Pharmaceutical Patents and Evergreening

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Originator

My personal views
Strong Interdependence

Healthcare Systems

Originators  Generics

New therapies  Cheaper drugs

New markets

Patients
Loaded Terms:

- Me-too
- Follow-up
- NCE
- 20y-patent exclusivity
- Me-too
- Basic patent
- Patent thicket
- Secondary patent
- Extension of monopoly
- Incremental innovation
Patents Covering Pharmaceuticals

Technical innovation continues after invention of the active

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**Research**

**Development**

**Marketing Approval & Launch**

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**Compound**

**Salts**

- Solid forms (solvates, polymorphs, particle size)

**Formulation, Release Profile**

- Manufacturing process, intermediates

- Additional indications (second medical use)

**Dosing regimen**

- Patient sub-populations

**Biomarkers**

**Combinations**

**Improved Formulations**
US: Divisionals – Evergreening?

- Practice of PTO leads to multiple divisional patents from single patent application:
  - Compound
  - Pharmaceutical composition
  - Method of treatment

COMBINED WITH

- 17y-patent term from grant

- NOW: 20y-patent term from filing
US: Multiple 30m-Stays – Evergreening?

- Hatch-Waxman patent linkage
  - Originator lists relevant patents (Orange Book)
  - Generic can refer to originator’s approval after 4y
  - 30m-stay of generic approval to resolve dispute

COMBINED WITH

- Grant of new patents (e.g. divisionals) – new 30m-stays

- NOW: Single 30m-stay
New Indications – Evergreening?

Basic Compound Patent

R&D&Reg (Indication A)

R&D&Reg (B)

Indication Patent (B)

NOW:
Allow carve-out of patented indications

Gx (A)

Gx (A, B)
New Formulations – Evergreening?

Approval (Formulation A)

Basic Compound Patent

Approval (B)
Withdrawal (A)

NOW: Allow referral to withdrawn A

Formulation Patent (B)

Gx (A)

Gx (B)
Secondary Innovation – Evergreening?

Approval (Formulation A)  Approval (B)

Basic Compound Patent

Formulation Patent (B)

NO

Gx (A)

Gx (B)
Example Cyclosporin Formulations

- 1983 Sandimmune® (cyclosporin) launched – breakthrough in transplantation medicine

- Cyclosporin difficult to formulate (insoluble in water)
  - Sandimmune® oral emulsion preconcentrate
  - High *intra* and *inter* patient variability
  - Food effect
**Technical Problem**
* Cyclosporin is Classified as a Critical Dose Drug

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Solution – New Formulation

*Acute Rejection: Neoral® versus Sandimmun®*

<table>
<thead>
<tr>
<th>LIVER TRANSPLANTS</th>
<th>Proportion of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Neoral®</td>
</tr>
<tr>
<td>Hemming¹ (n=41)</td>
<td>25.0</td>
</tr>
<tr>
<td>Mirza² (n=166)</td>
<td>25.0</td>
</tr>
<tr>
<td>Reggiani³ (n=55)</td>
<td>21.4</td>
</tr>
<tr>
<td>Van Buren⁴ (n=30)</td>
<td>13.0</td>
</tr>
</tbody>
</table>

Me-toos, Follow-ups – Evergreening?

Basic Compound Patent (A)

Me-too Follow-up

Basic Compound Patent (B)

NO

Gx (A)

Gx (B)
‘More than one patent per drug’ – Evergreening?

Basic Compound Patent

Approval (Formulation A)

Formulation Patent (A)

Gx (A)

Gx (A')

NO
Proposed Definition of Evergreening

Evergreening

= squeeze between regulatory rule and patent leading to unjustified or disproportionate prolongation of exclusivity
Avoid Evergreening ...

- By removing regulatory squeeze

**NOT**

- By changing patentability requirements
Search for Improved Therapies Worthwhile?

Diagram:
- Basic Compound Patent
- R&D&Reg (A)
- R&D&Reg (B)
- Secondary Patent (B)

Questions:
- ?
- ?
- ?

Legend:
- Arrow: Direction of research and development (R&D)
- Red X: Indicating a problem or issue
Innovation beyond Active

<table>
<thead>
<tr>
<th>Innovation Area</th>
<th>Generic</th>
<th>Generic Plus</th>
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</thead>
<tbody>
<tr>
<td>Indications – new therapies</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Treatment regimes – higher efficacy, better compliance</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Formulations – higher efficacy, better compliance, cheaper</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Manufacturing processes – cheaper or purer drugs, more environment-friendly production</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Solid forms – higher stability, less side effects</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
Expenses for Healthcare – Example Germany

Most important cost blocks for statutory insurers, 2009:

- Hospitals: € 56 bio
- Treatments by doctors: € 31 bio
- Drugs: € 32 bio
  thereof patent-protected: € 7 bio
- ...

Total expenses: €171 bio
Avoid Evergreening ...

- **NOT** by

- Prohibiting secondary patents
  - Stifles further innovation esp. in developing pharmaceutical industries

- Additional patentability requirements like s.3(d)
  - ‘enhanced therapeutic efficacy’
  - Unrealistic assumption that closest prior art is a marketed drug
  - Artificial burden
I have a dream ...

- Globally harmonized patentability standards
- Strong and efficient patent examination
- Fair balance of technical contribution and exclusivity
- Strong patents
- Strong presumption of validity
- Fair, predictable and efficient enforcement
- Business certainty

**Investment in risky and costly R&D – innovation helping patients**
MUMBAI -- Mumbai-based Glenmark Pharmaceuticals has shaken up India's Rs 3,000-crore lucrative anti-diabetes market dominated by multinationals with its new drugs, Zitamed and Zita. The drugmaker, which is locked in a bitter patent infringement battle with US drug firm Merck Sharp and Dohme's (MSD) over these drugs, has managed to rake in Rs 16 crore in just eight months since it launched them.

[...] Glenmark has priced these drugs 30 per cent cheaper than its competitors, [...]

"Glenmark's anti-diabetes drugs shake up Indian anti-diabetes market"
“Indian pharma's challenges

A shift to research and higher quality is overdue.

[...]

The longer-term solution is that the more innovative and enterprising Indian companies make a successful foray into drug discovery. Firms that are able to market patented products earn high margins on them, which enables such companies to plough back more resources into research and development as well as come up with more useful discoveries. The government can help in this. Strong public funding for joint research in therapeutic areas important for the Indian population can go a long way.”
Thank you for your attention