

India, Biotechnology and Patents

Industry Perspective

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Outline

- India and Biotechnology
- Indian Biotechnology: Strength, Opportunities, Weaknesses and Threats
- Patent issues

India and Biotechnology Base

- India is one of the emerging economies in the World.
- Shifting focus to one of the most promising industry of the future: Biotechnology
- Bio-diversity of India will be an advantage for Biotech companies.
- Vast reservoir of scientific human resource with reasonable cost, wealth of R&D institutions, centers of academic excellence in Biosciences
- Vibrant Pharmaceutical Industry and fast developing clinical capabilities collectively point to promising biotech sector
- Over 300 companies and 241 institutions use some form of biotechnology in agricultural, medical or environmental applications.

Core Areas of competence in India

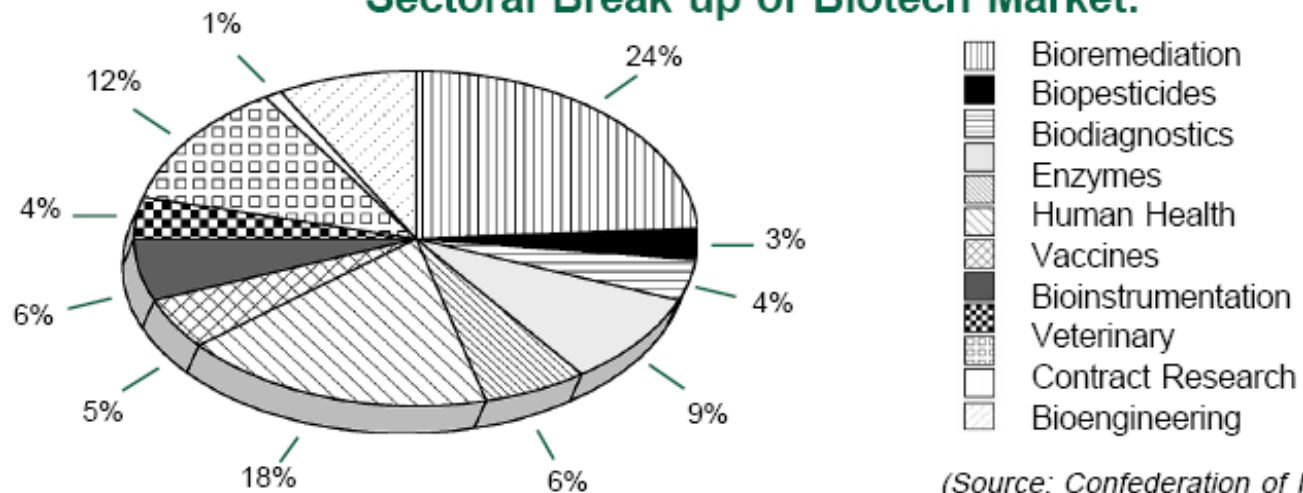
- Capacity in bioprocess engineering
- Skills in gene manipulation of microbes and animal cells
- Capacity in downstream processing and isolation methods
- Skills in extraction and isolation of plants and animals products
- Competence in recombinant DNA technology of plants and animals
- Excellence in traditional and molecular marker assisted breeding of plants and animals
- Infrastructure in fabricating bio-reactors and processing equipment

Biotechnology Industry in India

- Quite nascent stage
- Vast growth and opportunity
- Over 300 registered biotechnology companies, out of which ~100 in are modern biotech sector
 - Twelfth most successful biotechnology sector in the world as measured by number of companies (Ernst & Young)
 - 96 enterprises exclusively as Biotech companies, making India the third largest in Asia [after Australia (228) and China/Hong Kong (136)]

Biotechnology in India

Sectoral Break up of Biotech Market:



(Source: Confederation of Indian Industries)

Biotechnology market

- Total Biotech sector: \$420 million in 2002-2003
- Bio-pharma sector: \$290 million (70%)
- Bio-service sector including clinical research, contract research and contract manufacturing: \$30 million (7%)
- Agricultural Biotech sector: \$25 million (6%)
- Projections: Total Biotech sector to increase to
 - \$1.5 billion by 2007
 - \$4.5 billion by 2010

Pharmaceutical Biotechnology in India

- Market
 - 1997: \$3 billion
 - 2005: \$9 billion (expected)
- Vaccines (new generation and combinations)
 - Bharat Biotech, Bharat Serum, Biological E, Haffkine Bio-Pharmaceutical, Panacea, Pfizer, Serum Institute of India, Shanta Bio-techniques, Smithkline Beecham and Wockhardt
- Therapeutics
 - Biocon, Eli Lilly and Wockhardt
- Diagnostics
 - Bharat Biotech, Qualigen Diagnostics, Span Diagnostics, J. Mitra and xCyton Diagnostics

Examples of Indian Health Biotechnology Products

Sector	Type	Product name	Application	Producer ^a
Vaccines	Recombinant hepatitis B surface antigen	Shanvac-B	Hepatitis B	Shantha Biotechnics
	Recombinant hepatitis B surface antigen	Revac-B	Hepatitis B	Bharat Biotech
	Recombinant hepatitis B surface antigen	Gene Vac-B	Hepatitis B	Serum Institute of India
	Purified capsular polysaccharide Vi of <i>Salmonella typhi</i>	Typbar Vi	Typhoid	Bharat Biotech
Therapeutics	Recombinant human insulin	Wosulin	Diabetes	Wockhardt (Mumbai)
	Recombinant human erythropoietin α	Epox	Anemia	Wockhardt
	Recombinant human interferon α -2b	Shanferon	Cancer	Shantha Biotechnics
	Recombinant streptokinase	Shankinase	Cardiovascular	Shantha Biotechnics
		Indikinase	Cardiovascular	Bharat Biotech
	Liposomal amphotericin B injection	Fungisome	Visceral leishmaniasis	Lifecare Innovations (New Delhi)
	Recombinant human granulocyte colony-stimulating factor	Gramstim	Neutropenia	Dr. Reddy's Laboratories
Diagnostics	Immunoblot assays using recombinant HIV-1 antigens gp41 and C-terminus of gp-120 and HIV-2 antigen gp-36	HIV TRI-DOT	HIV-1 and HIV-2	J. Mitra (New Delhi)
	Immunoblot assay using recombinant HIV-1 antigens gp-41 and gp-120, HIV-2 antigen gp-36, and HCV antigens NS-3, NC-4 and NC-5	HIV-HCV Combo	HIV and hepatitis C	Bhat Biotech India (Bangalore)
	Enzyme-linked immunosorbent assay for recombinant HCV core antigens 1b & 3g, together with peptides for HCV antigens NS-3, NS-4 1, NS-4 2 and NS-5	HEP-Chex C	Hepatitis C	xCyton Diagnostics (Bangalore)
	Enzyme-linked immunosorbent assay for recombinant version of <i>Taenia solium</i> excretory/secretory antigens	Cysti-Chex	Neurocysticercosis	xCyton Diagnostics

^aSome products have more than one Indian manufacturer; only selected examples are shown.

Source: Indian Biotechnology-rapidly evolving and industry led Nature Biotechnology 22, Supplement December 2004 DC31-36

Indian Biotechnology: Strengths

- Human Resource: Trained manpower and knowledge base.
- Academic Resource: Good network of research laboratories.
- Industry Base: Well developed base industries (e.g. pharmaceuticals, seeds).
- International Experts: Access to intellectual resources of NRI's in this area.
- Clinical Capability: Extensive clinical trials and research access to vast and diverse disease in the huge population.
- Bio-diversity: India's human gene pools and unique plant, animal & microbial diversity offer an exciting opportunity for genomic research.
- Stem Cells Research: Several labs have commenced research in stem cells and have valuable stem cell lines.

Indian Biotechnology: Opportunities

- Large domestic market
- Large export potential
- Low cost research base for international companies in comparison with other countries
- Vast and diverse disease based patient populations provide unique opportunities for clinical research and clinical trials
- Supportive Government policy on embryonic stem cells research provides a useful opportunity for International companies to pursue such research in India
- Human bio-diversity provides unique research opportunity in genomics
- Plant & microbial bio-diversity provides vast prospecting opportunities for new drugs
- Conducive Government policy on GM crops provides useful opportunities for Agri-biotech companies

Indian Biotechnology: Weakness

- Missing link between research and commercialization
- Lack of venture capital
- Relatively low R&D expenditure by industry
- Image of Indian industry – doubts about ability of Indian products to meet International standards of quality

Indian Biotechnology: Threats

- Danger of anti-biotech propaganda gaining ground
- Inadequate protection of Intellectual Property Rights (IPR), significant improvement remains in the areas of implementation and enforcement

Key Methods of Doing Business in India

- Set up joint venture companies to locally manufacture the product
- Collaborative research
- Contract research
- Contract manufacturing
- Technology transfer
- Marketing arrangement for bio-supplies (appoint distributor/agent)
- Clinical research

Indian Policy on Biotechnology

- DBT (started in 1985) is developing policy for India
- Indian Council of Medical Research (ICMR)
- Indian Council of Agricultural Research (ICAR)
- Council of Scientific and Industrial Research (CSIR)
- Department of Science and Technology (DST)
 - Current focus on genomics, proteomics, transgenics, stem cell research and product development.
 - Technology Development Fund (TDF) and additional VC funds to promote small and medium biotech enterprises
- Regulatory framework is in place to approve GM crops and r-DNA products for human health
- State government initiatives: AP, KA, MH

IPR Issues

- IP is a central issue in any industry
- Robust intellectual property rights framework is the need of the hour
- India is already member of
 - Paris Convention
 - PCT
 - Berne Convention
 - Convention on biological diversity
 - WTO
- Should make legislation clear on the criteria for the patentability of biotechnological inventions
- Protection of IPR is still an issue and are managed on CnDA

Policy Reasons for Patents

- Patents provide owner with “market exclusivity” that creates increased profits → profits motivate innovation
- Patents require disclosure of new innovations that fosters dissemination of knowledge and further innovation
- Patents discourage the keeping of trade secrets

Biotechnology Business Reasons for Patents

- Biotech businesses require large front-end investment at high risk → patents provide market exclusivity (i.e. profits) that provide a big pay-off when something works
- Patents create a currency of “intellectual property” that allows small inventors/start-ups to obtain investment money
- Sometimes patents are the products

Indian Patent Act, 1970

- With limited resources for R&D, the Act was created to encourage process patenting rather than novel product development
- The weak patent system has had a significant impact on innovative capacities because it has emphasized process innovation, rather than product innovation
- Changes in the Patent Act,
 - Product Patents
 - Longer patent term (20 year)
 - Stronger compliance and enforcement mechanism
- Pressure to comply with TRIPS is raising awareness of IP issues

What can be Claimed?

- Diagnostic tests
- Research tools
- Gene therapy
- Therapeutic proteins Sensors
- Bioinformatics
- Sequences
- Pharmaceuticals

Patents in Biotechnology

- 1980 - Diamond v. Chakrabarty decision
- 1980 - First Cohen-Boyer recombinant DNA patent
- 1984 - Cell line derived from human leukemia patient patented
- 1986 - Genetically engineered corn patented
- 1988 - Harvard Onco-mouse patent - USPTO extends Chakrabarty decision to transgenic animals
- 1991 - Isolated human bone marrow stem cells patent

Bioinformatics in India

- The amalgamation of both biology and information technology
- IT industry looks at Bioinformatics as the next big opportunity
- Major concern:
 - Global market
 - increasing volume of data
 - Human resource in IT, lot of scope in data mining, data handling, fingerprinting, DNA sequencing etc.
 - Institutes are engaged in cutting edge research in genomics and proteomics
 - Expected to grow to \$6 billion in 2005
 - Wipro Health Sciences, SysArris and Kshema
 - Bio-IT need to have multiple platforms: wet lab services, clinical services etc.

Bioinformatics

- Data
 - Genomics
 - Proteomics
 - Clinical
 - High-throughput assays
- Tools
 - Software/hardware
 - Collection
 - Analysis
 - Visualization
 - Pattern recognition
 - Molecular modeling
 - Predictive

IP in Bioinformatics

- Types of Intellectual Property:
 - Software IP and marketing
 - Copyright
 - Licensing Agreements
 - Patents
 - Difficulties
 - No “typical” bioinformatics patent
 - Various business models
 - Cross-technical discipline

Types of Bioinformatics Patents

- Bioinformatics database structures (US Pat No. 6,023,659 (2000))
- Computer based methods of determining the actions of drug candidates on cellular targets (US Pat No. 6,300,078 (2001)).
- Methods for modeling molecular interactions for rational drug design (US Pat No. 5,787,279 (1998))
- Use of 3-D protein structures in rational drug design (US Pat No. 6,225,076 (2001))

Patent Issues for Industry

- Too broad (generic) claims
- Insufficient disclosure (How to make?)
- No written description (no compound, structure, properties etc.)
- Not enabled
- Does the invention really work?
- Prior art exclusion
- Obvious claims

Issues in patentability

- Does the identification and separation by conventional methods of genes which code for well-known compounds represent a discovery or an invention?

A classical example in this area is insulin, a protein that has been known for some time and is produced by a specific gene in the animal body. The structure of this gene was not known until recently.

Issues in patentability

- Are claims directed to genetically-engineered known compounds acceptable?

For example, should a claim directed to "genetically engineered insulin" be allowed, notwithstanding that the inventor discovered only one of the many gene manipulation methods, or should the claim be limited to a product by process?

Issues in patentability

- Are functional claims often so broadly worded, that they may prevent further research in a specific field for fear of infringement suits, acceptable or should the claims be limited to the actual description in the specification?

The Biggest Challenges

- Will the integrated Indian pharmaceutical companies focus on the generics or will they compete with the western research-based pharmaceutical companies in the race for new drug development?
- As for the Indian companies looking for international partners for research partnership, will the partnership be based on asymmetric model of outsourcing or if their innovative capability will allow them accessing to intellectual property on the final product.

A career in patent law

- Patent prosecution
- Patent litigation
- IP Licensing - Technology transfer
- Patent agents/attorneys
- Scientific/Law experience
- Firm or In-House

Key aptitudes for a patent attorney/agent

- Fluent in the technical literature
- Playing with words and writing
- Detail oriented
- Good with people - it's a service industry
- Understand the business
- Litigators should enjoy arguing and public speaking

A few important points

- Patentability and Infringement can be mutually exclusive
 - Having a patent does not mean that you can enjoy the monopoly? Check, your patent might be infringing other broad patent(s)?
 - You may not have freedom to operate even if you have a patent granted for the technology (Solution: Cross licensing)
- Freedom to practice even when you do not have a patent (Your process/technology may be clear prior art).

The future of Biotechnology

- Developing diverse, collaborative relationships to strengthen its industry
- Harmonizing standards with international standards in manufacturing and laboratory practices (ensuring foreign markets and enhancement of the industry's global and local standing)
- Cheaper labor, technical capacity and expertise may capture markets away from companies in the developed countries
- Illustrates the importance of fostering a regulatory and IP environment (encouraging innovative startup companies)

Further Readings

- Kumar N. K., et.al. **Indian Biotechnology – Rapidly evolving and industry led** *Nature Biotechnology* Volume 22 Supplement December 2004
- **Biotechnology in India A Promising Future** Economic News published for the Embassy of India (Economic Wing) Volume XIII Number 2 Winter 2002-03
- **Report on Biotechnology Industry in India** Ref. No. 521.76 DEJ/KEI Embassy of Switzerland 2004
- Lesser W. **Role of IPR in Biotechnology Transfer – Corporate Views** (www.wipo.org/about-ip/en/studies/pdf/ssa_lesser_biotech.pdf)
- Maria A. et. al. **Biotechnology in India** Report commissioned by French Embassy in India 247 pages.

List of useful websites

- www.dbtindia.nic.in
- www.ciionline.org
- www.aibaonline.com
- www.ableindia.org