



Guideline for Registration of Combination Products 2025

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**Medical Product Division
Bhutan Food and Drug Authority**

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1. Introduction

Combination products represent a unique and dynamic category within the healthcare industry, integrating two or more different types of medical products into a single entity. The convergence of these diverse components within a single product brings forth complex regulatory challenges that necessitate comprehensive guidelines to ensure safety, quality and efficacy/effectiveness.

This guidance document is intended to guide the applicant on registration of combination products, and the classification criteria of combination products to provide information on the regulatory framework for dealing with combination products submissions. This document should be read in conjunction with any relevant and applicable guidance documents. Combination products are either medicine-medical device combination or medical device-medicine combination.

2. Scope

- 2.1. This guideline shall apply to combination products of medical devices, medicines and biologics.

3. Objectives

- 3.1. To guide the applicant on proper classification of combination products and the submission of appropriate documents based on the combination products category.
- 3.2. To provide guidance to the regulators for consistent and uniform decision-making in the regulation of combination products.

4. Normative References

- 4.1. The Medicines Act of the Kingdom of Bhutan 2003
- 4.2. Bhutan Medicines Rules and Regulation 2019
- 4.3. Guideline for registration of medicinal products 2020
- 4.4. Guideline for registration of medical device 2022

5. Definitions

- 5.1. **Ancillary dossier:** It refers to the dossier required by the secondary section
- 5.2. **Authority:** It refers to Bhutan Food and Drug Authority

- 5.3. Combination product:** It refers to
- 5.3.1. A product comprised of two or more regulated components, i.e., medicine/ medical device, biological/medical device, or medicine/medical device/biological, that are physically, chemically, or otherwise combined or mixed and produced as a single entity;
 - 5.3.2. Two or more separate products packaged together (co-packaged) in a single package or as a unit and composed of medicine and medical device products, medical device and biological products.
- 5.4. Medical device-medicine products:** It refers to combination products when the 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 Medical Device section (MDS) is the primary agency of the combination products.
- 5.5. Medicine-medical device products:** It refers to combination products when its primary mode of action is based on pharmacological, immunological or metabolic action in/on the body where the Drug Evaluation section (DES) is the primary agency of the combination products.
- 5.6. Primary dossier:** It refers to the dossier required by the primary section.
- 5.7. Primary Mode of Action:** It refers to the mode of action that provides the greatest contribution to the overall therapeutic effects of the combination products.
- 5.8. Primary section:** It refers to the section with primary regulatory responsibility for combination products which is determined by the primary mode of action of the product.
- 5.9. Secondary section:** It refers to the section that regulates the other part(s) included in the combination products.

6. Acronyms

- 6.1. BFDA:** Bhutan Food and Drug Authority
- 6.2. DES:** Drug Evaluation Section
- 6.3. IFU:** Instruction For Use
- 6.4. MDS:** Medical Device Section
- 6.5. MPD:** Medical Product Division
- 6.6. PMOA:** Primary Mode of Action
- 6.7. TAT:** Turn around time
- 6.8. WLA:** WHO Listed Authority

7. General principle

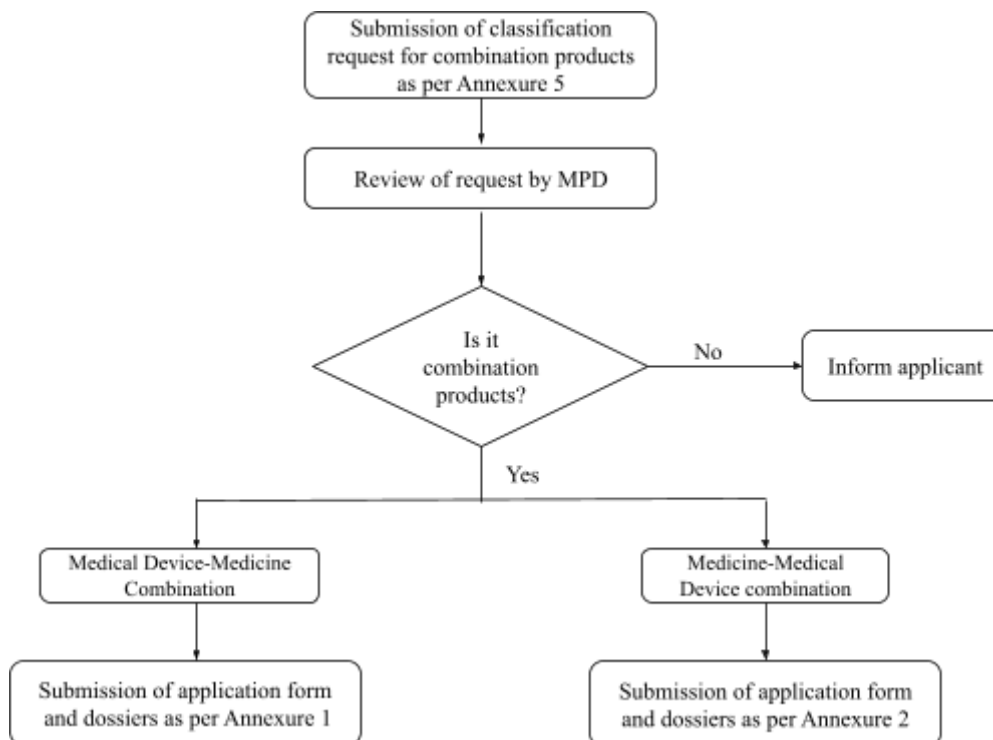
- 7.1. Medicine-medical device/medical device-medicine combination products are

regulated as medicines or medical devices based on the PMOA/the principal mechanism of action by which the claimed effect or purpose of the product is achieved.

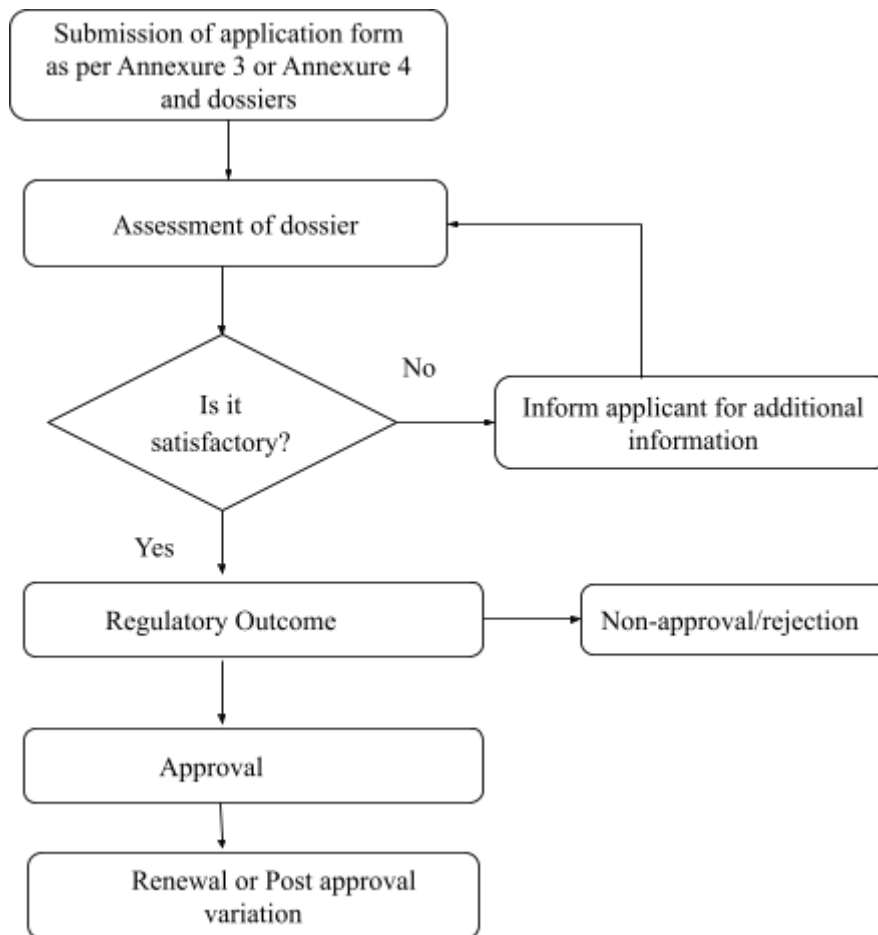
- 7.2. Other criteria that need to be considered while classifying the combination products are the statutory definitions and the proposed indication/claim.
- 7.3. Combination products regulated as medicines are based on pharmacological, immunological or metabolic action in/on the body and will be registered in accordance with the Guideline for registration of medicinal products.
- 7.4. Combination products regulated as medical devices do 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 and will be registered in accordance with the Guideline for registration of medical devices.
- 7.5. There are two routes of registration for combination products:
 - 7.5.1. Full route of registration: Combination products that are not eligible under Abridged route of registration.
 - 7.5.2. Abridged route of registration: Combination products that are WHO prequalified or is registered in any one of the WHO listed Authority (WLA)

8. Process flow chart

8.1. Preliminary assessment for combination products



8.2. Registration of combination products



9. Procedure

9.1. Preliminary assessment for combination products

- 9.1.1. The applicant should submit the request for classification of combination products as per Annexure 5 along with supporting documents
- 9.1.2. The request for classification of combination products should be reviewed to identify whether the product is combination products or not, based on the statutory definitions, the proposed indication/claim and PMOA.
- 9.1.3. In case of combination products, the applicant will be guided to submit application forms and dossiers.
- 9.1.4. The primary and secondary section responsible for the review of the product will also be identified.

9.2. Registration of combination products

- 9.2.1. The applicant shall submit the application form as per Annexure 3 or 4 based on the route of registration with the dossiers (primary and ancillary dossiers as per Annexure 1 and 2 respectively)

- 9.2.2. The application fee should be paid to the primary section
- 9.2.3. The dossier submitted should be assessed and evaluation queries may be issued to the applicant if clarification or additional information is required. The maximum number of queries from the Authority will be capped at two.
- 9.2.4. The product registration certificate is issued within a TAT of 60 calendar days considering the stop clock principle
- 9.2.5. The registration certificate number and certificate format for the product will be based on the primary section.
- 9.2.6. The product registration certificate is valid for three years
- 9.2.7. The renewal process is as per the relevant guideline for registration of medicinal products and medical devices respectively.

10. Reference

- 10.1. Guideline for Drug-Medical Device and Medical Device-Drug combination product, Ministry of Health, Malaysia, 2023
- 10.2. Guidance for Combination Products Classification, Saudi Food and Drug Authority, 2020

11. Annexure 1: Document requirement for Medical Device-Medicine combination

Sl. No.	Documents required	Full route	Abridged route
For primary dossier			
1	As per Guideline for registration of medical devices	Yes	Yes
For ancillary dossier			
1	Part I: General Information <ol style="list-style-type: none"> Generic or International Nonproprietary name (INN) Brand name or trade name (if applicable) Dosage form Strength Compendial/ In-house specifications List of all the ingredients in the dosage form and their amount on a per unit basis, as per the label claim and batch quantities Description of the organoleptic characteristics Commercial presentation of packaging and pack size The therapeutic category/pharmacological classification to which the pharmaceutical product belongs Indication Dose and directions for use for each indication Mechanism of Action(s) for the claimed indication List of all the major and common side effects. Side effects specific to the particular drug including newly recognized side effects should be identified. Information on use in pregnancy, breastfeeding and other special groups of patients including known contraindications and compatibility of use of the finished product during pregnancy and breastfeeding. Withdrawal Period for food producing animals (For Veterinary Medicines) 	Yes	Yes
2	Part II: Quality data of medicine component As per: ICH M4Q: Common technical document for the registration of pharmaceuticals for human use quality overall summary of module 2 and module 3: quality	yes	No

	or The ASEAN Common Technical Dossier (ACTD for the registration of pharmaceuticals for human use part ii: quality		
3	Part III: Non Clinical Document 1. Non Clinical Overview 2. Tabular Listing of Non Clinical Study 3. Non Clinical/ Biocompatibility Study Reports	Yes <i>(only for New chemical entities)</i>	No
4	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))	Yes <i>(only for New chemical entities)</i>	No

12. Annexure 2: Document requirement for Medicine-Medical Device combination

Sl.No.	Documents required	Full route	Abridged route
For primary dossier			
1	As per Guideline for registration of medicinal products	Yes	Yes
For ancillary dossier			
1	Device description including Instruction for use (IFU) / Product Catalog /Brochure	Yes	Yes
2	Relevant essential principle and evidence of conformity (for Risk Class C and D)	Yes	No
3	Performance data/Report or Certificate of Analysis	Yes	Yes
4	Clinical Evidence (for Risk Class C and D)	Yes	No
5	Risk analysis	Yes	No

13. Annexure 3: Application for registration of combination products (Abridged route)

APPLICATION FOR REGISTRATION OF COMBINATION PRODUCTS (Abridged route)

M/s.....hereby applies for registration of the combination product specified below for sale/distribution in Bhutan.

Combination product (tick whichever applicable)

- ☐ Medicine-Medical Device combination
- ☐ Medical Device-Medicine combination

Basis for Abridged registration (tick whichever applicable)

- ☐ The product is WHO prequalified
- ☐ The product has obtained regulatory approval from WHO Listed Authority (WLA)

Name of the WLA where the product is approved:

.....

Sl. no	Product name	Composition (With Strength)	Manufacturer	Pack size	Risk classification

Declaration (please tick the boxes):

- ☐ I hereby declare that the documents and information submitted is true to my knowledge and will be liable for any consequences if any information provided is proved to be false or misleading
- ☐ I declare that I have read the regulation and I am fully aware that my application may be rejected if I do not fulfill the conditions or contravene the provision(s) of the act and regulations made there under.
- ☐ If my application is granted, I shall abide by the Medicines Act and Regulations and any other standards set by the Authority.

Dated Signature of applicant with name and contact No.

14. Annexure 4: Application for registration of combination products (Full route)

APPLICATION FOR REGISTRATION OF COMBINATION PRODUCTS (Full route)

M/s.....hereby applies for registration of the combination product specified below for sale/distribution in Bhutan.

Combination product (tick whichever applicable)

☐ Medicine-Medical Device combination

☐ Medical Device-Medicine combination

Sl. no	Product name	Composition (With Strength)	Manufacturer	Pack size	Risk classification

Declaration (please tick the boxes):

☐ I hereby declare that the documents and information submitted is true to my knowledge and will be liable for any consequences if any information provided is proved to be false or misleading.

☐ I declare that I have read the regulation and I am fully aware that my application may be rejected if I do not fulfill the conditions or contravene the provision(s) of the act and regulations made there under.

☐ If my application is granted, I shall abide by the Medicines Act and Regulations and any other standards set by the Authority.

Dated Signature of applicant with name and contact No.

15. Annexure 5: Template for classification request for combination products

Date: (DD/MM/YYYY)

To
The Medical Product Division
Bhutan Food and Drug Authority

Subject: Request for Classification of Combination Products

Dear Sir/Madam,

We, (Firm Name) would like to submit this request for the classification of a combination product.

Details of products:

Generic name:

Brand name:

Manufacturer:

Intended use/indication:

Mode of action:

Supporting Documents:

-Product insert/IFU/Manual

-Packaging specimen

We hereby declare that all the information provided in this submission is true, complete, and accurate to the best of our knowledge

Yours Faithfully,

(Signature of applicant)

(Name and address)

Quality Policy of Medical Product Division

"We commit to provide consistent regulatory operations with risk based planning and continual improvement in compliance with the recognized standards to meet our consumers' satisfaction and confidence"

Bhutan Food and Drug Authority

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