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MEMORANDUM **NOTE DE SERVICE**

TO Rosslynn Miller-Lee
Executive Director,
Medical Device Evaluation Bureau
MDD

FROM Emily Hollink
DE MDD

SUBJECT Recommendation for Authorization under the COVID-19 Interim Order
OBJET Manufacturer: Siemens Healthcare Diagnostics Inc.

Technology: Antibody (serological) *Setting:* Laboratory

Device: Advia Centaur XP/XPT SARS-CoV-2 Total Assay
Applications: 316549

Background

Applications for the SARS-CoV-2 Total Assay were submitted for use on the Advia Centaur XP/XPT and Atellica IM instruments. The assay formulation is identical, but some of the performance characteristics were established specific to each instrument type, therefore the manufacturer submitted the information in two separate applications.

The information was reviewed under the Interim Order Respecting the Importation and Sale of Medical Devices for Use in Relation to COVID-19. This Interim Order allows 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.

The information submitted was evaluated based on the Health Canada Guidance: Requirements for Serological Antibody Tests Submitted under the COVID-19 Interim Order.

The Advia Centaur XP/XPT SARS-CoV-2 Total Assay received an instrument-specific US FDA Emergency Use Authorization (EUA) on May 29, 2020.

Intended Use

ADVIA CENTAUR SARS-COV-2 TOTAL (COV2T)
The ADVIA Centaur SARS-CoV-2 Total (COV2T) assay is for in vitro diagnostic use in the qualitative detection of total antibodies (including IgG and IgM) to SARS-CoV-2 in human serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur XP and ADVIA Centaur XPT systems.

This assay is intended as an aid in identifying patients with an adaptive immune response to SARSCoV-2, indicating recent or prior infection.

Test results should be interpreted in conjunction with clinical observations, patient history, epidemiological information, and other laboratory findings. A negative result does not exclude the possibility of exposure to or infection with SARS-CoV-2 and should not be used as the sole basis for patient management decisions. SARS-CoV-2 antibodies may be detectable after infection and a positive result may be indicative of acute or recent infection.

[IFU, 11206951_EN Rev. 01, 2020-05 Draft 2020-05-28 18:29:40]

ADVIA Centaur SARS-CoV-2 Total Quality Control (COV2T QC)
The ADVIA Centaur SARS-CoV-2 Total Quality Control (COV2T QC) is for in vitro diagnostic use in monitoring the precision and accuracy of the ADVIA Centaur COV2T assay using the ADVIA Centaur systems.

[*IFU 11206743_EN Rev. 01, 2020-05 Draft 2020-05-20 12:41:34*]

Discussion: The information provided meets the minimum requirements to authorize the Advia Centaur XP/XPT IM SARS-CoV-2 Total Assay under the Interim Order.

The Advia Centaur XP/XPT instrument has a Class IV medical device licence, thus this application builds off a platform in the highest risk class, and with experience of use in Canada. Pre-clinical studies included precision, hook effect, endogenous interference, and assessment of some of the requested potentially interfering substances outlined in the serological guidance. The remaining information will be requested as a post-authorization study, given the high demonstrated clinical sensitivity and specificity.

Clinical sensitivity was assessed using 262 specimens from 67 patients, and presented over time. The highest sensitivity for the test is observed 2 weeks post-PCR positive result, which is consistent with known available evidence on the development of antibodies post-infection. The clinical sensitivity of the SARS-CoV-2 Total Assay was found to be 100%.

Clinical specificity was assessed using 1589 negative samples from healthy individuals collected prior to the onset of COVID-19. Clinical specificity of the SARS-CoV-2 Total Assay was found to be 99.8%.

An independent study by Public Health England corroborated these findings, determining a sensitivity of 98.1% and a specificity of 99.9% in 536 positive and 994 negative samples, respectively, using the Atellica IM instrument. The information in the applications suggest that performance should be reasonably expected to be similar for the Advia Centaur XP/XPT instrument.

The labelling includes detailed information to communicate test performance. The minimum requirements outlined in both the Regulations and in the serological guidance have been met.

The assay is manufactured in the US.

Based on the scientific evidence available, it is reasonable that the test will be effective for the claimed intended use. In the current context related to COVID-19 pandemic, the risks related to the use of this assay are outweighed by the benefits associated with increased testing capacity that will be facilitated by the authorization for sale of this assay.

RECOMMENDATION:

Authorize the Advia Centaur XP/XPT SARS-CoV-2 Total Assay with the following conditions:

Within one month:

1) Submit a plan to Health Canada that will assess the performance of the test when used in the intended sites. This may be supported by identification of a minimum of two Canadian sites where the performance of the test will be monitored.

2) Given that some samples to assess cross reactivity are unavailable, provide a plan to assess cross-reactivity for the following substances or pathogens:

Mandatory cross-reactivity studies

- Human coronavirus 229E
- Human coronavirus NL63
- Human coronavirus HKU1
- Human coronavirus OC43
- Adenovirus
- Enterovirus (e.g. EV68)
- Human Metapneumovirus
- Parainfluenza virus 1 - 4
- Rhinovirus
- Respiratory syncytial virus

Optional organisms

- SARS
- MERS
- Norovirus
- *Haemophilus influenzae*
- *Legionella pneumophila*
- *Mycobacterium tuberculosis*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*
- *Bordetella pertussis*
- *Mycoplasma pneumoniae*
- *Chlamydia pneumonia*
- *Pneumocystis jiroveci (PJP)*
- *Candida albicans*
- *Pseudomonas aeruginosa*
- *Staphylococcus epidermis*
- *Staphylococcus salivarius*

3) Provide the results of an in-use stability study for the reagents when used on the Advia Centaur XP/XPT instrument.

When available:

4) To supplement the precision results already included in your application, provide the results of a full study evaluating the repeatability of the assay (20x2x2) or a full study evaluating reproducibility (3x5x5) per CLSI EP05-A3.

5) Provide updated labelling that reflects the validated storage conditions for specimens.

6) Provide the final shelf life and shipping stability reports.

[signed in docuBridge]		I concur / Je suis d'accord	
	2020-08-12		
Emily Hollink	Date	**Rosslyn Miller-Lee** Executive Director/ Directrice Executive Medical Devices Evaluation Bureau/ Bureau de l'évaluation des instruments médicaux	Date