Registration of Class B Medical Devices – *Guidance for Industry Consultation*

1 BACKGROUND

Medical devices are classified based on a rule based risk classification system into four risk classes – class A to D with class A being the lowest risk class and this is in line with the recommendations from the Global Harmonization Task Force (GHTF). The actual risk classification of each medical device depends on the claims made by the product owner and on its intended purpose. Class B medical devices are typically of low-moderate risk and includes devices such as hypodermic needles, suction apparatus, pregnancy test kits and ultrasound imaging equipment.

2 EVALUATION ROUTES

Currently, there are two evaluation routes for Class B medical devices:

(i) Full Evaluation Route
(ii) Abridged Evaluation Route

With the enhancements to the medical device regulatory framework announced on 20 April 2012, there will be two more evaluation routes for Class B medical devices:-

(i) Expedited Class B Registration (EBR) Evaluation Route
(ii) Immediate Class B Registration (IBR) Evaluation Route

The eligibility for the different evaluation routes depends on the numbers of prior approvals obtained from HSA's reference agencies at the point of submission. The types of approvals that qualify for abridged, EBR and IBR evaluation routes are:

- ✓ Australia Therapeutic Goods Administration (TGA)
- ✓ Health Canada (HC)
- ✓ Japan Ministry of Health, Labour and Welfare (MHLW)
  - Pre-Market Certification from a Japanese Registered Certification Body; OR
  - Pre-Market Approval from MHLW
- ✓ US Food and Drug Administration (US FDA)
  - 510K clearance
  - PMA
- ✓ European Union Notified Bodies (NB) via EC certificates issued according to

- Directive 93/42/EEC Annex II section 3 or Annex V for Class IIA devices
- Directive 98/79/EC Annex IV including sections 4 and 6 for List A IVDs
- Directive 98/79/EC Annex IV or Annex V with Annex VII for List B and self-testing IVDs

2.1 Full Evaluation Route

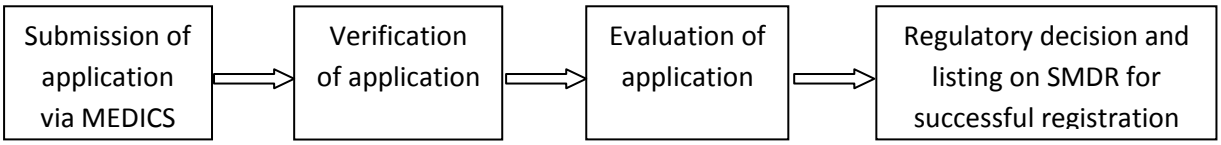
A medical device that has **not obtained any prior approval** from any HSA's reference agencies at the point of application will be subject to **full evaluation route**.

2.1.1 Submission Requirements

- Letter of Authorisation
- Annex 2: List of configurations of medical devices to be registered
- Common Submission Dossier Template (CSDT)
    a) Executive Summary
    b) Essentials Principles Checklist and Declaration of Conformity
    c) Device Description
    d) Detailed Information of Design Verification and Validation Documents
        - Full reports of Preclinical Studies including the detailed sterilization validation if applicable
        - Clinical Evidence, including publications and full reports of the studies referenced in the clinical evaluation report
    e) Proposed Device Labeling
    f) Risk Analysis
    g) Manufacturer Information
        - Name and address of the manufacturing site(s)
        - Proof of Quality Management System – e.g. ISO13485 Certificate, Conformity to US FDA Quality System Regulations or Japan MHLW Ordinance 169
        - Manufacturing Process – Flow Chart

For medical device with label claims beyond the inherent performance of the device, additional clinical data may be requested to substantiate the proposed label use.

2.1.2 Processing of application



Upon submission via MEDICS, an application fee will be charged immediately. The application dossier will be verified for completeness before the application is accepted for evaluation. Any omitted documents will need to be addressed via input requests.

Upon acceptance of the dossier for evaluation, the evaluation fees will be triggered. The payment mode (GIRO or progressive payment or others) will depend on the applicant's selection at the point of submission in MEDICS.

Evaluation of the dossier by HSA is based on the data set submitted by the applicant. An input request will be issued to the applicant if clarification or additional information is required. A regulatory decision is made based on the outcome of HSA's evaluation of the submitted dossier. Only application which satisfy the registration requirement will be listed on the Singapore Medical Device Register (SMDR).

The stop-clock starts whenever HSA issues an input request and ends when HSA receives a complete and satisfactory response from the applicant.

2.2 Abridged Evaluation Route

A medical device that has obtained at least one reference agency approval for a labeled use similar to that intended for marketing in Singapore at the time of submission will qualify for the abridged evaluation route.

2.2.1 Submission Requirements

- Letter of Authorisation
- Annex 2: List of configurations of medical devices to be registered
- Proof of approval by reference agency (e.g. approval letters, certificates)
- Common Submission Dossier Template (CSDT)

  a) Executive Summary

b) Essential Principles Checklist and Declaration of Conformity

c) Device Description

d) Summary of Design Verification and Validation Documents

- Summary of Preclinical Studies including the sterilization validation if applicable
- Clinical Evidence

e) Proposed Device Labeling

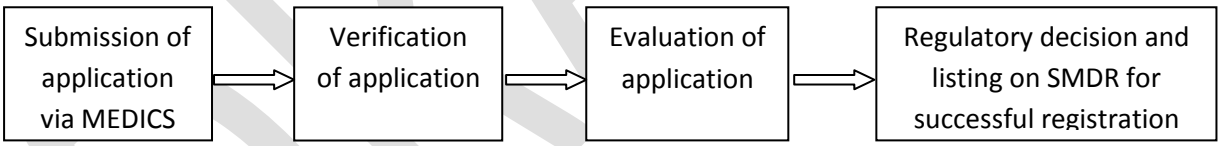
f) Risk Analysis (if applicable)

g) Manufacturer Information

- Name and address of the manufacturing site(s)
- Proof of Quality Management System – Eg: ISO13485 Certificate, Conformity to US FDA Quality System Regulations or Japan MHLW Ordinance 169

For medical device with label claims beyond the inherent performance of the device, additional clinical data may be requested to substantiate the proposed label use.

2.2.2 Processing of application



Upon submission via MEDICS, an application fee will be charged immediately. The application dossier will be verified for completeness before the application is accepted for evaluation. Any omitted documents will need to be addressed via input requests.

Upon acceptance of the dossier for evaluation, the evaluation fees will be triggered. The payment mode (GIRO orprogressive payment or others) will depend on the applicant's selection at the point of submission in MEDICS.

Evaluation of the dossier by HSA is based on the data set submitted by the applicant. An input request will be issued to the applicant if clarification or additional information is required. A regulatory decision is made based on the outcome of HSA's evaluation of the submitted dossier. Only application which satisfy the registration requirement will be listed on the SMDR.

The stop-clock starts whenever HSA issues an input request and ends when HSA receives a complete and satisfactory response from the applicant.

2.3 Expedited Class B Registration (EBR) Evaluation Route *(NEW for industry's feedback)*

2.3.1 Eligibility Criteria

The following medical devices are eligible for submission via the EBR evaluation route:

(A) EBR-1: a medical device that has

- obtained approval from at least **one** of HSA's independent reference agencies for a labeled use similar to that intended for marketing in Singapore; **and**

- [HSA's independent reference regulatory agencies are HC, MHLW, US FDA and TGA/EU NB and the corresponding approvals listed under **Section 2 Evaluation Route]**

- been marketed for at least 3 years in the above independent reference agency' jurisdiction [or in Singapore][1]; **and**

- no safety issues globally, defined as
  a) no deaths;
  b) no serious deterioration in the state of health[2] globally,

arising from the use of the medical device(s) as intended by the Product Owner, in the last three years; **and**

c) no open field safety corrective actions (including recalls) at the point of submission

OR

[1] Or the medical device has been used in Singapore for at least 3 years prior to the implementation of requirement for product registration for Class B medical devices on 1st January 2012

[2] Serious deterioration in the state of health, in relation to a person means: (a) a life-threatening illness or injury suffered by that person; (b) a permanent impairment of a bodily function of that person; (c) any permanent damage to any part of that person's body; or (d) a condition requiring medical or surgical intervention to prevent any such permanent impairment or damage.

(B) EBR-2: a medical device that has obtained approval from at least **two** of HSA's independent reference agencies for a labeled use similar to that intended for marketing in Singapore.

2.3.2 Submission Requirements

- Letter of Authorisation
- Annex 2 List of configurations of medical devices to be registered
- Proof of approval from independent reference agencies – [Note: one independent reference agency for EBR-1 and two independent reference agencies for EBR-2]
- Proof of marketing history in the same independent reference agency' jurisdictions e.g. Invoice with date, proof of sale – **[Note: for EBR-1 only]**
- Declaration of no safety issue globally (Refer to Annex C for the template for this declaration) – **[Note: for EBR-1 only]**
- Common Submission Dossier Template (CSDT)

  a) Executive Summary

  b) Essentials Principles Checklist and Declaration of Conformity

  c) Device Description

  d) Summary of Design Verification and Validation Documents

  - Summary of Preclinical Studies including summary of sterilization validation if applicable
  - Clinical Evidence

  e) Proposed Device Labeling

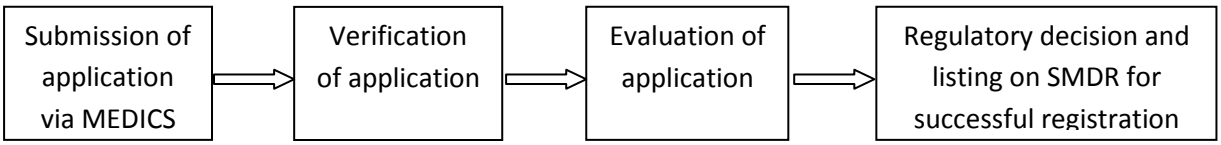
  f) Risk Analysis (if applicable)

  g) Manufacturer Information

  - Name and address of the manufacturing site(s)
  - Proof of Quality Management System – e.g. ISO13485 Certificate, Conformity to US FDA Quality System Regulations or Japan MHLW Ordinance 169

For medical device with label claims beyond the inherent performance of the device, additional clinical data may be requested to substantiate the proposed label use.

2.3.3 Processing of application



Upon submission via MEDICS, an application fee will be charged immediately. The application will be verified for eligibility for EBR and once confirmed, the application will be accepted for evaluation. The evaluation fees will be charged at this point. In view of the shortened processing timeline, progressive payment will not be an option available for applications submitted via this route. In the event that the application does not qualify for EBR, the application will be re-routed to the abridged evaluation route and the respective evaluation fee shall apply.

Evaluation of the dossier by HSA is based on the data set submitted by the applicant. An input request will be issued to the applicant if clarification or additional information is required. A regulatory decision is made based on the outcome of HSA's evaluation of the submitted dossier. Only application which satisfy the registration requirement will be listed on the SMDR.

The stop-clock starts whenever HSA issues an input request and ends when HSA receives a complete and satisfactory response from the applicant.

2.4 Immediate Class B Registration (IBR) Evaluation Route *(NEW for industry's feedback)*

2.4.1 Eligibility Criteria

A medical device that fulfils the following criteria will be eligible for IBR:

- approval by at least two of HSA's independent reference agencies for intended use similar to that submitting for registration in Singapore; **and**
- marketed for at least 3 years in both independent reference agencies' jurisdictions; **and**
- no safety issues globally, defined as

  a) no deaths;
  b) no serious deterioration in the state of health[2]

globally, arising from the use of the medical device(s) as intended by the Product Owner, in the last three years; **and**

c) no open field safety corrective actions (including recalls) at the point of submission

In addition, the medical device should not have **any** rejection/withdrawal in any reference agency or prior rejection/withdrawal in Singapore.

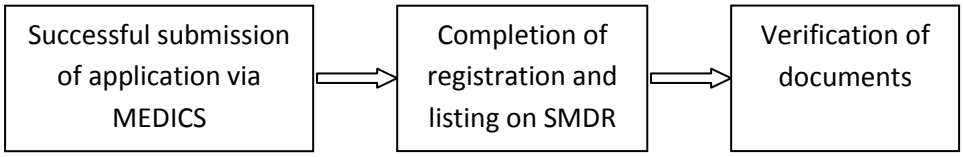
HSA's independent reference regulatory agencies are HC, MHLW, US FDA and TGA/EU NB and the corresponding approvals listed under **Section 2 Evaluation Route.**

2.4.2 Submission Requirements

- Letter of Authorisation
- Annex 2 List of configurations of medical devices to be registered
- Proof of approval from independent reference agencies
- Proof of marketing history in the same two independent reference agencies' jurisdictions e.g. Invoice with date, proof of sale
- Declaration of no safety issue globally (See Annex C for the template for this declaration)
- Common Submission Dossier Template (CSDT):
    a) Executive summary
    b) Device description
    c) *For sterile device only*: declaration of conformity to ISO sterilization standards for sterile medical devices. If not in conformity to ISO sterilization standards, a summary of sterilization validation is required.
    d) Proposed device labeling
    e) Manufacturer Information
        - Name and address of the manufacturing site(s)
        - Proof of Quality Management System – Eg: ISO13485 Certificate, Conformity to US FDA Quality System Regulations or Japan MHLW Ordinance 169

For medical device with label claims beyond the inherent performance of the device, additional clinical data may be requested post-registration to substantiate the proposed label use.

2.4.3 Processing of application



Upon successful submission via the MEDICS, the medical device will be listed on the SMDR immediately. The total fees will also be charged immediately upon successful submission for this route. As the device is listed immediately upon successful submission, applicants are reminded to ensure that all the required information is entered correctly and accurately.

HSA will verify the documents submitted in MEDICS after successful submission. Based on the intended use of the device by the Product Owner, additional licensing conditions may be imposed post-registration.

The IBR evaluation route facilitates immediate market access for the medical devices. Any IBR application which fails to fulfill ALL criteria specified under section 2.4.1 for the IBR evaluation route, not supported by the correct documents or a wrong risk class medical device submitted via the IBR evaluation route will result in cancellation of registration and total registration fee will NOT be refunded. This device will have to be re-submitted via other evaluation routes or submitted as other risk class. In these cases, the corresponding new application and evaluation fees shall apply.

3 GENERAL NOTES

All aspects of the medical device's quality including packaging, labelling (including instruction of use), and intended purpose/indications for use, intended for supply in Singapore shall be the same as that approved by the reference agencies that have approved the medical device. Registrants are required to attach appropriate explanation if there are differences from those stated in the certificates or the reference agency approved labelling.

For further information on the specific content and requirements for the letter of authorization and CSDT, please refer to GN-15, GN-17 and GN-18 guidance documents, respectively.

A summary of the evaluation routes and its corresponding documentation requirements is attached in Annex A and B respectively.

Annex A

Summary of Evaluation Routes

Evaluation Route	Full	Abridged	Expedited Class B registration - EBR *(NEW for industry's feedback)*	Immediate Class B registration – IBR *(NEW for industry's feedback)*
Criteria (at the time of submission)	• Not approved by any of HSA medical device's reference agencies	• At least 1 reference agency's approval	**EBR – 1** • At least 1 reference <u>independent</u> agency's approval • Marketed for ≥ 3 years in the above independent reference agency's jurisdiction* • No safety issues globally **OR** **EBR-2** • At least 2 <u>independent</u> reference agencies approvals	• At least 2 <u>independent</u> reference agencies' approvals • Marketed for ≥ 3 years in the above 2 independent reference agencies' jurisdiction • No safety issues globally • No prior rejection/withdrawal by independent reference agencies and Singapore
Targeted Turn-Around-Time	160 working days[#]	100 working days[#]	60 working days[#]	Immediate listing upon successful submission in MEDICS
Total Fee	S$4,000	S$2,300	S$1,400	S$1,400

*Or the medical device has been used in Singapore prior to the implementation of requirement for product registration for Class B medical devices on 1st January 2012

[#]Excluding company's response time to input request

Annex B

Summary of Submission Requirements

	Documentary Requirements	Full	Abridged	EBR -1 and 2 *(NEW for industry's feedback)*	IBR *(NEW for industry's feedback)*
1	Letter of authorization	✓	✓	✓	✓
2	Annex 2 List of Configurations	✓	✓	✓	✓
3	Proof of reference agency's approval(s)		✓	✓	✓
4	Proof of marketing history in the reference agencies' jurisdictions e.g. Invoice with date,			✓ Only required for EBR-1	✓
5	Declaration of no safety issues globally				✓
6	Executive Summary	✓	✓	✓	✓
7	Essential Principles Checklist and Declaration of conformity	✓	✓	✓	
8	Device description	✓	✓	✓	✓
9	Design verification and validation documents including : ○ Preclinical studies ○ Clinical evidence	✓ Detailed reports[1]	✓ Summary[2]	✓ Summary[2]	✓ Sterilisation validation for Sterile device only[3]
10	Proposed device Labelling[4]	✓	✓	✓	✓
11	Risk Analysis	✓	If applicable	If applicable	
12	Manufacturing site's name and address	✓	✓	✓	✓
13	Proof of Quality Management System – Eg: ISO13485 Certificate, Conformity to US FDA Quality System Regulations or Japan MHLW Ordinance 169	✓	✓	✓	✓
14	Manufacturing Process – Flow Chart	✓			

[1] Full study reports containing complete descriptions of the objectives, protocols, methods of data analysis, results and conclusions are to be provided.

[2] A summary of the studies undertaken is to be provided and should include a brief description of the study objectives, test methods, results and conclusions.

[3] A declaration of conformity to ISO Sterilization standards is acceptable. If not, a summary report of sterilisation validation is required.

[4] Medical device with label claims beyond the inherent performance of the device, additional clinical data may be requested to substantiate the proposed label use. For medical device submitted via IBR route, the additional data may be request post registration.

Annex C

Safety Declaration Template

[To be printed on Company Letterhead of Registrant]

Medical Device Branch
Pre-Marketing Division
Health Products Regulation Group
Health Sciences Authority

[Date]

Dear Sir/Madam,

Subject: Declaration of no safety concerns

I, *[name of Registrant]*, the applicant for registration of the medical device(s) stated below, hereby declare that there are:

☐ No deaths

☐ No serious deterioration in the state of health[1]

globally, arising from the use of the medical device(s) when used as intended by the Product Owner, in the last three years from *dd/mm/yyyy]*; **and**

☐ No open field safety corrective actions (including recalls)

This declaration shall apply to the following medical device(s):

[List containing product names of medical devices]

I, the applicant, am aware that a false declaration is an offence under the Health Products Act (Cap. 122D) and may result in the cancellation of registration of the above medical devices under Section 37(1) of the Act.

Yours Sincerely,

[Signature]

[Full Name and Title of Senior Company Official]

[Company stamp]

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[1] Serious deterioration in the state of health, in relation to a person means: (a) a life-threatening illness or injury suffered by that person; (b) a permanent impairment of a bodily function of that person; (c) any permanent damage to any part of that person's body; or (d) a condition requiring medical or surgical intervention to prevent any such permanent impairment or damage