TO **A**	Rosslynn Miller-Lee Executive Director, Medical Device Evaluation Bureau MDD
FROM **DE**	Emily Hollink Medical Device Directorate

Application Information *Information de soumission*			
Application ***Soumission*** 313727	**Name of device** ***Nom de l'homologation*** ANTI-SARS-COV-2 ELISA (IGG).	**Licence Number** ***No. de l'homologation*** N/A	**Risk Class** ***Classe de l'instrument***
Application Type ***Type de soumission*** APPLICATION UNDER IO	**Licence Type** ***Type d'homologation*** SINGLE DEVICE	**Manufacturer** ***Fabricant*** EUROIMMUN MEDICAL DIAGNOSTICS CANADA INC.	**Company ID** ***No. d'entreprise*** 116604

Division:	Date Assigned:	Date Completed:
IN VITRO DIAGNOSTICS	*Date assignée:* 2020-09-09	*Date d'achèvement:* 2020-09-17

Technology	Antibody
Test Setting	Lab

1 Background/*Antécédents*

On 2020-04-09, Health Canada received an application for authorization under the Interim Order for the ANTI-SARS-COV-2 ELISA (IGG) submitted and manufactured by EUROIMMUN MEDICAL DIAGNOSTICS CANADA INC.

Table 1. Summary of the application

Date	Comment
April 9 2020	The applicant submitted a request for IO authorization.
April 14 2020	The application underwent technical screening. A series of back and forth discussions took place between the applicant and Health Canada.
May 8 2020	The initial review was completed and an AI request was sent to the applicant.
May 19 2020 to May 27 2020	The applicant responded to the AI request in several installments.
August 20 2020	The AI response was reviewed.

Table 1. Summary of the application	
Date	**Comment**
August 21 2020	A second AI request was submitted to the applicant followed by several back and forth communications between Health Canada and the applicant.
August 31 2020	The response to the second AI request was submitted.

The ANTI-SARS-COV-2 ELISA (IGG) is intended for the semi-quantitative detection of SARS-CoV-2 antibodies (IgG) in serum, EDTA, heparin or citrate plasma using ELISA technology. The device is compatible with microplate readers that detect 450nm to 650nm wavelength.

The application was reviewed under the Interim Order 32 Respecting the Importation and Sale of Medical Devices for Use in Relation to COVID-19 pursuant to 33 subsection 30.1(1) of the Food and Drugs Act. This Interim Order will allow the Department to issue expedited authorization for sale or import of medical devices to deal with the current significant risk of COVID-19 to the health and safety of Canadians.

2 Intended Use

ANTI-SARS-COV-2 ELISA (IGG) Package Insert [EI 2606G A CA CQ3.docx, Version: 2020-08-2]

The EUROIMMUN Anti-SARS-CoV-2 ELISA (IgG) is an enzyme-linked immunosorbent assay intended for the qualitative in vitro determination of human antibodies of the immunoglobulin dass IgG against SARS-CoV-2 in human serum and plasma (EDTA, heparin or citrate) in the general population

- The assay is for use in conjunction with the testing strategy outlined by the respective public health authorities in charge.
- Negative results do not exclude SARS-CoV-2 infection and should not be used as the sole basis for patient management dedsions.
- False positive results for IgG antibodies may occur due to cross-reactivity from pre-existing antibodies or other possible causes.
- This assay is not intended to be used for screening patients or as an aid for diagnosis of patients with suspected COVID-19 infection.
- This assay is not intended for home-testing (or self-testing).
- Negative results must be combined with clinical observations, patient history and epidemiological information.
- False negative results can occur in elderly and immunocompromised patients.

3 Discussion/*Évaluation*

The information provided meets the minimum requirements for issue of Authorization under Interim Order 32.

The manufacturer holds a valid MDSAP Certificate.

This device has been authorised outside of Canada by the FDA (EUA dated 05/04/2020).

Studies for precision and endogenous interference were provided and were accepted.

Studies for limit of detection, cross-reactivity, class specificity and interference are on-going. Partial results were provided using contrived samples and were accepted. The outstanding results will be the subject of a condition.

Accelerated stability data was provided. Real time stability studies are ongoing and expected to be completed by August 2021.

Evidence of acceptable clinical performance was demonstrated through two studies. One study tested 1,151 negative clinical samples that demonstrated specificity between 98.7% to 100% depending on the population. In the second study, 75 clinical positive samples and 1419 negative clinical samples were tested and demonstrated sensitivity at 90.7% to 94.7% and specificity at 99.1% to 99.6%, depending on how borderline results were interpreted. In addition, a literature review was conducted which included peer-reviewed studies provided by the applicant as well as other publically-available studies. Overall, the literature does indicate that, although variable, the clinical performance of EUROIMMUN Anti-SARS-CoV-2 ELISA (IgG) is mostly acceptable.

Labelling meets the minimum requirements of the Regulations. The package insert includes the available information for LOD, precision, cross-reactivity, interference and clinical performance that was presented in this application. A limitations section indicates that the assay should be interpreted in conjunction with the patient's medical history, clinical signs and symptoms, and the results of other diagnostic tests.

In the context of the COVID-19 pandemic, the preliminary validation studies provided by the manufacturer are sufficient for an authorization given that the benefits that may be obtained from authorizing this assay for SARS-CoV-2 detection outweigh the risks related to the current COVID-19 national health emergency.

4 Recommendation

The application may be approved for authorization with the following conditions:

I. **CONDITION WITHIN SIX MONTHS OF AUTHORIZATION: Provide a detailed cross reactivity/analytical specificity study report. Every effort should be made to assess cross-reactivity using a minimum of 5 pre-pandemic samples positive for IgG antibodies directed against the pathogens listed below.**

Table 2: List of mandatory organisms to be tested for cross-reactivity

Epstein-Barr virus (infectious mononucleosis)
Human Metapneumovirus (hMPV)
Influenza A & B
Parainfluenza virus 1- 4
Rhinovirus

Table 3: List of optional organisms to be tested for cross-reactivity

Mycoplasma pneumoniae	Pneumocystis jiroveci (PJP)
Chlamydia pneumoniae	Candida albicans
Haemophilus influenzae	Pseudomonas aeruginosa
Legionella pneumophila	Staphylococcus epidermis
Mycobacterium tuberculosis	Staphylococcus salivarius
Streptococcus pneumoniae	HCV
Streptococcus pyogenes	Norovirus
Bordetella pertussis	
HIV	
HBV	

II. **CONDITION WITHIN THREE MONTHS: Provide a class specificity report. Evidence should demonstrate that the assay detects anti-CoV-2 IgG when both IgM and IgG antibodies to SARS-CoV-2 are present in the sample.**

III. **CONDITION WHEN AVAILABLE: Provide the results for the real-time stability testing to support the shelf life and in-use stability claims.**

IV. **CONDITION WITHIN ONE MONTH: Provide real-time shipping stability to support the current transportation protocol.**

I CONCUR / JE SUIS D'ACCORD

Signed in Docubridge

Emily Hollink Date

Signed in Docubridge

Rosslyn Miller-Lee Date
Executive Director/ Directrice Executive
Medical Devices Evaluation Bureau/ Bureau de l'évaluation des instruments médicaux