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GUIDELINE FOR REGISTRATION OF COVID-19 IVD TEST KITS

Medical Device Authority
MINISTRY OF HEALTH MALAYSIA

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Preamble

This present guideline serves as guidance for transition towards the submission of registration application of COVID-19 IVD test kits via Medc@st for all previous application that has obtained Special Access Notification or Conditional Approval.

This guideline also covers all new COVID-19 IVD test kits which have not obtained Special Access Notification or Conditional Approval previously.

Irrespective of the requirements of this Guideline Document, MDA has the right to request for information or material, or define conditions not specifically described in this document that is deemed necessary for the purpose of regulatory control.

MDA reserves the right to amend any part of the guideline whenever it deems fit.

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Glossary

Condition of Use

In COVID-19 screening test, it refers to the type of person (Professional or lay user) who used the device and it also covered the environment in which the test was taking place.

- **Professional use**

A condition that describes the respective device can only be used by trained users or personnel that possess good knowledge about the test. It also referred to medical device that can be used under supervision of a qualified personnel. Normally, this type of use is referred to workers that are working in diagnostic, research and health care facilities. (Source: Health Science Authority-GN08: Guidance on Medical Device Advertisement and Sales Promotion)

- **Self-Testing**

A condition that describes the respective device is used by different people with different backgrounds of knowledge. Normally, this type of test is referred to a lay user with no or minimum knowledge about the test. This type of test also can be taken at home or anywhere, is easy to use and produces rapid results.

- **Lay person (Self-Test GD)**

Individual that does not have formal training in a specific field or discipline. (Source: ISO 18113-1)

Notes:

1) Lay person includes a patient (care recipient), caregiver (includes non-healthcare professionals), or family member that directly uses the device or provides assistance in using the device.

Test Principle

- **Rapid Test Kit (RTK)**

An in vitro diagnostic rapid test for the qualitative detection of SARS-CoV-2 antigen and antibody

- **Assay**

A laboratory test to find and measure the amount of specific SARS-CoV-2 antigen and antibody

- **Point of Care (POC) or Near POC for molecular assay**

It refers to molecular assay performed outside a laboratory environment by a healthcare professional not necessarily a laboratory professional, generally near to, or at the side of the patient. Molecular assay involved could be rapid molecular assays, Reverse Transcription-Polymerase Chain Reaction (RT-PCR), and other nucleic acid amplification tests. The aim of POC is to collect the specimen and obtain accurate results in a very short period of time at or near the location

of the patient. (Source: Centers for Disease Control and Prevention, CDC and Guidance document- MDA/GD/0001)

COVID-19 Detection Methods

Molecular Assay

- **Real Time-Polymerase Chain Reaction (RT-PCR)**
  A diagnostic technique to detect viral genetic material (viral RNA) in a biological sample after having amplified it to allow for its detection. (Source: World Health Organization, WHO)

- **Loop-mediated isothermal amplification (LAMP)**

  Is an isothermal nucleic acid amplification method exponentially amplify specific nucleic acid sequences at a constant temperature. LAMP can be completed in 30 minutes. (Source: World Health Organization, WHO)

Antigen Test

Immunodiagnostic test that detects the presence of viral proteins (antigens) expressed by the COVID-19 virus in a sample from a patient's respiratory tract.

There are two types of antigen test mechanisms:

1) Lateral flow assays (RTK Antigen)
   To detect active infection through directional flow of patient sample over target proteins, usually on a flat card or cassette.
2) Immunoassays (Antigen Assays)
   To detect active infection through incubation of patient sample with test proteins, usually in a 96-well plate or similar.

Antibody Test

Antibody assay test look for a variation of IgA, IgG, and IgM antibodies in venous blood samples in SARS-CoV-2 infected person, either as a separate or combined antibody measurement in laboratory settings using enzyme linked immunosorbent assays (ELISA) or chemiluminescence immunoassays (CLIA)

Antibody RTK is a rapid point-of-care lateral flow immunoassay test product intended for qualitative detection of IgM or IgG in SARS-CoV-2 infected person within 15 minutes that use a minimal amount of blood on a disposable testing strip or devices

IgA antibodies appeared early in SARS-CoV-2 infection (5 to 7 days post-onset, sometimes within 2 days of symptom onset). Secretory IgA plays an important role in protecting mucosal surfaces against pathogens by neutralizing respiratory viruses, including SARS-CoV-2 (Source: Centers for Disease Control and Prevention, CDC)

IgM antibodies body will begin to develop around 8 days post infection and can persist for weeks to months following infection, though its persistence appears

to be shorter than IgG's; therefore, detection of IgM could suggest relatively recent infection (Source: Centers for Disease Control and Prevention, CDC).

IgG antibodies develop around 14 days post infection and its levels appear to decrease more slowly over time than levels of other classes of antibody. Therefore, assays that measure total antibody or IgG could have higher sensitivity as the time between infection and antibody testing increases (Source: Centers for Disease Control and Prevention, CDC).

- **Neutralizing Antibody**

A type of protein produced by immune cells of the host after reaction with specific foreign antigen such as receptor binding domain (RBD), a composition of spike (S) protein from SARS-CoV-2 virus. This protein can be detected by using rapid test kit (RTK), a lateral flow test of a device pre-coated with Angiotensin converting enzyme 2 (ACE2) and other assay such as Enzyme-Linked Immunosorbent Assay (ELISA). Both of the test practically used whole blood or plasma as a sample of specimen.

1 Abbreviation and Acronyms

SA	Special Access
CA	Conditional Approval
MDA	Medical Device Authority
CSDT	Common Submission Dossier Template
EL	Evaluation Letter
ER	Evaluation Report
IFU	Instructions for Use
RFU	Recommended for Use
RTK	Rapid Test Kit
RT-PCR	Reverse transcription polymerase chain reaction
LAMP	Loop-mediated Isothermal Amplification
POC	Point of Care
GDPMD	Good Distribution Practice for Medical Devices
QR code	Quick Response code
QMS	Quality Management System
TAT	Turn around Time
MDR 2012	Medical Device Regulations 2012
ELISA	Enzyme-Linked Immunosorbent Assay

2 Registration Requirement and Process flow

2.1 The application for registration shall be made to the Authority through an online, web-based system called —Medical Device Centralized Online Application System (MeDC@St 2.0) as per MDA guideline MDA/GL/MD-01 and MDA/GL/IVD-1.

2.2. The establishment should identify their scenario and provide the appropriate documentation before submitting an online application. Scenario (a) and Scenario (b) are the two types of scenarios about which establishments should submit applications via MeDC@St 2.0. This guideline's requirements are only pertinent to COVID-19 test kits & assays. Conformity Assessment Bodies are not required to conduct conformity assessments for the above-mentioned test kits. MDA had appointed Local Assigned Evaluation Laboratories to verify the performance of these test kits.

2.2.1 **SCENARIO (A)** is applicable for the **COVID-19 test kit has been recommended for use under special access or conditional approval.**

Scenario (a)	**Requirements**
Through Special Access or Conditional Approval, MDA has granted a letter of recommendation for use. To register the COVID-19 test kits, the establishment must have an establishment license and all related technical documentation. Please refer to MDA portal for the approved list. The foregoing requirements apply to all test kits currently on the market, as detailed below. 1. POCT PCR for COVID-19 2. PCR test kits 3. RTK COVID-19 Ag tests (Professional use) 4. RTK COVID-19 Ag – Self test kits 5. Ab Assays for COVID-19 test kits 6. Other types of screening tests for COVID-19. (Novel type)	a. Establishment must be licensed with MDA. MDA establishment license with in-vitro diagnostic (IVD) scope on the Good Distribution Practice of Medical Device (GDPMD) certification b. Valid ISO 13485 certificate form the legal manufacturer. c. Provide full details on the test kits such as name of manufacturer, Brochures , IFU and performance reports and other related information's d. Full technical documents in accordance to Medical Device Regulation 2012 e. For Self-test COVID-19 RTK, the test kit shall comply with the requirements specified in MDA guidance document, COVID-19 RTK (Self-test) Requirement, MDA/GD/0059. f. Manufacturer Clinical Performance Report shall meet the minimum requirement in accordance to the prevalence of SARS-Cov-2

Table 1 Scenario (a) Requirements

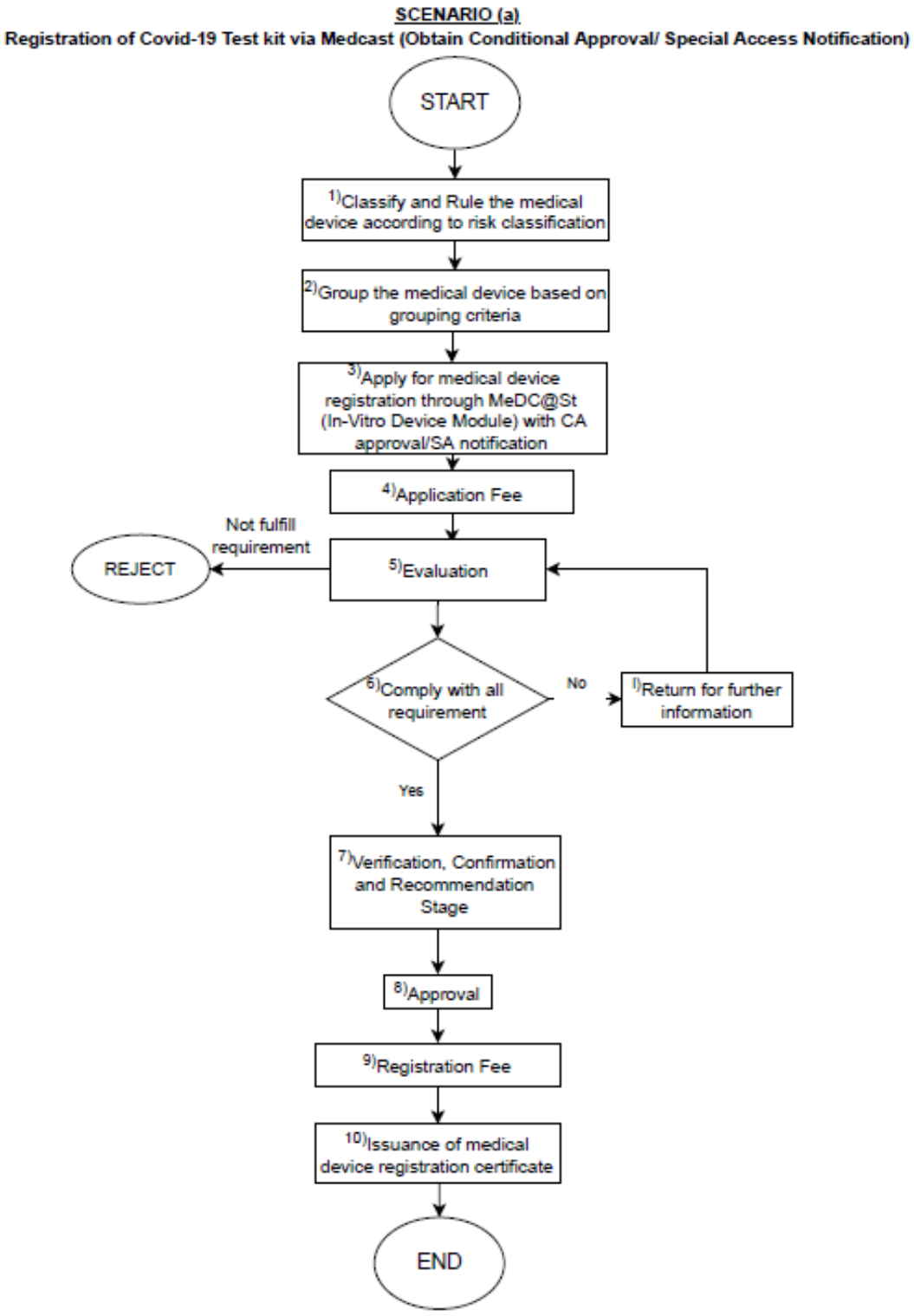

Figure 1 Registration of COVID-19 Test kit via Medcast (Obtained Conditional Approval/ Special Access Notification) Scenario (a)

Scenario (a): The table below provides explanation on Registration of COVID-19 Test kit via MeDC@St (Obtained Conditional Approval/ Special Access Notification).

Step	Explanatory Notes
1) Classify and Rule the medical device according to risk classification	The classification and Rule of medical device should be done according to the rules of medical device classification as specified in First Schedule of Medical Device Regulation 2012 and further elaborated in the Guidance Document on In-Vitro Diagnostic (IVD) Medical Device Classification System (MDA/GD/0001)
2) Group the medical device based on grouping criteria	The grouping of medical device should be done according to the rules of medical device grouping as specified in Second Schedule of Medical Device Regulation 2012 and further elaborated in the Guidance Document on product Grouping for Iv-Vitro Diagnostic (IVD) Medical Device (MDA/GD/0054)
3) Apply for medical device registration through MeDC@St System (In-Vitro Device Module)	Application for registration of medical device may be made after the requirements are met and the information and supporting documents (including Conditional Approval Letter/ Special Access Notification) to support the requirement are available. Application for medical device registration shall be made via MeDC@St. Applicant must create an account before making application via MeDC@St.
4) Application fee	According to Table of Fees under Fifth Schedule of Medical Device Regulation 2012
5)Evaluation	Dry Evaluation by MDA: i) Application that meets the requirements but incomplete documentations will be returned to the applicant for more information/documentation. **Notes: Refer to Table 3 Documents/Information required to be submitted**
6) Comply with all requirement	Comply with the requirements and the information and supporting documents to support the requirement are available.
7) Verification, confirmation and recommendation Stage	Verification, confirmation and recommendation by MDA.
8) Approval	Approval by MDA
9) Registration fee	According to Table of Fees under Fifth Schedule of Medical Device Regulation 2012
10) Issuance of medical device certificate	Issuance of medical device registration certificate.

2.2.2 **Scenario (b).** The COVID-19 test kits that are not listed in the MDA portal, those applications are considered as new applications.

Scenario (b)	**Requirements**
The COVID-19 test kit is deemed a new application because it is not listed on the MDA portal. Type of test kits for COVID-19 : 1. POCT PCR for COVID-19 2. PCR test kits 3. RTK COVID-19 Ag tests (Professional use) 4. RTK COVID-19 Ag – Self test kits 5. Ab Assays for COVID-19 test kits 6. Other types of screening tests for COVID-19. (Novel type)	a. Establishment must be licensed with MDA. MDA establishment license with in-vitro diagnostic (IVD) scope on the Good Distribution Practice of Medical Device (GDPMD) certification b. Valid ISO 13485 certificate form the legal manufacturer. c. Provide full details on the test kits such as name of manufacturer, Brochures, IFU and performance reports and other related information's d. Full technical documents in accordance to Medical Device Regulation 2012 e. For Self-test COVID-19 RTK, the test kit shall comply with the requirements specified in MDA guidance document, COVID-19 RTK (Self-test) Requirement, MDA/GD/0059. e. Manufacturer Clinical Performance Report shall meet the minimum requirement in accordance to the prevalence of SARS-Cov-2

Table 2 Scenario (b) Requirements

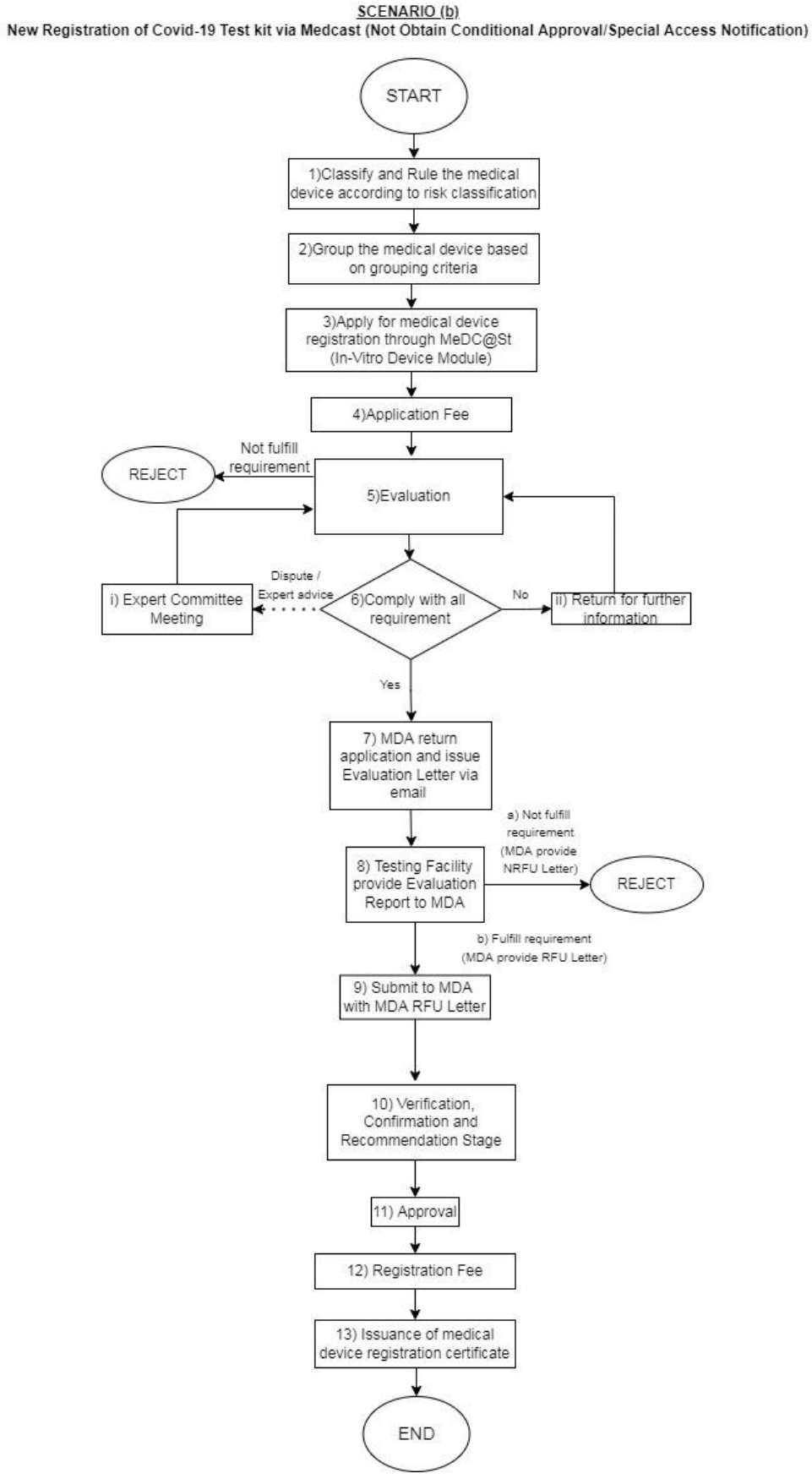

Figure 2 New Registration of COVID-19 Test kit via Medcast (Not Obtain Conditional Approval/Special Access Notification) Scenario (b)

Scenario (b): The table below describes how to register for COVID-19 test kits that do not have a Recommended Use Letter via Conditional Approval/Special Access Notification as a new application.

Step	Explanatory Notes
1) Classify and Rule the medical device according to risk classification	The classification and Rule of medical device should be done according to the rules of medical device classification as specified in First Schedule of Medical Device Regulation 2012 and further elaborated in the Guidance Document on In-Vitro Diagnostic (IVD) Medical Device Classification System (MDA/GD/0001)
2) Group the medical device based on grouping criteria	The grouping of medical device should be done according to the rules of medical device grouping as specified in Second Schedule of Medical Device Regulation 2012 and further elaborated in the Guidance Document on product Grouping for In-Vitro Diagnostic (IVD) Medical Device (MDA/GD/0054)
3) Apply for medical device registration through MeDC@St System (In-Vitro Device Module)	Application for registration of medical device may be made after the requirements are met and the information and supporting documents to support the requirement are available. Application for medical device registration shall be made via MeDC@St. Applicant must create an account before making application via MeDC@St.
4) Application fee	According to Table of Fees under Fifth Schedule of Medical Device Regulation 2012
5)Evaluation	Dry Evaluation by MDA: ii) Application that meets the requirements but incomplete documentations will be returned to the applicant for more information/documentation. **Notes: Refer to Table 3 Documents/Information required to be submitted**
6) Comply with all requirement	i) Any dispute or expert advice needed, the expert committee will be convened, if necessary. ii) The application will be return to the applicant if further information or any additional document needed. Comply with the requirements and the information and supporting documents to support the requirement are available.
7) MDA return application and issue Evaluation Letter via email	i) MDA will issue Evaluation Letter to applicant via Email for the application to undergo evaluation at testing facility assigned by MDA.
8) Testing Facility provide Evaluation Report to MDA	Testing Facility will send the Evaluation Report to MDA: a) If the evaluation report does not satisfy the requirements, it will be rejected, and an email with a Not Recommended of Use letter will be sent to the applicant via email

	b) MDA will send out an email to the applicant with a Recommended for Use Letter if the evaluation report results meet the requirements.
9) Submit to MDA with MDA RFU Letter/ NRFU letter	The applicant must submit the Recommendation for Use letter via MeDC@St to continue the registration procedure. In order to receive a rejection notice from MDA, applicants who receive a Not recommended for use letter by email must submit the letter via MeDC@St.
10) Verification, confirmation and recommendation Stage	Verification, confirmation and recommendation by MDA. (please refer to flow chart)
11) Approval	Approval by MDA (Please refer to Flow Chart)
12) Registration fee	According to Table of Fees under Fifth Schedule of Medical Device Regulation 2012
13) Issuance of medical device certificate	Issuance of medical device registration certificate. The registration certificate is valid for five years from the date of issuance.

2.3 The Risk Classification for COVID-19 IVD Test Kit is Class C Rule 3.

2.4 Table 3: specifies the documents required to be submitted for registration of COVID-19 test kits. The COVID-19 test kit registration Checklist for reference Table 3 lists the documentation that must be presented in order for COVID-19 test kits to be registered. For your reference, below is the COVID-19 test kit registration checklist.

Documents/Information required to be submitted	**Remarks (Yes/No)**
i. GDPMD scope for IVD (Attach copy of GDPMD certificate)	
ii. Letter of Authorization from Foreign Manufacturer with list of devices	
iii. Quality Management System Certificate, ISO13485	
iv. Common Submission Dossier Template (CSDT) in accordance with MDR 2012	
v. Essential Principles of Safety and Performance of Medical Devices (EPSP)	
vi. Description and Test Principle of COVID-19 Test Kit • Intended Use (to mention whether professional / self-test use)	

• Sample type • Instrument (if applicable)	
vii. List of Configuration (LoC) • Name of COVID-19 test kit • Identifier • Brand/Model	
viii. Pre-Clinical Studies **Analytical Performance** • Analytical Sensitivity • Analytical Specificity • Interference • Other Analytical tests	
ix. Clinical Evidence **Clinical Performance Report** • Clinical Sensitivity • Clinical Specificity **For self-test kit:** • Method Comparison- Performance Validation (Cross table) -The clinical performance of the Self-Test COVID-19 test kit by patient self-testing, and professional testing after supervised self-collection or professional collection. -Cross table for the method comparison of Self-Test COVID-19 test kit against RT-PCR • Layman usability *Provide raw data of Full Report ***Testing conducted for Clinical Evidence should have adequate sample size according to prevalence of the disease.** **Criteria molecular detection** • Rapid molecular – Point of care testing (Time, gene detection, sample extraction) 1 gene • RT-PCR – gene detection (at least two genes and channels)	
x. Medical device labelling, IFU & Product brochure **For Self-Test Kit:** IFU • IFU date and Version • BI & BM • Infographic Procedure	

Labelling Provide QR code on COVID-19 RTK (self-test) label to redirect to instructions for use (Audio-visual demonstration), disposal method and reporting mechanism together with medical device information such as name, brand, conditional approval letter reference number, batch /lot number /serial number. The QR code will also direct the purchaser to a form for capturing information on: i) purchaser information (name, and contact information); ii) date and time of purchase; and iii) the premise where the purchase is made. *Establishment should provide labelling in Bahasa Malaysia **Disposal Procedure** • Provide disposable bag with biohazard symbol and disinfectant for the disposable of the test kit (compulsory) *the disposable bag must fit for all materials provided • Instruction for disposal **Reporting COVID-19 Result Method** Methods of reporting to medical practitioners or healthcare facilities (if a positive result/ negative result/ invalid result is obtained)	
xi. Risk Analysis (according to ISO 14971)	
xii. Manufacturer Information (Manufacturing process; flowchart)	
xiii. Declaration of Conformity (in accordance to the template provided in MDR 2012)	

Table 3 Documents/Information required to be submitted

3 Evaluation Timeline

The following table specifies the evaluation duration (counted in working days upon receipt of complete application) for the application COVID-19 IVD test kits via Medc@st:

Scenario (a) Evaluation Timeline

MDA	60 working days
Testing Facility	-

Scenario (b) Evaluation Timeline

MDA	60 working days
Testing Facility	90 working days

4 Table of Fees

As per the Fifth Schedule of the Medical Device Regulations 2012, the descriptions of fees for Class C devices are as below:

Application Fee	RM 500
Registration Fee	RM 2000

MEDICAL DEVICE AUTHORITY

MINISTRY OF HEALTH, MALAYSIA

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