Intellectual Property Considerations in Biomanufacturing processes



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HIGHLIGHTS

- **Intellectual Property Rights in Biomanufacturing**
  - Introduction
  - Idea Generation
  - Invention Ownership



- **Cell pro Case Study**
- **Intellectual Property Strategic Considerations**
  - Process Development Phase
  - Biomanufacturing Scale-up Phase

Patenting Strategy for Biomanufacturing around the World

United States

Europe

India

Japan

China

INTRODUCTION

Biomanufacturing Process

- ***IDEA phase***
- ***PROCESS DEVELOPMENT***
- ***PLANT DESIGN phase***

❖ ***Process development and scale-up are essential to obtain a competitive commercial product.***

IPR Issues in Biomanufacturing :

- **IP Ownership issues – Joint ventures**
- **Patent Infringement issues for scale-up process**



PATENTS
Novel & Unobvious ideas

Vs

TRADE SECRETS
Ideas publicly not disclosed

IDEA GENERATION

❖ *Reservoir of ideas acts as a fuel for Scale-up of Biomanufacturing process.*

PATENT	TRADE SECRET	COPYRIGHT
• Novel & Unobvious Ideas reduced to practice.	• Ideas not publicly disclosed • May be Patentable – novel & unobvious & reduced to practice.	• Code .i.e. not product of nature is an expression of idea and copyrightable.

What is NOVELTY???

❑ Ideas not publicly disclosed by someone else before the inventor's thought of the idea.

- ***Novelty criterion is different for different countries – US / Europe / Japan – Aus.***



Novelty in US	Novelty in Europe	Novelty in Japan/ Australia
• Non - disclosure in public by inventor/ owner anywhere for > 1 yr before date of filing a patent application.	• **Absolute Novelty –** No disclosure in public made by I/O anywhere in the world.	• Non - disclosure in public made by I/O in each of these countries.

What is UNOBVIOUS??

❑ Idea must not be discernible –

- by combining 2 or more related references, published before the filing date of patent application.
- from routine experimentation based on published information.



❖ ***Obviousness determined by Patent Office Examiners and Judicial determinations during Patent Litigation.***

Prior to Patenting

INVENTION - Legal life cycle

Conception of Idea

- Person who conceive an invention – INVENTOR.

Reduction to practice

- Person who performs a process/ makes a product
  - TECHNICIAN.



❖ **Constructive Reduction to practice is filing a Patent Application describing and claiming the invention.**

"Technicians are not Inventors, they are the followers of Inventors"

BUT

✓ **Technician can become an inventor by solving a problem with NOVEL & UNOBVIOUS solution.**

INVENTION OWNERSHIP

- An Invention may have ***multiple inventors***.
- For multiple inventors, ownership of an invention is ***Joint & Several*** (like in real estate)

❖ Ownership Issues may arise during scale-up of Biomanufacturing process.

✓ ***Resolve invention ownership issues before manufacturing scale-up process is completed.***

❖ *If issue not resolved, company initiating the scale-up risks have to pay significant fee to operate the plant or being shut down by an injunction.*

❑ **Globalization of Mfg – leads to possibility that 1 or > 1 inventor of a company's IP will be from country outside US.**

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✓ **Imp to identify assignment issues (country specific) before drafting an assignment document transferring ownership to a Biomanufacturing company.**

Considerations for Ownership Transfer

EUROPE and ASIA	*JAPAN*
• Consideration given to an Inventor for assigning his/her rights is not merely 'Gratuitous'	• Japanese inventors have been awarded millions of dollars in remuneration, based on Royalty considerations.



❖ **Companies can use this multi-national inventorship to strategize Patent Ownership and Patent timing & claiming in countries where inventors reside as well as other countries where patent protection is sought.**

❖ **A Patent assignment should be recorded in the United States Patent Office.**

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❖ **For foreign applications, it should be recorded in the respective patent office of the country.**

Issues of Concern

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- ***Dynamism & Technology explosion in Biomanufacturing result in the flood of inventions and hence responsible for the problems of Patent Infringement.***

  ✓ ***<u>To resolve this, Careful Planning & Creative Strategy is must.</u>***

- ***Multiple inventors work on the same Invention without knowledge of each other. Legal consequences are usually tragic because in US 1st to invent will prevail. Everyone else has to attenuate/ completely change long term strategy – loss of time & money.***

Patent Infringement Issues

❖ *If 2 or more companies invent same or very closely related product/ process within the same time period.*

WHO WINS THE CONTEST ??

1) 1st Company to file a Patent Application wins the rights (except US).

- *It can block all other companies working on the technology from practicing in Europe.*

✓ ***Blocked Countries – WHAT TO DO??***

- *Watch patent applications published in European Patent Office for problem applications.*
- *Take action to narrow claims/ force owner to cancel claims (during patent examination).*
- *Submit Prior Art to the European Examiner.*

2) 1st Company to INVENT wins the patent rights in US.

Invention = Conception of idea + Reduction to practice

✓ ***Winner : Company with earliest conception date + diligence in constructive reduction to practice process.***

- *Inventorship contests decided by US – Patent Office.*

❖ *Example : Case of CellPro Vs Johns Hopkins University, Baxter Healthcare Corporation and Becton Dickinson and Co.*

CELLPRO - CASE STUDY

- In 1980s, scientists began making monoclonal antibodies (Abs) that would recognize and bind to the antigens (Ags) contained on the surface of blood cells.
- Once Ab binds to Ag on cell surface, cell is flagged and separated by FACS. MAbs which are uniform in their binding properties, produced by Hybridomas.

❖ Dr. Curt Civin discovered an Ag named My-10 that appears on the surface of immature stem cells not mature cells. He also disclosed a MAb named anti- My-10, which recognized My-10 Ag and which was useful in separating stem cells from mature cells.

❖ The patents (680 & 204) also disclosed how a hybridoma which manufactured the anti-My-10 Ab could be produced and a sample of hybridoma was deposited in ATCC.

❑ ***680 Claim 1: " A suspension of human cells comprising pluripotent lympho- hematopoietic stem cells substantially free of mature lymphoid and myeloid cells."***

❑ ***204 Claim 1: " A MAb which specifically binds to an Ag on nonmalignant, immature human marrow cells, wherein said Ag is stage specific and not lineage dependent & Ag is also bound specifically by Ab produced by hybridoma deposited in ATCC."***

- Dr Ronald Berenson, a scientist at the Fred Hutchinson Research Centre, developed a method of physically separating stem cells from mature cells that was similar to that disclosed in the Civin patents. The MAb developed by Berenson was designated as 12.8 Ab.
- Berenson and others at Hutchinson formed CellPro in 1989 and obtained licenses from Hutchinson for the use of Berenson's cell separation technology.
- In 1990, CellPro produced by cloning, a master cell bank containing 12.8 hybridomas used to produce working cell bank to produce 12.8 Abs.
- Therefore, CellPro had allegedly committed the Patent Infringement of '204 Antibody patent by Civin'.
- After legal prosecution of the patent history, CellPro was ordered to repatriate to the US – all clones or subclones of 12.8 Ab hybridoma cell line previously exported by it, as well as any further clones or subclones produced there from.





- ✓ The Federal Circuit found CellPro had infringed claims in the 2 patents in contention. CellPro was not only blocked from practicing its own technology but it owned damages to Johns Hopkins.
- ✓ CellPro could likely have paid the costs of losing the lawsuit but it could not survive the terms for its future business.

ANY MITIGATION POSSIBLE IN CASE OF CELLPRO???

- Since research was performed secretly, it was not possible to know that other inventors were out there until it was too late.

BUT

- It was worthwhile to perform watches of US published application database and other databases in the world . Companies can identify and study activities of their competitors.
- If a patent application is filed, application will publish about 18 months after filing date unless in US, the patent owner requests no publication at the time of filing or early publication.



INTELLECTUAL PROPERTY- STRATEGIC CONSIDERATIONS

❖ *Process Development Phase of Biomanufacturing Scale-up*

- For companies that are pioneers in their technology, far ahead of their competitors, patents have historically provided a way of recouping R & D costs by :
  - Excluding competitors from the area.
  - Charging royalties or other remuneration to approved companies to use the aspects of the patented technology.
- In the course of Scaling-up a Biomanufacturing process, the companies will encounter a supplier having patent on the desired particular process/ product.

✓ ***Cost of using this technology can be mitigated by having patents and patent applications that can be cross- licensed.***

- A Company's patent portfolio should not only protect the company's products and processes but also claim products/ process that company don't plan to use but could choose to license it.

✓ ***Such claims not only provide protection of IP but also:***

- Act as potential revenue generators for company.

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❖ ***Broader the SCOPE of claims, more difficult for competitors to enter technology area.***

- Companies should enter Joint ventures with a clear understanding of Invention ownership and determine market apportionment based upon the ownership.
  - ✓ ***Venture partners should make sure that inventions under consideration are patentable in all target countries.***

PATENTING FOR BIOMANUFACTURING AROUND THE WORLD

- *Patent protection for a scale-up operation requires the consideration of global strategy years before actual scale-up is performed.*
- ✓ ***Because of the interaction of US Laws, PCT and Paris Convention***
- Priority Date is very imp for the success of Global patent protection esp. in countries where the winner is '1st to file' patent application.



How global patenting works???

- Filing a Patent Application – in country where inventor/ company resides
- ✓ ***For example - In United States, date of filing = priority date***
- Company has 1 yr from priority date to perform foreign filing of patent application and retain the benefit of priority date.
- PCT allows company to file a PCT application that gives company rights to file in foreign countries for upto 30 months.
  - ✓ ***Save expenses for filing and translation of patent application***
- Most countries are members of PCT. If not, then company can file directly in the country within 1 yr of priority date.

Strategy for Patenting Globally

- Patent strategizing requires a company to :
  - *Identify the Product Markets*
  - *Identify the Location of Manufacturing facilities*



- To obtain full protection, company should file patent applications with :
  - *Product claims in its largest markets*
  - *Applications with process claims in countries with its manufacturing facilities.*

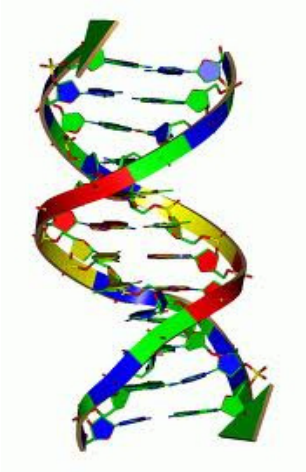
✓ ***Check whether all aspects of Biotechnology invention is Patentable in Manufacturing & Market countries.***

PATENTABILITY CRITERIA

UNITED STATES	EUROPE
PATENTABLE ??? ▪ Biotech Products/ Processes	***NON- PATENTABLE???*** ▪ Medical Procedures
▪ Medical Procedures	▪ Process for Cloning Humans
▪ Cloning	▪ Process for modifying Genetic identity of Humans & Animals
▪ Biological materials isolated from environment – Genes isolated and available for industrial production.	▪ Using Human embryos for commercial use ▪ Plant/ animal varieties/ biological process for their production
	▪ Human Body & its elements
▪ Plant or Animals if invention is not confined to a single variety	***PATENTABLE???*** ▪ Body elements isolated from the body ▪ Microbiological process/ products ▪ Isolated Genes for Industrial production

PATENTABILITY CRITERIA FOR JAPAN

- Japanese Patent Office is adopting “super enablement” standard along the lines of standard developed in US.
  - ***<u>For an invention to be Patentable - What is IMP???</u>***



- ***Creativity***
- ***Inventive Step***
- ***Utility***
- ***Non-obviousness***

BIOTECHNOLOGICAL INVENTIONS??

- **Genetic Engineering**
- **Micro - organisms**
- **Plants**
- **Animals**

PATENTIBILITY IN BIOTECHNOLOGY

GENETIC ENGINEERING

Inventions related to –

- **Gene**
- **Vector**
- **Recombinant Vector**
- **Transformant**
- **Fused cell**
- **Recombinant Protein**
- **Monoclonal Antibody**

MICRO-ORGANISMS

Inventions related to –

- **Micro-organisms *per se* as well as those relating to**
- **The Use of Micro-organisms**

PLANTS & ANIMALS

Inventions related to –

- **Plants/ Animals *per se***
- **Parts of Plants/Animals**
- **Process of creating P/A**
- **Use of P/A**

❖ ***Seedling Law in Japan is also there to protect new Plant varieties.***

❖ ***Both Patent Law + Seedling law can be used for Plant protection.***

PATENTABILITY IN INDIA

❑ INDIAN PATENT ACT – 1970

Main Features of Indian Patent Act :

- **Purpose:** To encourage the cheap acquisition of new technology and enhance technological reliance.
- It severely restricted the patenting of foods, chemicals and pharmaceuticals to some types of process patents.
- It created a culture that fostered the largest generic Drug business in the world.

❑ TRIPs AGREEMENT – 1995

- In 1995, India signed the TRIPs agreement to become a member of WTO.
- Patent protection for 20 years.
- No discrimination b/w imported and domestic products.
- Provide compulsory licensing.

❖ ***India is presently the largest market and largest exporter of generic drugs.***

❖ ***Drug Approval Process is the biggest barrier for Biotechnology expansion in India.***

✓ ***India is investigating the creation of agency like FDA (US) for Drug Approval and Export.***

INTELLECTUAL PROPERTY INDIA
PATENTS | DESIGNS | TRADE MARKS
GEOGRAPHICAL INDICATIONS

सत्यमेव जयते

PATENTABILITY IN CHINA

- **CHINA PATENT LAW – 1993**

Guidelines of China Patent Law :

- **What is *PATENTABLE??***

- **DNA fragments/ genes/ proteins / chemical substances.**
- **Process of creating Plants/ animals – Genetic Engineering**
- **Transgenic Plants/ animals & their Gene related Products**
- **Micro-organisms *per se***
- **Processes related to the use of Micro-organisms**

- **What is *NON-PATENTABLE ??***
  - **Plants/ animal varieties**

State Intellectual Propety Office of The P.R.C
中华人民共和国国家知识产权局

❖ ***Biomanufacturers face significant challenges in protecting their IP globally.***

✓ ***Developing a strategy for Patenting generally & Claiming particularly will provide maximum value possible.***

❖ ***Value is measured by protection of Biomanufacturer IP & protection against design-around products developed by competitors and licensing potential.***

Why Protect Intellectual Property in Biomanufacturing processes

- Patents are an important element in the innovation system particularly in medicine.
- Fosters economic growth
- Provides incentives for technological innovation
- Attracts investment that will create new jobs and opportunities.

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