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MEDICAL DEVICE GUIDANCE DOCUMENT

PLACEMENT OF HIV SELF-TEST (HIVST) KIT IN MALAYSIA MARKET

Medical Device Authority (MDA) has published this guidance document without seeking public comment as per the usual practice. This is to enable the guidance document to be published in the shortest possible period. MDA will not seek public comment prior to implementing a guidance document if the Authority determines that prior public participation is not feasible or appropriate. However, this guidance document is open for comment and any relevant comment received will be brought to attention for the betterment of this guidance document.

Medical Device Authority
MINISTRY OF HEALTH MALAYSIA

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Preface

This Guidance Document was developed by the Medical Device Authority (MDA) to assist establishments seeking to import, export, or market Human Immunodeficiency Virus Self-Test kits (HIVST) in Malaysia in complying with the registration requirements outlined in Act 737.

This Guidance Document also provides guidance for healthcare professionals to understand and comply with the legal requirements for HIVST registration.

This Guidance Document shall be read in conjunction with the current laws and regulations used in Malaysia, which include but not limited to the following-

a) Medical Device Act 2012 (Act 737); and
b) Medical Device Regulations 2012; and
c) Medical Device (Duties and Obligations of Establishments) Regulations 2019; and
d) Circular letter No. 2/2023 Permission for Placement in the Market of Human Immunodeficiency Virus (HIV) Disease Self-Test Kits

In this Guidance Document, the following verbal forms are used:
— "shall" indicates a requirement;
— "should" indicates a recommendation;
— "may" indicates a permission; and
— "can" indicates a possibility or a capability.

Notwithstanding the provisions of this Guidance Document, the MDA reserves the right to request additional information or materials, or to impose conditions not explicitly outlined in this document, as deemed necessary for regulatory control.

The MDA has made significant efforts to ensure the accuracy and completeness of this guidance document. However, in the event of any conflict between the content of this document and written law, the provisions of the law shall prevail.

MDA reserves the right to amend any part of the guidance document from time to time.

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Abbreviation and Acronyms

CSDT	Common Submission Dossier Template
GDPMD	Good Distribution Practice for Medical Devices
HIVST	Human Immunodeficiency Virus (HIV) Self-Test
IFU	Instructions for Use
IVD	In-Vitro Diagnostic
MDA	Medical Device Authority
MDR 2012	Medical Device Regulations 2012
NGO	Non-Governmental Organisation
QMS	Quality Management System
QR CODE	Quick Response code
RFU	Recommended for Use

PLACEMENT OF HIV SELF-TEST (HIVST) KIT IN MALAYSIA MARKET

1 Introduction

Human immunodeficiency virus (HIV) is a retrovirus that targets immune system cells (mainly CD4-positive T-cells and macrophages), making an individual more susceptible to various illnesses and infections. It is transmitted through sharing injection equipment or through direct contact with the bodily fluids of an infected individual. It most frequently happens during unprotected sex (sex without using a condom or HIV medication to prevent or treat HIV).

With 40.1 million cases reported to date, HIV continues to be a severe problem to worldwide public health. Additionally, 650,000 individuals passed away in 2021 from HIV-related causes, and 1.5 million people contracted the virus. This data has warned us, especially the diagnostic health sector, to find the best solution to solve the current issue.

The World Health Organization (WHO) has introduced HIV self-testing as an approach to reach people who may not test otherwise, including people from key populations, men and young people. HIV self-testing could be done by introducing HIV self-test (HIVST) kits in the in-vitro diagnostic market. This emerging technology could be used as an effective method for controlling HIV risk transmission, which could later help initiate the Pre-exposure prophylaxis (PrEP) programme for the high-risk infected person.

Detection method for HIVST

i. Type of test

a. Antibody Test

Antibody tests are done to detect HIV antibodies in a person's blood or oral fluids. Antibody tests can take 23 to 90 days to detect HIV after exposure. The most rapid test and the only FDA-approved HIVST is the antibody test (HIV-1 antibody, HIV-2 antibody). Antibody tests using venous blood can generally detect HIV sooner after infection than tests using fingertip blood or oral fluids.

b. Antigen/Antibody Test

The antigen/antibody test is done to detect for both HIV antibodies (HIV-1 antibody, HIV- 2 antibody) and antigens (p24 antigen). Antibodies are produced by a person's immune system upon exposure to viruses such as HIV. Antigens are foreign substances that activate a person's immune system. When a person is infected with HIV, an antigen called p24 is produced before antibodies are produced. Antigen/antibody testing is recommended for laboratory testing and is common in the United States. Laboratory antigen/antibody tests on intravenous blood can usually detect HIV 18 to 45 days after exposure. There is also a rapid antigen/antibody test that can be done at your fingertips.

Antigen/antibody tests performed on fingertip blood can take 18 to 90 days after exposure.

ii. Type of Sample

Whole blood or Oral fluids

HIVST specifically refers to a process in which a person collects his or her own specimen (oral fluid or blood) and then performs a test and interprets the result, often in a private setting, either alone or with someone he or she trusts.

2 Scope and application

This document is a written explanation to guide the establishment who deal with HIVST to comply to the requirements for pre-market, placement in the market and post-market including requirements on registration of HIVST, licensing of establishments dealing with HIVST, product labelling, sales, distribution and advertising and post-market surveillance and vigilance activities.

3 Terms and definitions

For the purposes of this document, the terms and definitions in Act 737, the regulations under it and the following terms and definitions apply.

3.1 Human Immunodeficiency Virus (HIV)

HIV (Human Immunodeficiency Virus) is a virus that attacks the body's immune system, specifically the CD4 cells (T cells), vital cells for fighting off infections, which if left untreated, HIV can lead to the disease AIDS (Acquired Immunodeficiency Syndrome).

3.2 conformity assessment

Technical term given to the process of evaluation and evidence generated and procedures undertaken by the manufacturer, under the requirements established by the Authority, to determine that a medical device is safe and performs as intended by the manufacturer and, therefore, conforms to essential principles of safety and performance for medical devices.

3.3 Conformity Assessment Body (CAB)

The conformity assessment body registered under Section 12 of Act 737.

3.4 Recognised regulatory authorities or notified bodies

Government agencies or notified bodies recognised by MDA that exercises a legal right to control the use or sale of medical devices within its jurisdiction, and can take legal action to ensure that medical devices marketed within its jurisdiction comply with legal requirements.

Note: refer Circular Letter No. 2/2014: Conformity Assessment Procedures for Medical Device Approved by Recognized Countries.

4 Regulatory requirements for establishment dealing with HIVST

HIVST is classified as an IVD medical device and is regulated under Act 737. Therefore, it must be registered before being imported, exported, or made available on the market, as stipulated in Section 5 of Act 737.

An establishment dealing with HIVST is subjected to the licensing requirements stipulated in Act 737, Section 15 and its regulations as follows;

i. A manufacturer of HIVST shall implement and be certified under ISO 13485 with IVD scope,
ii. An AR, importer and/or distributor of HIVST shall implement and be certified under GDPMD with IVD scope,
iii. Both manufacturer and AR shall obtain an establishment license with appropriate roles depending on the business activities that they carry out.

Detailed information on requirements and process flow of applying an establishment license can be found and referred in Guidance Documents on Licensing for Establishment MDA/GD/0027.

5 Performance evaluation

The performance evaluation of HIVST performed by the manufacturer should align with *ISO 20916: IVD Medical Devices-Clinical performance studies using specimens from human subjects - Good study practice* or any other relevant international standards to ensure that clinical performance studies are designed, conducted, and reported appropriately.

The performance evaluation of the HIVST kit shall meet the performance criteria as detailed out below:

Type of test to detect antibodies and antigens/antibodies (Based on specimen type)	Sensitivity	Specificity
i. Using blood samples	shall not be less than 99.0%	shall not be less than 99.0%
ii. Using saliva samples	shall not less than 92.0%	shall not be less than 99.0%

Note:
1. The sensitivity of the HIVST kit means the ability of the test kit to detect HIV 1 and 2 antibodies in a sample of a person infected with HIV.
2. The specificity of the HIVST kit means the ability of the test kit to detect the blood of a person who is free of HIV infection.

6 Conformity Assessment Procedure

Part II of the Third Schedule of Medical Device Regulation 2012 addressed the requirements as follows;

I. For locally made HIVST, the manufacturer shall collect and compile all evidence of conformity of HIVST to demonstrate the compliance to EPSP including performance evaluation,
II. For imported HIVST, the AR shall provide all evidence of conformity of HIVST from the manufacturer to demonstrate the compliance to EPSP.

Note: Evidence of conformity shall include conformity to requirements on QMS, PMS, technical documentation and DoC and shall be compiled based on CSDT elements.

An establishment shall appoint a Conformity Assessment Body (CAB) with expertise in the Medical Device Technical Areas, specifically IVD 0201 and IVD 0403 codes, to perform conformity assessment of the HIVST as follows;

i. Full conformity assessment for any HIVST that has not received premarket approval from any reference country (Refer to MDA Guidance Document MDA/GD/0003).
ii. Conformity assessment by way of verification for HIVST that has obtained premarket approval from any recognised regulatory authorities or notified bodies, as stated in the MDA Circular Letter No. 2/2014.

7 Registration requirements and process flow of HIVST

Manufacturer or AR is responsible to perform the following actions before making an application for registration of the HIVST:

a) Classify the HIVST based on the rules of medical device classification as specified in First Schedule of Medical Device Regulation 2012 (which further elaborated in the Guidance Document on In-Vitro Diagnostic (IVD) Medical Device Classification System (MDA/GD/0001));
b) Group the HIVST according to the rules of medical device grouping as specified in Second Schedule of Medical Device Regulation 2012 (which further elaborated in the Guidance Document on product Grouping for In-Vitro Diagnostic (IVD) Medical Device (MDA/GD/0054)); and
c) Prepare a summary of technical documents of HIVST in the CSDT templates. The CSDT shall contain compilation of evidence of conformity of HIVST collected during conformity assessment which addressed four elements of conformity assessment as follows:

    i. Quality Management System (QMS)
    ii. Post-market Surveillance System (PMS)
    iii. Technical Documentation
    iv. Declaration of Conformity (DOC)

Note: The AR of HIVST shall perform the above actions based on information provided by the manufacturer of HIVST.

Application for registration of HIVST shall be submitted to the Authority via the online system known as the Medical Device Centralized Online Application System (MeDC@St). For detailed information, reference to the guideline MDA/GL/No.2: How to Apply for In-Vitro Diagnostic (IVD) Medical Device Registration under Act 737 can be made.

The application shall be submitted together with all evidence of conformity including the report and certificate of conformity issued by the CAB via the online system.

Upon receiving a complete application and payment of the application fee, the Authority will process and review the application and decide whether to approve or reject it. If the application is approved and the registration fee is fully paid, the application status will be marked as complete. The Authority will then issue a registration e-certificate of HIVST, which can be downloaded via the system.

The application will be rejected under the following circumstances:

i. The HIVST is wrongly classified.
ii. Failure to provide additional information of the HIVST requested by the Authority within 90 days or any granted extension period.
iii. Submission of the application without the requested information, particulars, or documents.
iv. Non-compliance with registration requirements as evidenced by the provided documentation.

However, this will not affect the applicant's right to submit a new application and the application fee is not refundable.

7.1 Documents to be submitted for HIVST registration

The checklist of documents to be submitted for the purpose of HIVST registration is as per Table 1 below.

Table 1: Checklist documents for HIVST registration

No	Matters	Remarks (Yes/No)
1	Quality Management System Certificate, ISO13485 of legal manufacturer	
2	GDPMD scope for IVD (Attach copy of GDPMD certificate) – applicable for imported HIVST	
3	Letter of Authorization from Foreign Manufacturer with list of devices - applicable for imported HIVST	
4	Common Submission Dossier Template (CSDT) in accordance with MDR 2012, which contain the following elements:	
	i. Executive summary	
	ii. Essential Principles of Safety and Performance of Medical Devices (EPSP)	
	iii. Description and Test Principle of HIVST Kit ● Intended Use (to mention whether professional/self-test use) ● Sample type ● Instrument (if applicable)	
	iv. List of Configuration (LoC) ● Name of HIVST Kit ● Identifier ● Brand/Model	
	v. Pre-Clinical Studies (Analytical Performance): ● Analytical Sensitivity ● Analytical Specificity ● Interference ● Other Analytical tests	
	vi. Clinical Evidence ● Clinical Performance Report ● Layman usability report ● Comparison between self-test VS Professional test report	
	vii. Medical device labelling, IFU & Product brochure	
	viii. Risk Analysis (according to ISO 14971)	
	ix. Manufacturer Information (Manufacturing process; flowchart)	

5	Certificate and Reports of conformity assessment from CAB	
6	Declaration of Conformity (in accordance to the template provided in MDR 2012)	

7.3 Evaluation Time

The evaluation period for registering an HIVST kit is 30 working days from the date of submission of an application with complete documentation.

7.4 Table of Fees

Based on the classification rules specified in First Schedule of Medical Device Regulation 2012 for IVD medical devices, HIVST is classified as class D IVD medical device. Therefore, the application and registration fees of HIVST are as per Table 4.

Table 4: Description of fees

Type of Fee	Fee
Application Fee	RM 750
Registration Fee	RM 3,000

Note: The fees are prescribed in the Fifth Schedule of the Medical Device Regulations 2012.

8 Requirements on HIVST labelling

The labelling of HIVST shall comply with the labelling requirements specified in the Sixth Schedule of the Medical Device Regulation 2012 (further elaborated in the Guidance Document on Requirements for Labelling of Medical Devices, MDA/GD/0026).

8.1 Specific requirements for Instruction for Use (IFU)

IFU for HIVST shall comply with the labelling requirements specified in the 6th Schedule of Medical Device Regulations 2012 and contain the followings;

- IFU date and version
- Statement of “self-test use” in the IFU and product packaging
- English and translation in Bahasa Malaysia
- Infographic and link of video tutorial to explain on how to conduct self-test
- The link of the QR code (refer Fig. 1) of TEST NOW platform and the statement to visit the platform
- The disposal method of HIVST
- Contact details for the user to make a complaint if there are issues related to the use of the HIVST

Note: The TEST NOW platform is an online one-stop centre that provides HIV-related information including HIVST Kits as well as prevention, treatment and referral services. TEST NOW was developed in collaboration between Malaysia AIDS Foundation (MAF) and MOH.

8.2 Additional requirements on labelling

i. QR Codes

The establishment shall include QR codes on the HIVST label linking to;

- an audio-visual guide on the testing procedure and disposal method, and
- **TEST NOW Platform** to report HIV result and provide further assistance

Figure 1: QR Code to TEST NOW Platform

The statement of visit to the TEST NOW platform is needed to be stated in the IFU as to guide and introduce the user with the TEST NOW platform.

9 Additional requirements

9.1 Finger prick needle for HIVST using blood specimen

For blood sample collection, a sterile, single-use safety lancet suitable for lay users shall be provided with the HIVST. The lancet shall either be registered along with the HIVST as part of the same registration or registered separately.

9.2 Disposal of used HIVST

A disposable bag shall be included with the HIVST kit, ensuring it can accommodate all items used in the HIV self-testing. The IFU shall include guidance on the use of the disposable bag and the proper disposal of the HIVST kit.

10 HIVST Sales and Distribution Requirements

a) The following HIVST distribution activities are allowed:

i. Establishments (authorized representatives or manufacturers) to other establishments (appointed distributors);
ii. Establishment to public and private healthcare facilities; and
iii. Establishment to NGOs that collaborate with MOH, specifically for NGOs and its partner organizations that collaborate with the MOH.

b) HIVST can only be sold or supplied to the public by:

i. Community pharmacy licensed with the Pharmacy Services Program, MOH;
ii. Public and private healthcare facilities; and
iii. NGOs and its partner organizations that collaborate with the MOH

Note: HIVST kits may only be sold online by entities classified under b(i) and (iii). Deliveries shall be handled by appropriate logistics providers to ensure the safety and performance of the products.

c) The sale of HIVST by individuals either physically or online is strictly prohibited.

11 Advertisement Requirements

The HIVST advertisement shall be in accordance with requirements in Section 44 of Act 737, Medical Device (Advertising) Regulation 2019 and the codes of advertisement detailed out in Guidance Document MDA/GD/0032: Codes of Advertisement. An establishment may refer to Guideline MDA/GL/04: Application for Medical Device Advertisement Approval - Requirement for further information on application process of and criteria for advertisement approval.

12 Post-market Surveillance

An establishment shall comply with post-market obligations outlined in Chapter 3 of the Medical Devices Act 2012 (Act 737) and the Medical Devices (Duties and Obligations of Establishments) Regulations 2019. Each establishment is required to establish, implement and maintain a post-market surveillance system to monitor the safety and performance of HIVST and ensure the traceability of these devices throughout the supply chain in case any safety or performance issues arise.

An establishment shall refer to the guidance documents below to set up, implement and maintain the post market surveillance system and carry out the obligations and duties that have been specified in the legal documents mentioned above;

a) MDA /GD/0011, Complaint Handling;
b) MDA /GD/0012, Distribution Record;
c) MDA /GD/0013, Field Corrective Action;
d) MDA /GD/0014, Mandatory Problem Reporting; and
e) MDA /GD/0015, Medical Device Recall.

If an incident related to the HIVST comes to the establishment’s attention (whether due to failure or deterioration in the device's effectiveness resulting in false results, inadequacy in its labeling or instructions for use, or a serious threat to patients or the public), the establishment shall

1) report the incident to the Authority via the online reporting system, MeDCReST (www.medcrest.mda.gov.my),
2) carry out an investigation to identify and determine the root cause,
3) take appropriate actions to prevent the recurrence of incident (either carry out corrective or preventive actions, Field Corrective Actions (FCA) or recall)
4) Notify the actions to be taken and the status of the actions to the Authority

Note: Certain actions, such as issuing a Field Safety Notice or conducting a recall, must be communicated effectively to prevent the recurrence of incidents. When appropriate, a public announcement may be made through suitable channels to inform the public and relevant stakeholders.

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