# Regulatory Pathway Options Device Versus Drug

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## Introduction

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- Objectives of the presentation:
  - Examine the regulatory processes pertinent for products at the drug / device boundary in the USA and EU
  - Outline the regulatory processes for combination products
  - Assess the impact of labeling claims on the regulation of borderline or combination medical products
  - Highlight principles by reference to individual cases
- Not usually possible to “manipulate” a drug into being classified as a device or vice versa (but worth considering if one regulatory path is significantly shorter than the other!)

## Regulatory Framework

- US
  - Federal Food Drug and Cosmetic Act
  - Code of Federal Regulations
  - FDA (CDRH, CDER, CBER, OCP)
- EU
  - European Directives (MDD, AIMDD, IVDD, MP)
  - Competent Authorities (e.g MHRA)
  - Notified Bodies



## Devices in the US - Definitions

- Regulation is determined by the way a device is labelled, promoted or used
- Instrument, apparatus, implement, machine, contrivance, implant, in-vitro reagent, or other similar or related article, including a component part or an accessory which is:
  - Recognised in the official National Formulary or US Pharmacopoeia, or any supplement to them
  - Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease in man or other animals, or
  - Intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals, and which is not dependant upon being metabolised for the achievement of any of it's primary intended purposes

## Devices in US - Classification

- The FDA has established classifications for 1,700 different generic types of device, depending on *intended use* and *indications for use*
- Each type is assigned to one of three regulatory classes based on the level of control necessary to ensure safety and effectiveness
  - Class I: General Controls (+/- exemptions)
  - Class II: General Controls and Special Controls (+/- exemptions)
  - Class III: General Controls and Premarket Approval



## Devices in the EU - Definitions

- Instrument, apparatus, appliance, material or other article whether used alone or in combination, including software necessary for its proper application as intended by the manufacturer
- Product must have a 'medical purpose'
  - Diagnosis, prevention, monitoring, treatment, alleviation of disease
  - Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap
  - Investigation, replacement or modification of the anatomy or of a physiological process
  - Control of conception
- Does not achieve its function by pharmacological, immunological or metabolic means

## Devices in the EU - Classification

- Devices are classified into Classes I, IIa, IIb and III
- Classification is determined on the basis of:
  - Intended purpose
  - Degree of invasiveness
  - Duration of use
  - Active devices (i.e. intended to administer or exchange energy to or from the human body)
- Annex IX of the MDD provides the definitions and rules that are used to determine the classification of a particular medical device



## Regulation of Combination Products (US)

- Definition
  - A product comprising two or more regulated components that are physically or chemically combined and produced as a single entity
  - Two or more separate products packaged together in a single package or as a unit comprised of drug and device products
  - A drug / device product packaged separately that according to its label is intended for use only with another approved drug / device, where both are required to achieve the intended use
  - An investigational drug / device packaged separately that according to its proposed labelling is for use only with another individually specified investigational drug / device, where both are required to achieve the intended use
- FDA Office of Combination Products
  - Products reviewed by more than one agency center
  - Assigns center to have primary jurisdiction
  - Oversees review process to ensure timely and effective pre-market review and post-marketing regulation of combination products.

## Drug / Device Borderline (US)

- Apply definitions from the CFR to determine whether the product is a device or a drug:
  - If the primary intended use of the product is achieved through chemical action or by being metabolised by the the body, the product is usually determined to be a drug
  - If it is a combination product, go to the OCP
  - If you are unsure…….



## Regulation of Combination Products (EU)

- Medical devices incorporating a medicinal substance having an ancillary action
  - Regulated as a device (NB takes the lead)
  - Competent Authority for medicinal products reviews medicinal dossier
- Where a device and medicinal product form a single integral product which is intended exclusively for use in the given combination and which is not reusable, that single product is regulated as a medicinal product
- A device intended to deliver a medicinal product is itself regulated as a medical device
  - A kit comprising an insulin pen and insulin cartridges: the pen is subjected to the MDD whereas the insulin cartridge is regulated separately as a medicinal product

## Drug / Device Borderline (EU)

- To determine whether the medicinal product or medical device regime applies:
  - Consider the intended purpose of the product and the manner in which it is presented
  - Assess the method by which the principal intended action is achieved
- Although the manufacturers claims are important, it is not possible to place a product in one category or the other in contradiction with current scientific data or predicates
- Function of a medical device may be assisted by pharmacological, immunological or metabolic means, but as soon as these means exceed the 'ancillary' capacity, the product becomes a medicinal product



## Drug or Device?

- Illustration of main points using examples
- Sometimes a manufacturer/developer can manipulate the product to be one or the other
- Therefore it is important to understand the scope of the regulations
- Main guidance is European (e.g. MEDDEV 2.1/3 Rev 2) but applicable to the USA

## Examples

- Medical Devices
- Medical Devices with Ancillary Drugs
- Medical Devices with Accessories
- Medicinal Products
- Drug Delivery
- Drug or Device Depending on Location



## Medical Devices With Ancillary Drugs

- Bone cement with antibodies
- Coronary stents with cytotoxics
- Intrauterine contraceptive devices with spermicides
- Wound dressings with collagen
- Condoms with spermicide or cellulose/ antimicrobial

## Example: Bone Cement

- Plain bone cement is a medical device since it achieves its primary intended purpose (fixation of a prosthesis) by mechanical means
- Bone cements containing antibiotics, where the principle intended purpose remains fixation of a prosthesis, are also medical devices
- If the principle intended purpose is to deliver antibiotic, the product would be regulated as a medicinal product (drug delivery)



## Medical Devices With Accessories

- Contact lenses and cleansing solutions
- Condoms and lubricant
- Ostomy bags and skin care products
- Disinfectants for medical devices (endoscopes)

## Medicinal Products

- Spermicides
- Topical disinfectants for wounds (antiseptics)
- Intravenous fluids
- Antacids



## Example: Disinfectants

- The regulatory process is determined by the intended use and label claims. For example, a disinfectant:
  - used to disinfect medical devices, is regulated as a medical device
  - used to disinfect wounds would be regulated as medicinal product
  - used to disinfect hospital surfaces would be regulated under the:
    - Biocidal Products Directive (98/8/EC) in Europe
    - Federal Insecticide, Fungicide and Rodenticide Act, administered by the Environmental Protection Agency in the US

## Drug Delivery

- Device plus drug
  - Nebuliser plus beta agonist
  - Implantable infusion pump plus insulin
- Device plus drug
  - Pre-filled syringe
  - Transdermal patch
  - Aerosols with beta agonist



## Example: Needle Free Drug Delivery

- If device is re-usable with cartridges of drug, the device is a device and the drug is a drug (separate applications)
- If the device is single use, pre-filled, the whole thing is regulated as a medicinal product (one “drug” application with the “device” dossier “sent out” for review)
- If the device is multiple use but supplied with cartridges of drug as a “course” of medication, it would probably be regulated as a drug if only that device could be used

## Drug or Device Depending on Location

- Preservation fluid for organs intended for transplantation:
  - Regulated as a drug in the US
  - Regulated as a device in Canada
  - Differently regulated in different European countries – despite the harmonised Directive!
    - UK - not regulated
    - Germany – drug or device
    - France – device
    - Spain - drug



## Drug or Device Depending on Location

- Photosensitising drug and activating light source
  - US: The components are separately provided, but labelled for use together. The drug is regulated as a medicinal product and the light source as a medical device.
  - EU: drug is regulated as a medicinal product and the light source as a medical device. The two products are not 'linked', so healthcare providers select an appropriate activating light source independently of the drug

# Conclusions

- The *intended use* and *manufacturers claims* for medical products have a fundamental impact on the regulatory processes that are applicable for the product
- The majority of drugs and devices have a clear regulatory path to the market
- Regulatory strategies should be assessed and clarified at the earliest stage of product development, and revisited regularly throughout the programme so that opportunities to manipulate the regulatory pathway are not lost