HEALTH SCIENCES AUTHORITY

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PRODUCT REGISTRATION SUBMISSION GUIDE

E-Submission Guide for In Vitro Diagnostic Medical Devices for ASEAN CSDT and IMDRF ToC based Submissions in MEDICS

HSA Health Sciences Authority

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1. INTRODUCTION

1.1 Purpose

This document is intended to provide guidance on submission of a product registration dossier to HSA via the Medical Device Information and Communication System (MEDICS). This guide specifies the appropriate modules in MEDICS for uploading of the corresponding sections of the CSDT or IMDRF ToC dossier.

1.2 Background

Product registration applications for medical devices are submitted online to HSA and may be compiled and prepared from the ASEAN Common Submission Dossier Template (CSDT) or the International Medical Device Regulators Forum (IMDRF) In Vitro Diagnostic Device Market Authorization Table of Contents (IVD MA ToC).

Applications must be submitted online to HSA via MEDICS. The technical dossier and supporting documents shall be submitted in softcopy in MEDICS.

1.3 Scope

This document applies to in vitro diagnostic medical devices only.

2. SUBMISSION GUIDELINES

2.1 MEDICS application form

The technical dossier and supporting documents are to be submitted under the ‘Dossier & Supporting Document(s)’ section of the MEDICS application form. This section of the application form comprises several modules for uploading the documents.

To facilitate review of the pre-market application, applicants shall ensure that the relevant section of the dossier and supporting documents are uploaded correctly under each module. Document file names should also be meaningful and provide some indication of their content.

The “MEDICS application form” column in TABLE 1 lists the various modules in the ‘Dossier & Supporting Document(s)’ section of the MEDICS application form and includes a brief description of the expected contents to be uploaded under each of the modules.

2.1.1 Submissions based on CSDT

Please refer to “CSDT TR-02” column of TABLE 1 to determine which sections of the CSDT are to be uploaded under each module in MEDICS.

2.1.2 Submissions based on IMDFR nIVD ToC

Please refer to “IMDRF IVD ToC” column of TABLE 1 to determine which sections of the ToC are to be uploaded under each module in MEDICS.

2.2 Submitting responses to Input request queries via MEDICS

To facilitate identification and review of information uploaded onto MEDICS, a written response to each input request query shall be provided. If additional documents are submitted to support your response, please indicate the relevant file name(s) in your response. Responses to an input request may be included under ‘Applicant’s Response’ section in MEDICS, or consolidated into a separate document for submission to HSA.

2.3 Reference documents

Product Registration Submission	Document	Location
Based on the ASEAN CSDT	GN-18: Guidance on Preparation of a Product Registration Submission for In Vitro Diagnostic Medical Devices using the ASEAN CSDT TR-02: Contents of a Product Registration Submission for In Vitro Diagnostic Medical Devices using the ASEAN CSDT	www.hsa.gov.sg
Based on the IVD MA ToC	IMDRF In Vitro Diagnostic Medical Device Market Authorization Table of Contents (IVD MA ToC)	www.imdrf.org

3. TABLE 1 – SUMMARY OF SUBMISSION REQUIREMENTS

Legend:

F	Full evaluation route
A	Abridged evaluation route
E	Expedited evaluation route
I	Immediate registration route

	MEDICS Application Form - Dossier & Supporting Document(s)	Reference technical documents		Class B			Class C & D			
		IMDRF IVD ToC	CSDT TR-02	F	A	I	F	A	E	I
1	**Letter of authorization**									
	▪ Letter of Authorisation of Registrant by the Product Owner for all the products to be registered, using the latest template as per GN-15 Annex 1 Letter of Authorisation template	CH1.13 Letter of Authorization	NA	✓	✓	✓	✓	✓	✓	✓
2	**Annex 2 List of Configurations**									
	▪ A copy of Annex 2 for GN17 and GN18 List of Configurations, including the complete list of configurations of medical devices subject to the submission. This is to be submitted in a Microsoft Excel file.	CH1.05 Listing of Device(s)	4.2 Device Description	✓	✓	✓	✓	✓	✓	✓
3	**Proof of reference agency's approval(s)**									
	▪ Copies of approval letter(s) from each reference agency. For CE marked devices, the EU declaration of conformity by the product owner must be submitted, in addition to the EC certificate issued by the notified bodies.	CH1.07 Free Sale Certificate/ Certificate of Marketing authorization	3. Executive Summary		✓	✓		✓	✓	✓
4	**Proof of marketing history in the reference agencies jurisdictions e.g. Invoice with date, proof of sale or a declaration on marketing history**									
	▪ Invoice with date, proof of sale or a declaration on Marketing history as per Annex 2 of GN-15, to be completed by the local Applicant	NA	NA			✓ Only required for Condition 1			✓ Only required for ECR1	✓
5	**Declaration of no safety issues globally**									
	▪ Safety declaration template as per Annex 3 of GN-15, to be completed by the local Applicant	NA	NA			✓			✓ Only required for ECR1	✓
6	**Executive Summary**									
	▪ Introductory descriptive information on the medical device, the intended use and indications for use of the device.		3. Executive Summary	✓	✓	✓	✓	✓	✓	✓

	▪ Information on the use of the device, if any, such as targeted patient population, user profile (e.g. specific trained users), specific disease status or clinical condition (e.g. monitoring of a disease), assay principle (e.g. immunoassay) etc.	CH2.2 General Summary of Submission CH2.6 Global Market History								
	▪ If the medical device has any unique or novel feature or characteristic (e.g. nanotechnology), a description must be provided.									
	▪ Any high-level background information or details that the product owner wishes to highlight in relation to the device, its history or relation to other approved devices (e.g. predicate devices) or previous submissions (provides context to submission).									
	▪ List of countries from HSA's reference regulatory agency jurisdictions where the medical device is marketed.									
	▪ Date (accurate to MMYYYY) and country where the device was first introduced for commercial distribution, globally.									
	▪ Registration status (i.e. submitted, not submitted, pending approval, rejected or withdrawn) and approved intended use and indications of the medical device in HSA's recognised reference agencies, in a tabular format as per TR-02. If device is withdrawn/ rejected by any reference agencies, reason for rejection or withdrawal is to be provided.									
	▪ Declaration from product owner that labelling, packaging and IFU of the device for sale in Singapore are identical or not identical to that approved by reference agency being used as the basis for evaluation route. If not identical, please provide a description of the differences.									
	▪ If the subject device is different in any way (e.g. design, commercial name, specifications, intended use and indications for use) from those approved by the reference agencies, the differences should be described.									
	▪ To include a summary of reportable adverse events (AEs) and field safety corrective actions (FSCAs) for the medical device since its first introduction on the global market, in a tabular format as per TR-02.									
	▪ For FSCAs that are 'open', provide a description of any analysis and/or corrective and preventive actions undertaken by the product owner.									
	▪ If there have been no adverse events or FSCAs to date, provide an attestation from product owner on company letterhead, that there have been no adverse events or FSCAs since commercial introduction of the device globally.									

7	**Essential Principles Checklist and Declaration of conformity**									
	▪ Essential Principles conformity checklist (EP checklist). The checklist of conformity to the Singapore Essential Principles is to be submitted. Alternatively, the checklist to EU or Australian Essential Requirements can be submitted.	CH1.11.6 Declaration of Conformity CH3.3 Essential Principles (EP) Checklist CH3.4 Standards	4.1. Relevant Essential Principles and Method Used to Demonstrate Conformity ***NOTE:*** *Refer to GN-16 Guidance on Essential Principles for Safety and Performance of Medical Devices for more details*.	✓	✓		✓	✓	✓	
	▪ GN-11 Declaration of Conformity (DOC). Alternatively, the EC or AU DOC can be submitted.									
	▪ List the standards that have been complied with in the design and manufacture (including sterilization) of the device, if this has not been provided in the EP checklist or DOC.									
8	**Device description**									
	▪ A comprehensive description of the device including technology, functionalities and features. To include labelled pictorial representation (diagrams, photos, drawings) if applicable.	CH2.4 Device Description CH2.5 Indications for Use and/or Intended Use	4.2 Device Description	✓	✓	✓	✓	✓	✓	✓
	▪ Risk class and applicable classification rule for the medical device according to the Regulations.									
	▪ Product specifications including the version number of the software if applicable.									
	▪ List of medical device accessories intended to be used in combination with the devices. Accessories that can be sold separately should be identified and listed in the Annex 2 list of configurations if intended to be supplied in Singapore.									
	▪ Where safety and effectiveness data of similar or previous generation devices are used in the current submission, the following information is to be provided: o A list of such devices and specific information on the registration status of these devices with HSA are to be included (e.g. Device registration number). o A comparison, preferably in a table, of the design, specifications and intended use/indications for use between the subject device in the current submission and the comparator devices (similar and/or previous generation). To include labelled pictorial representation (diagrams, photos, drawings) where necessary.									

	▪ An indication of biological material or derivate used in the medical device, its origin and source/donor.									
	▪ Process validation results to substantiate that manufacturing procedures are in place to minimise biological risks, in particular, with regard to viruses and other transmissible agents. This also includes inactivation of infectious organisms in reagents and the production of reagents.									
9	**Design verification and validation documents including** ▪ **Preclinical studies e.g. physical test data, biocompatibility studies, animal studies and software verification and validation studies** ▪ **Metrological requirements** ▪ **Sterilisation validation (if applicable)** ▪ **Shelf-life studies and projected useful life**									
	▪ Evidence supporting the analytical performance (e.g. analytical sensitivity, analytical specificity and interference, precision, linearity/assay's measuring range/hook effect, traceability and expected values, cut-off value, trueness, specimen stability, performance characteristics for instrument) of the subject device.	CH3.5 Non-clinical Studies CH3.6 Other Studies CH3.7 Analytical Performance and Other Evidence Bibliography CH3.8 Other Evidence	4.3 Summary of Design Verification and Validation Documents	✓ Detailed reports	✓ Summary	✓ Sterilisation validation for Sterile devices only Software verification and validation studies for standalone medical mobile applications only	✓ Detailed reports	✓ Summary	✓ Summary	✓ Software verification and validation studies for standalone medical mobile applications only
	▪ Specify the claimed shelf life of the device components (e.g. reagents, calibrators/reference materials, control material, any other components susceptible to degradation).									
	▪ Evidence supporting the claimed shelf-life of device components. If applicable, both real time and accelerated stability studies are to be submitted. If real time aging has not been performed, adequate justification must be provided.									
	▪ Evidence supporting the stability during actual routine use of the device (real or simulated), including all applicable components (e.g. reagents, reaction cartridges).									
	▪ Information regarding and studies to support the stability of all of the sample type(s) identified in the labelling, including any and all recommended additives (e.g. anticoagulants).									
	▪ For IVD medical device that does not have expiry dates, the projected useful life of the device.									
	▪ Specify the version of the software to be supplied.									
	▪ An overview of all verification, validation and testing performed for the software both in-house and in a simulated or actual user environment prior to final release. Where the software has been validated together with the IVD instruments (e.g. IVD analysers), reports of such validation addressing the safety and performance considerations for the software is to be provided.									

	NOTE: *The version tested must be clearly identified and should match the release version of the software, otherwise to provide justification.*									
	▪ All unresolved anomalies in the release version of the software should be summarized, along with a justification for acceptability (i.e. the problem, impact on safety and effectiveness, and any plans for correction of the problems).									
	▪ Evidence supporting electrical safety and electromagnetic compatibility. For example, if a device is claimed to meet the requirements of IEC 60601-1 and IEC 60601-1-2, summary test reports and/or certificates are to be submitted for verification of conformance to these standards.									
	▪ Evidence to support the cybersecurity of connected medical devices such as wireless enabled, internet-connected and network-connected devices. For example, but not limited to: o Cybersecurity vulnerabilities and risks analysis o Cybersecurity control measures o On-going plans, processes or mechanisms for surveillance, timely detection and management of the cybersecurity related threats during the useful life of the device, especially when a breach has been detected.									
	▪ For non-IVD medical device accessories to be registered with the IVD medical device e.g. a lancet that is provided in the package to the user to perform a test, information on preclinical studies such as biocompatibility and sterilisation validation necessary to establish the safety and performance of these medical devices shall be provided.									
10	**Proposed Device Labelling**									
	▪ Primary and secondary labels in their original colour for the device and its accessories as applicable.	CH5.2 Product/Package Labels CH5.3 Package Insert/ Instructions for Use CH5.4 e-labelling CH5.5 Patient Labelling CH5.6 Technical/Operator Manual	4.4 Device Labelling ***NOTE:*** *Refer to GN-23 Guidance on Labeling for Medical Devices for more details.*	✓	✓	✓	✓	✓	✓	✓
	▪ If representative labels are provided, variable fields on the artwork must be highlighted, and ranges of values for the variable fields should be indicated.									
	▪ Copy of the IFU to be supplied in Singapore for the device and its accessories as applicable.									
	▪ Indicate format of the IFU to be supplied with every medical device e.g. paper or electronic.									

11	**Clinical evidence**									
	▪ A clinical evaluation report reviewed and signed by an expert in the relevant field that contains an objective critical evaluation of all of the clinical data submitted in relation to the device. Clinical evidence should include the following: o Clinical (Diagnostic) Sensitivity o Clinical (Diagnostic) Specificity o Method Comparison o Matrix Comparison o Clinical Cut-off o Reference Interval (Expected values) o Additional requirements for IVD medical device for self-testing and near patient testing (if applicable)	CH4.2 Overall Clinical Evidence Summary CH4.5 Other Clinical Evidence	4.3.2. Clinical Evidence ***NOTE:*** *Refer to GN-20 Guidance on Clinical Evaluation for more details.*	If applicable	If applicable	If applicable	✓	✓	✓	If applicable
12	**Risk Analysis**									
	▪ Risk analysis describing the risks identified, severity of harm and probability of occurrence including the mitigation measures. A risk management report to substantiate that all known and foreseeable risks have been reasonably mitigated and the residual risks have been reduced or controlled to an acceptable level is to be submitted.	CH3.2 Risk Management	4.5 Risk Analysis	✓	✓		✓	✓	✓	
13	**Manufacturing Information (sites name and address)**									
	▪ Name and address for all manufacturing and sterilisation sites (including contract manufacturers and contract sterilisers).	CH6A.3.2 General Manufacturing Information	4.6. Manufacturer Information	✓	✓	✓	✓	✓	✓	✓
14	**Proof of QMS - E.g.: ISO13485 Certificate, Conformity to US FDA Quality System Regulations or Japan MHLW Ordinance 169**									
	▪ ISO 13485 certificates are to be provided for manufacturing and sterilisation sites of finished devices.	CH1.06 Quality Management System, Full Quality System or Other Regulatory Certificates	4.6. Manufacturer Information	✓	✓	✓	✓	✓	✓	✓
	▪ For sites without ISO 13485 certification, comparable audit reports for the actual site e.g. US FDA Quality Systems Regulations or Japan MHLW Ordinance 169 can be submitted.									
15	**Manufacturing Process - Flow Chart**									
	▪ Manufacturing process flow diagram.	CH6B.6.3 Production and service controls information	4.6. Manufacturer Information	✓			✓	✓	✓	
16	**Other document, please specify**									
	▪ Information on previous regulatory decisions (e.g. withdrawals or rejections by HSA) for the devices ***NOTE:*** *You may be required to provide the previous submission or registration information where necessary.*	CH1.09 Pre-Submission Correspondence and Previous Regulator Interactions	NA	If applicable	If applicable	If applicable	If applicable	If applicable	If applicable	If applicable

	▪ Information on any ongoing AE or FSCA reported to HSA for the subject device. ▪ Justification for an unmet clinical need ***NOTE:*** *Only required for Priority Review Scheme Route 1*									

HEALTH SCIENCES AUTHORITY

Health Products Regulation Group
Blood Services Group
Applied Sciences Group

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