Current Initiatives Relevant to Nanomedicines in Japan

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Current regulation of nanomedicines

- ✓ Nanomedicines have been regulated within the general framework of the Pharmaceutical Affairs Law on a product-by-product basis.
- ✓ At present, we have no specially designed regulations for nanomedicines and existing guidance documents are applicable.

- ✓ Regulators and reviewers are gathering and analyzing information about state-of-the-art nanomedicines technology.

Current regulation of products that combine drug and device

- ✓ The basic regulatory policy of drug and device is equivalent whether they are nano-based or not.

  To evaluate their quality, safety and efficacy and to approve them only when their benefit/risk balance is positive.

- ✓ Although there is no specific definition for drug/device combination products, they are regulated as drugs or medical devices according to their main function or purpose, and assignment by the MHLW to the PMDA for evaluation is done on a case-by-case basis. Innovative products that combine with nanomedicines and device would be regulated in a similar way.

- ✓ Continued dialogue is essential among regulators to keep pace with innovation and relevant evaluation methods. Information about state-of-the-art technology in this field should be also exchanged and shared among regulators.

Measures for scientific uncertainty

✓Upon request, PMDA offers consultations to give guidance and advice on clinical trials for new drugs and medical devices.

✓PMDA also established new categories of consultation services:

- consultations on submission documentation for cell-and tissue-based products
- consultations on pharmacogenomics/biomarkers.

✓MHLW supports research activities with respect of nanomedicines and study of evaluating and ensuring the quality of nanomedicines.

The MHLW-supporting research activities with respect to nanomedicines

Background Science and Technology Basic Law

- Objectives : To achieve a higher standard of science and technology, and to contribute to the development of the economy and society of Japan.

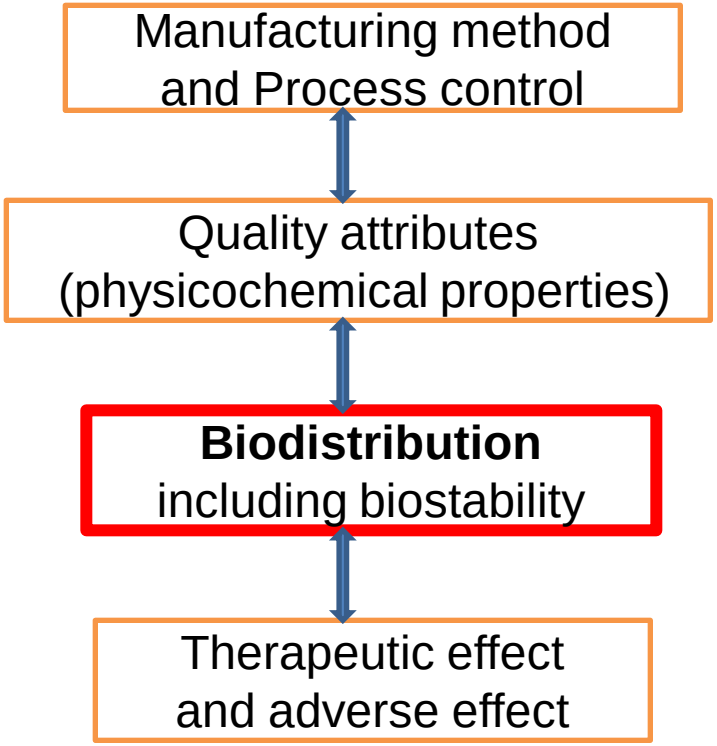
1. **Health and Labour Sciences Research Grants (2002-)**
2. **Collaboration with other ministry concerning to nanomedicines.(2003, 2004)**
3. **5-year Strategy for the Creation of Innovative Pharmaceuticals and Medical Devices (2007-2011)**
4. **Establishment of a new section at National Institute of Health Sciences (NIHS) (2008)**

Research activities of nanomedicines at MHLW/NIHS

Study of evaluating and ensuring the quality of nanomedicines

Objective: Development of an evaluation strategy of nanomedicines from the standpoint of quality, efficacy and safety

Nanomedicines are mainly developed for control of **biodistribution** of APIs



Knowledge about the relationship between each element is important for ensuring efficacy and safety as medicines.

Especially, knowledge about **biodistribution** is considered to be the key.

Output

Identification of critical quality attributes of nanomedicines.

Development of nanomedicines in Japan

1. Nanoparticulates with a particle size of around 100 nm effectively accumulate in vascular lesions or inflammatory sites including cancerous tissue.

2. The EPR (Enhanced Permeation and Retention) effect was discovered by Japanese researchers.
(Matsumura, Y., and Maeda, H. *Cancer Res*. **46**, 6387-6392 (1986))

3. Since then, many nanometer-sized DDS drugs such as block copolymer micelles using the EPR effect have been developed.

Approved nanomedicines# in Japan

- Lipid microspheres
  (Palux, Liple, Limethason, Diprivan, POPION)
- Liposomes
  (AmBisome, Doxil, Visudyne)
- Polymer-conjugated proteins
  (SMANCS, PEGASYS, PegIntron, SOMAVERT)
- Antibody-conjugated drugs
  (MYLOTARG, Zevalin)
- Nanoparticles (EMEND, Resovist, Abraxane)

 # These pharmaceuticals are classified as "nanomedicines" by their sizes in this slide.

Future Issues

Research for evaluating nanomedicines

- Analytical method of nanomedicines
- The evaluation method of biodistribution of nanomedicines
- In this research, discussion should take place about the regulation of nanomedicines.

Dialogue

- Discussion between industry, academia, and regulatory authorities about the appropriate regulation of nanomedicines, for enhancing the medical applications of this technology.
- International cooperation with other organizations

Documentation

- Points to consider documents for development of nanomedicines

Thank you for your attention.

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