Regulation on Combination Products in Japan

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Definition for CP

- MHLW/PMDA have no independent definition for Combination products (CP).
- But CP is generally recognized as a product that drug and medical device are physically or chemically integrated.

Definitions
(The Pharmaceuticals Affairs Law)

Article 2

- The term “drug” used in this Law refers to the articles specified in the following items.

  (1) Articles which are recognized in the Japanese Pharmacopoeia,

  (2) Articles (excluding quasi-drugs) which are intended for use in the diagnosis, treatment or prevention of diseases in humans or animals, and which do not belong to equipments/instruments, dental materials, medical or sanitary products(hereinafter referred to as “equipments/instruments etc.”),

Definitions

(The Pharmaceuticals Affairs Law)

Article 2

(3) Articles (excluding quasi-drugs and cosmetics) which are intended to affect the structure or functions of the human or animal body and which do not belong to equipments/instruments etc.

4. The term "medical device" used in this law refers to equipments/instruments etc. specified in Cabinet Ordinance, which are intended for use in the diagnosis, treatment or prevention of diseases in humans or animals, or which intended to affect the structure and functions of the human or animal body.

Has CP approved in Japan ?

- MHLW/PMDA have approved couple of medical devices which are generally recognized as CP.

  Drug eluting stent
  Heparin coated catheter
  Steroid eluting lead
  . . .

- For medical devices, approval for the original drug is not required. The approval as a product application would be sufficient.

- Once categorized as medical device, device regulation scheme applies to the product.

Rule of Classification of CP

- CP is regulated under the same regulation. (Pharmaceutical Affairs Law)
- MHLW/PMDA have no fixed procedure in determining the regulatory category(drug or device).
- We determine appropriate regulatory category for each application of CP case-by-case basis, based on a primary mode of action (PMOA) of the products.

Premarket review route of CP

- There is no specific review route for CP.
- Consultative/collaborative review among related divisions in PMDA and MHLW.
- We don’t have specific review timeline for CP. However, review timeline is set according to the application category (drug or medical device, brad new or generic, etc) .

User fee of CP

- User fee depends on its application category of the products as drug or medical device.

  JPY 30m for new drug

  JPY 9.4m for new and high-risk device

Submission requirement for CP

- Submission requirements for premarket approval and clinical trial application are same as for other drugs and/or medical devices.

Clinical data

- In general, clinical data from Japan is required for drugs.

- For medical device, in some cases, such as extrapolation could be scientifically explained by the result of foreign clinical trial, we don't require additional local clinical data.

  (same as for other drugs or medical devices)

Post approval modification of CPs

- Generally, submission should be required when CP was modified.

  (same as for other drugs and medical devices)

Labeling

- No specific requirement for label and instruction for related CPs.
- General labeling requirements are same as for other drugs and/or medical devices.

GMP/QMS practice

- The requirements are the same as for other drugs and medical devices.
- When CP is regulated as Drug, it is subject to GMP inspection.
- When CP is regulated as Medical Device, it is subject to QMS(ISO13485 based) inspection.

Adverse event/vigilance reporting requirements

- Marketing Authorization Holders of drug or medical device have to report adverse event such as death, disorder and infection in accordance with PAL.

- There is no specific requirement for CP, because CP is classified as either drug or medical device.

Conclusion

- There's no independent definition for CP in Japan.
- CP is regulated as drug or medical device according to PMOA, that is judged on case by case.
- MHLW/PMDA will accept discussion between applicant and regulatory authority if they would like to.