

Combination Products Regulation in Japan

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Products regulated by PAL

■ Products regulated under Pharmaceutical Affairs Law are as follows;

● Drugs :

- ✓ The articles recognized in the Japanese Pharmacopoeia.
- ✓ The articles which are intended for use in the diagnosis, treatment or prevention of disease in humans or animals, and which are not equipment/instruments etc.
- ✓ The articles which are intended to affect the structure or functions of the human or animal body, and which are not equipment/instruments etc.

● Medical devices :

- ✓ Equipment/instruments etc. specified by the government ordinance which are intended for use in the diagnosis, treatment or prevention of disease in humans or animals, or intended to affect the structure and functions of the human or animal body.

● Cosmetics

● Quasi-drugs

Definition

- We have no specific definition for combination products in legal matter.
- A product consisted, comprised or combined of a **drug** and a **medical device** in the following way is regarded as a so-called combination product.
 - Physically/chemically combined
(like drug eluting stents, heparin-coated catheter , drug pre-filled syringe, drug-eluting patches)
 - co-packaged
(like surgical kit containing catheters, rubbing alcohol, etc.)
- Separate “cross labeled” products are not recognized as combination products.
(like drug for photodynamic therapy and laser)

Drug ? or Device ?

- A combination product is judged as a drug or a medical device by the primary mode of action of each product on case by case basis.
- Following three divisions/office of MHLW are involved in such judgement.
 - Licensing and Evaluation Division
 - Medical Devices Evaluation Office
 - Compliance and Narcotics Division
- In case the product is judged as a pharmaceutical, Office of New Drug of PMDA leads for its review. If the product is judged as a medical device, Office of Medical Devices of PMDA leads for its review. Both offices co-operate with each other in review process.

Marketing Application, GMP/QMS and PMS

- There is no unique type of marketing application for combination products.
 - A combination product judged as a **drug** is a subject of **drug** SHONIN application and a combination product judged as a medical **device** is a subject of **device** SHONIN application.
 - A single SHONIN application (drug or medical device) is sufficient for a final product of a combination product.
- There is no special requirement for GMP/QMS or PMS for combination products.
 - A combination product judged as a **drug** is a subject of **drug**'s GMP and PMS, and a combination product judged as a medical **device** is a subject of **device**'s QMS and PMS.

Examples

■ Drug-eluting stents

- stents coated by drug-containing polymer
- regulated as a medical device
- reviewed by a medical device team of PMDA

■ Drug-prefilled syringe

- drug already filled in syringe
- regulated as a drug
- reviewed by a drug team of PMDA

(A normal syringe is certificated by third party certification.)

Examples

■ Device coated with drug

✓ Heparin-coated catheter

device

✓ Hydroxy apatite artificial bone with BMP

device?

■ Drug with device for delivering system

✓ Drug-eluting contact lens

drug?

✓ Drug-eluting transdermal patch

drug

✓ Gelatin sponge with BMP

drug?

Examples

- **Iontophoresis system with a drug reservoir**
 - In case of disposable system in which a reservoir is pre-filled with a drug and cannot be re-filled, the whole system is judged as a drug.
 - In case of non-disposable system in which a reservoir can be re-filled with a drug repeatedly, and iontophoresis system and a drug is distributed separately, the system is a medical device and a drug is regulated as a drug.
- **Following points should be considered**
 - ✓ Primary mode of action
 - ✓ Separate distribution