MINISTRY OF HEALTH MALAYSIA

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

First Edition – 15th March 2017

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Medical Device Authority
Ministry of Health Malaysia

PREAMBLE

- This present guideline serves as a guidance for the submission of registration application of drug-medical device/ medical device-drug combination products.

- Drug-medical device/ medical device-drug combination products are regulated according to the classification whether as drug or medical device.

- 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.

- Any drug substances used as ancillary to medical device which is listed as a scheduled poison shall be regulated in accordance with the Poison Act 1952.

- 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 combination products registration application.

- 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 2018

- Any enquiry on registration of combination products may refer to the relevant agency:

1. Secretary,
   Drug Control Authority,
   National Pharmaceutical Regulatory Agency,
   Ministry of Health Malaysia,
   Lot 36, Jalan Universiti,
   46200 Petaling Jaya, Selangor.
   Tel : +603-78835400 Fax :03-7956 2924
   E-mail : helpdesk@npra.gov.my
   Portal : http://npra.moh.gov.my/

2. Chief Executive
   Medical Device Authority (MDA),
   Ministry of Health Malaysia,
   Level 5, Menara Prisma,
   No. 26, Jalan Persiaran Perdana,
   Precint 3, 62675 Putrajaya.
   Tel : +603-8892 2400 Fax : +603-8892 2500
   E-mail : mdb@mdb.gov.my
   Portal : http://www.mdb.gov.my

GLOSSARY

Agency:

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

Ancillary Dossier:

Dossier required by the secondary agency

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

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

Secondary Agency:

Agency that regulate 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
NPRA	National Pharmaceutical Regulatory Agency
PSUR	Periodic Safety Update Report

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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;
ii. Two or more separate products packaged together 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 products 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 products (example: first aid kit consist of medical device and non-scheduled poison products)

Appendix 1 shows an illustrative table of the example of Drug-Medical Device/Medical Device-Drug Combination Product classification

Prior to registration, an applicant may apply classification application to NPRA through product classification form (BPFK 300-1) which is available at http://npra.moh.gov.my

2.0 REGISTRATION PROCESS OF COMBINATION PRODUCTS

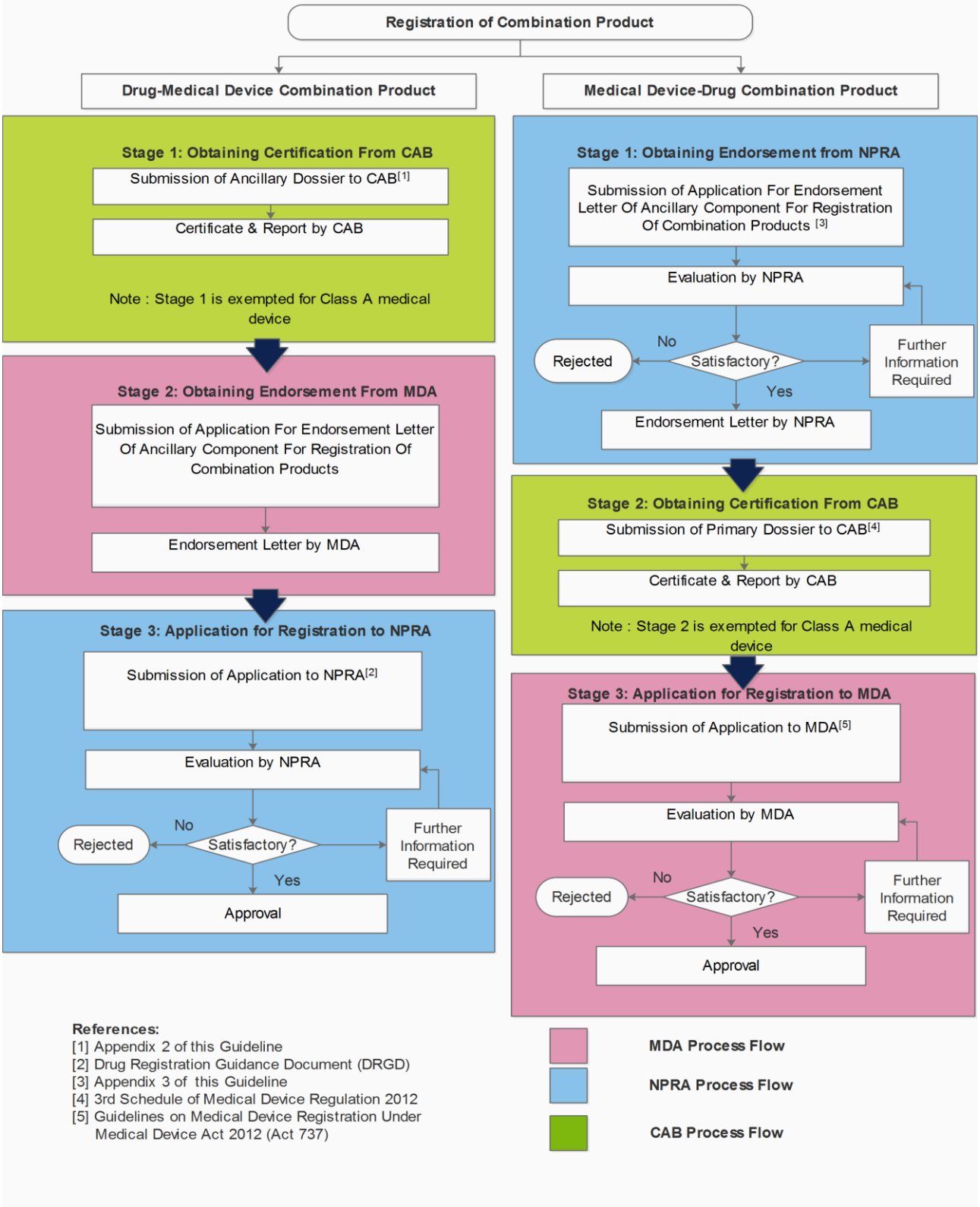
The primary agency for registration of combination product is based on the primary mode of action/the principal mechanism of action by which the claimed effect or purpose of the product is achieved:

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

ii. Medical devices 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 products is illustrated in **Figure 2**.

Figure 2 : Flow Of Registration Process Of Combination Products



*Note : Applicant may submit application for endorsement letter and registration of combination product concurrently to both secondary and primary 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.

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 3 stages:

i. Stage 1 – Obtaining Certification from CAB
ii. Stage 2 – Obtaining Endorsement from MDA
iii. Stage 3 – Application For Registration to NPRA

All the stages shall be completed, with the exception of Class A medical device (refer MDA GD-04: The rules of classification for general medical devices); in which it is exempted from Stage 1.

Stage 1: Obtaining Certification From CAB

The ancillary dossier in which the ancillary medical device component falls under Class B, C and D against the Classification of Medical Device found in First Schedule Medical Device Regulation 2012 shall be prepared in the format as specified in Appendix 2 and shall be submitted to CAB. Ancillary component that falls under Class A is exempted from this preliminary Stage 1 process.

Evaluation on ancillary component shall be done by CAB. CAB shall issue a certificate and report upon satisfactory review of ancillary component

Stage 2: 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 Products (Appendix 4: Form for Endorsement Letter of Ancillary Component for Registration of Combination Products)
ii. Ancillary Dossier (Appendix 2: Ancillary Medical Device Dossier Requirement for Drug- Medical Device Combination Product)
iii. Certificate and report issued by CAB

Ancillary medical device component that falls under Class A medical device is not required to submit document as specified in (ii) and (iii) above.

MDA shall issue an endorsement letter upon satisfactory review.

Stage 3: Application for Registration to NPRA

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

i. Certificate and report issued by CAB (not applicable for Class A medical device)
ii. Endorsement letter issued by MDA
iii. Data on drug in accordance to DRGD Section B: Product Registration Process

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 3 stages:

i. Stage 1 - Obtaining Endorsement from NPRA
ii. Stage 2 - Obtaining Certification from CAB
iii. Stage 3 - 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 Products (Appendix 4: Form for Endorsement Letter of Ancillary Component for Registration of Combination Products)
ii. Ancillary Dossier (Appendix 3: Ancillary Drug Dossier Requirement for Medical Device-Drug Combination Product)

NPRA shall issue an endorsement letter upon satisfactory evaluation.

Stage 2: Obtaining Certification from CAB

Applicant shall submit the primary dossier to CAB to undergo conformity assessment. CAB shall issue certificate and report upon satisfactory conformity assessment.
Class A medical device is exempted from Stage 2.

Stage 3: 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 in accordance with the guideline *MDA/GL/MD-0*1 on How to Apply for Medical Device Registration under Medical Device Act 2012 (Act 737) with the following documents:

i. Endorsement letter issued by NPRA
ii. Certificate and report issued by CAB

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

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	**Dossier Requirement for Medical Device Component**
Drug-Medical Device Combination Product	Refer to DRGD, Appendix 2: Requirements for Product Registration	Refer to Appendix 2: Ancillary Medical Device Dossier Requirement for Drug-Medical Device Combination Product
Medical Device-Drug Combination Product	Refer to Appendix 3: Ancillary Drug Dossier Requirement for Medical Device-Drug Combination Product	Refer to MDA/GD-04: Common Submission Dossier Template First Edition March 2014

4.0 TIMELINE FOR REGISTRATION OF COMBINATION PRODUCTS

The following table specifies the duration (counted in working days upon receipt of complete application) that are 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>Refer to CAB Evaluation Timeline</td><td>Evaluation timeline by NPRA:<table><tr><th>Category</th><th>Duration</th></tr><tr><td>New Chemical Entity</td><td>245</td></tr><tr><td>Biologic Component</td><td>245</td></tr><tr><td>Generics (Scheduled Poison)</td><td>90</td></tr><tr><td>Generics (Non-Scheduled Poison)</td><td>90</td></tr></table></td></tr>
<tr><td>Stage 2</td><td>Evaluation timeline by MDA:<table><tr><th>Class of Medical Device</th><th>Duration</th></tr><tr><td>A</td><td>15</td></tr><tr><td>B</td><td>30</td></tr><tr><td>C</td><td>90</td></tr><tr><td>D</td><td>110</td></tr></table></td><td>Refer to CAB Evaluation Timeline</td></tr>
<tr><td>Stage 3</td><td>Evaluation timeline by NPRA:<table><tr><th>Category</th><th>Duration</th></tr><tr><td>New Drug Products</td><td>245</td></tr><tr><td>Biologics</td><td>245</td></tr><tr><td>Generics (Scheduled Poison)</td><td>210</td></tr><tr><td>Generics (Non-Scheduled Poison)</td><td>210</td></tr></table></td><td>Evaluation timeline by MDA:<table><tr><th>Class of Medical Device</th><th>Duration</th></tr><tr><td>A</td><td>30</td></tr><tr><td>B</td><td>60</td></tr><tr><td>C</td><td>180</td></tr><tr><td>D</td><td>220</td></tr></table></td></tr>
</table>

5.0 FEES FOR REGISTRATION OF COMBINATION PRODUCTS

Every application for registration shall be accompanied with a fee imposed by the respective agencies as specified in the table 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 medical device-drug combination product:

Category of ancillary drug component	**Processing Fees**
1. New Chemical Entity 2. Biologic Component 3. Generics (Scheduled Poison) 4. Generics(Non-Scheduled Poison)	RM 1,000.00

5.2 FEES IMPOSED BY MDA

Application shall be accompanied with fees as specified to Fifth Schedule of Medical Device Regulation 2012.

Medical Device-Drug Combination Product (RM)		**Drug-Medical Device Combination Product (RM)**
Application Fee	Registration Fee	Administration Fee
750	5000	100

5.3 FEES IMPOSED BY CAB

Refer Circular Letter of Medical Device Authority No.2 Year 2014.

6.0 CHANGES/VARIATION TO PARTICULARS OF A REGISTERED COMBINATION PRODUCT

6.1 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 to Section 5.2 : Amendments To Particulars Of A Registered Product of DRGD.

Application for changes to particulars of ancillary medical device component for a registered drug-medical device combination product shall be submitted to MDA for endorsement letter. The endorsement letter shall then be required to be sent to NPRA for notification.

6.2 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 to 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 for endorsement letter. The endorsement letter shall then be required to be sent to MDA for notification.

APPENDIX 1: THE ILLUSTRATIVE TABLE OF DRUG-MEDICAL DEVICE/MEDICAL DEVICE-DRUG COMBINATION PRODUCT

Table 1 : Example of Drug-Medical Device Combination Product Classification

NO	PRODUCT	INTENDED PURPOSE/ INDICATION AND MODE OF ACTION (MOA)	CATEGORY	CUSTODIAN AGENCY
1.	**Drug-Eluting Beads** (Produced from biocompatible polyvinyl alcohol hydrogel modified with sulphonate groups in phosphate buffered saline.)	It is an embolic agent which is intended to be loaded with a chemotherapy agent, eg. doxorubicin for the purpose of treatment of malignant hyper vascularized tumour(s) by embolisation of vessels and occlusion of blood flow supplying malignant hyper vascularized tumour(s) and as a secondary action, delivers/elutes a local, controlled, sustained dose of the chemotherapy agent directly to the tumour(s).	If the beads are sold separately from the drug, it will be classified as **MEDICAL DEVICE** If the beads and drug are packaged and sold together, it will be classified as **Drug-Medical Device combination product regulated as DRUG**	**MDA** **NPRA**
2.	**Drug - Delivery Products Regulated as Drug Products** (eg. insulin prefilled pen/ syringes, asthma inhalers, intrauterine contraceptives whose primary purpose is to release progestogens)	To administer pharmacologically active substance	**Drug-Medical Device combination product regulated as DRUG** **NOTE:** The device component will be regulated on a case to case basis.	**NPRA**

Table 2 : Example Of Medical Device-Drug Combination Product Classification

NO	PRODUCT	INTENDED PURPOSE/ INDICATION AND MODE OF ACTION (MOA)	CATEGORY	CUSTODIAN AGENCY
1.	**Soft tissue filler/ Dermal filler**	To correct cutaneous contour deformities of the skin (e.g., moderate to severe facial wrinkles and folds such as nasolabial folds, scars), particularly in cases of aging or degenerative lesions.	**MEDICAL DEVICE** (If it incorporates an ancillary local anaesthetic eg. lidocaine, it will be classified as a **Medical Device-Drug combination product regulated as MEDICAL DEVICE)**	**MDA**
2.	**Synthetic fluid tissue reconstructive material**	As a submucosal implant in the urinary tract for urinary incontinence or vesicoureteral reflux. It may also be injected into the vocal cords to treat the effects of paralysis, atrophy, or scarring. After application, this device cannot be reused.	**MEDICAL DEVICE** (If it incorporates an ancillary pharmacologically active substance eg. local anaesthetic such as lidocaine, it will be classified as a **Medical Device-Drug combination product regulated as MEDICAL DEVICE)**	
3.	**Dental Products**			
	i. Root canal filling incorporating antibiotic	To seal the canal and disinfect the dentinal walls by diffusing through dentine. The antibiotic provides ancillary actions as bactericidal antibiotic and anti-inflammatory	**Medical Device-Drug combination product regulated as MEDICAL DEVICE**	**MDA**

NO	PRODUCT	INTENDED PURPOSE/ INDICATION AND MODE OF ACTION (MOA)	CATEGORY	CUSTODIAN AGENCY
		agent to assist in reducing pain and in maintaining a bacteria-free environment within the root canal.		
4.	**General Purpose Surgical or Barrier Drapes** (A sterile protective covering made of natural or synthetic materials, or both.)	To isolate a site of surgical incision or a surgical field from contamination (e.g., microbial, substance) in various clinical settings (e.g., in an operating room or catheterization laboratory). The device may also be used to protect a patient from heat/flame during a surgical procedure. This is a reusable or single use device.	**MEDICAL DEVICE** (If it incorporates an ancillary pharmacologically active substance, it will be classified as **Medical Device-Drug combination product regulated as MEDICAL DEVICE)**	**MDA**
5.	**Drug-Eluting Stents (DES)**	For use in angioplasty or coronary stenting procedures.	**Medical Device-Drug combination product regulated as MEDICAL DEVICE**	**MDA**
6.	**Drug-Eluting Beads** (Produced from biocompatible polyvinyl alcohol hydrogel modified with sulphonate groups in phosphate buffered saline.)	It is an embolic agent which is intended to be loaded with a chemotherapy agent, eg. doxorubicin for the purpose of treatment of malignant hyper vascularised tumour(s) by embolisation of vessels and occlusion of blood flow supplying malignant hyper vascularized tumour(s) and as a secondary action, delivers/elutes a local, controlled, sustained dose of the	If the beads are sold separately from the drug, it will be classified as **MEDICAL DEVICE** If the beads and drug are packaged and sold together, it will be classified as **Drug-Medical Device**	**MDA** **NPRA**

NO	PRODUCT	INTENDED PURPOSE/ INDICATION AND MODE OF ACTION (MOA)	CATEGORY	CUSTODIAN AGENCY
		chemotherapy agent directly to the tumour(s).	**combination product regulated as DRUG**	
7.	**General-body orifice lubricant incorporating an ancillary local anaesthetic** (e.g.lidocaine)	Lubricant intended to facilitate entry of a diagnostic or therapeutic device into a body orifice by reducing friction between the device and the body; Lubricant during catherisation, probing, endoscopy, changing fistula catheters, intubation, and prevention of iatrogenic injuries to the rectum and colon.	**Medical Device-Drug combination product regulated as MEDICAL DEVICE**	**MDA**
8.	**Enteral Feeding Kit** *(containing Iodine Pack drug)*	A collection of sterile devices that includes tubing and other materials intended to administer nutrient liquids directly into the stomach, duodenum, or jejunum of a patient by means of gravity or an enteral pump.	**Medical Device-Drug combination product regulated as MEDICAL DEVICE**	**MDA**

*Note: Table 1 and Table 2 are examples of combination product classification. These examples are non-exhaustive.

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

The following classification for the ancillary medical device component based on the risk classification of medical device shall be required for the submission of the dossier:

a. Class B
b. Class C
c. Class D

Refer to MDA/GD-04 The Rule of Classification for General Medical Device.

Table 3: General Requirements for Ancillary Medical Device Dossier

Part	**Section**	**Level Of Risk Classification Of Ancillary Medical Device Component**		
		Class B (Low-Moderate Risk)	**Class C (High-Moderate Risk)**	**Class D (High Risk)**
1	Executive Summary	√	√	√
	a) An overview which covers an introductory descriptive information on the medical device, the intended uses and indications for use of the medical device, novel features and a synopsis of the content of the CSDT;	√	√	√
	b)Commercial marketing history which covers the list of countries where the medical device is marketed and the dates of introduction into those countries	√	√	√
	c)Intended uses and indications in its label	√	√	√
	d)List of regulatory approval or marketing clearance obtained including the registration status, intended use and	√	√	√

	indications of the medical device in other countries; copies of certificates or approval letters from each country and declaration on labelling, packaging and instructions for use			
	e)status of any pending applications for regulatory approval or marketing clearance	X	X	√
	f) important safety and performance related information, which shall include :			
	(i) summary of reportable adverse events and field corrective actions;	√	√	√
	(ii) a description of the medical device if the medical device contains animal or human cells, tissues and/or derivatives thereof, rendered non-viable cells, tissues and/or derivatives of microbial or recombinant origin and/or irradiating components, ionising or non-ionising (if applicable)	√	√	√
2	Relevant essential principles and rule used to demonstrate conformity*	√	√	√

*note : The Essential Principles And Rule Used To Demonstrate Conformity shall be prepared in a form of a checklist that is in accordance with Schedule 1, Appendix 1 of Medical Device Regulation 2012. Example of Essential Principles Conformity Checklist can be found in Schedule 2, Table 1 of Medical Device Regulation 2012)

Ancillary Medical Device components that have been approved by recognized countries as specified in Circular Letter No. 2 Year 2014 are allowed to undergo Conformity Assessment by way of Verification prescribed in the Circular Letter.

APPENDIX 3: ANCILLARY DRUG DOSSIER REQUIREMENT FOR MEDICAL DEVICE-DRUG COMBINATION PRODUCT

Part I: General Information	
No.	**Section A: Combination Product Particulars**
1.	Combination Product Name
2.	Name & Strength of Active Substance and Excipient
3.	Dosage Form
4.	Product Description
5.	Pharmacodynamics
6.	Pharmacokinetics
7.	Indication
8.	Recommended Dose
9.	Route of Administration/Mode of Delivery
10.	Contraindication
11.	Warning and Precautions
12.	Interaction with Other Medicaments (If Applicable)
13.	Pregnancy and Lactation (If Applicable)
14.	Side Effects (If Applicable)
15.	Symptoms and Treatment of Overdose (If Applicable)
16.	Storage Condition (If Applicable)
17.	Shelf Life (If Applicable)
18.	Declaration of human/ animal origin (If Applicable)
No.	**Section B: Drug Product Formula**
1.	Batch Manufacturing Formula
No.	**Section C: Mock-up Label**
1.	General Labelling Requirement “Controlled Medicine/ Ubat Terkawal” (for Scheduled poison only unless exempted)
2.	Specific labelling requirement as stated in DRGD (if applicable)

PART II: QUALITY OF DRUG COMPONENT	
1.	Information on Development Studies
2.	Manufacturing Process and Process Controls
3.	Control of Excipients (if applicable)
	a. Specifications of Excipient
	b. Justification of Specifications (if applicable)
4.	Control of Drug Substances
	a) Nomenclature, Structure of Drug Substance, General Properties
	b) Manufacturer Name and Address
	c) Description of Manufacturing Process and Process Controls (only for biologic component)
	d) Controls of Materials (only for biologic component)
	e) Controls of Critical Steps and Intermediates (only for biologic component)
	f) Process Validation and/or Evaluation (only for biologic component)
	g) Manufacturing Process Development (only for biologic component)
	h) Elucidation of Structure and Characteristics(only for biologic component)
	i) Impurities (only for biologic component)
	j) Specifications
	k) Batch Analysis (only for biologic component)
	l) Certificate of Analysis for TWO batches
	m) Justification of Specifications (only for biologic component)
	n) Reference Standards or Materials (only for biologic component)
	o) Container Closure System (only for biologic component)
	p) Stability (only for biologic component)
PART III: NON CLINICAL DOCUMENT (Applicable only to New Chemical Entity and Biologic Component)	
	Section A: Table of Contents
No.	**Section B: Nonclinical Overview**
1.	Overview of the Nonclinical Testing Strategy
2.	Pharmacology
3.	Pharmacokinetics
4.	Toxicology

5.	Other Non-Clinical Study
6.	Integrated Overview & Conclusions
7.	List of Literature Citations
No.	**Section C: Nonclinical Written and Tabulated Summaries**
No.	**Section D: Nonclinical Study Reports**
No.	**Section E: List of Key Literature References**
PART IV: CLINICAL DOCUMENT (Applicable only to category New Chemical Entity and Biologic Component)	
No.	**Section A: Table of Contents**
No.	**Section B: Clinical Overview**
1.	Product Development Rationale
2.	Overview of Biopharmaceutics
3.	Overview of Clinical Pharmacology
4.	Overview of Efficacy
5.	Overview of Safety
6.	Benefits & Risks Conclusions
No.	**Section C: Clinical Summary**
1.	Summary of Biopharmaceuticals Studies and Associated Analytical Methods
2.	Summary of Clinical Pharmacology Studies
3.	Summary of Clinical Efficacy
4.	Summary of Clinical Safety
5.	Synopses of Individual Studies
No.	**Section D: Tabular Listing of all Clinical Studies**
No.	**Section E: Clinical Study Reports**

Appendix 4

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

CHECKLIST FOR SUBMISSION

DOCUMENTS	COMBINATION PRODUCT		Please tick if the document is attached
	DRUG-MEDICAL DEVICE	**MEDICAL DEVICE-DRUG**	
Ancillary Medical Device Dossier *(Appendix 2 of Guideline For Registration of Drug-Medical Device and Medical Device-Drug Combination Products)*	√ (not required for ancillary medical device Class A)	X	
Ancillary Drug Dossier *(Appendix 3 of Guideline For Registration of Drug-Medical Device and Medical Device-Drug Combination Products)*	X	√	
Report and Certificate of Medical Device Safety and Performance Assessment (CAB)	√	X	
Product catalogue	√	X	
For ancillary medical device Class A with measuring function and calibration and metrology report shall be provided.	√	X	
For ancillary medical device Class A supplied sterile, validation report shall be provided.	√	X	

The form and supporting documents can be sent either via email (in PDF format) or post to:

For Ancillary Medical Device Components	**For Ancillary Drug Components**
Chief Executive, Medical Device Authority, Level 5, Menara Prisma, Persiaran Perdana, Presint 3, 62675 Putrajaya. E-mail: mdb@mdb.gov.my	Secretary, Drug Control Authority, National Pharmaceutical Regulatory Agency, Lot 36, Jalan Universiti, 46200 Petaling Jaya, Selangor. E-mail: helpdesk@npra.gov.my

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*):

**Note:The application for obtaining endorsement letter and combination product registration must be submitted by the same applicant*

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:	
Medical Device Grouping:	
Medical Device Description:	
Brand/Model:	
Intended use of the device:	
Manufacturer's Name:	
Class : *(According to Guidance Document GD-04: The Rules of Classification For General Medical Devices)*	
Grouping List :	**(Not Applicable to single medical device)**

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 2 of Guideline For Registration of Drug-Medical Device and Medical Device-Drug Combination Products)
- Ancillary Drug Dossier (refer Appendix 3 of Guideline For Registration of 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).

ii. The device(s) conform(s) to all relevant essential principles for safety and performance, set out in the Appendix 1 of Third Schedule of the MDR 2012.

☐ **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 :