Clinical Research Infrastructure: from the Perspectives of Medical Care, Law, and Legislation

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Criticism against the clinical trials in Japan

time-consuming, low quality, slow, and expensive

Possible reasons:
1) low incentives for test patients
2) low incentives for researchers to perform such trials
3) weakness of the clinical trial performance system
4) shortages of physicians and medical treatment facilities which regularly perform clinical trials.
An even more fundamental problem for Japan = the conspicuous fall of the number of new drugs with new functions originating in Japan.

Background factors:
the rigidity of regulations for early stage clinical research, inadequacy of support systems, etc.
→ Establishment of systems similar to the FDA’s IND program is required.
A proposal to the government

Establishment of an agency specialized for promotion & total management of health-related researches in Japan (“Japanese INH”)

- Specialized and total funding agency of public research fund.
- Advise research policies from the aspect of health promotion and industrial promotion.
- Total management of National Agencies’ IPs

Establishment of an agency specialized for assessment of efficacy, safety & quality of new medical technology & products, for protection of test patients’ rights in clinical research and for regulation of clinical development processes (“Japanese FDA”).

- Assess & approve new medical technology & products
- Advise firms from the aspect of regulatory science for consistency of clinical researches & earlier finish of clinical development
- Protection of test patients from adverse effects of new medical technology & products during the clinical development processes and scientific surveillance of them after marketing.
Proposed functions of “Japanese NIH”

★ Unified management of public funds for health-related researches which has been managed by MHLW, METI and MECSST.
★ Strategic fund allocation from the aspect of economic growth and national industrial competitive capability
★ Strategic management of National Agencies’ IPs
★ Strategic planning to promote domestic health-related industries
★ Planning & management of national research projects to establish de facto standard innovative technology
★ Support for consortium type special projects

Partially realized by establishment of the Health-related Research Promoting Committee in April, 2008.
Proposed reform of pharmaceutical regulations

1. Unification of regulatory system for clinical trials and that for clinical research other than clinical trials
2. Unification of regulatory system for clinical research on new diagnostic & treatment practices and that on new drugs & medical devices
3. Change to regulatory system with three basic categories: drugs, medical devices, and biological products
4. Unification of duplicate evaluations by the PMDA and the MHLW.
5. Unification of the organization responsible for safety measures of the PDMA and the MHLW.

Partially realized by establishment of the Advanced Medical Treatment Evaluation System in April, 2008.
1. **Unification of regulatory system for clinical trials and that for clinical research other than clinical trials**

Remaining problems of Advanced Medical Treatment Evaluation System:

1) The results are of no legal value for being unconnected to the approval screening process under pharmaceutical laws and regulations.
2) Pharmaceutical consultations and support for approval applications are not accepted.
3) Protection of test patients’ rights is inadequately guaranteed.

Early stage consultation and support systems should be constructed in the PMDA.

— unification of the Advanced Medical Treatment Evaluation System and the Initiator Instigated Clinical Trial System

→ scientific, ethical, and waste-free clinical research (clinical trials) to achieve smooth screenings and approvals.
2. Unification of regulatory system for clinical research on new diagnostic & treatment practices and that on new drugs & medical devices

Although ground-breaking diagnostic & treatment technologies are highly likely to be related to the development of future drugs & medical devices, they often regulated according only to ethical guideline for clinical research on new diagnostic & treatment practices and, in this regard, are outside the framework of the Pharmaceutical Law.

→ Unification of regulatory system for these novel technologies and that on new drugs & medical would speed up their practical application and merchandising by appropriate guidance and support from the beginning, ensuring scientific and ethical clinical research.
3. Change to regulatory system with three basic categories: drugs, medical devices, and biological products

Under the present system, biological products are categorized to drugs or medical devices. But drug-induced AIDS, BSE, drug-induced hepatitis etc. seen in recent years are mainly problems related to characteristic of biological products.

Shares of biological products in innovative medical technology & drugs technologies have been rapidly increasing.

Biological products should be established as a third basic category.

→ Establish appropriate screening & surveillance criteria for products’ safety.
Issues to realize proposed reform

- Staff for new agencies
  - Increased number of staff for scientific assessment and for watch of medical technology & drugs
  - Systems for interchange of personnel between government and universities or firms

- New criteria of PMDA’s consultation fee
  (Reduction for start-ups and universities)

- Legal responsibility and compensation policy of medical and administrative staff for adverse effects of newly developed medical technology & drugs
Possible influences of DPJ’s landslide victory on pharmaceutical regulations I

1. Some diet members of DJP have strong negative conviction against clinical researches & drugs (as typically shown by their attitudes in legislation process of the New Organ Transplantation Law). Others of leading coalition are patients with drug-induced infections.
   → Possibility that unrealistically strong protection of test patients and drug safety could be required
   → Increased cost & time to perform clinical trials in Japan
Possible influences of DPJ’s landslide victory on pharmaceutical regulations II

2. DPJ will promote the social security systems much more than social insurance systems
   → Government medical investment will be fundamentally allocated to cover medical costs of poorer patients. Governmental expenses to compensate medical adverse effects will be increased.
   (as typically shown in legislation process of the Special Law to Relieve Victims of Drug-Induced HCV)
   → Decreased budget for substantial medical system, further decrease of drug prices, increase of consumption tax rate
   → Further delay of marketing of new drugs & medical devices in Japan, overseas transference of Japanese firms.

3. DPJ’s key policy: cut ministries’ “wasteful” expenses
   → Minimization of social capital investment
   → Decline of scientific researches in Japan, Withdrawal of foreign firms’ investment
1. It is difficult for pharmaceutical companies to obtain IPs in cooperative research with public institutes in Japan. IPs rules should be changed in order to promote cooperative research with foreign companies.  
   —Who obtains IPs in a cooperative study depends on each contact.

2. Is it breach of Fare Trade Regulations for pharmaceutical companies to fund clinical researches of medical institutes? (Is it judged as illegitimate facilitation of non-approved use of products?)  
   —No. Donations purposing truly public welfare are always legitimate. If companies specifies details of these funded researches, they should contract with institutes.

3. It is not legally required to obey GCP to proceed clinical researches other than clinical trials. (Obedience to MHLW Ethical Guideline & Helsinki Declaration is enough.)