sandwich immunometric assays	Yes	
Sample matrix	**Equivalence between sample types/Matrix equivalency studies** • POC needs data for fingertip sample type. • If no data for each sample type, a specimen equivalency study is requested • Patient serum used to validate the tests: number and variety of sera (assessed during review). • Validation of anticoagulants **For antigen test**: Equivalency between swabs recommended if all the studies were done with one swab	Yes	
Interference and Cross Reactivity	• **Endogenous substances** including : Hb, bilirubin, Proteins, TG, HAMA, RF, Total IgG, Total IgM. • **For antigen tests**, either naturally present in respiratory specimens or artificially introduced into the nasal cavity or nasopharynx • **Exogenous:** Common medication • **Cross-reactivity** with non-targeted commensal and pathogenic microorganisms. **Antigen assay**: in silico analysis alone is not acceptable. If wet testing is also provided only wet testing results should be listed in package insert. **For antibody assays : Class specificity** : For IgM assays, to determine if reactivity with SARS-CoV-2 specific IgG is a potential assay interferent and vice versa for IgG assays. Detection of total Ab detection: no need for class specificity	Yes	
Precision	Evidence of repeatability	Yes	
Seroconversion	Seroconversion panel testing, ***if available***.	Yes	
Stability	**Description of 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	Yes	

	review and the stability studies started immediately following authorization		
Robustness	Use variation : sample and reagent volume, operating temperature and humidity, reading time and illumination (visual reading)	No	
Point of Care	**Near patient studies** performed in clinical setting by intended users. Minimum of 9 operators and questionnaire to assess IFU clarity.	N/A	
Labeling	**Instructions for use** **Reagent labels** Intended Use Statement will be assessed during review	Yes	
Quality	• **QMS certificate provided?** • **Evidence of lot release programme**	yes	

File Disposition:

Recommend for Review