MINISTRY OF HEALTH MALAYSIA

GUIDELINE FOR DRUG-MEDICAL DEVICE AND MEDICAL DEVICE-DRUG COMBINATION PRODUCTS

- ENDORSEMENT LETTER APPLICATION
- ADVERSE DRUG REACTION AND INCIDENT REPORTING

Fifth Edition – 17th October 2024

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Medical Device Authority
Ministry of Health Malaysia

PREAMBLE

- This present guideline serves as guidance for endorsement letter application, post-approval changes/ variation application for ancillary component, adverse drug reaction and incident reporting for registered combination product.

- Drug-medical device/ medical device-drug combination products are regulated according to the classification whether as drug or medical device based on the primary mode of action (PMOA).

- Combination products regulated as drug by Drug Control Authority is in accordance with the requirements set forth in the Control of Drugs and Cosmetics Regulations 1984 which is promulgated under Sale of Drug Act 1952 and any other relevant documents published by NPRA.

- Combination products regulated as medical device by Medical Device Authority is in accordance with the requirements set forth in the Medical Device Act 2012 (Act 737) and its subsidiary legislations, and any other relevant documents published by MDA.

- The written laws shall take precedence over this guidance document in any event of discrepancy.

- The scope of this guideline includes information relating to dossier requirements and procedures for submission of endorsement letter application, post-approval changes/variation application for ancillary component, adverse drug reaction and incident reporting for registered combination product.

- Applicants shall familiarize with the contents of this guidance document and the governing legislations before they submit registration applications.

- The Authority may request for information or specify conditions not described in this document that is deemed necessary to ensure the safety, quality, efficacy and performance of the combination product.

- The Authority reserves the right to amend any part of this guideline whenever it deems fit.

- This guidance shall be fully enforced on 1st July 2019, while the implementation of adverse drug reaction and incident reporting (Section 7.0) shall be fully enforced starting 1st July 2022.

- Any enquiry on application of combination product may be submitted to the relevant agency:

1. Director
   National Pharmaceutical Regulatory Agency,
   Ministry of Health Malaysia,
   Lot 36, Jalan Universiti (Jalan Profesor Diraja Ungku Aziz)
   46200 Petaling Jaya, Selangor.
   Tel : +603-78835400 Fax :03-7956 2924
   E-mail: npra@npra.gov.my
   Portal: http://npra.gov.my/

2. Chief Executive
   Medical Device Authority (MDA),
   Ministry of Health Malaysia,
   Level 6, Prima 9, Prima Avenue II,
   Blok 3547, Persiaran APEC,
   63000 Cyberjaya, Selangor
   Tel: +603-8230 0300 Fax: +603-8230 0200
   E-mail: combination.product@mda.gov.my
   Portal: http://www.mda.gov.my

GLOSSARY

Agency:

Refers to National Pharmaceutical Regulatory Agency (NPRA) or Medical Device Authority (MDA).

Ancillary Dossier:

Dossier required by the secondary agency.

Approval Letter:

A document that is issued by the secondary agency after satisfactory review of the changes/ variation to particulars of a registered combination product.

Authority:

The Drug Control Authority established under regulation 3 of the Control of Drugs and Cosmetics Regulations (CDCR) 1984 or The Medical Device Authority established under the Medical Device Authority Act 2012 (Act 738).

Drug-Medical Device Combination Product (DMDCP):

Primary mode of action is based on pharmacological, immunological or metabolic action in/on the body where NPRA is the primary agency of the combination product.

Endorsement Letter:

A document that is issued by the secondary agency after satisfactory review of the ancillary component.

Establishment:

a) A person who is either a manufacturer, importer, or distributor who is responsible for placing any medical device in the market but does not include a retailer; and
b) an authorized representative appointed by a manufacturer having a principal place of business outside Malaysia,

and such person and authorized representative being –

i. a person domiciled or resident in Malaysia; or
ii. a firm or company constituted under the laws of Malaysia,

and carrying on business or practice principally in Malaysia.

Incident:

An event that causes, or has a potential to cause, unexpected or unwanted effects involving the safety of any person who used a combination product or any person associated with the use of a combination product.

Medical Device-Drug Combination Product (MDDCP):

Primary mode of action in or on the human body is not based on pharmacological, immunological or metabolic means, but that may be assisted in its intended function by such means where MDA is the primary agency of the combination product.

Primary Agency:

Agency with primary regulatory responsibility for a combination product which is determined by the primary mode of action of the product.

Primary Dossier:

Dossier required by the primary agency.

Primary Mode of Action:

Mode of action that provides the greatest contribution to the overall therapeutic effects of the combination product

Product Registration Holder:

The company or corporate or legal entity in the field of pharmaceuticals who has been granted the marketing authorization of a product.

Secondary Agency:

Agency that regulates the other part(s) included in the combination product

ABBREVIATIONS AND ACRONYMS

CAB	Conformity Assessment Body
CDCR	Control of Drugs & Cosmetics Regulations 1984
COA	Certificate of Analysis
CSDT	Common Submission Dossier Template
DCA	Drug Control Authority
DRGD	Drug Registration Guidance Document
GMP	Good Manufacturing Practice
MDA	Medical Device Authority
MVG	Malaysian Variation Guidelines
MVGB	Malaysian Variation Guideline for Biologic
NPRA	National Pharmaceutical Regulatory Agency

CONTENTS

1.0 INTRODUCTION

1.1 DEFINITION OF MEDICAL DEVICE

The term medical device includes:

a. any instrument, apparatus, implement, machine, appliance, implant, in-vitro reagent or calibrator, software, material or other similar or related article intended by the manufacturer to be used alone or in combination, for human beings for the purpose of—

   i. diagnosis, prevention, monitoring, treatment or alleviation of disease;
   ii. diagnosis, monitoring, treatment, alleviation of or compensation for an injury;
   iii. investigation, replacement or modification, or support of the anatomy or of a physiological process;
   iv. support or sustaining life;
   v. control of conception;
   vi. disinfection of medical device; or
   vii. providing information for medical or diagnostic purpose by means of in-vitro examination of specimens derived from the human body, which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but that may be assisted in its intended function by such means; and

b. any instrument, apparatus, implement, machine, appliance, implant, in-vitro reagent or calibrator, software, material or other similar or related article, to be used on the human body, which the Minister may, after taking into consideration issues of public safety, public health or public risk, declare to be a medical device by order published in the Gazette

1.2 DEFINITION OF DRUG

Under the CDCR 1984, Regulation 2: "*Product*" means:

a. a drug[1] in a dosage unit or otherwise, for use wholly or mainly by being administered to one or more human beings or animals for a medicinal purpose[2]; or
b. a drug[1] to be used as an ingredient of a preparation for a medicinal purpose[2].

Under Sales of Drug Act 1952, Section 2:

1. "***drug***" includes any substance, product or article intended to be used or capable, or purported or claimed to be capable, of being used on humans or any animal, whether internally or externally, for a medicinal purpose.
2. "***medicinal purpose***" means any of the following purposes:
    a. alleviating, treating, curing or preventing a disease or a pathological condition or symptoms of a disease;
    b. diagnosing a disease or ascertaining the existence, degree or extent of a physiological or pathological condition;
    c. contraception;
    d. inducing anaesthesia;
    e. maintaining, modifying, preventing, restoring, or interfering with, the normal operation of a physiological function;
    f. controlling body weight;
    g. general maintenance or promotion of health or well being

1.3 DEFINITION OF COMBINATION PRODUCT

The term combination product includes:

i. A product comprised of two or more regulated components, i.e., drug/ device, biological/ device, or drug/ device/ biological, that are physically, chemically, or otherwise combined or mixed and produced as a single entity; OR
ii. Two or more separate products packaged together (co-packaged) in a single package or as a unit and comprised of drug and device products, device and biological products.

Products that are excluded from the term combination product and will be regulated separately:

i. A drug, device, or biological product packaged separately that according to its investigational plan or proposed labelling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product labelling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or

ii. Any investigational drug or device packaged separately that according to its proposed labelling is use only with another individually specified investigational drug, device, or cosmetic product where both are required to achieve the intended use, indication or effect.

iii. Convenience pack product (example: first aid kit consists of medical device and non-scheduled poison product)

iv. Natural products and Health Supplement products.

Refer Table I: Medical Device-Drug-Cosmetic Interphase (MDDCI) and Combination Products Classification Decision in Appendix 2, DRGD for examples of Drug-Medical Device/Medical Device-Drug Combination Product classification.

Prior to registration, an applicant may apply for classification to NPRA through product classification form which is available at http://npra.gov.my.

2.0 REGISTRATION PROCESS OF COMBINATION PRODUCT

The primary agency for registration of combination product is based on the primary mode of action/ the principal mechanism of action by which the claimed effect or purpose of the product is achieved:

i. Drug is based on pharmacological, immunological or metabolic action in/on the body; shall be regulated by NPRA;

ii. Medical device does not achieve its primary mode of action in or on the human body by pharmacological, immunological or metabolic means, but that may be assisted in its intended function by such means; shall be regulated by MDA.

Flow of registration process of combination product is illustrated in **Figure 1** below.

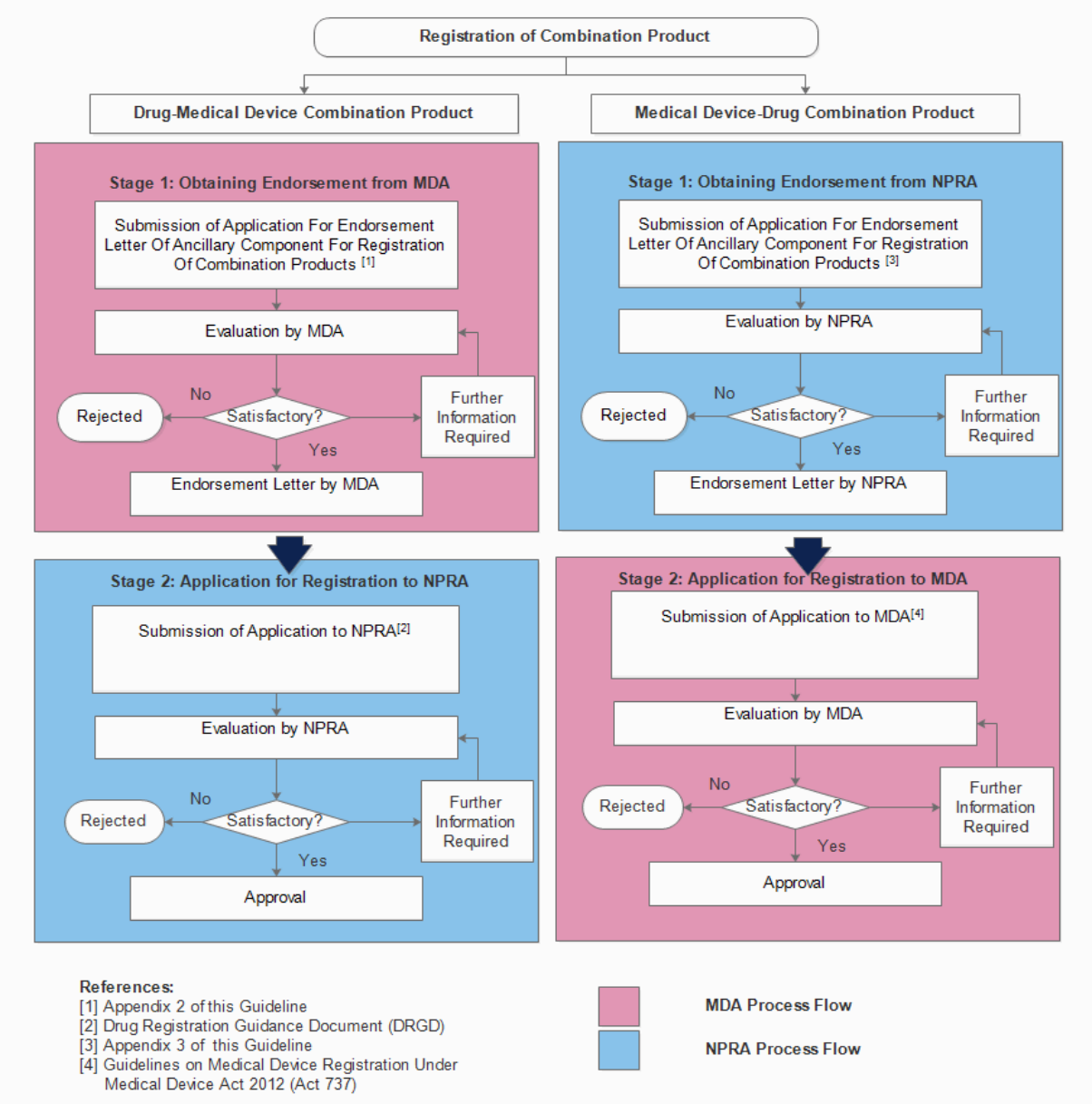


Figure 1: Flow of Registration Process of Combination Product

Explanatory Notes :

i. Applicant may submit application for endorsement letter and registration of combination product concurrently to both primary and secondary agency. However, the approval of combination product registration is subject to primary agency based on the fulfilment of registration requirements, as well as the receipt of endorsement letter from secondary agency.

ii. Refer **Appendix 5** for a process flow pertaining evaluation of medical device component for a combination product.

iii. Stage 1 Obtaining Endorsement from MDA for Drug-Medical Device Combination Product is NOT required for:
   a. low risk ancillary medical device components (e.g. syringe without needle for oral use, spoons, measuring cups, inhalers, spacers) is provided within the secondary packaging of the marketed Drug-Medical Device Combination Product (co-packed) and does not form as a single entity
   b. Non-sterile and non-measuring low risk ancillary medical device that form a single entity/ integrated product with the Drug-Medical Device Combination Product.
   c. ancillary medical device components that have already obtain registration approval from MDA. Proof of medical device registration certificate are required to be presented to NPRA when applying for Drug-Medical Device Combination Product registration.

iv. Stage 1 Obtaining Endorsement from NPRA for Medical Device-Drug Combination Product is NOT required for non-invasive (external use and/ or localised effect) medical device.

2.1 DRUG-MEDICAL DEVICE COMBINATION PRODUCT REGISTRATION PROCESS (NPRA AS PRIMARY AGENCY)

The registration process of Drug-Medical Device combination product shall undergo the following 2 stages:

i. Stage 1 – Obtaining Endorsement from MDA
ii. Stage 2 – Application for Registration to NPRA

All the stages shall be completed, with the exception as mentioned in Figure 1: Explanatory Notes, No. iii, , which may proceed directly to Stage 2- Application for Registration to NPRA.

Stage 1: Obtaining Endorsement from MDA

Applicant shall submit the following documents to MDA manually:

i. Application form for Endorsement Letter of Ancillary Component for Registration of Combination Product (Appendix 3: Form for Endorsement Letter of Ancillary Component for The Registration of Combination Product)
ii. Ancillary Dossier (Appendix 1: Ancillary Medical Device Dossier Requirement for Drug- Medical Device Combination Product)

MDA shall issue an endorsement letter upon satisfactory review.

The Authority may, in writing, at any time after the receipt of an application, request the applicant to give to the Authority within 90 days, particulars or document on the application or sample of the medical device.

If any additional information, particulars or document, or sample of the medical device required is not given by the applicant within the period specified in the request or any extension of time granted by the Authority, the application shall be deemed to be withdrawn and shall not be further proceeded with, but without affecting the right of the applicant to make fresh application.

Stage 2: Application for Registration to NPRA

For the purpose of registration of Drug-Medical Device combination product, applicant shall submit an application for registration with the following documents to NPRA via the online QUEST system at http://npra.gov.my:

i. Endorsement letter issued by MDA
ii. Data on drug in accordance to Section B: Product Registration Process, DRGD

Recommendations from the evaluation on Drug-Medical Device combination product shall be presented to the Drug Evaluation Committee followed by the meeting of DCA for approval/rejection.
The Drug-Medical Device combination product shall be registered after the approval by the DCA.

Applicant shall refer to the product registration approval notification sent by the Authority or the Approved Product Registration List in NPRA website.

2.2 MEDICAL DEVICE-DRUG COMBINATION PRODUCT REGISTRATION PROCESS (MDA AS PRIMARY AGENCY)

The registration process of Medical Device-Drug combination product shall undergo the following 2 stages:

i. Stage 1 - Obtaining Endorsement from NPRA
ii. Stage 2 - Application for Registration to MDA

All the stages shall be completed, with the exception of non-invasive (external use and/ or localised effect) medical device,such as skin barrier product (lotion, emulsion, ointment,

cream), irrigation solution, dressing comprising a matrix, which may proceed directly to Stage 2- Application for Registration to MDA.

Stage 1: Obtaining Endorsement from NPRA

Applicant shall submit the following documents to NPRA manually:

i. Application Form for Endorsement Letter of Ancillary Component for Registration of Combination Product (Appendix 3: Form for Endorsement Letter of Ancillary Component for The Registration of Combination Product)
ii. Ancillary Dossier (Appendix 2: Ancillary Drug Dossier Requirement for Medical Device-Drug Combination Product)

NPRA shall issue an endorsement letter upon satisfactory evaluation.

Stage 2: Application for Registration to MDA

For the purpose of registering a medical device-drug combination, applicant shall submit an application to MDA via the MeDC@St system with the following documents:

i. Endorsement letter issued by NPRA
ii. Data on medical device in accordance to guideline MDA/GL/MD-01 on How to Apply for Medical Device Registration under Medical Device Act 2012 (Act 737)

MDA shall register the Medical Device-Drug combination product and issue a medical device registration certificate upon approval.

The Authority may, in writing, at any time after the receipt of an application, request the applicant to give to the Authority within 90 days, particulars or document on the application or sample of the medical device.

If any additional information, particulars or document, or sample of the medical device required is not given by the applicant within the period specified in the request or any extension of time granted by the Authority, the application shall be deemed to be withdrawn and shall not be further proceeded with, but without affecting the right of the applicant to make fresh application.

3.0 DOSSIER REQUIREMENT FOR COMBINATION PRODUCT

The following dossier shall be submitted by the applicant for the purpose of registering combination product:

Table 1: Dossier Requirement for Combination Product

	Dossier Requirement for Drug Component (submission to NPRA)	**Dossier Requirement for Medical Device Component (submission to MDA)**
Drug-Medical Device Combination Product	(Primary Dossier) Refer to Appendix 15: Requirements for Full and Abridged Evaluations, DRGD	(Ancillary Dossier) Refer to Appendix 1: Ancillary Medical Device Dossier Requirement for Drug-Medical Device Combination Product
Medical Device-Drug Combination Product	(Ancillary Dossier) Refer to Appendix 2: Ancillary Drug Dossier Requirement for Medical Device-Drug Combination Product	(Primary Dossier) Refer to MDA/GD-04: Common Submission Dossier Template First Edition March 2014

4.0 TIMELINE FOR REGISTRATION OF COMBINATION PRODUCT

The following table specifies the duration (counted in working days upon receipt of complete application) that is required to perform product/ancillary dossier evaluation by each respective agency. Due to the nature of combination product which requires evaluation effort from both the Primary Agency and Secondary Agency, applicants are kindly advised to be vigilant on the overall timeframe required for combination product registration.

<table>
<tr><th>Stage</th><th>Drug-Medical Device Combination Product</th><th>Medical Device-Drug Combination Product</th></tr>
<tr><td>Stage 1</td><td>Evaluation timeline by MDA:<table><tr><th>Category</th><th>Duration (working days)</th></tr><tr><td>Drug-Medical Device Combination Product <u>WITH</u> Approval from Reference Countries*</td><td>90</td></tr><tr><td>Drug-Medical Device Combination Product <u>WITHOUT</u> Approval from Reference Countries*</td><td>180</td></tr></table></td><td>Evaluation timeline by NPRA:<table><tr><th>Category</th><th>Duration (working days)</th></tr><tr><td>Biologic Component</td><td rowspan="2">180</td></tr><tr><td>Non-Biologic Component</td></tr></table></td></tr>
<tr><td>Stage 2</td><td>Evaluation timeline by NPRA:<table><tr><th>Category</th><th>Duration (working days)</th></tr><tr><td>New Drug Product</td><td>245</td></tr><tr><td>Biologic</td><td>245</td></tr><tr><td>Generic(Scheduled Poison)</td><td rowspan="2">210</td></tr><tr><td>Generic (Non-Scheduled Poison)</td></tr></table></td><td>Evaluation timeline by MDA:<table><tr><th>Class of Medical Device</th><th>Duration (working days)</th></tr><tr><td>A</td><td>30</td></tr><tr><td>B</td><td>60</td></tr><tr><td>C</td><td>60</td></tr><tr><td>D</td><td>60</td></tr></table></td></tr>
</table>

**Refer Appendix 1: Ancillary Medical Device Dossier Requirement for Drug-Medical Device Combination Product*

5.0 FEES FOR REGISTRATION OF COMBINATION PRODUCT

Every application for registration shall be accompanied with a fee imposed by the respective agencies as specified in Section 5.1 and 5.2.

Any payment made shall **NOT** be **REFUNDABLE** once the application has been submitted and payment confirmed.

Applications without the correct fees will not be processed.

5.1 FEES IMPOSED BY NPRA

Under the CDCR 1984, Regulation 8(3): The Authority may charge any applicant such costs as it may incur for the purpose of carrying out any evaluation or investigation prior to the registration of any product.

No.	Category of Product	* Processing Fees	Analysis Fees	Total Fees
Drug-Medical Device Combination Product				
1.	Pharmaceutical a. New Drug Products b. Biologics	RM 1,000.00	Single active ingredient : RM 3,000.00	RM 4,000.00
			Two or more active ingredients : RM 4,000.00	RM 5,000.00
2.	Pharmaceutical a. Generic (Scheduled Poison) b. Generic (Non-Scheduled Poison)	RM 1,000.00	Single active ingredient : RM 1,200.00	RM 2,200.00
			Two or more active ingredients: RM 2,000.00	RM 3,000.00

** As stipulated in the CDCR 1984, Regulation 8.*

Fees imposed for endorsement of medical device-drug combination product: No processing fees will be charged by NPRA until further notice.

5.2 FEES IMPOSED BY MDA

The fees stipulated below are per application basis. Mode of payment: BayarNow

Medical Device-Drug Combination Product (RM)		**Drug-Medical Device Combination Product (RM)**	
Application Fee	Registration Fee	Drug-Medical Device Combination Product **WITH** Approval from Reference Countries*	Drug-Medical Device Combination Product **WITHOUT** Approval from Reference Countries*
750	5000	300	600
Mode of Payment: FPX through MeDC@St 2.0+		Mode of Payment: BayarNow	

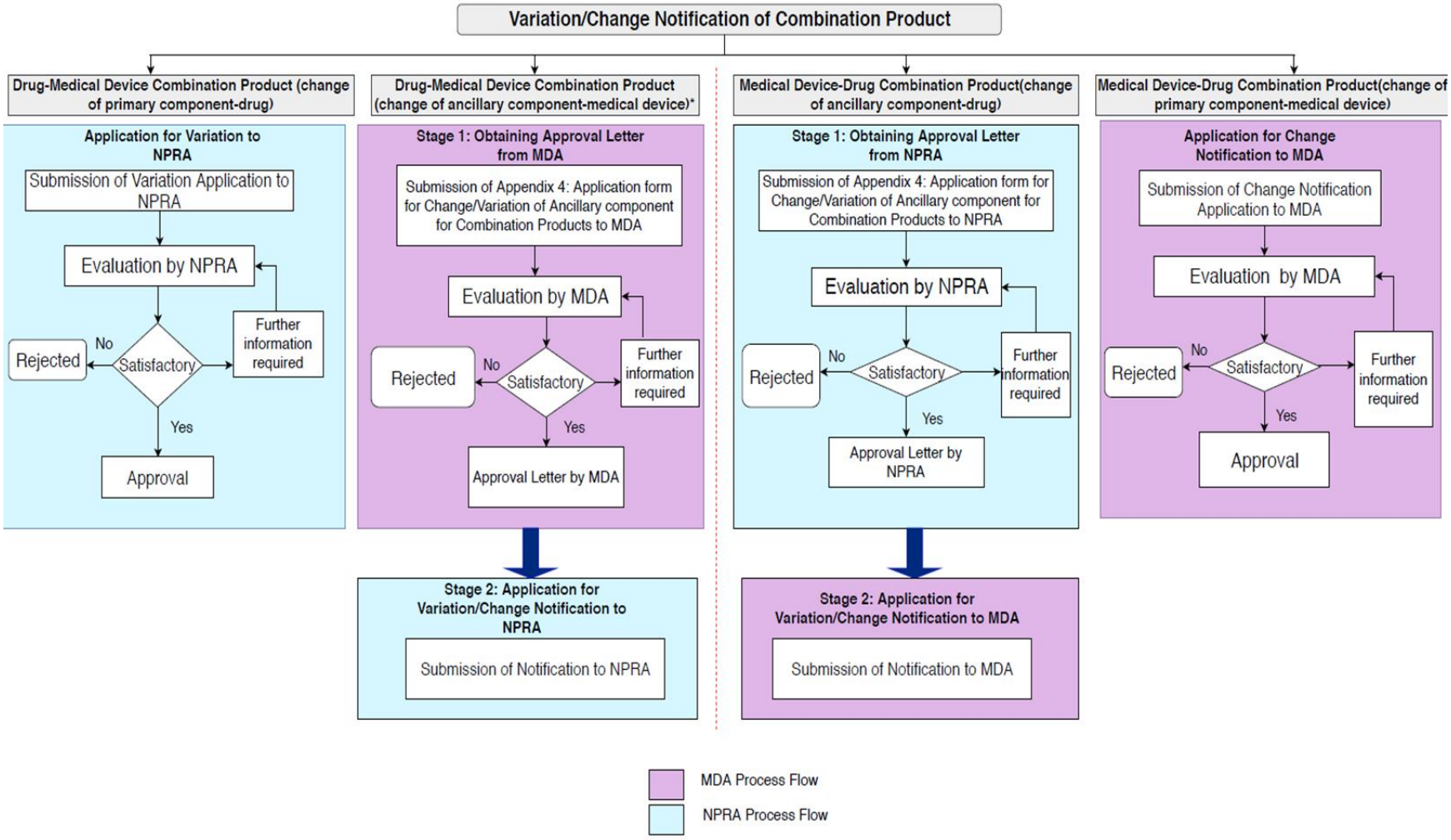
**Refer Appendix 1: Ancillary Medical Device Dossier Requirement for Drug-Medical Device Combination Product*

**Upon receiving a complete application, MDA's Finance Unit will issue an invoice for the for the payment fee to the applicant via email. The invoice will only be sent to the applicant's email address stated in the application form.*

**Applicant can visit BayarNow at http://bayarnow.mda.gov.my to make the payment. CASH WILL NOT BE ACCEPTED. We will not be responsible for the cash sent or brought to MDA.*

6.0 POST-APPROVAL CHANGES/ VARIATION TO PARTICULARS OF A REGISTERED COMBINATION PRODUCT

Figure 2: Flowchart of Variation/Change Notification Process of Combination Products



Explanatory Note*: Ancillary medical devices that have already obtain prior registration approval with MDA and subsequently approved of their change notification application with MDA SHALL not be required to proceed with this requirement

6.1 POST-APPROVAL CHANGES/ VARIATION TO PARTICULARS OF A REGISTERED DRUG-MEDICAL DEVICE COMBINATION PRODUCT

Application for changes to particulars of drug component for a registered Drug-Medical Device combination product shall be required to comply with Section 20: Amendments to Particulars of a Registered Product, DRGD.

Application for changes to particulars of ancillary medical device component for a registered drug-medical device combination product shall be submitted to MDA manually according to Appendix 6 along with Appendix 4: Application Form for Post-Approval Changes/ Variation of Ancillary Components for Combination Products. MDA shall issue an approval letter upon satisfactory evaluation, and this approval letter shall then be sent to NPRA for notification.

Note:

i. Application for changes to particulars of ancillary medical device component is not mandatory for low-risk ancillary medical device components
ii. Ancillary medical devices that have already obtain prior registration approval with MDA; and subsequently approved of their change notification application with MDA **SHALL not be required** to proceed with this requirement.

6.2 POST-APPROVAL CHANGES/ VARIATION TO PARTICULARS OF A REGISTERED MEDICAL DEVICE-DRUG COMBINATION PRODUCT

Application for changes to particulars of medical device component for a registered medical device-drug combination product shall be required to comply with the Guidance Document of Change Notification to Registered Medical Device.

Application for changes to particulars of ancillary drug component for a registered medical device-drug combination product shall be submitted to NPRA manually according to the categories and supporting documents in the current MVG or MVGB guidelines along with Appendix 4: Application Form for Post-Approval Changes/ Variation of Ancillary Components for Combination Products to the respective sections. Timelines for the evaluation of the application will follow as per the respective guidelines.

NPRA shall issue an approval letter upon satisfactory evaluation, and this approval letter shall then be sent to MDA for notification.

7.0 ADVERSE DRUG REACTION AND INCIDENT REPORTING

7.1 ADVERSE DRUG REACTION REPORTING

For adverse drug reaction (ADR) reporting, the latest edition of Malaysian Guidelines on Good Pharmacovigilance Practices (GVP) for Product Registration Holders shall be referred.

7.2 INCIDENT REPORTING

The management of incident for registered combination product is illustrated in Figure 3 and Table 2.

Figure 3: Management of Incident Involving Registered Combination Product by the Industry

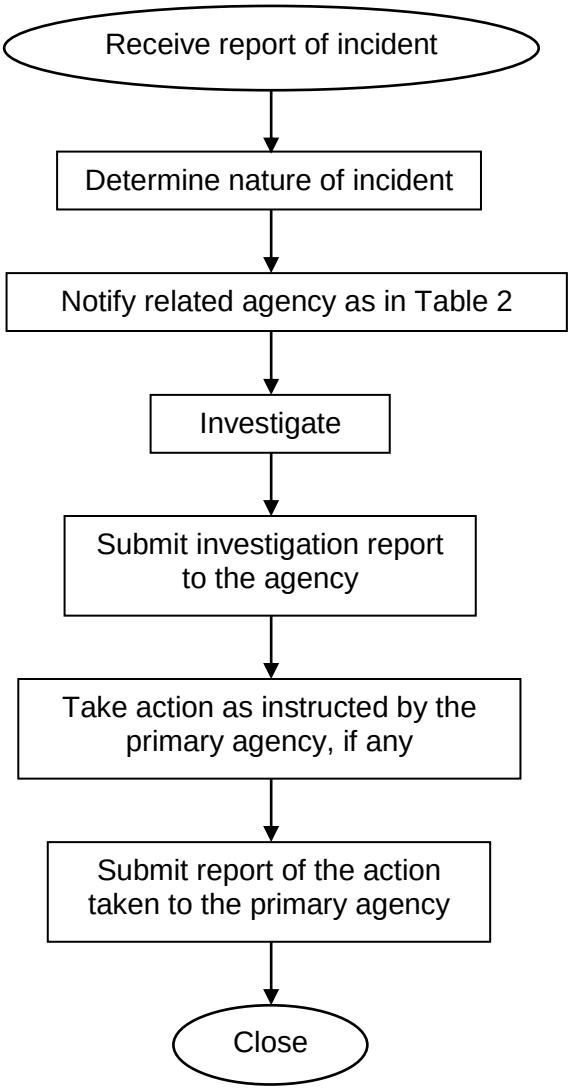


Table 2: Management of Incident Involving Registered Combination Product by the Industry

	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5	Scenario 6
Example of Product	Bone cement	Metered-dose inhaler	Drug-eluting stents	Insulin prefilled pen	Drug-eluting stents	Peritoneal dialysis bag
Primary Agency	MDA	NPRA	MDA	NPRA	MDA	NPRA
Nature of Incident	Device issue	Drug issue	Device & drug issues	Device & drug issues	Drug issue	Device issue
Notification to	MDA	NPRA	Both agencies (concurrent)	Both agencies (concurrent)	Both agencies (concurrent)	Both agencies (concurrent)
Investigation report to	MDA	NPRA	Both agencies (concurrent)	Both agencies (concurrent)	Both agencies (concurrent)	Both agencies (concurrent)
Regulatory instruction (if any) by	Primary agency					
Report of 'action taken' to	Primary agency					

Explanatory Notes:

i. Drug issues (other than ADR) may include quality defect/regulatory non-compliance related to safety

ii. In the event where the assessment on 'nature of incident' was not agreed by the primary agency, the agency will inform the company to notify the ancillary agency and the first notification timeline will be counted for.

iii. In the event where the nature of incident cannot be determined, notification of incident shall be submitted to both agencies (concurrent notification).

7.2.1 NOTIFICATION OF INCIDENT

All incidents that have caused user/patient harm shall be reported to the relevant agency as in Table 2. The incident reporting form for combination product shall be used (Appendix 7).

The reporting timelines are categorized below:

Characteristic of Incident	**Timeline to submit notification/initial report**
Local Event	
Related to the failure of the product or a deterioration in its effectiveness, or any inadequacy in its labelling or in its instructions for use	Within 30 calendar days from the discovery
Has led to the death or serious deterioration in the state of health of a patient, user or other person, or could do so were the incident to recur	Within 10 calendar days from the discovery
A serious threat to public health	Within 48 hours from the discovery
Foreign Event	
Individual incident report	Not required on routine basis ***Note:*** *For medical devices: only if the medical device is registered in Malaysian market**
Notification of any significant safety issue** such as new information impacting on risk(s) benefit profile of the product including international regulatory decision or action	No later than 3 calendar days
Withdrawal/suspension of registration in any country**	Within 24 hours from the discovery

*Refer Mandatory Problem Reporting Guidance Document

**Refer Malaysian Guidelines on Good Pharmacovigilance Practices (GVP) for Product Registration Holders

7.2.2 INVESTIGATION REPORT

The investigation report shall be submitted to the relevant agency as in Table 2, within 30 calendar days, or within a timeframe as directed by the agency.

The primary agency shall provide regulatory instruction when deemed necessary, and the company shall provide follow-up report on the action that has been taken within a timeframe

as directed by the agency. The report is considered accepted if no feedback received from the primary agency within 45 calendar days and no further action is needed.

The company shall provide response to the complainant within an agreed timeframe after completion of the investigation, or following the standard operating procedure that is in place.

7.2.3 SUBMISSION OF NOTIFICATION AND INVESTIGATION REPORTS

All notification of incident and investigation reports shall be submitted **via e-mail** to the following departments:

<table>
<tr><th colspan="2">Incident Report</th></tr>
<tr><td>Surveillance & Complaints Section,
Centre of Compliance & Quality Control,
National Pharmaceutical Regulatory Agency,
Lot 36, Jalan Universiti (Jalan Profesor Diraja Ungku Aziz),
46200 Petaling Jaya, Selangor.
E-mail: qpr@npra.gov.my</td><td>Post Market & Surveillance Vigilance Unit,
Medical Device Authority,
Level 6, Prima 9, Prima Avenue II,
Blok 3547, Persiaran APEC,
63000 Cyberjaya, Selangor.

E-mail: mpr@mda.gov.my</td></tr>
<tr><th colspan="2">Adverse Drug Reaction Report</th></tr>
<tr><td colspan="2">Pharmacovigilance Section,
Centre of Compliance & Quality Control,
National Pharmaceutical Regulatory Agency,
Lot 36, Jalan Universiti (Jalan Profesor Diraja Ungku Aziz),
46200 Petaling Jaya, Selangor.

E-mail: fv@npra.gov.my</td></tr>
</table>

APPENDIX 1: ANCILLARY MEDICAL DEVICE DOSSIER REQUIREMENT FOR DRUG-MEDICAL DEVICE COMBINATION PRODUCT

Documentation requirements shall be based on availability of regulatory approval or clearance as outlined in **Table 3** from the following countries/jurisdiction:

Table 3: Recognised regulatory agencies approval / clearance

Recognised Regulatory Authority	Approval Type
Therapeutic Goods Administration (TGA), Australia	TGA Marketing Authorization Approval (as medicinal product) TGA license
Health Canada, Canada	Drug Identification Number (DIN) Health Canada medical device license
European Medicines Agency (EMA) or Other Competent Authorities from EU Member Countries European Union (EU)	Marketing Authorization and Marketing Authorization Number EC Certification (CE Marking) against EU MDD, EU IVDD and EU AIMDD, as below: For general medical device: • Annex II Section 3 or Annex V of MDD (for Class IIA) • Annex II Section 3 or Annex III coupled with Annex V of MDD (for Class IIB) • Annex II Section 3 and 4 of MDD (for Class III) • Annex II Section 3 and 4 of AIMDD (for active implantable medical device) EC Certification (CE Marking) against EU Medical Device Regulations and EU IVD Regulations Article 117 opinion report issued by a Notified Body
Pharmaceuticals and Medical Devices Agency (PMDA), Japan	Manufacturing/Marketing Approval Certificate (as medicinal product) Pre-Market Certification from a Japanese Registered Certification Body (RCB and PMDA)

Recognised Regulatory Authority	Approval Type
	Pre-Market Approval from MHLW
Food and Drug Administration (FDA) USA	Marketing Authorization and National Drug Code (NDC) USFDA 510 (k) clearance letter USFDA Pre-Market Approval (PMA) Letter
Medicines & Healthcare products Regulatory Agency (MHRA), United Kingdom	For Great Britain and Northern Ireland: • Public Access Database for Medical Device Registration • UKCA Certification • EC (CE Marking) and UKNI Certification

Combination Product which:

i. HAS already obtained regulatory clearance as specified in **Table 3** is entitled for abridged documentation requirements (documentation proof of regulatory clearance must be enclosed together along with the dossier).

ii. HAS NOT obtained regulatory clearance as specified in **Table 3** is required to submit all of documentation requirements.

Table 4 detailed out about documentation requirements for ancillary medical device dossier. The information contained in the dossier should be supported by relevant supporting documents for example copies of labels, certificates and reports. Those documents must be legible and within its validity period. Refer **MDA/GD/0008 Common Submission Dossier Template (CSDT)** for further explanation on the elements stated below.

Table 4: Documentation requirements for ancillary medical device dossier

Element/Section		Description
1.	Overview of the Medical Device	**A complete description of the medical device** provides descriptive information on how the device functions, the basic scientific concepts that form the fundamentals for the device, the component materials and accessories used in its principles of operation as well as packaging. The intended use and indications for use of the medical device, principles of operation or mode of action and information on container closure system shall be provided. Please state it is a single-entity or co-packed combination product.

Element/Section		Description
2.	Labelled pictorial representation for the Medical Device	**Labelled pictorial representation** (e.g.diagrams, photographs and drawings), clearly indicating key parts/components, including sufficient explanation to understand the drawings and diagrams.
3.	Description of the accessories	**A description of the accessories**, other medical devices and other products that are not medical devices, which are intended to be used in combination with the medical device (e.g. other low-risk medical devices)
4.	Instruction of use (IFU) / Product Catalogue / Brochure	**Instructions of use** including the procedures, methods, frequency, duration, quantity and preparation to be followed for safe use of the medical device. Instructions needed to use the device in a safe manner shall, to the extent possible, be included on the device itself and/or on its packaging by other formats/forms (e.g. product insert & packaging)
5.	Contraindications, Warnings, Precautions and Potential Adverse Effects related to the Medical Device*	**Contraindications** which are a general description of the disease or condition and the patient population for which the device should not be used for the purpose of diagnosing, treating, curing or mitigating. Contraindications are conditions under which the device should not be used because the risk of use clearly outweighs any possible benefit; **Warnings** to inform on specific hazard alert that a user needs to know before using the device. **Precautions** to exercise special care necessary for the safe and effective use of the device. They may include actions to be taken to avoid effects on patients/users that may not be potentially life-threatening or result in serious injury, but about which the user should be aware. Precautions may also alert the user to adverse effects on the device of use or misuse and the care necessary to avoid such effects. **Potential adverse effects** or side effects from the use of the medical device, under normal conditions. These are potential undesirable and serious outcomes (death, injury, or serious adverse events) to the patient/user if the device is used under normal condition.
6.	Materials*	**Materials** include a. List of materials of the medical device making either direct (e.g. with the mucous membrane) or indirect contact (e.g., during extracorporeal circulation of body fluids) with a human body; and b. Complete chemical, biological and physical characterization of the materials of the medical device making either direct (e.g. mucous membrane) or indirect contact (e.g., during extracorporeal circulation of body fluids) with a human body
7.	Commercial marketing history	**3 years commercial marketing history** which covers the list of countries where the medical device AND/OR combination product

Element/Section		Description
		is marketed, list of regulatory approval or marketing clearance obtained including the registration status and status of any pending request for market clearance (documentation proof of regulatory clearance must be enclosed together along with the dossier).
8.	Post Marketing Information	**3 years summary of reportable adverse events** and field corrective actions (FCAs) related to the medical device OR declaration of no safety issues associated with the combination product globally.
9.	Summary of design verification and validation documents	**Pre-clinical studies**: This section should summarize or reference or contain report and/or certification and/or declaration of; a. Biocompatibility test conducted on materials used in a medical device. At a minimum, biocompatibility tests must be conducted on samples from the finished, sterilized device. All materials that are significantly different must be characterized. Information describing the tests, the results and the analyses of data must be presented; b. Pre-clinical physical tests (e.g. mechanical & functional tests, electrical safety tests, accelerated aging tests, etc) conducted on the medical device. Complete pre-clinical physical test data must be provided, as appropriate; and c. Pre-clinical animal studies to support the probability of effectiveness in humans. The data collected for the study includes any pre-clinical laboratory or animal studies, as appropriate for the medical device. The conclusion of the study should address the device's interactions with animal fluids and tissues and the functional effectiveness of the device in the experimental animal model(s). The rationale (and limitations) of selecting the particular animal model should be discussed. The report of all tests mentioned above must include the objectives, methodology, results, analysis and manufacturer's conclusions. Where no testing was undertaken for the medical device, a rationale for that decision must be provided. For combination product WITH approval from reference countries, this section should summarize or reference or contain report and/or certification and/or declaration of the tests conducted, include the objectives, methodology, results, analysis and manufacturer's conclusions. **Clinical Evidence:** Clinical evidence should be thorough and objective (i.e., it should consider both positive and negative data), with the goal of demonstrating valid clinical proof of the medical device's safety and performance. Where applicable, this evaluation may take the form of a. a systematic review of existing bibliography - The literature search protocol, the literature review report, and published

Element/Section		Description
		articles and other references selected as relevant to the medical device in concern are all required to be included in the report b. clinical experience with the same or similar devices - The manufacturer may generate post market surveillance reports, registries or cohort studies, adverse events databases, data for the medical device in question from individual patients under compassionate usage programs prior to marketing of the medical device, details of critically applicable field corrective actions (e.g. recalls, notifications, hazard alerts) c. clinical investigation - These may include clinical investigation plan, case report forms, monitoring and audit reports, regulatory authority approvals and associated correspondence as required by applicable regulations and final report. For combination product WITH approval from reference countries, summary of clinical evidence/data addressing relevant safety and performance-related to the medical device shall be provided (e.g Human Factors Studies)
10.	Risk analysis*	**Risk analysis** should summarize or reference or contain information on risk analysis conducted for the medical device is to be provided in the form of a risk management report.
11.	Manufacturing information	**Manufacturing information** should summarize or reference or contain documentation related to the manufacturing processes, including quality assurance measures. It should be provided in the form of a list of resources and activities that transform inputs into the desired output. Relevant Quality Management System (QMS) for the medical device AND/OR combination product (e.g Good Manufacturing Practice or ISO13485) shall be provided.
12.	Relevant essential principles and rule used to demonstrate conformity	**The Essential Principles** that are applicable to the device and the general rule or method used to demonstrate conformity to each applicable Essential Principle.

Explanatory Notes: *This section is not compulsory for combination product WITH approval from reference countries .

APPENDIX 2: ANCILLARY DRUG DOSSIER REQUIREMENT FOR MEDICAL DEVICE-DRUG COMBINATION PRODUCT

Part I: General Information	
1.	Combination Product Name
2.	Name & Strength of Active Substance and Excipient
3.	Product Description
4.	Indication/ Intended use
5.	Recommended Dose (If Applicable)
6.	Mechanism of Action of the Ancillary Drug
7.	Route of Administration/ Mode of Delivery (Ancillary drug follows the finished combination product)
8.	Contraindication
9.	Warning and Precautions
10.	Interaction with Other Medicaments (If Applicable)
11.	Pregnancy and Lactation (If Applicable)
12.	Side Effects (If Applicable)
13.	Symptoms and Treatment of Overdose (If Applicable)
14.	Storage Condition (If Applicable)
15.	Shelf Life (If Applicable)
16.	Declaration of Human/ Animal origin (If Applicable)
PART II: QUALITY OF DRUG COMPONENT	
1.	Manufacturing Process and Process Controls
2.	Control of Excipients (If Applicable)
	a) Specifications of Excipient
	b) Justification of Specifications
3.	Control of Drug Substances
	a) Nomenclature, Structure of Drug Substance, General Properties
	b) Manufacturer Name and Address with GMP compliance evidence
	c) Specifications
	d) Certificate of Analysis for TWO batches

	e) Stability (only for Biologic Component)
	f) Viral Inactivation/ Removal Studies and Transmissible Spongiform Encephalopathy (TSE)/ Bovine Spongiform Encephalopathy (BSE) Risk Assessment (only for Biologic Component)
PART III: NON CLINICAL DOCUMENT	
1.	Non Clinical Overview
2.	Tabular Listing of Non Clinical Study
3.	Non Clinical/ Biocompatibility Study Reports
PART IV: CLINICAL DOCUMENT	
1.	Product Development Rationale
2.	Tabular Listing of Clinical Study
3.	Clinical document pertaining to the medical device with ancillary component (i.e.: Clinical Evaluation Report (CER), in-house clinical report, published clinical paper (if any))

APPENDIX 3: APPLICATION FORM FOR ENDORSEMENT LETTER OF ANCILLARY COMPONENT FOR THE REGISTRATION OF

KEMENTERIAN KESIHATAN MALAYSIA
Ministry of Health Malaysia
Portal: www.moh.gov.my
Email: kkm@moh.gov.my

APPLICATION FORM FOR ENDORSEMENT LETTER OF ANCILLARY COMPONENT FOR THE REGISTRATION OF COMBINATION PRODUCT

Product already registered with MDA/ NPRA:

Yes ☐ Registration Number: _____ No ☐

CHECKLIST FOR SUBMISSION

DOCUMENTS	**COMBINATION PRODUCT**		Please tick if the document is attached
	DRUG-MEDICAL DEVICE	**MEDICAL DEVICE-DRUG**	
Ancillary Medical Device: I. Official/ Cover Letter II. Checklist for subbmission of ancillary medical device component (Section 6 of this document) III. Ancillary Device Dossier (1 copy in the form of electronic copy, CD or Thumb Drive) *(Appendix 1 of Guideline For Drug-Medical Device and Medical Device-Drug Combination Products)*	/	X	
Ancillary Drug: I. Official/ Cover Letter II. Checklist of the relevant drug category (Bioloigc Component or Non-Biologic Component) III. Ancillary Drug Dossier (2 copies in the form of electronic copy, CD) *(Appendix 2 of Guideline For Drug-Medical Device and Medical Device-Drug Combination Products)*	X	/	

Explanatory Notes: [/] – Required; [X] – Not required

For Ancillary Medical Device Components:
The form and supporting documents can be sent manually (hardcopy document with PDF electronic copy on a CD or Thumb Drive) to:

Chief Executive,
Medical Device Authority,
Level 6, Prima 9, Prima Avenue II, Blok 3547, Persiaran APEC,
63000 Cyberjaya, Selangor.
E-mail: combination.product@mda.gov.my

For Ancillary Drug Components:
The form and supporting documents can be sent manually to:

Product & Cosmetic Regulatory Coordination Section,
Centre of Regulatory Coordination & Strategic Planning,
National Pharmaceutical Regulatory Agency.
Lot 36, Jalan Universiti (Jalan Profesor Diraja Ungku Aziz),
46200 Petaling Jaya,Selangor

Please complete all information requested. All fields are mandatory unless stated otherwise.	
1. APPLICANT DETAILS	
Name of Applicant:	
NRIC No. / Passport:	Designation:
Name & Address of Company:	
ROC No.:	
City:	State:
Telephone No.:	Fax No.:
Email Address:	
Role of Applicant:	
☐	Product Registration Holder
☐	Manufacturer *Establishment License No.:*
☐	Authorized Representative *Establishment License No.:*
☐	Others (*please specify*):
2. COMBINATION PRODUCT DETAILS *Please provide product packaging label, product catalogue and product insert*	
☐	Drug-Medical Device
☐	Medical Device-Drug
Product Name:	Manufacturer's Name:
Brand/Model:	
Product Description:	
Intended Use/Indication:	

3. ANCILLARY MEDICAL DEVICE DETAILS

(Only applicable to Drug-Medical Device Combination Product)

Name of Medical Device	
Description of Medical Device	
Intended Use of Medical Device	
Brand/Model of Medical Device	
Name & Address of Manufacturer for the Medical Device	

Table 1: List of Configurations (if applicable)

No.	Name of device, accessories, constituent-components, or articles as per product label:	Model	Device Description

Note: If more than one (1) single medical device, please fill out in a separate sheet.

4. ANCILLARY COMPONENT DETAILS

Please provide details of the ancillary component according to the following:

- Ancillary Medical Device Dossier (refer Appendix 1 of Guideline For Drug-Medical Device and Medical Device-Drug Combination Products)
- Ancillary Drug Dossier (refer Appendix 2 of Guideline For Drug-Medical Device and Medical Device-Drug Combination Products)

5. ATTESTATION & DECLARATION

I, <Name of applicant>, ID <NRIC No. / Passport >, on behalf of <Name of company>
the product holder/manufacturer/authorize representative of this ancillary component, hereby declare that :

(tick where applicable)

☐ **Drug-Medical Device**:

i. This/these ancillary medical device(s) component is/are according to the definition of medical device set out in Section 2, Medical Device Act 2012 (Act 737).

☐ **Medical Device-Drug**:

i. This ancillary drug component is according to the definition of drug set out in Control of Drugs and Cosmetics Regulations 1984 which is promulgated under Sales of Drugs Act1952.

I hereby attest that the information and attachment provided on this form are accurate, correct, complete and current to this date.

Signature:

Applicant's Name:

Designation :

Date :

Company stamp :

6. CHECKLIST FOR SUBMISSION OF ANCILLARY MEDICAL DEVICE COMPONENT				
Company's Name: **Product Name:** **Medical Device Name:** **Applicant Name:**			**For MDA Use Only:** Submission ID: **MDA/ENL/** Date of Receipt:	
No:	**Sections**	**Y/N/NA**	**ObjectiveEvidence / Name of document**	**For MDA Use Only**
1.	Complete Application Form (Appendix 3) with a cover letter, hardcopy document & electronic copy (CD/Thumb drive)			
2.	Recognised regulatory agencies approval / clearance		Name of regulatory authority:_____ Approval type:_____	
3.	Overview of the Medical Device			
4.	Labelled pictorial representation for the Medical Device			
5.	Description of the accessories			
6.	Instruction of use (IFU) / Product Catalogue / Brochure			
7.	Contraindications, Warnings, Precautions and Potential Adverse Effects related to the Medical Device			
8.	Materials			
9.	Commercial marketing history			
10.	Post Marketing Information			
11.	Summary of design verification and validation documents			
12.	Risk analysis			
13.	Manufacturing information			
14.	Relevant essential principles and rule used to demonstrate conformity			
15.	RM300/RM600 Fee (Bank Draft payable to 'KUMPULAN WANG PIHAK BERKUASA PERANTI PERUBATAN')			

Explanatory note: Please tick Yes (Y), No (N) or NA (not applicable) to indicate that the requested documentation has been included in your submission. Explain responses in further detail and list related attachments under the Objective Evidence/Name of document column.

APPENDIX 4: APPLICATION FORM FOR POST APPROVAL CHANGES/ VARIATION OF ANCILLARY COMPONENTS FOR COMBINATION

KEMENTERIAN KESIHATAN MALAYSIA
Ministry of Health Malaysia
Portal: www.moh.gov.myEmail: kkm@moh.gov.my

APPLICATION FORM FOR CHANGE/VARIATION OF ANCILLARY COMPONENTS FOR COMBINATION PRODUCTS

CHECKLIST FOR SUBMISSION

DOCUMENTS	COMBINATION PRODUCT		Please tick if the document is attached
	DRUG-MEDICAL DEVICE	MEDICAL DEVICE-DRUG	
Documentations as per in Guidance Document for Change Notification by MDA	/	X	
Documentations as per in Variation Guidelines by NPRA	X	/	
Endorsement Letter Issued by MDA	/	X	
Endorsement Letter Issued by NPRA	X	/	

Explanatory Notes: [/] – Required; [X] – Not required

For Ancillary Medical Device Components:

The form and supporting documents can be sent manually (hardcopy document with PDF electronic copy on a CD or Thumb Drive) to:

Chief Executive,
Medical Device Authority,
Level 6, Prima 9, Prima Avenue II, Blok 3547, Persiaran APEC,
63000 Cyberjaya, Selangor.
E-mail: combination.product@mda.gov.my

For Ancillary Drug Components:

The form and supporting documents can be sent manually to:

Product & Cosmetic Regulatory Coordination Section,
Centre of Regulatory Coordination & Strategic Planning,
National Pharmaceutical Regulatory Agency.
Lot 36, Jalan Universiti (Jalan Profesor Diraja Ungku Aziz),
46200 Petaling Jaya,Selangor

Please complete all information requested. All fields are mandatory unless stated otherwise.	
1. APPLICANT DETAILS	
Name of Applicant:	
NRIC No. / Passport:	Designation:
Name & Address of Company:	
ROC No.:	
City:	State:
Telephone No.:	Fax No.:
Email Address:	
Role of Applicant:	
☐ Product Registration Holder ☐ Manufacturer *Establishment License No.:* ☐ Authorized Representative *Establishment License No.:* ☐ Others (*please specify*):	
2. COMBINATION PRODUCT DETAILS	
☐ Drug-Medical Device (Registration Number :)	
☐ Medical Device-Drug (Registration Number :)	
☐ Previous Endorsement Letter(s) Reference No :	
Product Name:	Manufacturer's Name:
Brand/Model:	
Product Description:	

Intended Use/Indication:

3. ANCILLARY MEDICAL DEVICE DETAILS *(Only applicable to Drug-Medical Device Combination Product)*	
Name of Medical Device	
Description of Medical Device	
Intended Use of Medical Device	
Brand/Model of Medical Device	
Name & Address of Manufacturer for the Medical Device	

Table 1: List of configurations

No.	Name of device, accessories, constituent-components, or articles as per product label:	Model	Device Description

Note: If more than one (1) single medical device, please fill out in a separate sheet.

4. ATTESTATION & DECLARATION

I, <Name of applicant>, ID <NRIC No. / Passport >, on behalf of <Name of company>
the product holder/manufacturer/authorize representative of this ancillary component, hereby declare that :

(tick where applicable)

☐ **Drug-Medical Device**:

i. This/these ancillary medical device(s) component is/are according to the definition of medical device set out in Section 2, Medical Device Act 2012 (Act 737).

☐ **Medical Device-Drug**:

i. This ancillary drug component is according to the definition of drug set out in Control of Drugs and Cosmetics Regulations 1984 which is promulgated under Sales of Drugs Act1952.

I hereby attest that the information and attachment provided on this form are accurate, correct, complete and current to this date.

Signature:

Applicant's Name:

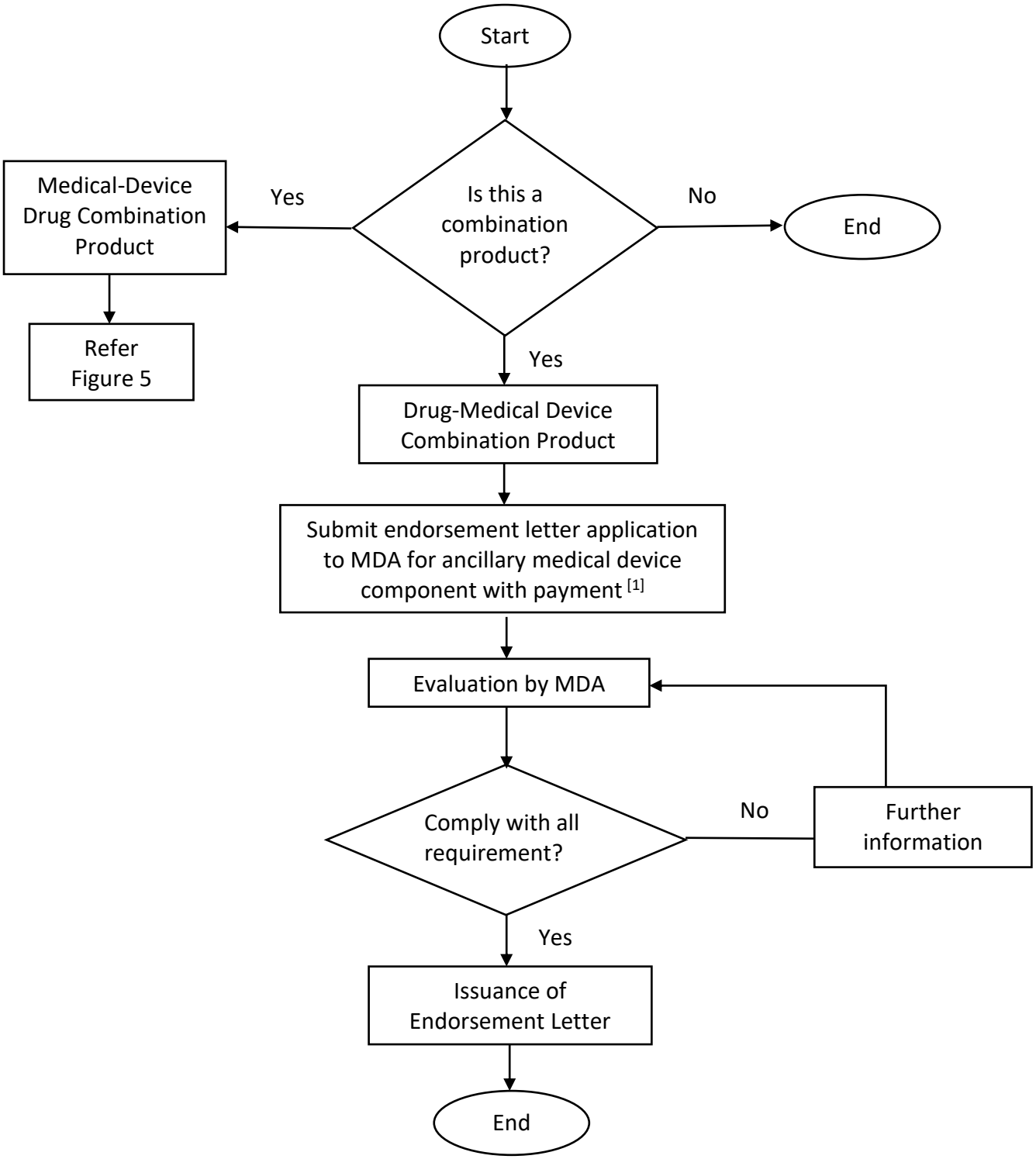
Designation :

Date :

Company stamp :

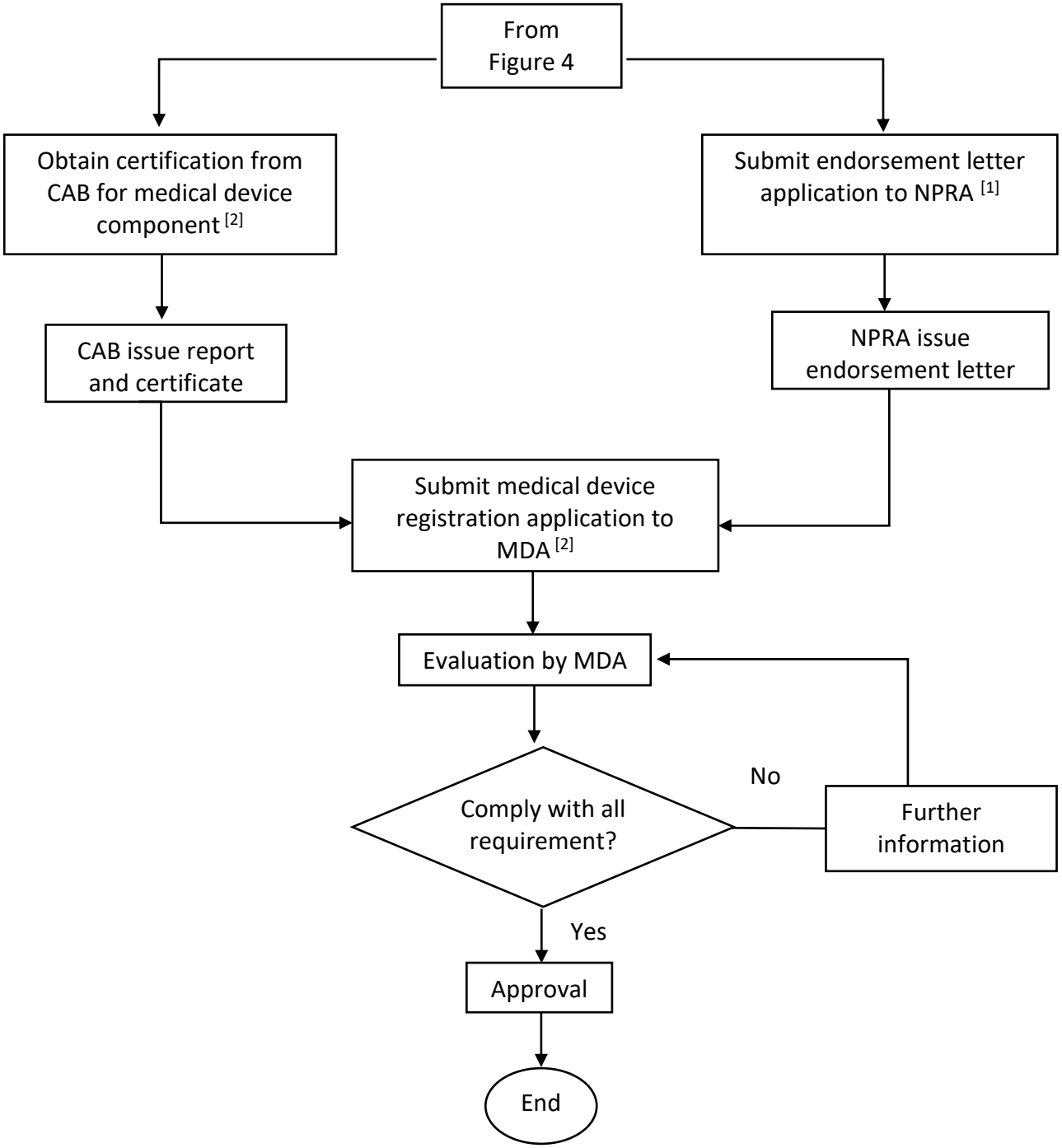
APPENDIX 5: ENDORSEMENT LETTER APPLICATION FLOW CHART FOR ANCILLARY MEDICAL DEVICE COMPONENT

Figure 4: Endorsement Letter Application Flow Chart for Ancillary Medical Device Component



[1] Refer Appendix 3, Guideline For Drug-Medical Device And Medical Device Drug Combination Products.

Figure 5: Application for Medical Device-Drug Combination Product Flow Chart



[1] Refer Appendix 3 Guideline For Drug-Medical Device And Medical Device-Drug Combination Products.

[2] Refer to MDA/GL/MD-01: How to Apply for the Medical Device Registration under Act 737

APPENDIX 6: CHANGE TO ANCILLARY MEDICAL DEVICE COMPONENTS

6.1 CATEGORIES OF CHANGES

Change to ancillary medical device components may be categorized into the following categories:

a) **Technical Changes** – major changes to particular of ancillary medical device components

b) **Administrative Changes** – minor changes to particular of ancillary medical device components

c) Any other changes that affect their safety and performance requires new endorsement letter application

MDA/GD/0020 - Change Notification for Registered Medical Device, a Guidance Document published by MDA can be referred for clarification of the terminologies used in this Appendix

The following Tables (Table 5 and Table 6) outline the guiding principles for identification of various types of change to ancillary medical device components.

(Note: Any other change that occurs to the ancillary medical device components that does not affect their safety and performance; AND not outlined in these Tables does not trigger the need for change notification)

The guiding principles for identification of Technical Changes of various types of change to medical devices are presented in Table 5. Applicant are required to provide the documents for each change that occur to the ancillary medical device components as outlined in the table.

Table 5: Technical Changes

Types of change	Documents to be submitted
4.1 Change in manufacturing facility, process and quality management system (QMS)	
(a) All changes to manufacturing and/or sterilisation facilities with no changes to the manufacturing and/or sterilisation processes. *Example:* *Change of manufacturing site.*	i) Revised QMS certificate(s) (if applicable); ii) Medical Device labelling stating changes for each amended section (if applicable); iii) Declaration that there is no change to manufacturing and sterilisation process; iv) Sterilisation validation report.
(b) All changes to manufacturing processes (including changes made to outsourced processes) that result in a change in specifications of a medical device. *Example:* *Change in the equipment used for cutting the result in the change in length of sutures.* *Moulding or cutting manufacturing process.*	i) Revised QMS certificate(s) (if applicable); ii) Summary of new manufacturing process; iii) Validation report covering new processes; iv) Pre-clinical studies (if applicable); v) Software validation report (for software); vi) Clinical safety report (for operating principles and design characteristics change) (if applicable); vii) Risk analysis.
(c) All changes to sterilisation processes (including changes made to outsourced processes) *Example:* *Change in moist heat sterilisation parameters, or change in sterilisation method from ethylene oxide to gamma radiation, or change from batch release to parametric release.*	i) Sterilisation technique (certificate); ii) Medical Device labelling stating changes for each amended section (if applicable); iii) Sterilisation validation report (including the sterilisation protocol, sterilisation standards applied, sterility assurance level, sterilisation revalidation report); iv) QMS certificate(s).

Types of change	Documents to be submitted
4.2 Changes in design or specifications of a medical device	
(a) All changes to the control mechanisms, operating principles and/or design characteristics of a medical device. *Example:* *Change from a quantitative assay to a qualitative assay.* *Addition of a footswitch to an X-ray system that previously do not operate via a footswitch mechanism.*	i) Revised QMS certificate(s) (if applicable); ii) Pre-clinical studies; iii) Risk analysis; iv) Clinical studies (if applicable); v) Software validation report (for software, if applicable); vi) Detailed summary of software changes (for software, if applicable).
(b) Changes that only involves a design change that does not affect the safety or performance of the medical device (e.g. changes that improve the medical device ergonomics, aesthetic modification of the medical device).	i) Revised QMS certificate(s) (if applicable); ii) Risk analysis; iii) Usability testing report (if applicable).
(c) All changes in specifications (including shelf life and stability) of a medical device.	i) Revised QMS certificate(s) (if applicable); ii) Pre-clinical studies (if applicable); iii) Clinical safety report (if applicable); iv) Risk analysis; v) Software validation report (for software, if applicable); vi) Detailed summary of software changes (for software, if applicable).
(d) Change to software that affect safety and performance of the device such that the treatment or diagnosis of the patient is altered. *Example:* *Upgrade of software version changes the performance characteristics like specificity or sensitivity of the diagnostic medical device.*	i) Revised QMS certificate(s) (if applicable); ii) Risk analysis; iii) Software validation report; iv) Detailed summary of software changes.

Types of change	Documents to be submitted
4.3 Changes to materials in a general medical device	
(a) All changes to biological materials that involve a change in type, source, processing and/or supplier of cells, tissues and/or derivatives of animal, human, microbial or recombinant origin without a change in the intended purpose of the biological material. *Example:* *Change in source of hyaluronic acid from Streptococcus zooepidemicus to Streptococcus equi.*	i) Revised QMS certificate(s) (if applicable); ii) Pre-clinical studies, including biological safety data; iii) Clinical safety report (if applicable); iv) Information of sources/donors; v) Risk analysis;
(b) All changes to materials or material formulation (of non-biological origin), including changes to medical device coating or surface modification techniques, that involve materials that make direct/indirect contact with body tissues and fluids, or are absorbed by the body. *Example:* *Replacement of catheter surface coating from PEBA to PEEK.*	i) Revised QMS certificate(s) (if applicable); ii) List of materials making direct/ indirect contact with human body; iii) Pre-clinical studies; iv) Clinical safety report (if applicable); v) Risk analysis.
(c) All changes to materials that are used for shielding in medical devices emitting ionising radiation. *Example:* *Change in shielding material of X-ray system from lead to tungsten.*	i) Revised QMS certificate(s) (if applicable); ii) Information on radiation source; iii) Information on materials for shielding of radiation; iv) Radiation safety test/test report; v) Risk analysis.
(d) All changes to the radiation source (e.g. radioisotopes).	i) Revised QMS certificate(s) (if applicable); ii) Information on radiation source; iii) Radiation safety test/test report; iv) Risk analysis.

Types of change	Documents to be submitted
4.4 Changes to materials in an in-vitro diagnostic (IVD) medical device	
All changes to the radiation source (e.g. radioisotopes in radioimmunoassay).	i) Revised QMS certificate(s) (if applicable); ii) Pre-clinical performance evaluation data; iii) Clinical performance evaluation data; iv) Information on source of material; v) Radiation safety test/test report; vi) Risk analysis.
4.5 Changes to ancillary medical devices information	
(a) If within the medical device list of configurations, the change only— i) involves the addition or reduction of new medical devices of the same design OR ii) involves addition of a new medical device with design change that does not affect the safety or performance of the medical device (e.g. changes that improve medical device ergonomics, aesthetic modification of the medical device).	i) Justification for addition of medical device(s) to be grouped within the medical device group; ii) List of configurations of medical devices; iii) Regulatory approval documents from the recognized countries (if applicable); iv) Medical Device information; v) Pre-clinical studies (where applicable); vi) Software validation report (for software, if applicable); vii) Manufacturing information (if applicable).
(b) All changes to the medical device that: i) involve changes of medical device name and/or medical device identifier and/or brief description of item(s) in the list of configurations; OR ii) involve changes of medical device propriety name due to company acquisition/merging	i) Declaration from manufacturer to state that there is no change to medical device in all aspects, including intended use, technical specifications; ii) List of configurations of medical device;

The guiding principles for identification of Administrative Changes of various types of change to medical devices are presented in Table 6. Applicant is required to provide the documents for each change that occur to the ancillary medical device components as outlined in the table.

Table 6: Administrative Changes

Types of change	Documents to be submitted
5.1 Change in manufacturing facility, process and quality management system (QMS)	
(a) All changes to certificates for manufacturing and sterilization facilities that - i) involves an update of certificate QMS validity date only OR; ii) change in scope of the QMS certification which affect the medical device (that is not due to safety, and/or performance of the medical device) OR; iii) involves a cancellation of QMS scope on the certificate for any of the multiple existing manufacturing facilities that is related to the medical device (that is not due to safety, and/or performance of the medical device)	Valid QMS certificate and report.
5.2 Changes in design or specifications of a medical device	
All changes in software related to design or specifications of a medical device requires new endorsement application, (a) Unless the change only involves a change to software version number that does not affect safety	i) Software validation report. ii) Detailed summary of software changes. The change notification for this item may be consolidated for a maximum period of 6 months.

Types of change	Documents to be submitted
or performance of the medical device, such as— i) software changes solely to correct an inadvertent software error which does not add new functions, does not pose any safety risk and is intended to bring the system to its original specification; ii) software changes which augment interfacing to other non-medical peripherals such as printers or VDUs and which has no diagnostic or therapeutic function; or iii) software changes which only modify the appearance of the user interface with no risk to diagnostic or therapeutic function of the medical device.	
5.3 Changes to ancillary medical devices information	
(a) All deletions of a medical device from medical device listing *Example:* *The change only involves the reduction in the number of medical devices in the grouping due to obsolescence and not due to safety or performance considerations.*	i) Justification for deletion of medical device(s) to be grouped within the medical device; ii) Declaration from manufacturer to state that there is no change to medical device in all aspects, including intended use, technical specifications; iii) List of configurations of medical devices
(b) A change in regulatory status on rejection or withdrawal in any recognized countries for any medical device.	i) Existing regulatory approval; ii) Documents from relevant regulatory authorities citing reason for the change in regulatory status; iii) Reason for company to withdraw from regulatory authorities (if applicable).
(c) All changes in the manufacturer information that only- i) involve changes in the manufacturer's name and	i) Revised QMS certificate(s) ii) Medical Device labelling stating changes for each amended section (if applicable);

Types of change	Documents to be submitted
address; OR ii) involve changes in the manufacturing site's name only; with no change in the manufacturing site's address	iii) Declaration that there is no change to manufacturing and sterilization process;
(d) All changes to the medical device that: i) involves changes of medical device name and/or medical device identifier and/or brief description of item(s) in the list of configurations; OR ii) involve changes of medical device propriety name due to company acquisition/merging	i) Declaration from manufacturer to state that there is no change to medical device in all aspects, including intended use, technical specifications; ii) List of configurations of medical device;

6.2 SUMMARY TABLE OF CHANGES

The following provides guidelines on completing the Summary Table of Change Notification.

(a) This summary table is to be completed and submitted for all change applications.

(b) List the proposed changes, according to the "category of change", to the registered medical device(s) in the summary table below. All applicable types of changes are to be included; any change not specified in this table will not be included for the change notification.

(c) Information to be included in the table is explained below:

i) **Type of changes:** Please state clearly the **type of change**, **category of change** and **reference number of the endorsement letter of ancillary medical device**

- With reference to the 'type of changes' categories in 6.1, highlight the type of change proposed.
- Specify the **reference number of the endorsement letter of ancillary medical device** included in this change
- ***NOTE*** *All applicable types of changes are to be included. If the types of change proposed affects/results in another type of change, all types of changes shall be included. For example, change in material of medical device and change (update) of labelling often occur together.*

ii) **Present:** Please state clearly the current scope and aspects of the medical device to be changed.

iii) **Proposed:** Please state clearly the proposed scope and aspects of change.

iv) **Reason for change:** Please state clearly the rationale for the proposed scope and aspects of change.

v) **Status of proposed change in recognized countries:** Please state the reference agency status (approved/authorized for marketing) for these proposed changes.

(a) Type of changes	(b) Present	(c) Proposed	(d) Reason for change	(e) Status of proposed change in recognised countries
Type of change: *e.g. Change in material: Delivery tube material changed from polyvinyl chloride(PVC) to silicone* **Category of change:**	*Delivery tube material: polyvinylchloride (PVC)* **Endorsement Letter Reference No:** **List of medical device** i) ii) iii)	*Delivery tube material: silicone*	*Improve patient safety by changing to DEHP-free tubing material*	*Australia TGA – pending* *EU Notified Body – approved/authorised for marketing* *Health Canada – not supplied* *US FDA – not supplied* *Japan MHLW – not supplied*
Type of change: *e.g. Change in manufacturing facility* **Category of change:**	*Name and address of current manufacturing facility A* **Endorsement Letter Reference No:** **List of medical device** i) ii) iii)	*Name and address of new manufacturing facility B*	*Reason for to move manufacturing activities from facility A to facility B*	*Australia TGA – pending* *EU Notified Body – approved/authorised for marketing* *Health Canada – not supplied* *US FDA – not supplied* *Japan MHLW – not supplied*

6.3 FEES IMPOSED BY MDA

The fees stipulated below are per application basis. Mode of payment: BayarNow

No	Type of Change	Fee (RM)
1.	Technical Change	150
2.	Administrative Change	30

**Upon receiving a complete application, MDA's Finance Unit will issue an invoice for the for the payment fee to the applicant via email. The invoice will only be sent to the applicant's email address stated in the application form.*

**Applicant can visit BayarNow at http://bayarnow.mda.gov.my to make the payment. CASH WILL NOT BE ACCEPTED. We will not be responsible for the cash sent or brought to MDA.*

6.4 EVALUATION TIMELINE

The following table specifies the evaluation duration (counted in working days upon receipt of complete application) for the application of endorsement letter of Ancillary Medical Device Component.

No	Type of Change	Evaluation Timeline (working days)
1.	Technical Change	60
2.	Administrative Change	30

The Authority may, in writing, at any time after the receipt of an application, request the applicant to give to the Authority within 90 days, particulars or document on the application or sample of the medical device.

If any additional information, particulars or document, or sample of the medical device required is not given by the applicant within the period specified in the request or any extension of time granted by the Authority, the application shall be deemed to be withdrawn and shall not be further proceeded with, but without affecting the right of the applicant to make fresh application.

APPENDIX 7: RELEVANT POST-MARKETING ACTIVITIES FORM

1. Incident Reporting Form for Combination Product

INCIDENT REPORTING FORM FOR COMBINATION PRODUCT

This reporting form is to be used by establishment/product registration holder (PRH) to submit mandatory problem report relating to any incident involving its product recorded inside or outside Malaysia only if the product / medical device is registered in Malaysian market. Please submit completed form with Reference Number to MDA and NPRA via e-mail to:

SURVEILLANCE & COMPLAINTS SECTION, CENTRE OF COMPLIANCE & QUALITY CONTROL National Pharmaceutical Regulatory Agency (NPRA), Lot 36, Jalan Universiti (Jalan Profesor Diraja Ungku Aziz), 46200 Petaling Jaya, Selangor. E-mail: qpr@npra.gov.my	**POST MARKET & SURVEILLANCE VIGILANCE UNIT** Medical Device Authority (MDA), Level 6, Prima 9, Prima Avenue II, Blok 3547, Persiaran APEC, 63000 Cyberjaya, Selangor. E-mail: mpr@mda.gov.my

Reference no.*			
Type of report*	☐ Initial ☐ Follow-Up / Update ☐ Final		
Location of Incident*	☐ Inside Malaysia ☐ Outside Malaysia		
Location Information			
Name of institution			
Address			
Telephone No.		E-mail	
Contact person at site of incident			
Product Information*			
Product name			
Brand name			
Manufacturer name			
Batch / Lot / Serial No.			
Registration No.			

Manufacturing date		Expiry date	
Incident Information			
Report category*	☐ Quality defect, failure or deterioration of product/device effectiveness / Non-compliance or inadequacy in labelling/ packaging/Instructions for Use (IFU) and/or other regulatory requirement ☐ Led to death or injury, or serious deterioration in the state of health of a person / May led to death or serious deterioration in the state of health of a person or could do so were the incident to recur ☐ Serious threat to public health		
Description of incident*			
Date of incident*			
Date of establishment awareness on the incident*			
User at time of incident	☐ Healthcare provider ☐ Patient ☐ Others, please specify: _____		
Usage of product device	☐ Initial Use ☐ Single use / Disposables ☐ Re-use of single use ☐ Reuse of Reusable ☐ Re-serviced / Refurbished ☐ Others		
Current status of product	☐ Implanted ☐ Explanted ☐ Quarantine at user's site ☐ Quarantine at establishment's site ☐ Disposed ☐ Returned to manufacturer ☐ Others, please specify: _____		
List of other product/ devices involved in the incident (if applicable)			

Result of manufacturer investigation*			
Corrective Action and Preventive Action (CAPA) has been taken by the manufacturer*	☐ Yes ☐ No, please justify: _____		
IN MALAYSIA, this incident will lead towards *	☐ Field Corrective Action (FCA) / CAPA ☐ Recall ☐ No action required		
Was this incident reported to other Regulatory Authorities?*	☐ Yes, please select the Competent Authority the incident has been reported to: ☐ US FDA ☐ EU ☐ Australia ☐ Canada ☐ Japan ☐ Others, please specify: _____ ☐ No		
Details of Reporting Person			
Person name			
Establishment name / Product Registration Holder*			
Establishment License No. *(Under Act 737) *For medical device only*			
Address			
Telephone No.		Fax No.	
E-mail			
Patient Information *(if available)*			
Gender		Age	

Patient outcome*	☐ Death ☐ Life threatening ☐ Hospitalised ☐ Congenital anomaly ☐ Required intervention to prevent permanent impairment / damage ☐ Others, please specify: _____

Other Information	
Manufacturer / authorised representative aware of other similar incident (frequency, number)	
Countries where this similar incident occurred	

I attest that the information provided by the user / manufacturer submitted is true and correct. [1]*

Signature : _____

Name of reporting person : _____

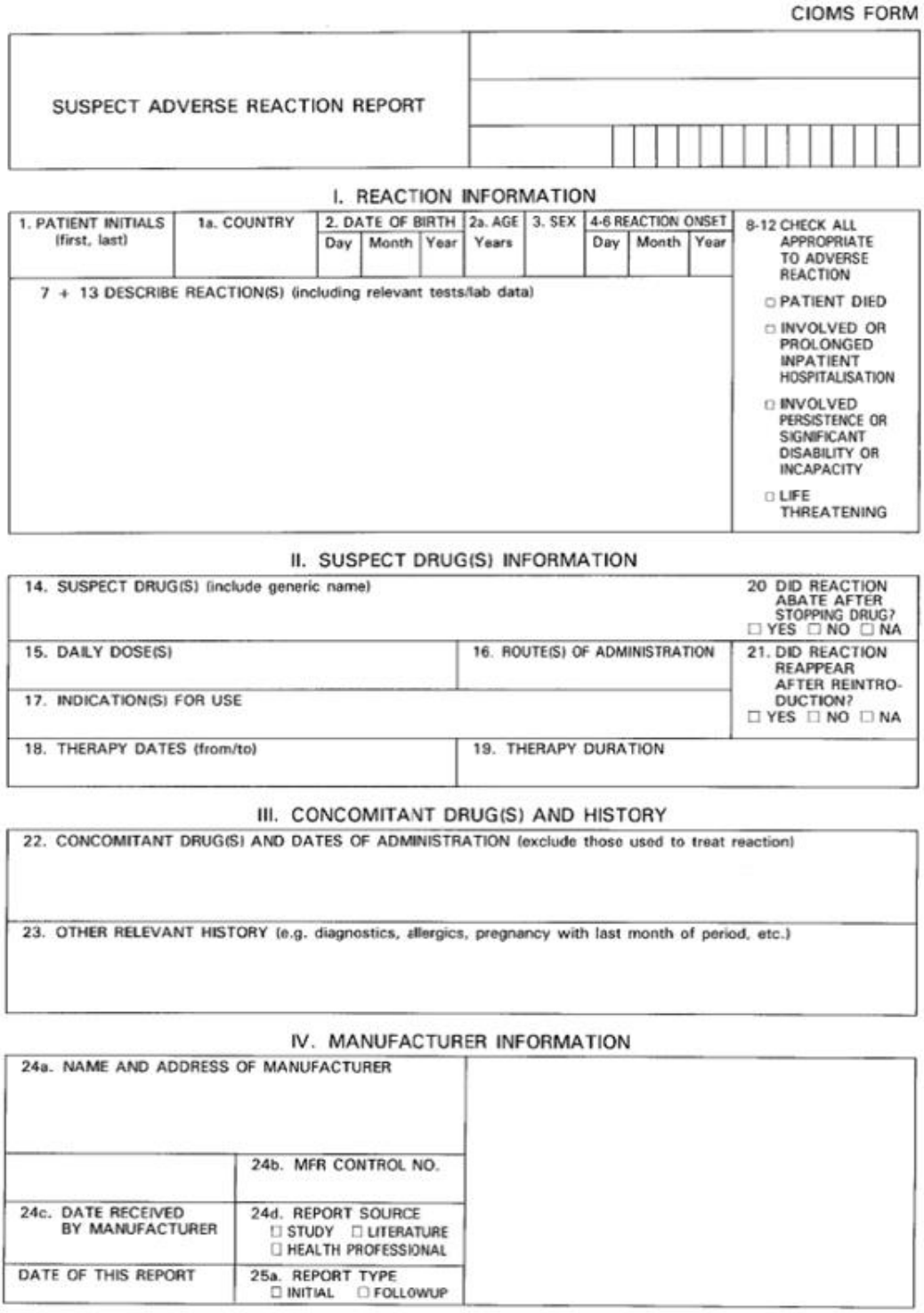
Date of this notification : _____

Establishment stamp : _____

[1] *Submission of this report does not constitute an admission that the user, establishment, or product caused or contributed to the incident.*

** All fields are required.*

2. CIOMS Form for Adverse Drug Reaction Reporting



CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE Years	3. SEX	4-6 REACTION ONSET Day	Month	Year	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
										☐ PATIENT DIED ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION ☐ INVOLVED PERSISTENCE OR SIGNIFICANT DISABILITY OR INCAPACITY ☐ LIFE THREATENING

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)		20 DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA
15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION	21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA
17. INDICATION(S) FOR USE		
18. THERAPY DATES (from/to)	19. THERAPY DURATION	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER		
	24b. MFR CONTROL NO.	
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE ☐ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL	
DATE OF THIS REPORT	25a. REPORT TYPE ☐ INITIAL ☐ FOLLOWUP	

APPENDIX 8: LIST OF RELEVANT REFERENCES

A) MEDICAL DEVICE AUTHORITY (MDA)

7.1 Legislation

1. Medical Device Act 2012 (Act 737)
2. Medical Device Regulations 2012

7.2 Circular Letter

1. Circular Letter PBPP No.2/2014: Conformity Assessment Procedures For Medical Device Approved By Recognized Countries
2. Circular Letter PBPP No.3/2017: Implementation And Enforcement Of Guideline For Registration Of Drug-Medical Device And Medical Device-Drug Combinations Products (Revision 1)

7.3 Guidance Document

1. MDA/GL/MD-01 (Third Edition): How to Apply for the Medical Device Registration under Act 737
2. MDA/GD/0005: Product Grouping
3. MDA/GD/0006: Definition of Medical Device
4. MDA/GD/0007: The Essential Principles of Safety and Performance of Medical Devices
5. MDA/GD/0008: Common Submission Dossier Template (CSDT)
6. MDA/GD/0009: Rules of Classification for General Medical Devices
7. MDA/GD/0014: Mandatory Problem Reporting
8. MDA/GD/0020: Change Notification for Registered Medical Device
9. MDA/GD/0025: Declaration of Conformity (DoC)
10. MDA/GD/0026: Requirements for Labelling of Medical Devices
11. MDA/GD/0031: Conformity Assessment for Medical Device

B) NATIONAL PHARMACEUTICAL REGULATORY AGENCY (NPRA)

7.1 Legislation

1. Poisons Act 1952
2. Sales of Drugs Act 1952 and Regulations
3. Control of Drugs and Cosmetics Regulations 1984 (CDCR 1984)
4. Dangerous Drugs Act 1952 (DDA 1952)

7.2 Directives & Circulars for Combination Products

1. Directive Letter Bil 4/2017: Direktif Kuatkuasa Pemakaian Guideline For Registration of Drug-Medical Device and Medical Device-Drug Combination Product
2. Circular: Lanjutan Tarikh Pelaksanaan Pemakaian Guideline For Registration Of Drug-Medical Device And Medical Device-Drug Combination Products
3. Circular: Keperluan Acknowledgement Receipt/ Endorsement Letter bagi Pendaftaran Baru/ Pendaftaran Semula Produk Kombinasi Ubat-Peranti Perubatan (Drug-Medical Device Combination)

7.3 Guidance Document

1. Drug Registration Guidance Document (DRGD)
2. Malaysian Guidelines on Good Pharmacovigilance Practices (GVP) for Product Registration Holders
3. Malaysian Variation Guideline For Biologics (MVGB)
4. MALAYSIAN VARIATION GUIDELINE FOR PHARMACEUTICAL PRODUCTS (MVG)