For the Future of Medical Innovation

Policy Package for medical innovation, in line with fiscal and economic policy

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**SOCIAL SECURITY POLICY OF MHLW**

PRESENTED TO THE COUNCIL ON ECONOMIC AND FISCAL POLICY
Carrying out the integrated reform of the social security and tax systems, including strengthening the systems and ensuring fair burdening.

Carrying out the reforms in social security system, aiming at two points below in fiscal reform period.
1. Promoting private businesses in social systems
2. Incentive-targeted reform

Restructuring Japanese health care system with innovation, contribute to economy and government finance

Example
- Outcome based physician fee system
- Benchmarking medical medical practices

New social security system consistent with economic and fiscal policy
1. Strengthen and streamline current systems
2. Consistent with economic and fiscal policy
3. Long-term vision based system restructuring

New Policy Package

I Strengthen social security
Reform on health care delivery system

II New social security policy with new viewpoints
Healthy Society
Global pharm. policy
Global contribution
Fair burden

Healthy aging model society
Containment of cost increase
Promoting Generic drug with strong R&D pharm. industry

Comprehensive medical and industrial policy

Stable delivery of quality drugs
Introducing innovation while promoting low priced drugs

Containment of Health care cost
- moderate national burden
- drug usage review
- drug price revision

Industry Competitiveness
- R&D based pharm. industry
- Generic industry
Promoting generic drug use / strong pham. industry

New target for generic drug use

70% in 2017 was determined by the Council's discussion

Original MHLW proposal

Intermediate review (2017)
Principles

I Promoting Innovation
II High-quality, and cost-efficient health care delivery system
III Review current policy from global point of view

I Promoting Innovation
- revitalizing clinical research in Japan
- Open innovation with collaboration between industry and academia
- Consideration of innovation in health insurance reimbursement policy

II Health care delivery system
- Generic drug use acceleration
- Stable supply of basic, essential drugs
- Modernize drug distribution system, proper and accurate pricing practices

III Reviewing policy
- Encouraging and supporting globalization and global contribution
- Harmonization of international drug regulation
- New vision for pharmaceutical industry, through dialogs with key leaders
Example of Innovation Promotion Actions (presented to the Council)

Revitalization of clinical research in Japan
- Patient registration data base in National Medical Center as an infrastructure for clinical trials

Reward innovative product in health insurance reimbursement policy
- Consider proper recognition of innovativeness

Distribution system
- Discuss modernization of Japanese drug distribution system
  * proper item-by-item price bargaining between hospitals and distributors are essential for recognition of innovation

Ensuring Government-Industry-Academia Collaboration
- Include AMED and other academia leaders to the Dialog between Government and industry

Encouraging globalization and out-bound business development
- Compiling international drug regulation harmonization strategy

* Ensuring delivery of basic drugs and essential drugs.
* Taking appropriate actions also for medical devices industry.
What is “Frailty”

“Frailty” is the situation of the aged which the ability of daily living get lowered and has more risk for disability or mortality.

Changes by aging
- Low appetite
- Low social activity
- Low muscle power
- Low recognition
- Comorbidity

Risk indicators
- Low nutrition
- Sarcopenia
- Mild Cognitive Impairment

Multi phases of “Frailty”
- Social
- Physical
- Mental

Maintaining of living ability is possible by appropriate intervention

Action
- Comprehensive action is needed
- Appropriate prevention method should be applied to aged persons.

Further research and action should be made in areas such as;
- Education
- Assessment
- Intervention
- Integrated care

Many aged become disable through the stage of “frailty”

(comorbidity)
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PROMOTION OF MEDICAL RESEARCH AND DEVELOPMENT
For promoting medical innovation, comprehensive, integrated and consistent policy is needed.
Promote the strategy package facilitating all the process from R&D, clinical research/trials, pre- and post-marketing safety, insurance coverage, through globalization of innovative products which are to be put into practical use. Specifically, this package is targeting innovative pharmaceuticals/medical devices/regenerative medicine which can cure serious illnesses (such as rare diseases/cancer etc.) unless established therapy is available.

### Prioritized Policy I

**SAKIGAKE**

- **Pre-Clinical Research**
- **Clinical Research /Trial**
- **Approval**
- **NHI* Price Listing**

*National Health Insurance

### Prioritized Policy II

- **facilitate the environment for industry activities**
- **International Deployment**

### Scheme to rapid authorization of unapproved drug

#### Accelerate R&D through supporting each stage

- **Coalition between “Network for Drug Discovery” and “Pharmaceutical Affairs Consultation on Research and Development (R&D) Strategy”**
- **Support of Drug-Repositioning (DR) and development of off-label use**
- **Development of safety assessment technique for using IPS derived cells** followed by international standardization
- **R&D through public-private joint project**
- **High-quality clinical trials by Clinical Trial Core Hospital • NC and coalition with research group for rare diseases**
- **Support for orphan drug R&D Support for ultra-orphan through the R&D to Early designation**
- **Support for Drug Development through Medical Information and Communication Technology (MICT)**
  - DB of Medical Information
  - Rapid and effective Clinical Trials
  - Incorporation into review for approval
- **Analysis by Modeling and Simulation (M&S) conducted by PMDA**
- **Utilizing “Pre-application Consultation”**
- **Improving the predictability of NHI drug price**
  - Discussion on Premium to promote the development of new drugs and to eliminate off-label use
- **Strengthening measures on post-marketing safety**
  - Development of system of patient registry
  - Research on biomarker
- **Utilization of the data from clinical research of rare disease / cancer for post-marketing surveillance**
- **Support for SME and venture**
  - Discussion on funding system for review user fee to be implemented
- **Support for orphan drug R&D**
- **Strengthening industry competitiveness**
  - tax incentive
  - HR Development
- **Mutual understanding of the process from R&D to approval with the trading partner, to promote export**

### Strengthen the structure of PMDA

(consultation, review, safety measures in terms of quality and quantity)

### Promotion of Regulatory Science

(Developing guidelines/assessment for the state-of-the-art technology)
Overall picture of SAKIGAKE designation system

Diagram of actual process

[Cases of regular approval review]
- Consultation for regulatory strategy
- Clinical trials I/II
- Clinical trial consultation
- Phase III trials
- Approval review

[Cases of SAKIGAKE designation]
- Consultation for regulatory strategy
- Nonclinical studies
- Clinical research
- Clinical trials I/II
- Clinical trial consultation
- Phase III trials
- Approval review
- Prior assessment
- Speedy review designation
- Prior assessment
- Approval review
- (1) Priority consultation
- (2) Prior review
- (3) Priority review
- (4) Review partner system
- (5) Improvement of post-marketing safety measures (re-examination period, etc.)

* In some cases, the results of phase III studies are accepted after application.
Approval system responding to practical application of products for regenerative medicine, etc. (approval with conditions/for limited period)

<Problem in applying existing approval system for products for regenerative medicine, etc.>
Because human cells are used and the quality is uneven reflecting individual difference, it takes a long time to collect and evaluate the data in order to confirm the efficacy.

[Existing path to approval]

- Clinical research
- Clinical trials (confirmation of efficacy and safety)
- Approval
- Marketing

[Approval system responding to early practical application of products for regenerative medicine, etc.]

- Clinical research
- Clinical trials (speculation of efficacy, confirmation of safety)
- Approval with conditions/for limited period
- Marketing
- Continued marketing

* Faster access for patients!

- Efficacy is speculated based on a certain number of limited cases within shorter period than before.
- For safety, acute adverse reactions, etc. can be evaluated in short period.

- Risks are explained to patients and their consent is obtained. Post-marketing safety measures are taken.
Compared to Basic research, academic infrastructures for clinical research are not sufficient in Japan, so seeds in basic research are not developed as medicine.

There are only few medical institutions that can conduct high-quality clinical research and clinical trials.

### International comparison of papers in major medical journals

<table>
<thead>
<tr>
<th>Basic Research</th>
<th>Three major medical journals combined</th>
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<tbody>
<tr>
<td>1 USA</td>
<td>2,011</td>
</tr>
<tr>
<td>2 Germany</td>
<td>386</td>
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<tr>
<td>3 UK</td>
<td>284</td>
</tr>
<tr>
<td>4 Japan</td>
<td>266</td>
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<table>
<thead>
<tr>
<th>Clinical Research</th>
<th>Three major medical journals combined</th>
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<td>1 USA</td>
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<tr>
<td>2 UK</td>
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<td>3 Canada</td>
<td>435</td>
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<tr>
<td>16 China</td>
<td>97</td>
</tr>
<tr>
<td>25 Japan</td>
<td>55</td>
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※1 Nature Medicine, Cell, Journal of Experimental Medicine  
※2 New England Journal of Medicine, Lancet, JAMA
The Core Clinical Research Hospitals

Under new medical service law, new scheme of the Core Clinical Research Core Hospitals was introduced in this April.

It is expected that:
1. Core Hospitals will gather more patients with rare diseases for trials
2. Core Hospitals will attract more excellent researchers
3. Core Hospitals will have more consultations from other research institutions and accept more contracted clinical researches
Proper and global standard regulations are indispensable for promoting research and development, and have more competitive industry

Example:
Regulation on clinical researches
Restoring public trust in clinical researches
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CONSIDER REWARD FOR INNOVATION IN REIMBURSEMENT PRICES
Recent trend in number of approval and listing of new drugs

- The number of listing tends to be increased as the number of approval is increased.
- Products listed as new drugs was increased about 3.5-fold from 10 years ago.
- Drugs are more actively developed.
- Acceleration of approval review contributed.

Number of drugs approved
- The figures for FY 2014 and FY 2015 were estimated based on the mean growth rate from FY 2005 to FY 2013.

Number of new drugs listed
- The figures for FY 2013 to FY 2015 were estimated based on the mean growth rate from FY 2009 to FY 2012.
Japanese Pricing method for new drugs

New drugs

With similar drugs

Price determination by comparable drug (I)

Corrective premium
5%~120%

Average foreign price adjustment
(in case of 125% and over, or 75% and lower)

Adjustment between specifications

Without similar drugs

Price determination by comparable drug (II)

Cost calculation method

New drugs lacking in novelty
### History of Price Premiums for New Drugs

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<tbody>
<tr>
<td>Innovative</td>
<td>40%</td>
<td>40~100%</td>
<td>50~100%</td>
<td>70~120%</td>
<td>70~120%</td>
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<td>Utility I</td>
<td>10%</td>
<td>15~30%</td>
<td>25~40%</td>
<td>35~60%</td>
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<td>Utility II</td>
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<td>5~20%</td>
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<td>Marketability I</td>
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<td>10%</td>
<td>10%</td>
<td>10~20%</td>
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<tr>
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<td>3%</td>
<td>3%</td>
<td>5%</td>
<td>5%</td>
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<tr>
<td>Pediatric use</td>
<td>—</td>
<td>—</td>
<td>3~10%</td>
<td>5~20%</td>
<td>5~20%</td>
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<tr>
<td>First Approval</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>10%</td>
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Price Premium for Innovative drug in cost calculation method

Until 2014

Average Profit* % ±50 %

From 2016

Average Profit* - 50 % ~ +100%

*Current Pharmaceutical industry’s average Profit rate is: 15.9%.
→ 7.95%~31.8% after premium adjustment
Pricing of new drugs under premium to promote creation of new pharmaceuticals and development of approvals of off-label use

(Trial continues since April 2010.)

Price under this system

Price of new drugs if the drug does not meet the condition (under present system)

Supplementary resolution for the next revision of medical fees

○ Confirm and review domestic research/development of drugs that genuinely contribute the quality of medical care and the its financial effects. Additionally, examine the review of current methods such as the products subject to the premium

○ Continuously examine the pricing of long-term listed products or generic drugs

Brand drug
A Yen

Drug Price

Premium

Reduction based on sales price

Chuikyo

Conditions: Disparity ratio of the price of the drug comparing to market price does not exceed the average ratio.

Listing new drugs

Launch of the first generics or 15yrs after of launch of brand drugs

The first grand revision after the launch of new generics

time
The innovative medical device reimbursement price is revised every two years according to its actual market price. The market price include that of same functional devices, so the price is subject to market prices of other companies’ products.
Special Calculation Method for Innovative Medical Devices

New Schemes (After 2014 revision)

The Innovative device A is not affected by market prices of other companies’ devices.

- **Innovative devices Device A**
  - First entry
  - New Functional category for A
  - Price revision Based on A
  - Price revision Based on B
  - Price revision Based on B & C

- **Same function Device B**
  - Second entry
  - Same function as A
  - Same price as B

- **Same function Device C**
  - Third entry
  - Same price as B
  - Price revision Based on A
  - Price revision Based on B & C

- **Same category**
  - After two revisions