Drug Re-Examination/Data Exclusivity in JAPAN and Neighboring Countries

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What is the Re-examination Term?

Re-examination term
- Term for carrying out post-marketing examination to ensure efficacy and safety of the drug
- No marketing application for generic drugs during this term

Substantial Regulatory Data Exclusivity!
# Re-examination System in Japan

<table>
<thead>
<tr>
<th>Event</th>
<th>Date of</th>
<th>Date of</th>
<th>Expiration of</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st marketing approval</td>
<td>1st marketing approval</td>
<td>2nd marketing approval</td>
<td>Exclusivity</td>
</tr>
<tr>
<td>Filing date</td>
<td>Issue date</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patent term</td>
<td>Maximum 25 years + β</td>
<td></td>
<td></td>
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<tr>
<td>Re-examination term</td>
<td></td>
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<tr>
<td>New active ingredient</td>
<td>8 years + α</td>
<td></td>
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<tr>
<td>Orphan or Pediatric*</td>
<td>10 years + α</td>
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<td></td>
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<tr>
<td>Additional indication</td>
<td>4 years + α</td>
<td></td>
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</tbody>
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α: Term between generic drug application and its approval/price listing

β: Term between generic drug approval and its price listing

Pediatric*: Pediatric can be extendable to original term up to 10 years
Grounds for 8th Year Re-examination (1/2)

Safety Measures

- Peak for modification/revision of important drug info is the 7th year. Most of such modifications are made five to eight years after approval of the new active ingredient, the peak being the seventh year.

- 70% of the modifications/revisions are revised within 8 years. About 70% of all drug package inserts are revised within 8 years after approval of the new active ingredient. Dealt with by revision of implementing rules, not laws.

Re-examination on the 8th year

JPMA
Grounds for 8th Year Re-examination (2/2)

Period from Marketing Approval of Drugs to Revision of Cautions during Use of Drug

- New active ingredient (6th year reexamination)
- New active ingredient (10th year “)
- New administration route (6th year “)
- Accumulated Percentage

Note 1) Those added changes to cautions during use dictated by a directive of the manager of the safety policy department from July 2003 to July 2006 are counted.

Note 2) Drugs containing new active ingredients which have been approved since 1989 are counted.

Source: Pharmaceutical and Medical Safety Bureau, Ministry of Health, Labour and Welfare
Introduction of Twice-a-Year Generic Drug Price Listing System

Twice-a-Year Generic Drug Price Listing

Promotion of Generic Drugs

In the past
Expiration of approval

This Jul. → Next Jul.
March → This July
Price listing
Period between approval and price listing: 4 ~16 months

Expiration of approval

After 2007
Expiration of approval

This Jun. → This Dec.
February → This June
Period between approval and price listing: 4 ~10 months

JPMA
Korean DE
Korean Effective PMS: 4 - 6 years

• Items to be re-examined six (6) years:
  ✓ New Drugs.
  ✓ Ethical Drugs different from already licensed drugs in terms of active ingredients or mixture ratios.
  ✓ Ethical Drugs different from already licensed ones in the route of administration, while containing the same active ingredients.

• Items to be re-examined four (4) years:
  ✓ Ethical drugs which are identical to already licensed drugs in terms of active ingredients and route of administration but distinctively different in added indications.
  ✓ Other drugs whose re-examination is deemed necessary by the Commissioner of the Korean FDA.

• During PMS period, third parties cannot obtain approval for generic versions of the same product unless they can submit data which are: a) different from the data submitted for the first approval; and b) equivalent to or exceeds the scope of data submitted for the first approval. → The re-examination (PMS) period in effect works as data exclusivity in Korea.
DE in Korea-US Free Trade Agreement

• The Korean Patent Act currently provides six (6) or four (4) years of data exclusivity under the “drug re-examination” system.

• As part of the FTA, Korea agreed to provide five (5) or three (3) years of data exclusivity for information relating to the safety and efficacy submitted in support of the marketing approval of pharmaceutical product.

• South Korea-US Free Trade Agreement


• **Five (5) years' data exclusivity** applies, from the date of marketing approval, to all safety and efficacy information submitted in the process of a marketing approval if the origination of this information involves a considerable effort (Article 18.9.1, FTA).

• **Three (3) years' data exclusivity** applies, from the date of marketing approval, to new clinical information that is submitted in the process of obtaining marketing approval for product containing a chemical entity (Article 18.9.2, FTA).
Incrementally Modified Drug

Three categories of drug approval
1. New Drug Approval
2. Drug approval with minimum required Data
   - so called as "Incrementally Modified Drug", which is similar to the U.S. 505(b)(2)
3. Generic drug Approval

Korean Incrementally Modified Drug (IMD) Approval
✓ IMD modification can encompass modification of the structure, formulation, or indication of existing drugs. IMD is generally recognized as an improved version of the original drug in terms of safety, efficacy or convenience.
✓ Hanmi's Incrementally Modified Drug, Esomezol, Enters US market recently. This is the first Korean case of overcoming the Hatch-Waxman patent barrier of the US.
✓ Pharmaceutical Companies can reduce astronomical budget required to develop a new drug.

Be careful about Green List of Patent Linkage
Chinese DE
Regulations for Implementation of the Drug Administration Law of the People’s Republic of China (Decree of the State Council No. 360)

**Article 35** - The State protects undisclosed data of drug study and others which are independently acquired and submitted by drug manufacturers or sellers to obtain production or marketing approval of the drugs in question which contain new chemical entities. No one may make unfair commercial use of the said data.

Within six years from the date a drug manufacturer or seller obtains the approval documents for producing or marketing a drug containing new chemical entities, if any other applicant uses the data mentioned in the preceding paragraph to apply for approval for production or marketing of the drug in question without permission of the original applicant who has obtained the approval, no approval may be given to any other applicant by the drug regulatory department except that the data submitted are acquired independently.

No drug regulatory department may disclose the data set forth in the first paragraph of this Article except

(1) for the need of public interests; or

(2) where steps are taken to ensure that the data are protected against unfair commercial use.
Possible Problem on Data Exclusivity?

✓ It is still unclear how this DE would apply to import drugs, which are manufactured abroad to be marketed within China.

✓ The last portion of the article sets out exception when the State may disclose clinical trial data. Therefore it does not support the construction that the state will not give marketing approval to a generic company following the establishment of the national standards of the new drug.

✓ 2013 Special 301 Report pointed that there is evidence that generic manufacturers have, in fact, been granted marketing approvals by the State Food and Drug Administration (SFDA) prior to the expiration of this period, and in some cases, even before the originator’s product has been approved.
The United States is very concerned about barriers in China to IPR protection for pharmaceutical products. In the patent area, China’s revised implementation of Article 26.3 of its patent law has led the State Intellectual Property Office (SIPO) to refuse to consider post-filing supplementary test data supporting previously filed patent applications, contrary to the practice of the major patent offices around the world. This has led Chinese authorities not only to reject pending patent applications but also retroactively to revoke previously granted patents. These revisions make obtaining protection of patents of a reasonable scope very difficult in China when compared to other major markets. In addition, the United States continues to encourage China to provide an effective system for expeditiously addressing patent issues in connection with applications to market pharmaceutical products.

In addition, the United States continues to have concerns about the extent to which China provides effective protection against unfair commercial use, as well as unauthorized disclosure, of undisclosed test or other data generated to obtain marketing approval for pharmaceutical products. China’s law and its WTO accession commitments require China to ensure that no subsequent applicant may rely on the undisclosed test or other data submitted in support of an application for marketing approval of new pharmaceutical products for a period of at least six years from the date of marketing approval in China. However, there is evidence that generic manufacturers have, in fact, been granted marketing approvals by the State Food and Drug Administration (SFDA) prior to the expiration of this period, and in some cases, even before the originator’s product has been approved. The United States was encouraged by China’s 2012 JCCT commitment to define “new chemical entity,” a term that is central to the marketing approval process, in a manner consistent with international research and development practice. The United States looks forward to China’s implementation of this commitment without undue delay.
New Drug Observation Period?

Provisions for Drug Registration (SFDA Order No. 28)
Section 3 - New Drug Observation Period

**Article 66** - In order to protect the public health, the State Food and Drug Administration may set an observation period for any new drug approved for production. The observation period of a new drug shall be no longer than five years from the date the drug is approved for production. During the observation period of a new drug, the State Food and Drug Administration shall not approve other manufacturers to produce, change dosage form of or import the drug.

=> It is still unclear how this Observation Period would apply to import drugs. Applications for clinical trials submitted by Chinese local company will be acceptable.

**Article 71** - Starting from the date a new drug enters the observation period, other registration applications for the same drug shall no longer be accepted. The other applicants’ applications for the same drug already accepted but not yet approved for clinical trials shall be returned; upon the expiration of the observation period of the drug, the registration of a generic or import drug may be applied for.

=> Such Period is applied to the drug of a non-originator, a local company. Due to that, even an IND request of the drug originator cannot be accepted.
Thank you very much for your kind interest and attention!!

Yoichi