Strategies for Global Patent and Regulatory Protection of Life Science Inventions

Presented by: Lisa Mueller
Agenda

- Patenting of Life Science Inventions
  - Variations in patent laws from country to country
  - Unique Life Science Inventions - Plants

- Regulatory Challenges and Strategies
  - U.S. FDA Basics
    - Product authorizations
    - Definitions
    - Standards for Approval
    - Data Exclusivity
    - Patent Linkage
  - Global Regulatory Challenges
Patenting of Life Science Inventions
Patent Laws Vary from Country to Country

- **Patentable Subject Matter**
  - U.S.: Isolated DNA, proteins, certain types of diagnostic methods, “abstract” software and business methods are not patentable
  - EP and other countries: Isolated DNA, proteins, antibodies and diagnostic methods are patentable (provided practiced on a sample and not on a human or animal body) but animals, plants, methods of treatment may not be

- **Novelty**
  - U.S. and may countries (Australia, Canada, China, Japan, etc.) have a grace period
  - Europe – no grace period*
Patent Laws Vary from Country to Country

- Obviousness/Inventive Step
  - U.S.: Tests recited in *Graham v. Deere* and *KSR*
    - Determine scope and content of prior art
    - Determine differences between claimed invention and prior art;
    - Level of ordinary skill in the art
  - EP: Problem-Solution Approach (China follows a similar approach)
    - Determine the closest prior art
    - Establish the “objective technical problem to be solved”
    - Determine whether or not the claimed invention would have been obvious to one skilled in the art starting from the closest prior art and the objective technical problem
Patent Laws Vary from Country to Country

- JP: Would a person skilled in the art have been able to make the invention easily based on the prior art known prior to the filing date
- AU: Determine whether an invention would have been obvious to ‘a person skilled in the relevant art’ in light of the “common general knowledge” prior to the filing date (Canada follows a similar approach)
Patent Laws Vary from Country to Country

- Enablement/Sufficiency
  - U.S.: Specification must enable a representative number of “species” to support a genus; method of treatment claims require that there be a correlation between *in vitro* or *in vivo* animal model assay data and the claimed method of treatment (if there is no human data)
  - EP: Specification only need disclose *at least one way of practicing an invention*
  - CN: Specification must provide qualitative or quantitative data of experimental tests to allow a person skilled in the art to be convinced that the technical solution of the invention enables the use to be carried out and/or the effect as expected to be achieved
  - CA: Specification should establish the utility of the invention, by demonstration or sound prediction
Patent Laws Vary from Country to Country

• Miscellaneous items:
  • Limited or shortened time periods or requirements to file a divisional application
    • CA: Divisional can only be filed if there is a unity rejection
    • BR: Very short time period for filing a divisional application
  • Strict double patenting practice: U.S., CA and MX
  • Only one independent claim per category permitted (EP, CL)
  • In certain jurisdictions claims can only be narrowed, not broadened, once examination is requested (BR)
  • Different approaches to claim amendments:
    • U.S.: No new matter
    • EP: Cannot amend in such a way to add subject-matter which extends beyond the content of the application as filed – very strict
      • Directly and unambiguously derivable
Patent Laws Vary from Country to Country

• IT’S EXPENSIVE!
  • Filing fees
    • Search, examination and publication fees
  • Plus:
    • Excess number of pages (over 100 in the U.S., over 35 in EP)
    • Claims over a certain number (U.S. over 20 total and 3 independent; over 15 in EP)
    • Yearly maintenance fees even during prosecution
## Costs and time lines

<table>
<thead>
<tr>
<th>Country</th>
<th>Cost (filing and prosecution)*</th>
<th>Time line for grant</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S.</td>
<td>$15,000-50,000*</td>
<td>3-7 years</td>
</tr>
<tr>
<td>Europe</td>
<td>$15,000-50,000*</td>
<td>3-8 years</td>
</tr>
<tr>
<td>Australia</td>
<td>$7,000-8,500</td>
<td>2-3 years</td>
</tr>
<tr>
<td>Brazil</td>
<td>$10,000-80,000*</td>
<td>10-18 years</td>
</tr>
<tr>
<td>China</td>
<td>$15,000-20,000</td>
<td>3-5 years</td>
</tr>
<tr>
<td>India</td>
<td>$7,500-15,000</td>
<td>5-7 years</td>
</tr>
<tr>
<td>Japan</td>
<td>$7,000-12,000</td>
<td>About 3 years</td>
</tr>
<tr>
<td>Mexico</td>
<td>$12,000-15,000</td>
<td>3-5 years</td>
</tr>
<tr>
<td>New Zealand</td>
<td>$1,500-4,500</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Russia</td>
<td>$10,000-15,000</td>
<td>2-3 years</td>
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</table>
Unique Life Science Inventions - Plants

- Plants can be protected in a number of different ways
  - **Utility patents** – not restricted to how the plant is reproduced
    - Inbred and hybrid lines, unique processes, etc.
  - **Plant Patents** – Asexually reproduced plants (cuttings, buds, grafting, etc.).
    - Ornamental plants, fruit & nut trees
  - **Plant Variety Protection Act**
    - Administered through the Department of Agriculture
    - Protects seed propagated plants
      - Potatoes, wheat, watermelon, lettuce, grass, peas, tomato (F1 hybrids), beans, oats, etc.
      - Need seed sample – 3,000 untreated seeds of which at least 85% will germinate
    - Protection available in many countries under the UPOV convention
  - Can file for more than one of the above
Developing a Global Strategy

• Filing considerations for Tech Transfer Office
  • Is there a licensee or potential licensee?
  • If not:
    • Have you actively licensed this type of technology previously?
      • Is this a “hot”/high value area:
        • e.g. CAR-T technology, oncology drug/biologic, CRISPR technology, etc.
    • What is the commercial value to a licensee?
      • Is it a platform technology?
        • Genentech – Cabilly
      • New plant variety versus new oncology drug/biologic
Developing a Global Strategy

• Invest in a strong first filing (preferably a provisional)
  • Disclose all embodiments in the specification (not just in the examples)
    • Include:
      • Representative number of species to enable any claimed genus
      • Sequence listing (if necessary)
      • Describe the correlation between in vitro or in vivo animal model assay data provided in the specification and any claimed method of treatment
Developing a Global Strategy

- Include as much experimental data as possible
  - Include data demonstrating unexpected or surprising results
  - Consider the use of prophetic examples
  - Describe combinations of features
    - Be careful when using laundry lists
      - EP does not allow:
        ▪ Accept arbitrary selections from two or more lists (no cherry picking)
        ▪ Allow combinations of features from different embodiments/aspects
Developing a Global Strategy

• Regarding the claims:
  • Include one or more generic independent claims encompassing various combinations of the independent claims
  • Use multiple dependency
  • Write as many claims as possible
  • Include both method of treatment (U.S.) and first medical use, EPC2000 or second medical use claims (Swiss-type)
  • Consider including a “clause” section before the claims
Developing a Global Strategy

• Don’t forget to include any information regarding government funding in your application
• File the application in the name of the assignee
  • Make sure assignment of application to the applicant (assignee) occurs during the priority year
• Use rolling “provisional” approach during the priority year
Developing a Global Strategy

- File a PCT application within the priority year
  - Consider filing a Chapter II Demand to proceed through International Preliminary Examination if a favorable search report and written opinion is not received
Developing a Global Strategy

- Use PCT-Patent Prosecution Highway Pilot (PCT-PPH) upon notification of one or more allowable claims if a search report and/or international preliminary report on patentability (IPRP)
Developing a Global Strategy

• Enter National Phase from the PCT
  • Licensee: Confer on country selection
  • No Licensee, consider:
    • Commercially relevant countries for technology
    • High value technology consider minimum filing list: CA, EP
      • Perhaps JP, MX, AU
        • Consider BRIC countries
Developing a Global Strategy

• Enter National Phase from the PCT
  • Reduce number of claims upon entry as necessary to avoid excess claim fees and to comply with independent claim rules
    • Use “clauses” for basis of support for new claim set
    • Exception: Canada - File with as many claims as needed to cover the invention
      • Why?
        • No claim fees
        • Cannot file a divisional unless there is a unity rejection
          - Strong double patenting prohibition
  • File the broadest possible claim set for examination in jurisdictions that only allow narrowing claim amendments during prosecution (BR)
Developing a Global Strategy

• Prosecution
  • Consider accelerating examination in Europe
    • Free and can be filed at any time – only catch:
      • File a response within the two/four month period set in the Examination Report
    • Remember strict approach to claim amendments in Europe
  • Submit supplemental data to overcoming obviousness/inventive step rejections (EP, US)
  • Don’t forget to cite relevant prior art and the status of prosecution and additional filings as required in other jurisdictions (US, IL, IN)
  • Try to keep claim amendments and arguments as consistent as possible in one jurisdiction to another (to extent possible)
  • Consider keeping a continuation/divisional on file for very important inventions in the event of an IPR, opposition, etc.
Regulatory Challenges and Strategies
U.S. FDA Basics - Product Authorizations

- **Approval**: Used to describe an *affirmative authorization* by the FDA as to the safety and/or efficacy of a product
  - Note that the use of terms such as “FDA approved” are not permitted when the FDA has not affirmatively confirmed safety and/or efficacy (Drugs that follow an OTC monograph, devices marketed based on substantial equivalence determinations [510(k)s])
- **Licensing**: Used to describe the system of *authorizing* both the product and process for a biological product
  - Biologics licenses are also referred to as approvals
- **Clearance**: Used to describe the process of *affirming a notification* that a medical device is substantially equivalent to another marketed device
  - FDA can grant or retract any product authorization at any time
Key Definitions: Drugs

- **Drugs are articles intended:**
  - For use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals;
  - To affect the structure or any function of the body of man or other animals; and
  - For use as a component of any article specified above

- **New Drug:**
  - Any drug which:
    - Is not generally recognized as safe and effective for use under its intended condition among experts qualified by scientific training and experience, or
    - Has not been used to a material extent or time for its intended condition, other than in investigations
Standards for Approval: FDCA Drugs

- **New Drug Application (NDA)**
  - Substantial evidence (consisting of adequate and well-controlled investigations) that the drug will have the effect it purports or is represented to have under the conditions of use, and
  - Safe for use under such conditions

- **Abbreviated New Drug Applications (ANDA)**
  - Information to show that the:
    - Active ingredient(s), labeling, route of administration, dosage form, and strength of the new drug are the same as those of the listed drug
    - New drug is bioequivalent to the listed drug
Key Definitions: Biological Product

• A biological product is defined as any of the following applicable to the prevention, treatment or cure of a disease or condition in humans:
  • Virus
  • Therapeutic serum
  • Toxin
  • Antitoxin
  • Vaccine
  • Blood
  • Blood component or derivative
  • Allergenic product
  • Protein (except a chemically synthesized protein) or analogous product
  • Arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound)
# Small Molecules vs. Biologics

<table>
<thead>
<tr>
<th></th>
<th>Small Molecules</th>
<th>Biologics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Size (MW)</strong></td>
<td>Small (&lt;1000)</td>
<td>Large (&gt;10,000)</td>
</tr>
<tr>
<td><strong>Source</strong></td>
<td>Chemical synthesis</td>
<td>Cultures of living cells</td>
</tr>
<tr>
<td><strong>Form</strong></td>
<td>Generally oral solids</td>
<td>Often injected or infused</td>
</tr>
<tr>
<td><strong>Example</strong></td>
<td>PREVACID MW=369.35</td>
<td>SYNAGIS MW=148,000</td>
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Standards for **Licensing**: PHS Act

- **BLA**
  - Biological product is safe, pure, and potent, and
  - Facilities in which the biological product is manufactured, processed, packed, or held (manufacturing facilities) meet standards designed to assure that the biological product continues to be safe, pure, and potent

- **Biosimilar**
  - Biological product is “highly similar” to the reference product notwithstanding minor differences in clinically inactive components, and
  - No clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product

- **Interchangeable**
  - Biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product
Data Exclusivity

- U.S. law provides a **data exclusivity regime** for innovator products once approved or licensed by the FDA
  - Establishes a set period of length of time that the FDA is prevented from relying on the originator’s data to approve products of potential generic/biosimilar competitors
  - Originator/Innovator companies have a certain period of time to market their products without competition from incoming generics, thereby resulting in significant financial benefits
## Types of Data Exclusivity

<table>
<thead>
<tr>
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<th>Drug Products (Small Molecules)</th>
<th>Biological Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>New “molecule” exclusivity</td>
<td>5 years from date of FDA approval</td>
<td>12 years from date of FDA approval</td>
</tr>
<tr>
<td>Orphan Drug Exclusivity</td>
<td>7 years from date of FDA approval</td>
<td>None</td>
</tr>
<tr>
<td>Pediatric Exclusivity</td>
<td>Additional 6 months (after all other forms of protection have expired)</td>
<td>Additional 6 months (after all other forms of protection have expired)</td>
</tr>
</tbody>
</table>
Patent Linkage

• **U.S. law provides a patent linkage system for issued patents that cover an approved or licensed drug or biological product**
  - Orange Book - drug products (e.g. small molecules)
    - List API, formulation and (approved) method of treatment patents
    - Cannot list method of manufacturing patents
    - Example: http://www.accessdata.fda.gov/scripts/cder/ob/search_product.cfm
  - Purple Book - biological products
    - Can list any type of patent
Why is patent linkage important?

- **Drug Products:** When a generic applicant files an ANDA it must certify against any patents listed in the Orange Book
  - Generic must make one of the following certifications:
    - No patent information has been filed (known as a “Paragraph I” filing);
    - Patent(s) have expired (known as a “Paragraph II” filing);
    - FDA should approve of its generic version after the date the last patent expires (known as a “Paragraph III” filing); or
    - Generic product does not infringe the listed patents and/or that those patents are not enforceable (known as a “Paragraph IV” filing)
  - Filing an ANDA is considered to be an act of patent infringement
Why happens when there is a Paragraph IV certification?

- Begins a cascade of events:
  - Generic must notify the originator within 20 days of the filing of the ANDA
  - Originator has 45 days to file a patent infringement action against the generic
  - If a patent infringement action is filed, the FDA cannot approve the generic manufacturer’s application until:
    - Generic prevails in the patent infringement litigation; or
    - 30 months from the date the patent owner receives notice of the Paragraph IV certification (which can be modified if either party to the action fails to reasonably cooperate in expediting the action)
  whichever comes first
Biosimilar Patent List Exchange Process

• **Purple Book**
  - Lists product and proprietary names
  - Date of licensure
  - Whether the listed biological product is a reference product
  - NO information on patents
    • Complicated patent “list exchange” process

• **Filing a biosimilar application is an act of infringement**
  - No 30 month stay as with drug products
1. Biosimilar Applicant (BA) “shall provide” a copy of the biosimilar application and manufacturing information to BLA holder (on a confidential basis)

2. BLA holder is required to provide a list of patents infringed and whether and are available for license

3. BA is required to provide a list of additional patents infringed and non-infringement, invalidity contentions

4. BLA holder is required to provide patent infringement and validity contentions

5. Parties negotiate a list of patents to be litigated

6. Complaint served

7. BA gives BLA holder 180-days notice of first commercial marketing

8. BLA holder files for preliminary injunction

Phase I

Phase II
## Global Regulatory Challenges

<table>
<thead>
<tr>
<th>Country</th>
<th>Local Clinical Trials</th>
<th>Data/Market Exclusivity</th>
<th>Patent Linkage</th>
<th>Biosimilar Pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>Yes</td>
<td>8+2+1</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Japan</td>
<td>In principle yes</td>
<td>8 years (10 years orphan drugs)</td>
<td>Yes*</td>
<td>Yes</td>
</tr>
<tr>
<td>Brazil</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Russia</td>
<td>Yes</td>
<td>6 years*</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>India</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>China</td>
<td>Yes</td>
<td>6 years*</td>
<td>Yes*</td>
<td>Yes</td>
</tr>
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Questions
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Lisa provides strategic counsel on complex patent issues to clients in the pharmaceutical, biopharmaceutical, biotechnology and chemistry sectors. She brings an in-depth knowledge and extensive experience to her work advising clients on patent protection, freedom to operate and invalidity of blockbuster drugs they aim to produce and distribute.

A thought leader on pharmaceutical and biopharmaceutical patent law, Lisa speaks frequently to legal and industry groups, and publishes widely. At Michael Best, she serves as Chair of the Life Sciences and Chemical Practices Group, and as a member of the Management Committee and the Venture Best industry group. She is the author of an award-winning blog, BRIC Wall, which provides unique insights on patent law developments in the life sciences industry in Brazil, Russia, India and China.

Admissions
• Illinois
• Supreme Court Illinois
• United States District Court, Northern District of Illinois
• United States Patent and Trademark Office

Education
• Valparaiso University School of Law, Juris Doctor (J.D.), magna cum laude, 1992
• Valparaiso University, Bachelor of Science (B.S.), 1990; Chemistry and Biology