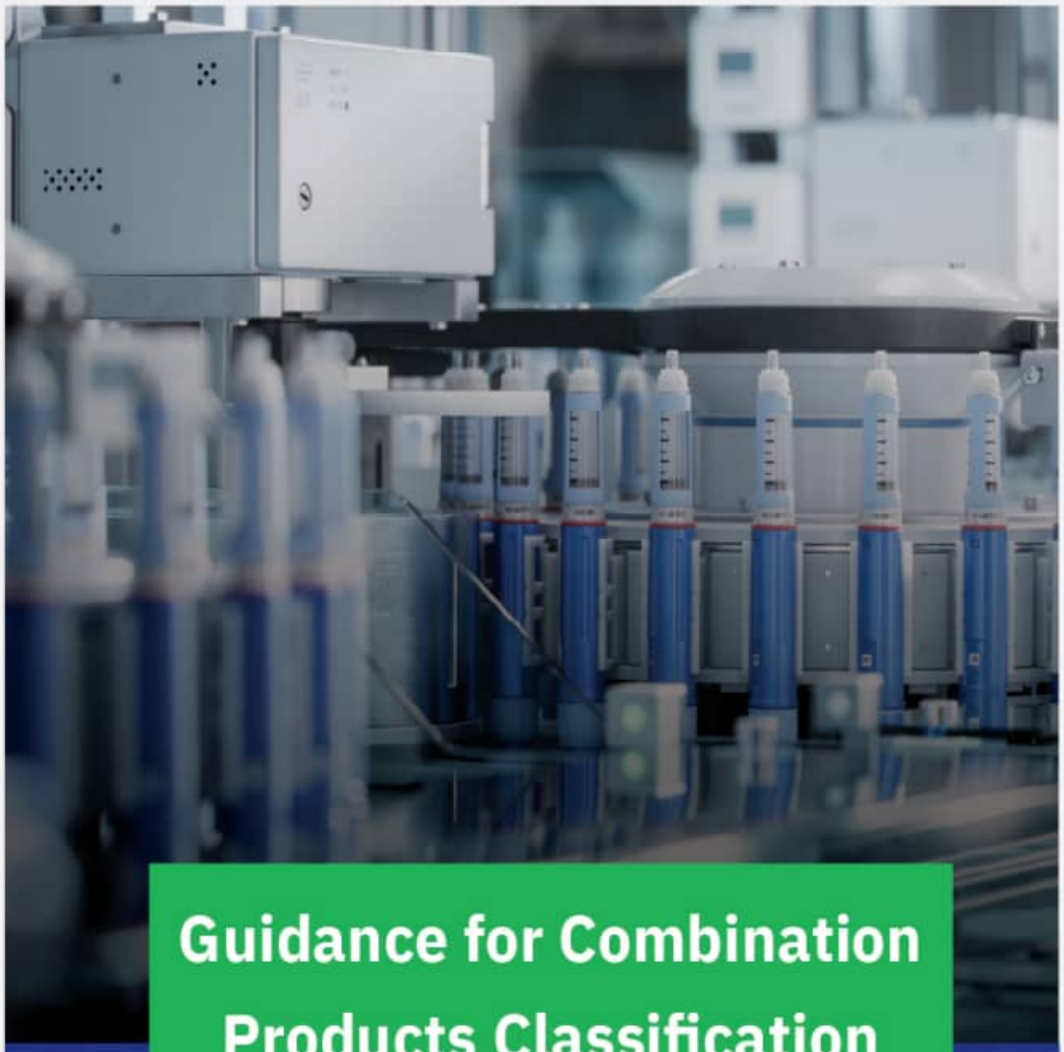
Kingdom of Saudi Arabia
Saudi Food & Drug Authority



Guidance for Combination Products Classification and Registration

Version 2.0

Vision

To be a leading international science-based regulator to protect and promote public health

Mission

Protecting the community through regulations and effective controls to ensure the safety of food, drugs, medical devices, cosmetics, pesticides and feed

Document Control

Version	Author	Date	Comments
Draft	Products Classification Department	19-02-2020	Draft for public comments
Draft	Products Classification Department	23-07-2020	Draft for public comments
1.0	Products Classification Department	7-10-2020	Implemented
Draft	Products Classification Department	15-5-2024	Draft for public comments
Draft	Products Classification Department	12-08-2025	Draft for public comments
2.0	Products Classification Department	5-03-2026	Implemented

Table of Contents:

1.Introduction

1.1 Objectives

This guidance provides definition of the combination products and provides applicants with clear criteria for their classification. It outlines the regulatory framework governing the submission and review of combination products. This document should be read in conjunction with other relevant and applicable Saudi Food & Drug Authority (SFDA) guidance documents.

1.2 Scope

This guidance pertains to combination products as defined in the definition section of this document; it also describes the criteria of classifications of such products. If a company is unable to determine the classification of its product, it may submit a classification request along with the required documents via the Products Classification Service available through the GHAD system, SFDA's unified digital platform for regulatory submissions. It is important to note that the Saudi Food & Drug Authority (SFDA) reserves the right to request information, material or defined conditions not specifically described in this document, in order to allow the authority to take the appropriate decision. It is also important to note that the SFDA has the right to change the designated sector after the classification decision been made to protect the public health, harmonize with any new/updated regulation or for any other compelling reasons. In most cases, the decision will follow this guideline.

1.3 Definitions

- **Biological medicinal products:** Medicinal products derived from a variety of natural sources such as human or animal tissues, or microbiological origins and produced by Culture & purification techniques. They include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, and tissues.

- **Combination Product:** A product consists of two or more of items that subject to more than one different SFDA's regulation. It may include:

A) Integrated combination product:

• A product consists of two or more regulated components that are combined/integrated as a single product.

B) Non-integrated combination product:

• A product consists of two or more separated items that are contained in the same package. [Co-packaged combination product].

• Any regulated product packaged separately where the labeling information refers to be used with another specific regulated product where both are required to achieve the intended purpose of use. [Cross-labeled combination product].

Consulted Sector:

A) The sector that provides the necessary consultation/review to the leading sector regarding the ancillary part of the combination product.

OR

B) The sector that regulates the other regulated component of the combination product.

Cosmetic Products:

Any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odors.

Drug:

Any pharmaceutical product manufactured in a pharmaceutical dosage form and contain one or more of active substance used externally or internally in treatment of a disease in human, or prevent the disease.

- **Human cells, tissues, or cellular or tissue-based products (HCT/Ps):**

  It means articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. Examples of HCT/Ps include, but are not limited to, bone, ligament, skin, dura mater, heart valve, and cornea.

- **Immunological means:**

  An action initiated by a substance or its metabolites on the human body and mediated or exerted (i.e. stimulation, modulation, blocking, replacement) by cells or molecules involved in the functioning of the immune system (e.g. lymphocytes, toll-like receptors, complement factors, cytokines, antibodies).

- **Leading Sector:**

  The sector that has the primary responsibility of regulating the combination product.

Medical device:

Any instrument, apparatus, implement machine, implant device, 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 diagnosis, prevention, monitoring, controlling, treatment or alleviation of disease or injuries or compensation for injuries. It is also used for investigation, replacement, modification, or support of the anatomy or of a physiological process, supporting or sustaining life (Vital functions of a human being), control of conception or assist for that, disinfection of medical devices and supplies and providing information for medical or diagnostic purposes by means of in vitro examination of specimens derived from the human body. It does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means.

Medical Supplies:

Medical products and materials, used for treatment or diagnosis, or compensation, or straighten, or for handicapped cases, or other medical uses for human being, including medical gases.

Metabolic means:

An action which involves an Alteration, including stopping, starting or changing the rate of the normal chemical Processes participating in, and available for, normal body function. The fact that a product is itself metabolized does not imply that it achieves its principal intended action by metabolic means.

Pharmaceutical Dosage Form:

Physical manifestation of a product that contains the active ingredient(s) and/or inactive ingredient(s) that are intended to be delivered to the patient in individual doses.

Pharmacological means:

An interaction at a molecular level between a substance or its metabolites and a constituent of the human body which results in initiation, enhancement, reduction or blockade of physiological functions or pathological processes. Examples of constituents of the human body may include, among others: cells and their constituents (cell membranes, intracellular structures, RNA, DNA, proteins, e.g. membrane proteins, enzymes), components of extracellular matrix, components of blood and components of body fluids.

Primary mode of action (PMOA):

The mode of action by which the combination product achieves its intended purpose/effect, i.e. pharmacological immunological, metabolic. It is objective and must be based on the state of art scientific data.

1.4. References:

This guideline should be read in conjunction with any relevant documents such as:

- Implementing Regulation of the Law of Pharmaceutical and Herbal establishments and products
- Implementing Regulation of the Law of Medical Devices
- Regulatory Framework for Drugs Approval
- MDS-REQ1 Requirements for Medical Devices Marketing Authorization
- SFDA Products Classification Guidance

2 Examples of combination products

2.1. Single entity combination products (integrated combination products):

a. Prefilled drug delivery systems (syringes, insulin injector pen, metered dose inhaler)

d. Device coated or impregnated with a drug or biologic (transdermal patch, drug-eluting stent)

> **NOTE 1:**
> Please refer to MDS-G008 Guidance on Medical Devices Classification, for more examples on combination products with medical device primary mode of action.

2.2. Co-packaged combination products (non-integrated combination products):

a. First aid kits containing devices (bandages, gauze), and drugs (antibiotic ointments, pain relievers)

b. Drug or vaccine vial packaged with a delivery device.

> **NOTE 2:**
> Please refer to Appendix.1 of this document for more examples.

2.3. Cross-labeled combination products (non-integrated combination products):

a. Light-emitting device and a light-activated drug

b. Drug/biological product utilizes a device where it is required that the two should be cross-labeled.

3 Product classification/Designating Criteria

The classification of the combination product and the assignment of the combination product to the leading sector regulation for premarket review is based on certain criteria such as the following:
(Please see Appendix 1: the illustrative examples of combination products as guidance for classification only)

3.1 The statutory definitions

3.2 The proposed indication/claim,

3.3 The primary mode of action (PMOA) by which the claimed effect or purpose is achieved.

For example in Drug/Device combination product:

- Product Subject to Drug Regulation if the the primary mechanism of action is achieved by pharmacological, immunological, or metabolic means,

- Product Subject to Medical Device Regulation if the the primary mechanism of action is NOT achieved by pharmacological, immunological, or metabolic means.

3.4 If the combination product have separate mode of actions; none of them is inferior to the other; the assignment will be based on the sector that regulates products with the similar questions of safety and efficacy for the product as whole.

3.5 In case of there is no such sector, the determination will then be dependent on the sector that has the most expertise related to the most significant safety and effectiveness questions presented by the combination product. However, all components of the combination product must meet acceptable standards of safety, efficacy and quality.

3.6 The classification of the product in a stringent regulatory authority.

4 Regulatory framework for combination products classification and registration submissions:

4.1 Classification and designation Process:

4.1.1. Applicant may submit a classification request through the Products Classification Service at GHAD system in case of uncertainty.

4.1.2. The Products Classification Department (PCD) will review the request and identify whether the product is a combination product or not.

4.1.3 The PCD will determine/designate the leading sector that has the primary review responsibility for the product and the consulted sector that will provide the necessary information or expertise to the leading sector. (See Section 3 of this document)

4.1.4. A decision on this review decided upon by the PCD, if the decision cannot be reached by the PCD, the submission will referred to The Joint Advisory Committee for Regulating and Classification of Combination Products for a final decision.

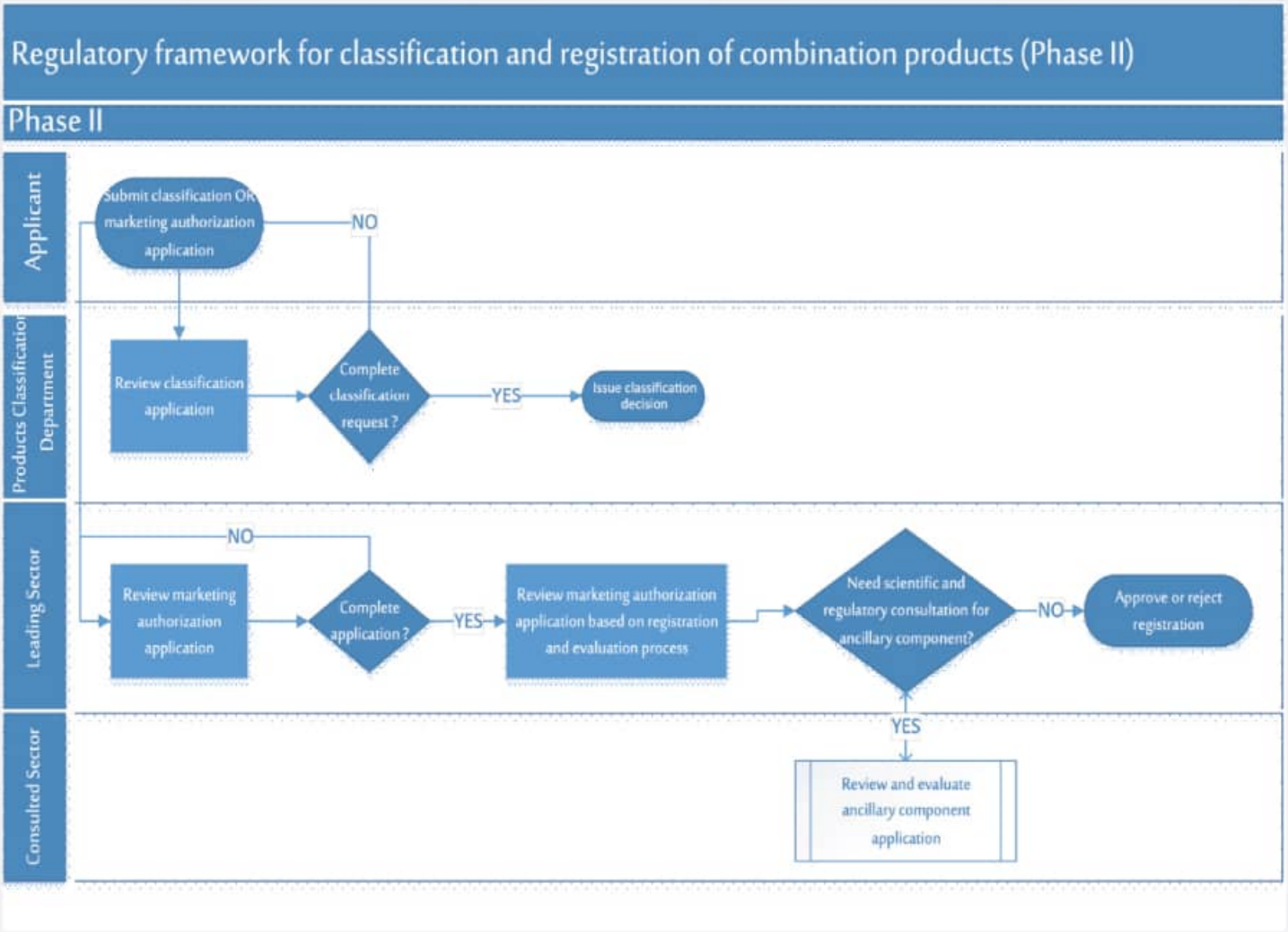
4.1.5. If applicant wishes to appeal on the decision, a letter of appeal should be submitted through GHAD system, with justifications within 60 days of receiving the decision.

4.2. Registration Process:

4.2.1. Applicant may submit a registration/marketing authorization application to the leading sector (either drug or medical device) based on the primary mode of action (PMOA), as the leading sector has the responsibility for regulating the combination product and thus it is the applicant's contact point for the registration application.

4.2.2. The approval of combination product registration is subject to the leading sector based on fulfilment of all registration and/or technical requirement of both primary and ancillary components.

4.2.3. The leading sector may seek (if needed) the consulted sector's review for any regulatory and/or scientific questions regarding the ancillary part of the combination product.


Regulatory framework for classification and registration of combination products (Phase II)
Phase II
Applicant
Products Classification Department
Leading Sector
Consulted Sector
Submit classification OR marketing authorization application
NO
Review classification application
Complete classification request ?
YES
Issue classification decision
NO
Review marketing authorization application
Complete application ?
YES
Review marketing authorization application based on registration and evaluation process
Need scientific and regulatory consultation for ancillary component?
NO
Approve or reject registration
YES
Review and evaluate ancillary component application

5 Data requirements for registration/marketing authorization

Note	Submission requirement	Time
Phase I: **2026-2027**	The combination product marketing application should be prepared according to the guidance of submission of the leading sector.	**Non**
Phase II: **2027-2030**	**Drug leading sector:** The applicant may submit • Drug full eCTD • Ancillary medical device requirement (please refer to appendix 2)	**Voluntary**
	Medical device leading sector **The applicant may submit** • Full technical documentation in compliance with MDS-REQ1 • Ancillary drug dossier (please refer to appendix 3)	
Phase III: **2030**	**Drug leading sector:** The applicant MUST submit • Drug full eCTD • Ancillary medical device requirement (please refer to appendix 2)	**Mandatory**
	Medical device leading sector The applicant MUST submit • Full technical documentation in compliance with MDS-REQ1 • Ancillary drug dossier (please refer to appendix 3)	

6 Timeline for classification and registration of combination products

6.1. Classification process timelines and fees:

The Service	Timelines	Fee (SAR)
Classification Request	3 working days	1,000 (non-refundable)
Appeal on classification decision	60 working days	Free

6.2. Registration process timelines:

Leading Sector	Drug		Medical Device	
Timelines	Type of submission	Duration of Registration	Class of Risk	Duration of Marketing Authorization
	New Drug	280 working days	Class A, B, C, D	35 working days
	New Drug not registered in an SRA	405 working days	In-Vitro Diagnostics (All classes)	35 working days
	Medicinal Biological	280 working days		
	Medicinal Biological not registered in an SRA	405 working days		
	Radiopharmaceutical	280 working days		
	Generic	200 working days		
	Renew	40 working days		

Please refer to the followings to review the approved timelines

- **Regulatory Framework for Drugs Approval**
- **Requirements for Medical Devices Marketing Authorization (MDS-REQ 1)**

Appendix 1

The Illustrative Examples of Combination Products

Product	Intended purpose/ Primary Mode of Action	Assignment
Drug-Eluting Stents	For use in angioplasty or coronary stenting procedures.	Combination product regulated as Medical Device
Prefilled drug delivery systems (e.g. prefilled insulin, asthma inhalers)	To administer pharmacologically active substance	Combination product regulated as Drug
Blood bag containing anticoagulant/	To collect and preserve blood and its components (not for direct intravenous infusion)	Combination product regulated as Medical Device
Intravascular catheter securement device containing antimicrobial /antiseptic agent	The antimicrobial agent provides ancillary antimicrobial activity to reduce skin colonization and catheter colonization, suppress regrowth of microorganisms, and reduce catheter-related bloodstream infections in patients with central venous or arterial catheters.	Combination product regulated as Medical Device
Breath collection/analysis devices and 13C-Urea for H. pylori diagnosis	Intended for use in the qualitative detection of urease associated with H. pylori in the human stomach and is indicated as an aid in the initial diagnosis and post-treatment monitoring of H. pylori infection	Combination product regulated as Medical Device
Embolic Drug-Eluting Bead	Intended to embolize vessels of hypervascular tumors (HVTs) in the liver using interventional arterial administration. The beads are capable of loading chemotherapy	Combination product regulated as Medical Device
A self- contained, portable infusion system delivers the medication at a constant flow	Intended for postoperative pain management for patients of 18 years and above	Combination product regulated as Drug

Appendix 2

Documentation requirements for ancillary medical device dossier

SN	Section	Element/Section
1	Device Description	Detailed description, specifications, intended use, variants, and accessories
2	Labeling and IFU	Information to be provided by the Manufacturer that include labels, Instruction of use (IFU) and any promotional material
3	Essential Principles Checklist	Essential principles checklist and method of conformity to applicable essential principles with evidence of compliance with essential principles

Appendix 3

Documentation requirements for ancillary drug dossier

Part I: General Information		
SN	**Section**	**Element/Section**
1	Combination Product Name	Name of the overall product as submitted
2	Active Substance & Strength	Name & Strength of Active Substance and Excipient
3	Dosage Form	Dosage Form (referring to actual form of ancillary drug before incorporated in the Medical Device)
4	Product Description	Pharmaceutical characteristics and visual description
5	Pharmacodynamics	Mechanism of action of the active ingredient
6	Pharmacokinetics	Absorption, distribution, metabolism, and excretion profile
7	Indication / Intended Use	Clinical indication aligned with the combination product
8	Dosage	Recommended Dose (As optional)
9	Route of Administration	Route of Administration/Mode of Delivery (Ancillary drug follows the finished combination product)
10	Contraindications	Known medical contraindications
11	Warning and Precautions	Standard safety and precautionary measures
12	Interactions	Drug-drug or drug-device interactions
13	Pregnancy and Lactation	Risk classification and recommendations (If Applicable)
14	Adverse Effects	Known and potential side effects (If Applicable)
15	Overdose Management	Symptoms and Treatment of Overdose (If Applicable)
16	Stability Data	Shelf life and storage conditions(If Applicable)
17	Origin Declaration	Declaration of human/ animal origin (If Applicable)

Appendix 4

What is New in The Guidance for Combination Products Classification (Version 2.0)?

The following table shows statements that added, deleted or replaced to the first version on 07/10/2020:

Section	Current Amendment
1.3 Definitions	Updated
4 Regulatory framework for combination products classification and registration submission	Newly added 4.1 Classification process 4.2 Registration process
5 Data requirements for registration/marketing authorization	Newly added
6 Timeline for registration of drug/device combination products	Updated
Appendix 1	Updated
Appendix 2	New
Appendix 3	New

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