FREQUENTLY ASKED QUESTIONS (FAQS) ON DRUG-MEDICAL DEVICE COMBINATION PRODUCTS

No	FAQ
1.	**Question:** **How to apply for an Endorsement Letter Application for ancillary medical device components?** Answer: Please refer Appendix 5 of the Guideline: Endorsement Letter Application Flow Chart for Ancillary Medical Device Component
2.	**Question:** **What are the documents required for submission?** Answer: Applicant need to provide the following: • A cover letter • Application form for Endorsement Letter of Ancillary Medical Device Component (Appendix 3) • Checklist for submission of ancillary medical device component • Hardcopy documents (including ancillary medical device dossier and supporting documents) • Electronic copy (CD/thumb drive)
3.	**Question:** **Where shall the applicant submit the required documents:** Answer: 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
4.	**Question:** **What is the validity of the endorsement letter?** Answer: The endorsement letter for ancillary medical device component shall be valid provided that there are no other changes to the particulars of the ancillary device component. Any changes to the current requirements will be updated from time to time.

No	FAQ
5.	**Question:** **Registered medical devices are required to undergone conformity assessment conducted by Conformity Assessment Body (CAB) in accordance to Act 737. Does ancillary medical device component have to undergo the same process as well?** Answer: Ancillary medical devices component for a Drug-Medical Device Combination Product is not subjected to undergone conformity assessment conducted by CAB. This drug-medical device combination product 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. Refer Appendix 5: Endorsement Letter Application Flow Chart for Ancillary Medical Device Component.
6.	**Question:** **What are the examples of combination products?** Answer: Refer Table III: Medical Device-Drug-Cosmetic Interphase (MDDCI) Product Classification Decision in Drug Registration Guidance Document (DRGD) for examples of Drug-Medical Device/Medical Device-Drug Combination Product classification.
7.	**Question:** **Does the low-risk medical device component require endorsement letter as a prerequisite for drug approval by NPRA?** Answer: Endorsement letter is not mandatory for low-risk medical device components.
8.	**Question:** **Does the drug-medical device combination product endorsement letter be used for different drug approval application with the same medical device brand name?** Answer: Yes, applicant is required to list down the drug products information in the endorsement letter form and it is only applicable for the same medical device brand name and submission type, provided that the performance of the ancillary medical device component is not affected by the different drug product.

<table>
<tr><th>No</th><th>FAQ</th></tr>
<tr><td>9.</td><td>
Question:
What are the documentation requirements that qualify a drug-medical device combination product to be eligible under the abridged evaluation route?

Answer:
The documents that qualify for the application to be eligible under the abridged evaluation route are as depicted in Table 4 of the Guideline

<table>
<tr><th>No</th><th>Recognised Regulatory Authority</th><th>Approval Type</th></tr>
<tr><td>1</td><td>Therapeutic Goods Administration (TGA), Australia</td><td>TGA Medicinal licence</td></tr>
<tr><td>2</td><td>Health Canada, Canada</td><td>Health Canada Medicinal Licence</td></tr>
<tr><td>3</td><td>European Medicines Agency (EMA) or Other Competent Authorities from EU Member States

European Union (EU)</td><td>Certificate of Medicinal Products

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 Declaration of Conformity

Article 117 opinion report issued by a Notified Body</td></tr>
<tr><td>4</td><td>Pharmaceuticals and Medical Devices Agency (PMDA), Japan</td><td>Premarket approval from PMDA</td></tr>
<tr><td>5</td><td>Food and Drug Administration (FDA) USA</td><td>USFDA Approved Drug Letter

USFDA 510 (k) clearance letter

USFDA Pre-Market Approval (PMA) Letter</td></tr>
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No	FAQ
10.	**Question:** **How many references country approval is needed for ancillary medical device component to make it eligible for an abridged evaluation route?** Answer: One (1) reference country approval is sufficient for the ancillary medical device components to be eligible for an abridged evaluation route.
11.	**Question:** **What are low-risk medical devices?** Answer: Description of low-risk medical devices includes the following: 1. A non-invasive ancillary medical device component which come into contact with injured skin; intended to be used as a mechanical barrier, for compression or for absorption of exudates only, i.e. they heal by primary intent; 2. A non-invasive ancillary medical device component intended for channelling or storing a. body liquids or tissues b. liquids or c. gases for the purpose of eventual infusion, administration or introduction into the body 3. An invasive ancillary medical device component, used transiently (under 60 minutes) with respect to body orifices (other than those which are surgically invasive) and which: a. not intended for connection to an active medical device, or b. intended for connection to a Class A medical device only 4. An invasive ancillary medical device component, short term use (under between 60 minutes to 30 days) and are intended for use in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in a nasal cavity 5. Reusable surgical instruments 6. Active ancillary medical device component intended for diagnosis; intended solely to illuminate the patient's body, with light in the visible or near infra-red spectrum 7. Ancillary medical device component manufactured from or incorporating animal or human cells/tissues/derivatives thereof, whether viable or non-viable; intended to come in contact with intact human/patient skin only
12.	**Question:** **What are the examples of low-risk medical device?** Answer: Examples of low risk medical devices are asthma inhaler, syringe without needle, measuring cup, measuring spoon, medicine dropper, dosing spoon, pipette

No	FAQ
13.	**Question:** **What are medium-high risk medical devices?** Answer: Description of low-risk medical devices includes the following 1. For non-invasive ancillary medical components: a. intended to be used principally with wounds which have breached the dermis, including devices principally intended to manage the microenvironment of a wound b. intended to be used principally with wounds which have breached the dermis and can only heal by secondary intent c. intended for channelling or storing i. body liquids or tissues ii. liquids or iii. gases; and they may be connected to a medium-high risk, active medical device d. intended for use of i. channeling blood, or ii. storing or channeling other body liquids, or iii. for storing organs, parts of organs or body tissues e. blood bags f. intended to modify the biological or chemical composition of i. blood, ii. other body liquids, or iii. other liquids intended for infusion into the body; and intended for infusion into the body 2. For invasive ancillary medical components: a. Intended to be used short-term/long term and are invasive with respect to body orifices (other than those which are surgically invasive) b. Intended to be used long term in the oral cavity as far as the pharynx, in an ear canal up to the ear-drum or in a nasal cavity c. Intended to be connected to a medium-high risk, active medical device and are invasive with respect to body orifices (other than those which are surgically invasive) d. All surgically invasive devices intended for transient/short term/long term use, except reusable surgical instruments e. All implantable devices, and long-term surgically invasive devices 3. For active ancillary medical components: a. All active therapeutic ancillary device components intended to administer or exchange energy b. All active ancillary device components intended to control or monitor the performance of medium-high risk, active therapeutic devices

No	FAQ
	c. Active ancillary device components intended for diagnosis, except to be used solely to illuminate the patient's body d. intended to emit ionizing radiation and intended for diagnostic and/or interventional radiology, including devices which control or monitor such devices, or those which directly influence their performance e. intended to administer and/or remove medicinal products 4. Misc ancillary medical device components: a. Incorporating animal or human cells/tissues/derivatives thereof, whether viable or non-viable; unless such devices are manufactured from or incorporate non-viable animal tissues or their derivatives that come in contact with intact skin only b. intended specifically to be used for sterilizing medical devices, or disinfecting as the prior/end point of processing c. intended specifically to be used for disinfecting, cleaning, rinsing or, when appropriate, hydrating contact lenses d. All contraceptive ancillary medical device components
14.	**Question:** **What are the examples of medium-high risk medical devices?** Answer: Examples of medium-high risk medical devices are prefilled drug delivery systems (prefilled pen, prefilled syringe, syringe for injection, insulin injector pen), intrauterine with hormone action, implant with hormone action, Continuous Ambulatory Peritoneal Dialysis (CAPD) products with CAPD system (dialysate bag, drainage bag, transfer tubing, linking connector, disc, injection port, overpouch etc), drug eluting beads
15.	**Question:** **What are the products that are excluded from the term combination product and will be regulated as drug product only?** Answer: The examples include: i. Nasal spray with /without dosing control ii. Drug packed with dropper for internal/external use, of which it is a part of the container/packaging iii. Eye/ear/nose drop packing iv. Drug packed with applicator for skin/external body orifice (nostril, mouth, ear canal, anus and vaginal) without dosing control: e.g applicator for skin, vaginal, anus and ear canal v. Nail brush

No	FAQ
16.	**Question:** **What are the products that are excluded from the term combination product and will be regulated separately?** 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)
17.	**Question:** **Will MDA establish a communication channel for manufacturer to submit the ancillary drug-medical device combination product dossier directly to MDA?** Answer: Yes. The medical device manufacturer may submit the information/dossier via electronic copy (CD) or thumb drive directly to MDA to maintain confidentiality of the contents. The information will be regarded as confidential and will only be evaluated in support of the applications. The confidential information will not be disclosed to any third party without a written authorization from the medical device manufacturer.
18.	**Question:** **Can a risk analysis report that accounts for the finished drug-medical device combination product be accepted by MDA?** Answer: Yes, the report can be accepted for a single-entity combination product
19.	**Question:** **Can Instruction for use (IFU) or Package Insert for the finished drug-medical device combination product be accepted by MDA?** Answer: Yes, the IFU and package insert can be accepted for a single-entity combination product

No	FAQ
20.	**Question:** **What are the recommended standards used when conducting performance testing?** Answer: Depending on the type of devices, the reports shall be submitted as per standards listed below: • ISO 594-1: Conical Fittings with 6% (Lure) Taper for Syringes, Needles and Certain Other Medical Equipment - Part 1: General Specifications • ISO 594-2: Conical Fittings with 6% (Lure) Taper for Syringes, Needles and Certain Other Medical Equipment - Part 1: Lock Fittings • ISO 720: 1985: Glass - Hydrolytic Resistance of Glass Grains a 121º C - Method of Test and Classification • ISO 7864: Sterile Hypodermic Needles for Single Use • ISO 7886-1: Sterile Hypodermic Syringes for Single Use - Part 1: Syringes for Manual Use • ISO 7886-2: First Edition 1996-05-15: Sterile Hypodermic syringes for Syringes for Single Use - Part 2: Syringes for use with power driven syringe pumps • ISO 7886-3: First Edition 1996-05-15: Sterile Hypodermic syringes for Syringes for Single Use - Part 3: Auto-disposable syringes for fixed-dose immunization • ISO 11040-4: Prefilled Syringes Part 4: Glass Barrel for Injectables • ISO 10993-1: Biological Evaluation of Medical Devices - Part 1: Evaluation and Testing • ISO 11608-1: Pen-Injectors for Medical Use – Part 1: Pen-injectors – Requirements and test methods • ISO 11608-2: Pen-Injectors for Medical Use – Part 2: Needles – Requirements and test methods • ISO 11608-3: Pen-Injectors for Medical Use – Part 3: Finished Cartridge – Requirements and test methods • ISO 11608-4: Pen-Injectors for Medical Use – Part 4: Requirements and test methods for electronic and electromechanical pen-injectors • ISO 21649: Needle-Free Injectors for Medical Use - Requirements and Test Methods. • ASTM D4169:, Standard Practice for Performance Testing of Shipping Containers and Systems • ANSI/AAMI/ISO 17665-1: 2006, Sterilization of Health Care Products – Moist Heat – Part 1: Requirements for the development, validation, and routine control of a sterilization process for medical devices • ANSI/AAMI/ISO 11135-1:2007,Sterilization of Health Care Products – Ethylene oxide – Part 1: Requirements for development, validation, and routine control of a sterilization process for medical device • USP 27:2004, Sterility, Biocompatibility, Biological Tests and Assays, Bacterial Endotoxin Test (LAL), Pyrogen Test (USP Rabbit Test), or other applicable tests related to the drug/biological product and delivery of the drug/biological product

No	FAQ
	• AAMI/ANSI/ISO 11737-1:2006, Sterilization of medical devices-microbiological methods-Part 1: Determination of the population of microorganisms on product • ANSI/AAMI/ISO 11607:2006, Packaging for terminally sterilized medical devices The report of all tests mentioned above must include the objectives, methodology, results, analysis and manufacturer's conclusions.
21.	**Question:** **What are the options that can to be included in Clinical Evaluation Report to address relevant safety and performance concerns regarding the drug-medical device combination product for a combination product with approval from reference countries?** Answer: It may include the following information 1. Data on post-market clinical follow-up studies for combination product 2. Data on human factors study for the combination product 3. Excerpts from the drug common technical document (CTD) clinical overview for the combination products
22.	**Question:** **Manufacturing process has been reviewed for combination products that has obtained approval from reference countries. Does the applicant have to submit the information to MDA for approval again?** Answer: The requirements on manufacturing process can ONLY be excluded if the ancillary medical device is co-packaged together with its primary drug component **AND** received approval or marketing clearance as a medical device in reference countries. A single entity drug-medical device combination product is required to include the Manufacturing Process information as outlined in the dossier.
23.	**Question:** **Is European Union Essential Requirement Checklist (EU ERC) acceptable?** Answer: Yes, the applicant may provide EU ERC as a supporting document. List of reference standards only will NOT be accepted.

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<tr><td>24.</td><td>Question:
What is the fee imposed for endorsement letter application for drug-medical device combination product?

Answer:
The fee imposed are as follow:
<table>
<tr><th colspan="2">Drug-Medical Device Combination Product (RM)</th></tr>
<tr><td>Drug-Medical Device Combination Product <u>WITH</u> Approval from Reference Countries</td><td>Drug-Medical Device Combination Product <u>WITHOUT</u> Approval from Reference Countries</td></tr>
<tr><td>300</td><td>600</td></tr>
</table>
</td></tr>
<tr><td>25.</td><td>Question:
What is the mode of payment?

Answer:
The payment shall be made via bank draft payable to "KUMPULAN WANG PIHAK BERKUASA PERANTI PERUBATAN"

It should be submitted to:

Chief Executive
Medical Device Authority (MDA)
Ministry of Health Malaysia
Level 6, Prima 9, Prima Avenue II
Blok 3547, Persiaran APEC
63000 Cyberjaya, Selangor
(Attn: Management and Service Unit)

Note: Information on reference number and phone number of the applicant must be written at the back of the bank draft, not in the table section. Kindly print invoice / payment advice along with the bank draft according to the category. The payment of different category shall be made separately.</td></tr>
<tr><td>26.</td><td>Question:
Can MDA request additional information / document that is not described in the Guideline?

Answer:
MDA 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.</td></tr>
</table>

No	FAQ
27.	**Question:** **Where do I send my query on drug-device combination products to MDA?** Answer: You may send an email to combination.product@mda.gov.my for any query on drug-device combination product