Application procedure for manufacturers seeking a recommendation of their serology tests/kits during the COVID-19 outbreak in Belgium.

Approval procedure

1. Minimal eligibility criteria for antibody tests can be found in **Annex 1** to this communication. Minimal eligibility criteria for antigen tests can be found in **Annex 2** to this communication.

2. The manufacturer submits its application for recommendation to serology@fagg-afmps.be. Use the following phrase in the subject line: recommendation – "name manufacturer" – "name device".

   Requests shall be accompanied by (when applicable):
   - A declaration of conformity with the IVD Directive (98/79/EC).
   - A list of (harmonized) standards that have been applied.
   - Relevant standard certificates (e.g. EN ISO 13485:2016).
   - Instructions for use.
   - Labels.
   - Information on the instrumentation that needs to be used with the test (e.g. open or closed platform test). For closed platform tests, provide a list of Belgian laboratories with compatible instruments.
   - Any relevant scientific validation data that pertain to the test.

3. For non CE-marked devices: file an application for performance evaluation as clarified on: https://www.fagg-afmps.be/sites/default/files/content/ivdapplication_formv1.pdf.

4. The FAMHP and Sciensano verify the request. Only complete requests will be processed.

5. When the request fulfils all eligibility criteria, the FAMHP and Sciensano choose which Belgian laboratory is suited to perform a validation study. This validation includes verification of the clinical performance (sensitivity/specificity) of the product. The laboratory will be selected according to the expertise and technical platforms required for optimal testing and taking into account available laboratory resources. The FAMPH informs the manufacturer on how many sample tests should be sent to what laboratory.

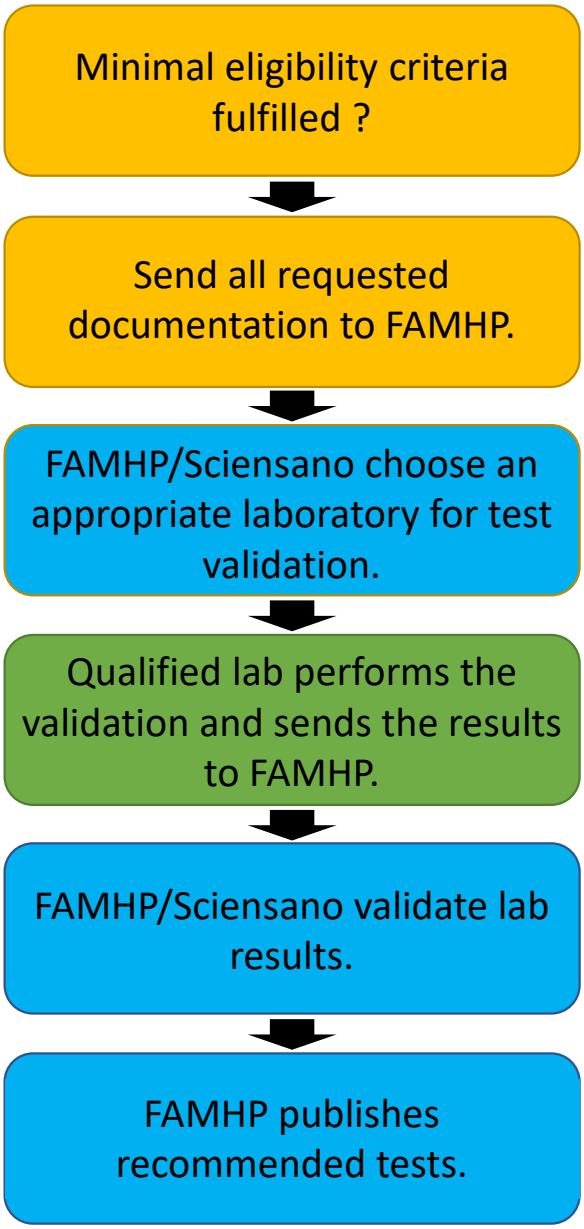
6. The results from the validation study will be sent by the laboratory to the FAMPH. After positive evaluation of the results by the FAMHP and Sciensano, the FAMHP will publish the test on a list of recommended serology tests for SARS-CoV-2.

Workflow

Steps performed by manufacturer

Step performed by validation lab

Steps performed by FAMHP/Sciensano



Annex I - Specifications for SARS-CoV-2 antibody tests for professional use

Intended Use	Determination of the immune status against SARS-CoV-2. Detection of SARS-CoV-2-specific IgG antibodies or a combination of IgG and IgM/IgA antibodies in plasma, serum, venous or capillary blood. Not suitable for diagnosing active infections.
Instructions for Use	In line with IVDD (98/79/EC) Annex 1 requirements. [1]
Labelling	In line with IVDD (98/79/EC) Annex 1 requirements.
Manufacturing	Conforms to EN ISO 13485:2016.
Target population	Specify the target population for the test: e.g. suspected or confirmed patients, general population.
Target user	Healthcare professional.
Method	Provide a short, clear description of the method principle.
Target protein	Indicate which viral protein is used to capture possible antibodies.
Specimen	Specify which specimen types can be used in the test.
Validation of specimens	When applicable; demonstrate equivalency between different specimen types.
Cross-reactivity	Assessment of cross reactivity with other pathogens likely present in the surrounding area including, where possible, other common pathogenic coronaviruses. The effect of the following infections should be evaluated: • Infections with the common human pathogenic coronaviruses like HCoV-HKU1, -NL63, -OC43, or -229E. • Infections with influenza viruses and other respiratory viruses. • Acute bacterial pneumonia. The effect of the following vaccinations could be evaluated: • Vaccination against influenza viruses.
Interference	Assessment of possible interference from substances/conditions. E.g. autoantibodies, triglycerides, bilirubin, common medicines and medicines used to alleviate or treat infections. Indicate at what concentration possible interfering substances have been measured.
Precision	Both repeatability and reproducibility should be assessed.
Cut-off value	When applicable, provide a rationale for the chosen cut-off value.
Clinical sensitivity	For samples taken between 5-15 days after onset of symptoms: ≥ 90 % (with 95 % confidence intervals). For samples taken later than 15 days after onset of symptoms: ≥ 97 % (with 95 % confidence intervals).

	Comparison with results from a validated molecular test using nasopharyngeal samples should be performed. The time delay between symptom onset or a positive nucleic acid test result and a positive serological test should be stated.
Clinical specificity	≥ 98,5 % (with 95% confidence intervals).
Controls	Rapid tests[2] shall include a procedural control detecting the capability of the assay. Other tests: when not included in the kit, specify which external controls have been validated and indicate within which predetermined limits control results should fall.
Instrumentation	When applicable; indicate what instrumentation and software is needed to read/run the test and provide at least one validated combination for tests that can be read/run on multiple platforms.

References

1. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31998L0079
2. Rapid tests are defined as qualitative or semi-quantitative tests, which involve non-automated procedures and have been designed to provide a fast result.

Annex II - Specifications for SARS-CoV-2 antigen tests for professional use

Intended Use	Determination of the presence of SARS-CoV-2 by detection of viral antigen(s).
Instructions for Use	In line with IVDD (98/79/EC) Annex 1 requirements. [1]
Labelling	In line with IVDD (98/79/EC) Annex 1 requirements.
Manufacturing	Conforms to EN ISO 13485:2016.
Target population	Specify the target population for the test: e.g. suspected patients, general population.
Target user	Healthcare professional.
Method	Provide a short, clear description of the method principle.
Target antigen	Indicate which viral antigen is captured.
Specimen	Specify which specimen types can be used in the test.
Validation of specimens	When applicable; demonstrate equivalency between different specimen types.
Cross-reactivity	Assessment of cross reactivity with other pathogens likely present in the surrounding area including, where possible, other common pathogenic coronaviruses. The effect of the following infections should be evaluated: • Infections with the common human pathogenic coronaviruses like HCoV-HKU1, -NL63, -OC43, or -229E. • Infections with influenza viruses and other respiratory viruses. • Acute bacterial pneumonia.
Interference	Assessment of possible interference from substances/conditions. E.g. autoantibodies, triglycerides, bilirubin, common medicines and medicines used to alleviate or treat infections. Indicate at what concentration possible interfering substances have been measured.
Precision	Both repeatability and reproducibility should be assessed.
Cut-off value	When applicable; provide a rationale for the chosen cut-off value.
Clinical sensitivity	Comparison with results from a validated molecular test using nasopharyngeal samples should be performed. Specify at what time (e.g. days after symptom onset or a positive PCR result) samples have been taken. Sensitivity and PPV values should be stated.
Clinical specificity	≥ 98 % (with 95 % confidence intervals).
Controls	Rapid tests[2] shall include a procedural control detecting the capability of the assay.

	Other tests: when not included in the kit, specify which external controls have been validated and indicate within which predetermined limits control results should fall.
Instrumentation	When applicable; indicate what instrumentation and software is needed to read/run the test and provide at least one validated combination for tests that can be read/run on multiple platforms.

References

1. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31998L0079
2. Rapid tests are defined as qualitative or semi-quantitative tests, which involve non-automated procedures and have been designed to provide a fast result.