Application Information *Information de soumission*			
Application *Soumission* 312756	**Licence Name** *Nom de l'homologation* DIAPLEXQ NOVEL CORONAVIRUS (2019-NCOV) DETECTION KIT	**Licence Number** *No. de l'homologation* N/A	**Risk Class** *Classe de l'instrument* 4
Application Type *Type de soumission* Interim Order	**Licence Type** *Type d'homologation* Test Kit	**Manufacturer** *Fabricant* LIFE SCIENCES RESEARCH INSTITUTE (LSRI)	**Company ID** *No. d'entreprise* 151657

Note to File Purpose *Objet de Note au dossier*		
Subject/*Objectif* **Review of additional information**		
Division: IVDD	Date Assigned: *Date assignée:* **March 27, 2020**	Date Completed: *Date d'achèvement:* **March 27, 2020**
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1 Background/*Antécédents*

This is the review of a response received on March 26, 2020 for additional information requested on March 26, 2020.

2 Evaluation/*Évaluation*

1. Provide the revised package insert with an updated intended use that reads as follows:

"DiaPlexQ™ Novel Coronavirus (2019-nCoV) Detection Kit is a real-time RT-PCR test intended for the presumptive qualitative detection of nucleic acid from the SARS-CoV-2 in respiratory specimens such as nasopharyngeal swab or oropharyngeal swab or sputum from individuals suspected of COVID-19 that meet the CDC SARS-CoV-2 clinical criteria.
Results are for the presumptive detection and identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of active infection with SARS-CoV-2 but do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause od disease.
Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information."

The test is intended for use by trained clinical laboratory professionals.

Response:
A package insert has been provided with the following intended use:

"DiaPlexQ™ Novel Coronavirus (2019-nCoV) Detection Kit is a real-time RT-PCR test intended for the presumptive qualitative detection of nucleic acid from the SARS-CoV-2 in respiratory specimens such as nasopharyngeal swab or oropharyngeal swab or sputum from individuals suspected of COVID-19 that meet the CDC SARS-CoV-2 clinical criteria.
Results are for the presumptive detection and identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of active infection with SARS-CoV-2 but do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease.
Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information."
The test is intended for use by trained clinical laboratory professionals.
a) The patients being tested meet the CDC SARS-CoV-2 clinical criteria.
b) Positive results are indicative of active infection.
c) Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.
d) The test is intended for use by trained clinical laboratory professionals.

Reviewer's Discussion
The intended use is not adequate. The package insert has no version number and date.. In addition, it does not include a summary of the inclusivity and clinical study and some sections are empty (e.g. Sections 5.8 (Expected values), 5.9 (Disposal), 5.10 (Cleaning and disinfection)). Once the manufacturer has correctly addressed all the identified issues, a revision to the IFU will be requested to:

a) delete sections 5.8, 5.9 and 5.10.
b) include under the Performance characteristics section a summary of the inclusivity study and the clinical study including the results.
c) Revise the Intended use to read:
"DiaPlexQ™ Novel Coronavirus (2019-nCoV) Detection Kit is a real-time RT-PCR test intended for the presumptive qualitative detection of nucleic acid from the SARS-CoV-2 in respiratory specimens such as nasopharyngeal swab or oropharyngeal swab or sputum from individuals suspected of COVID-19 that meet the CDC SARS-CoV-2 clinical criteria.

Results are for the presumptive detection and identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of active infection with SARS-CoV-2 but do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease.
Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information."
The test is intended for use by trained clinical laboratory professionals.
d) Include a version number and date in the package insert,

2. Which matrix did you use to dilute and test the SARS-CoV-2 transcript RNA samples used in the sensitivity (LOD) study and analytical specificity studies. Was it an artificial or clinical matrix, and what was the composition?

Response:

a. The matrix used for diluting and testing the SARS-CoV-2 transcript RNA samples is RNase free water including Human RNA 2 ng/uL (RNase free water). Whole process has been provided in the attached document (additional info March 23).

Reviewer's Discussion

The analytical sensitivity study should be performed in an artificial or clinical matrix to simulate the clinical sample matrix. This has not been demonstrated by the manufacturer. In addition, as they are claiming multiple clinical matrices (nasopharyngeal swab or oropharyngeal swab or sputum) results from one upper respiratory matrix and one lower respiratory matrix should be provided.
Another request should be made.

AI: The analytical sensitivity study should be performed in an artificial or clinical matrix to simulate the clinical sample matrix. RNase free water is not an acceptable matrix. In addition, as you are claiming multiple clinical matrices (nasopharyngeal swab or oropharyngeal swab or sputum) results from one upper respiratory matrix and one lower respiratory matrix should be provided. If this study has not been completed, please provide a timeframe for completion.

3. What was the percent identity matches against publicly available SARS-CoV-2 sequences that was detected by the DiaPlexQ™ Novel Coronavirus (2019-nCoV) Detection Kit?

Response:

100% and please find attached document (additional info March 26) for In silico analysis: GISAI list of 126 COVID-19.

Reviewer's Discussion

The manufacturer has confirmed that the *in silico* analysis has demonstrated 100% identity of

publicly available SARS-CoV-2 sequences with the DiaPlexQ™ Novel Coronavirus (2019-nCoV) Detection Kit.

3 Conclusion

Evidence of analytical sensitivity using artificial or clinical matrix to simulate the clinical sample matrix has not been provided. The request should be made again with more clarity and the manufacturer should be asked if the study has not been performed and if so a timeframe for completing it.

The package insert is not complete [has no version number and date, and it does not include a summary of the inclusivity and clinical study, some sections are empty and not applicable (e.g. Sections 5.8, 5.9, 5.10)] and the intended use should also be revised. A final revision to the package insert will be requested if the manufacturer addresses all pending issues.

As this is a new manufacturer for Health Canada, evidence of QS should be provided as per the Interim Order Guidance document.

AI: Provide a copy of the manufacturer's Quality Manufacturing System Certificate, or alternatively evidence of Good Manufacturing Practices.

4 Recommendation

Request the following information:

1. The analytical sensitivity study should be performed in an artificial or clinical matrix to simulate the clinical sample matrix. RNase free water is not an acceptable matrix. In addition, as you are claiming multiple clinical matrices (nasopharyngeal swab or oropharyngeal swab or sputum) results from one upper respiratory matrix and one lower respiratory matrix should be provided. If this study has not been completed, please provide a timeframe for completion.
2. Provide a copy of the manufacturer's Quality Manufacturing System Certificate, or alternatively evidence of Good Manufacturing Practices.