Differences Between Pharmaceuticals and Medical Devices

and

Implications for Regulatory Systems

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What is a “medical device”?

Converging medical technologies

Source: Eucomed (modified)

Converging medical technologies

Source: Nikkei Weekly 20 Feb. 2006

Drugs and medical devices differ

Drugs

- Discovered
- Stable formulation once developed
- Highly mechanized manufacture
- Consumed by use
- Systemic toxicity
- Large populations of exposure
- Patient may choose to stop use

Medical devices

- Designed
- Constant iterative improvements or changes
- Often manufactured by hand operations
- Available for study after use
- Adverse events most often local in nature
- Relatively limited populations of exposure
- Generally not subject to ethnic differences
- Most intended for professional use

Source: S. Alpert, M.D., PhD. (Medtronic, Inc.); Asian Harmonization Working Party, Seoul, Sept. 2006 (adapted)

Drugs and medical devices differ

Drugs

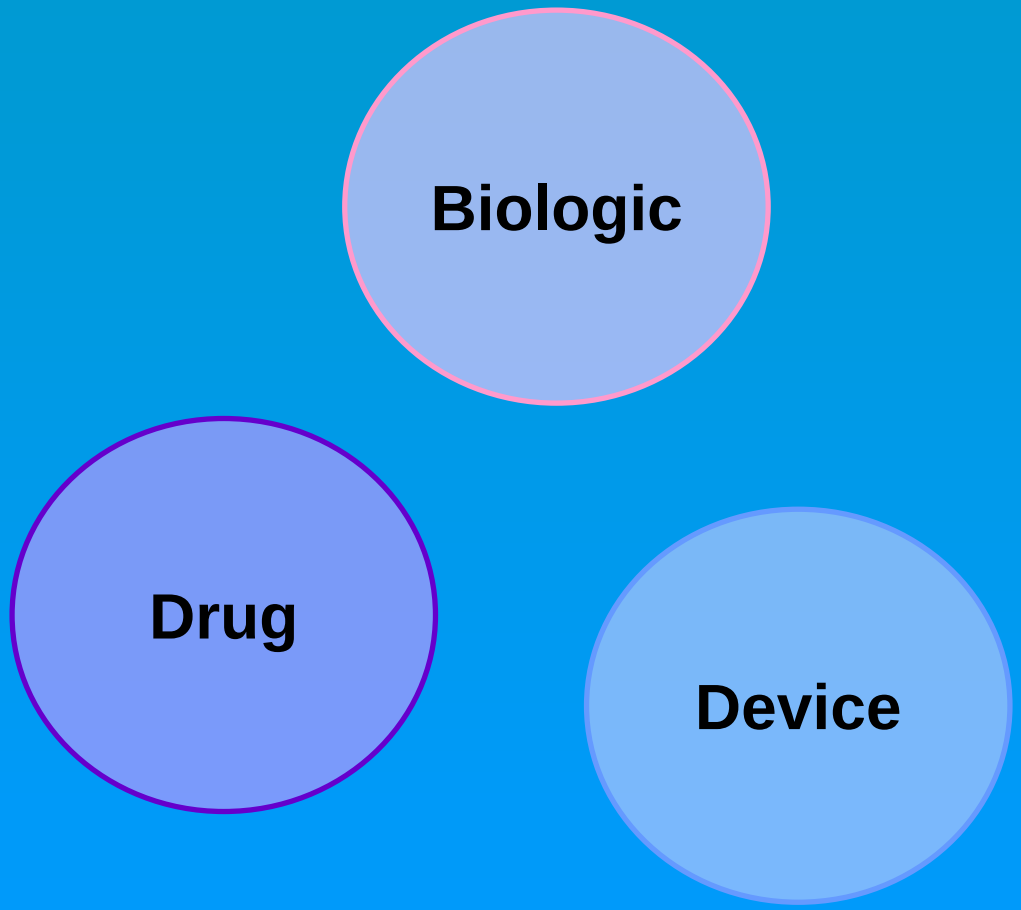
- Pure molecules
- Toxicology primary concern
- Short half-life in body
- Long market life
- Drug interactions of concern
- Wrong drug/dose
- Clinically studied
- Good Manufacturing Practices (cGMP)

Medical devices

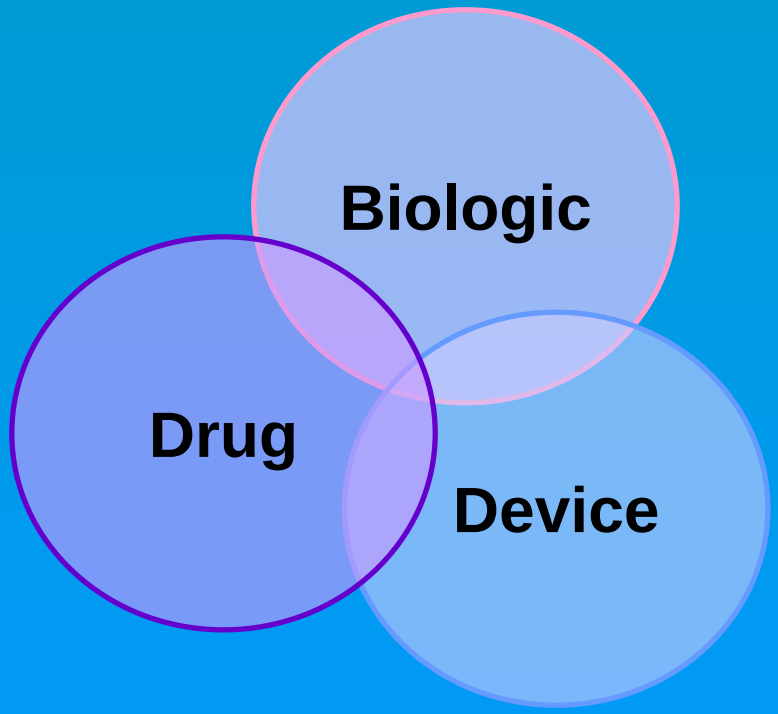
- Complex components and assemblages
- Biocompatibility
- Durable
- Rapid product cycles
- Device malfunctions possible
- Use error possible
- Often studied on bench
- Quality management systems (ISO 13485)

Source: D. Schultz, M.D., US FDA CDRH; Development of New Technology and Challenges to Regulatory Harmonization; APEC 2005 Pharmaceutical Regulatory Science Forum, Taipei, Nov. 2005 (adapted)

Converging medical technologies



Converging medical technologies



What is a “medical device”?

USA definition:

“… an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is …

(2) **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

(3) **intended to affect the structure of any function of the body of man** of other animals, ...

What is a “medical device”?

USA definition:

“… and which **does not achieve its primary intended purposes through chemical action** within or on the body of man or other animals and which is **not dependent on being metabolized for the achievement of its primary intended purposes**” [emphasis added]

Source: 21 U.S.C. 201(h)

What is a “medical device”?

Europe definition:

“… any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application **intended** by the manufacturer to be used for human beings for the purpose of:

- **diagnosis, prevention, monitoring, treatment or 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, …

What is a “medical device”?

Europe definition:

“… and which **does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means**, but which **may be assisted in its function by such means**” [emphasis added]

Source: Council Directive 93/42/EEC of 14 June 1993 concerning medical devices

What is a “medical device”?

Global Harmonization Task Force (GHTF) definition:

“… 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,
- **Investigation, replacement, modification, or support of the anatomy or of a physiological process** …

What is a “medical device”?

Global Harmonization Task Force (GHTF) definition:

“… and 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 function by such means**” [emphasis added]

Source: GHTF/SG1/N29R16:2005; Information Document Concerning the Definition of the Term “Medical Device”

What is a “medical device”?

- Medical devices distinguished from drugs and biological products on basis of intended mode(s) of action
  - Not metabolic, pharmacologic, or immunologic
  - May be assisted by such means
- Internationally harmonized definition exists
  - Not yet uniformly adopted
  - Opportunity for international harmonization
- No international definition of “combination products” that may cross borderlines (yet)
  - Opportunity for international harmonization → GHTF

Intended primary mode of action

Drug eluting stent

Regulated as a drug or
as a medical device?

Source: S. Alpert, M.D., PhD. (Medtronic, Inc.); Asian Harmonization Working Party, Seoul, Sept. 2006 (adapted)

Intended primary mode of action

Drug eluting stent

Regulated as a drug or as a medical device?

Drug eluting disc

Regulated as a drug or as a medical device?

Source: S. Alpert, M.D., PhD. (Medtronic, Inc.); Asian Harmonization Working Party, Seoul, Sept. 2006 (adapted)

Intended primary mode of action

Drug eluting stent

- Primary intended mode of action
  - stent opens artery
- Secondary action
  - drug reduces inflammation and restenosis of artery

➢ **Regulated as a device**

Source: S. Alpert, M.D., PhD. (Medtronic, Inc.); Asian Harmonization Working Party, Seoul, Sept. 2006 (adapted)

Intended primary mode of action

Drug eluting stent

- Primary intended mode of action
  - stent opens artery
- Secondary action
  - drug reduces inflammation and restenosis of artery

➢ Regulated as a device

Drug eluting disc

- Primary intended mode of action
  - chemotherapy for brain tumor
- Secondary action
  - local delivery of drug by device

➢ **Regulated as a drug**

Source: S. Alpert, M.D., PhD. (Medtronic, Inc.); Asian Harmonization Working Party, Seoul, Sept. 2006 (adapted)

Objectives of regulatory systems

- Protection of public health
  - Timely access of patients and clinicians to technology
- Efficient use of public and private resources
- Risk-based and proportionate controls
  - Protect patients, users, and others
  - Promote innovation and trade
- Transparency, predictability, consistency, and objectivity
- Scientifically appropriate pre-market assessment and post-market surveillance

Objectives of regulatory systems

- "One size does *not* fit all products"
  - Drugs *vs.* devices
  - Different risk-based classes of medical device
- How products will be used, and by which users, is important
- Product's most important intended therapeutic or diagnostic action is useful in deciding how to regulate
- Entire life cycle of product should be considered in determining appropriate regulatory controls

Drugs and medical devices regulatory systems differ – some examples

Drugs

- Clinical trials generally required
- Phased clinical trials
- Often randomized double blind clinical trials, sometimes with placebo
- No explicit risk stratification
- Emphasis on kinetics, metabolism, and eventual disposition in body
- Generally stable formulation
- Good Manufacturing Practices (cGMP)

Medical devices

- Clinical trials often unnecessary
- Un-staged clinical trials
- Often unfeasible and/or unethical to attempt double blind clinical and/or placebo trials
- Risk-based classification (e.g., four classes)
- Emphasis on interaction with body, possible failure modes
- Rapid, frequent changes
- Quality management systems (ISO 13485)
- Regulation over device lifetime

Summary

- Harmonized definition of “medical device” exists
- Devices and drugs differentiated on basis of intended primary mode of action
- Medical devices and drugs differ
  - Regulatory systems should be different
  - Different risk-based classes of medical device require proportional regulatory controls