PMDA Update

Science-Based Initiatives of PMDA

From “accelerated” to “advanced” review

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<tr>
<th>Type of Financial Interest within last 12 months</th>
<th>Name of Commercial Interest</th>
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<tr>
<td>☐ Grants/Research Funding</td>
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<tr>
<td>☐ Stock Shareholder</td>
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<td>☐ Consulting Fees</td>
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<td>☐ Employee</td>
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<td>☐ Other (Receipt of Intellectual Property Rights/Patent Holder, Speaker’s Bureau)</td>
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Today’s Content

1. Introduction

2. Promotion of Developing Innovative Products

3. Promotion of Regulatory Science to the Global Level
1. Introduction
As at 2006, new drug marketing in Japan lagged on average 4 years behind the initial global launch, a gap of around 2.5 years over the US, the country with the smallest lag. *

1,417 days (=approx. 4 years)

<table>
<thead>
<tr>
<th>Country</th>
<th>Days Until Marketing</th>
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<tr>
<td>Japan</td>
<td>915 days</td>
</tr>
<tr>
<td>France</td>
<td>757 days</td>
</tr>
<tr>
<td>Denmark</td>
<td>620 days</td>
</tr>
<tr>
<td>Germany</td>
<td>583 days</td>
</tr>
<tr>
<td>Sweden</td>
<td>538 days</td>
</tr>
<tr>
<td>Switzerland</td>
<td>512 days</td>
</tr>
<tr>
<td>UK</td>
<td>505 days</td>
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* The average of the number of days until marketing in the respective country following initial launch of the global top 100 products. Since the number of the top 100 products available varies with the country, the marketing lag has been calculated using only the number of products marketed in the respective country. For example, for the US where all drugs are available it was calculated using 88 of the 100 best-selling drugs after deduction of duplicate ingredients and those launched prior to 1981.

Source: OPIR Research Paper No. 31 (May 2006)
Enhancement of Consultation from earlier stage

Basic Research → Applied Research → Research with specific objectives (disease treatment, etc.) aiming at practical use → Development Research → Application Review → Approval

[Old Model]

[New Model]

Accelerate the application & approval period
PMDA achieved shorting approval time of new drug

New active substance (NAS) approval time by approval year

Note: The EMA approval time includes the EU Commission time.
2. Promotion of Developing Innovative Products

- Pharmaceutical Affairs Consultation on R&D Strategy
- SAKIGAKE Designation
- Conditional and Time-limited Authorization of Regenerative Medical Products
(1) Pharmaceutical Affairs Consultation on R&D Strategy

Basic Research

Applied Research

Research with specific objectives (disease treatment, etc.) aiming at practical use

Development Research

Non-clinical trial

Clinical Trial

Application Review -> Approval

[Old Model]

[New Model]

Consultation

Communication from the early development

LATER SATGE

EARLIER SATGE
Process of Pharmaceutical Affairs Consultation on R&D Strategy

Towards Pre-Consultation, Technical Experts explain the procedure & contents on the Consultation

Pre-Consultation (Free)
Technical Experts cope with the summary of the consultation contents. Where necessary, Review Team attend

Points on summary
Where necessary, external experts join

Scientific discussion (fix the record within 1 month)
Mainly, Review Team and Technical Experts cope with consultation

Face to Face Consultation (charge)

University/ARO/Research Institute

Would like to consult the process of commercialization of seeds

Would like to confirm own seed to fit the Consultation

Individual meeting (Free)

 Towards Pre-Consultation, Technical Experts explain the procedure & contents on the Consultation
Seamless Activity from Research to Approval - Collaboration PMDA & AMED -

Basic Research

Applied Research

Research with specific objectives (disease treatment, etc.) aiming at practical use

Development Research

Non-clinical trial

Clinical Trial

Application Review -> Approval

Drug Discovery Support Network

Pharmaceutical Affairs Consultation On R&D Strategy (Scientific Advice)

AMED* • Japan Agency for Medical Research and Development

Close Collaboration PMDA
Partnership Agreement with AMED* (August 19, 2015)

1. Utilizing Pharmaceutical Affairs Consultations on R&D Strategy
2. Support AMED to evaluate projects
3. Mutual cooperation to improve clinical research infrastructures
4. Sharing information
Drug Lag = Development Lag + Review Lag

Review speed is similar, but, development is …

Need “align start line”.

Development time | Application | Review time | Approval
---|---|---|---
EMA | | | |
PMDA | | | |

Development lag
(2) SAKIGAKE - Which train is better for drug marketing?

Local train

- Slowly moving
- Step by Step
- Stay in line while getting on the train
- Self service

Trans-Europe Express

SAKIGAKE leads significant products for earlier approval

- Rapidly moving
- Shortcut
- Priority-lane and pre-boarding
- Concierge service
SAKIGAKE- Streamlining of Process

**Designation Criteria**
- New mechanisms compared to existing approved products
- Medical products for diseases in dire need of innovative therapy
- Applied for approval firstly or simultaneously in Japan
- Prominent effectiveness can be expected based on non-clinical study and early phase of clinical trials

**Advantage for Designated Products**

<table>
<thead>
<tr>
<th>Prioritized Consultation</th>
<th>Prior-Review Consult. (Rolling Review)</th>
<th>Prioritized Review [12 → 6 months]</th>
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<tr>
<td>[Waiting time: 2 → 1 month]</td>
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- Review Partner [PMDA manager as concierge]
- Post Market Measures [Extension of re-examination period considered]
Designated:
6 Pharmaceuticals, 2 Medical Devices, 3 Regenerative Products
(3) Conditional and Time-limited Authorization of Regenerative Medical Products

Conventional Regulatory Approval Process

Clinical trial
(Confirmation of efficacy and safety)

Approval

Marketing

Regulatory System that Facilitate Early Patient Access

Clinical research

Clinical trial
(likely to predict efficacy, confirmation of safety)

Conditional and time-limited authorization

Marketing
Further confirmation of efficacy and Safety

Marketing Authorization
or
Revocation of the conditional approval

Continued marketing

Re-Application (or Expiration)
within max. 7yrs
Regenerative Medical Products Approval

1 Product approved on 18 September 2015
Note: application in September/in October 2014

HeartSheet® for serious heart failure due to ischemic heart disease
(conditional and time-limited authorization – 5 years, conducting post-marketing efficacy studies)

[Conditional and time-limited authorization(HeartSheet®)]
- Target: Serious heart failure due to Ischemic Heart Disease
- Product: Autologous skeletal myoblast
- Manufacturing Process
  - Biopsy from Quadriceps -> manufactured at company CPF -> sheet culture in hospital CPF

Figures quoted from the company press release docs

Conditional approval requirement (part)
I. Confirmation of efficacy (survival) with 60 HeartSheet cases vs 120 existing treatment cases
II. Time limitation of approval: 5 years
3. Promote Regulatory Science to the Global Level
Science Board

Established in May 2012; to discuss how PMDA can better cope with products with advanced science & technology, in each developmental stage (basic research, development support, product review, and PMS).

Board members

Academia (Knowledge of the Latest Innovative Technologies)
Outcome of the Science Board

1st term (FY2012 - 2013)
- Summary of discussion on the assessment of the current status of personalized medicine related to development and regulatory review (2014)
- Summary of discussion on non-clinical pharmacological studies on anticancer drugs (2013)
- Current perspective on evaluation of tumorigenicity of cellular and tissue-based products derived from induced pluripotent stem cells (iPSCs) and iPSCs as their starting materials (2013)

2nd term (FY2014 - 2015)
- Discussion on Evaluation of Medical Devices in Pediatric Use (2015)
- Report on the use of non-clinical studies in the regulatory evaluation of oncology drugs (2016)
- Current Status and Perspectives of Placebo-Controlled Studies (2016)
The report regarding the use of non-clinical studies in the regulatory evaluation of oncology drugs (#2 of the 2nd term) was also scientifically evaluated by the academia and published in a science journal.

Summary

Towards “Integration of Knowledge/Experience” for Public Health

Photo for first climbers to Mt. Everest in 1953
Thank you very much for your attention!
Danke für Ihre Aufmerksamkeit!

Ask