المملكة العربية السعودية
الهيئة العامة للغذاء والدواء

Guidance for Combination Products Classification

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Guidance for Combination Products Classification

Saudi Food & Drug Authority

Kingdom of Saudi Arabia

Saudi Food & Drug Authority

Vision and Mission

الرؤية والرسالة

Vision

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

الرؤية

أن تكون هيئة رائدة عالمياً تستند إلى أسس علمية لتعزيز وحماية الصحة العامة

Mission

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

الرسالة

حماية المجتمع من خلال تشريعات ومنظومة رقابية فعالة لضمان سلامة الغذاء والدواء والأجهزة الطبية ومنتجات التجميل والمبيدات والأعلاف

Document Control

Version	Author	Date	Comments
First Draft	Products Classification Department	19-02-2020	Initial draft for public comments
Second Draft	Products Classification Department	23-07-2020	Second draft for public comments
Final	Products Classification Department	7-10-2020	FINAL

Table of Contents:

1. Introduction

1.1 Objectives

This guidance provides definition of the combination products, and it intends to guide applicants on 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 the any relevant and applicable 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 the company could not identify the classification of its product, it could submit a classification request along with the required documents through the electronic Products Classification System (e-PCS). 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 or for any other compelling reasons. In most cases, the decision will follow this guideline.

1.3 Definitions

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.

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 different SFDA's jurisdictions in terms of regulatory path, marketing and/or manufacturing. It includes:

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.

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: An article intended for use in the diagnosis, cure mitigation, treatment, or prevention of disease and which is intended to affect the structure or function of the body.

Food: Any substance whether processed, semi-processed or unprocessed, which is intended for direct human consumption or to be used in manufacturing, preparing or treating a foodstuff.

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

Medical device: means any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent or calibrator, software, material or other similar or related article:

A) Intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of:
   - Diagnosis, prevention, monitoring, treatment or alleviation of disease,
   - Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
   - Investigation, replacement, modification, or support of the anatomy or of a physiological process,
   - Supporting or sustaining life,
   - Control of conception,
   - Disinfection of medical devices,
   - Providing information for medical or diagnostic purposes by means of in vitro examination of specimens derived from the human body; and

B) Which 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.

Primary mode of action (PMOA): Is the mode of action by which the combination product achieves its overall therapeutic intended purpose/effect.

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

NOTE:
Please refer to MDS-G42 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**:
>
> Please refer to MDS-G7 Guidance on Criteria of Medical Devices Bundling/Grouping within one MDMA Application.

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.

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

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

immunological, or metabolic means but may be assisted in that effect or purpose 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 General Framework for Dealing with Combination Products Requests

4.1 The sponsor may submit a classification request through the electronic-Products Classification System (ePCS) in case of uncertainty.

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

4.3 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)*

4.4 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.

4.5 If the sponsor wishes to appeal on the decision, a letter of appeal should be submitted through the ePCS, with justifications within 60 days of receiving the decision.

5 Data requirements

The combination product marketing application should be prepared according to the guidance of submission of the leading sector.

6 Timeline for registration of drug/device combination products

- Please refer to the target performance timelines for other regulated products such as food and cosmetics published in SFDA website.

<table>
<tr><th></th><th>Drug-Medical Device Combination Product</th><th>Medical Device-Drug Combination Product</th></tr>
<tr><td>Leading Sector</td><td>
<table>
<tr><th>Type of submission</th><th>Duration of Marketing Authorization</th></tr>
<tr><td>New Drug</td><td>280 working days</td></tr>
<tr><td>New Drug not registered in an SRA</td><td>405 working days</td></tr>
<tr><td>Medicinal Biological</td><td>280 working days</td></tr>
<tr><td>Medicinal Biological not registered in an SRA</td><td>405 working days</td></tr>
<tr><td>Radiopharmaceutical</td><td>280 working days</td></tr>
<tr><td>Generic</td><td>155 working days</td></tr>
<tr><td>Renew</td><td>40 working days</td></tr>
</table>
</td><td>
<table>
<tr><th>Class of Risk</th><th>Duration of Marketing Authorization</th></tr>
<tr><td>Class A, B, C, D</td><td>35 working days</td></tr>
<tr><td>In-Vitro Diagnostics, all classes</td><td>35 working days</td></tr>
<tr><td>HCT/Ps</td><td>35 working days</td></tr>
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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 microorganism's, and reduce catheter-related bloodstream infections in patients with central venous or arterial catheters.	Combination product regulated as Medical Device
A toothbrush (manual or powered) co-packaged with a tooth paste	For use in tooth care and oral hygiene	Combination product regulated as Medical Device *(need to notify (list) the cosmetic product in eCOSMA.)*
Food product co-packaged with a medicinal herbal product	For use to provide nutritional and health/medicinal effects	Combination product regulated as Herbal product in Drug Sector *(need to register the food product)*

Appendix 2

What is New in The Guidance for Combination Products Classification (Second Draft)?

The following table shows statements that added, deleted or replaced to the past version on 19-02-2020:

Section	Current Amendment
Definition of Foodstuff	Modified: **Food**: Any substance whether processed, semi-processed or unprocessed, which is intended for direct human consumption or to be used in manufacturing, preparing or treating a foodstuff.
Timeline for registration of drug/device combination products	Modified: Target performance timelines for Drug-Medical Device Combination Product Marketing Authorization