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BIOPHARMA AND INDIA

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Partner

Mantra

…The object which the Amending Act wanted to achieve ….to prevent ever-greening; to provide easy access to the citizens of this country to life saving drugs; and to discharge their Constitutional obligation of providing good health care to its citizens…

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Section 3(d)

The mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or the mere use of a known process, machine or apparatus unless such process results in a new product or employs at least one new reactant is not an invention

Section 3(d)

Salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of a known substance shall be considered to be the same substance unless they differ significantly in properties with regard to efficacy

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Section 3 (e)

A substance obtained by a mere admixture resulting only in the aggregation of the properties of the components thereof or a process for producing such substance is not an invention

Novartis/ Glivec

- Free base compound Imatinib patented in various countries including USA and the EU in 1993
- Novartis converted the Imatinib to Imatinib Mesylate
- India did not allow product patents at that time

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Novartis/Glivec

- Imatinib mesylate crystallised to obtain beta crystalline form which was the subject matter of the Indian application in 2005
- Claim, API beta crystalline form of Imatinib mesylate is more effective than the free base and displays improved bio-availability

Novartis/Glivec

- Claim was 30% improvement in the bio-availability over the base compound
- No data produced at the time of the application as 3 (d) came into force in 2005
- Novartis conducted experiments after the application was refused and re submitted the data

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Novartis Litigation

- Novartis filed a patent application in the Chennai patent office in 1998 as a post box application
- It also filed an EMR pending grant
- On the basis of the EMR sued CIPLA, Ranbaxy and other generics
- Madras HC upheld the EMR and granted restraining orders

Novartis Litigation

- Bombay HC rejected the action on grounds that
  - the patent application was challenged
  - drug was more expensive
  - was imported only
  - not in the public interest
- The EMR came to an end on rejection of the application

Novartis Litigation

- Assistant Controller rejected the application after opposition on grounds of
  - Lack of novelty
  - Obviousness
  - Section 3(d)- lack of enhanced “efficacy”
  - Wrongful Priority

Novartis Litigation

- Improved efficacy claim
  - Only 30% increase in bioavailability
  - This could be due to difference in solubility
  - Comparison with Imatinib free base and not Imatinib Mesylate
  - Free base can be used equally in the treatment

Novartis Litigation

- Novartis filed two writ petitions in the Madras HC seeking
  - Reversal of the Assistant Controller's decision
  - Declaration that Section 3(d) unconstitutional and non compliant with TRIPS

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Madras HC

- Madras HC held that section 3(d) is constitutional and complies with TRIPS
- Reverted the matter to the IP Appeal Board for appeal
- Ruled on the meaning of “Therapeutic Effect”

Meaning of Efficacy

- In pharmacology meaning of efficacy is “the ability of a drug to produce the desired therapeutic effect”
- Therapeutic means “healing of the body- having good effect on the body”
- Efficacy is independent of potency of the drug

Meaning of Efficacy

- If the discovery of a new form of a known substance must be treated as an invention, then the applicant should show that the substance so discovered has a better therapeutic effect

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Efficacy

- The patent applicant would know the "therapeutic effect" of the known substance /previous patent
- He would also know the difference between the known substance/patented drug and the drug in respect of which patent is asked for

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Efficacy/Derivatives

- Meaning of “any derivatives differ significantly in properties”
- Derivatives should contain such properties which are significantly different with regard to the efficacy

HC on Efficacy

- The test is that the applicant has to show enhancement in the known efficacy
- The applicant can show this by giving necessary comparative details …resulted in enhancement of the known efficacy of the original substance and the derivative….will not be same substance since the properties differ significantly with regard to efficacy

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IP Appeal Board

- The beta crystalline form of Imatinib Mesylate is novel and inventive (non obvious)
- Failed section 3(d); claimed invention does not demonstrate significantly enhanced efficacy
- Therapeutic effect means curative effect

IP Appeal Board

- Non disclosure of prior art in the specification at the time of the application
- Non disclosure of the clinical data in the specification at the date of the application
- High price of the drug could lead to unrest and public disorder

Supreme Court

- Does the beta crystalline form comply with section 3 (d)
- Is it novel and inventive
- Does it violate public disorder

SC/ Section 3(d)

- Section 3(d) not limited to pharmaceutical products or processes
- Cannot be limited curative effect but extend to an advantage or perhaps therapeutic advantage

SC/Efficacy

- Greater effectiveness; greater safety; palliative care
- Clinical trial data
- Known substance clearly anticipated/ enabling disclosure

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SC/Section 3(d)

- What is a derivative
- What is a known substance
- What is new use
- Standard of proof

EPO and Section 3(d)

- Article 10(2)b Directive 2004/27/EC5

A medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailibity

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EPO/Section 3(d)

The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy. In such cases additional information providing proof of the safety and/or efficacy ….must be supplied

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EPO /Therapeutic Effect

- If the assumption is that compounds with similar chemical structure will have similar therapeutic activity then it will not be allowed
- If it shows advantageous activity not possessed by the disclosed prior art then it will be allowed

EPO APPROACH

- Assumption is that solid state inventions are close to the prior art because they may have the same chemical compound/entity but different physical/physiochemical form

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EPO

Requirements

- Clear/precise description of the invention and distinction from the prior art
- Sufficient/complete disclosure on how the invention was obtained
- Clear description of novelty/enabling disclosure

EPO

- Inventive step/obviousness

"Problem solution" and not "obvious to try"

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EPO/New Forms

- Structurally it is novel and not obvious over the prior art
- If structurally not novel or is obvious then need to demonstrate improvement over the prior art
- Improvement has to be increased/ enhanced effect

EPO/New Forms

- EPO does not contain “therapeutic effect” It is not defined or adhered to
- Confined to the advantageous/problem solution
- In contrast 3 (d) requires curative effect/ healing of a disease

EPO Practical Steps

- Description in the specification
- Disclosure of data at the time of the application
- Cite prior art and distinguish invention

Clear Precise Claims

- Solvates/hydrates/ crystals/co-crystals
- Polymorphs
- Parameters

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Clear Precise Claims

- Product by Process
- New product obtained by a known process
- A new process resulting in the same product is not allowed

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Clear and Precise Claims

- Parameters
- Single crystal x-ray diffraction
- PXRD
- Raman Spectroscopy/IR
- TGA/DTA/DSC

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Parameters

- Technical parameters
- Essential parameters
- Do not use parameters or methods that cannot be compared with the prior art

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Parameters

- Include the method of measuring the parameters
- Give necessary details
- Number of peaks: sufficient to clearly distinguish from prior art
- In claims describe the peaks rather than the whole spectrum

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Process

- Old process resulting in new product
- The application does not clearly describe the method used to define the parameters
- The method for preparation of the seed crystals is not described

Other Points

- Prior art must be sufficiently disclosed at the time of the application
- The level of disclosure required is the same as that for the base compound
- Provide the values for the significant region of the spectrum
- Disclose data at the time of the Application not later

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Comparative data

- Comparative data (absolutely essential)
- If parameter not disclosed in the prior art- provide it
- If not known provide the corresponding value of the prior art parameter

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Inventive Step

- The UK/EPO approach is the problem/ technical solution approach
- Assumption is that should be the approach of the Indian Patent Offices
- It is not the US Obvious to Try

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Inventive Step

- The prior art is determined and the closest prior art is identified
- The technical problem is determined by the difference between the claimed invention and the prior art
- Identify the technical effect induced by the difference

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Inventive Step

- Confirm that the technical problem has been solved
- Assess whether in the light of the prior art it would have been obvious to the person skilled in the art

Attitude of Indian Patent Offices

- Polymorphs are common in APIs
- Crystallisation normal part of development of the API
- It is a routine task in development of the API
- New crystalline forms are predictable
- The intended medical use has been disclosed

Pre Grant Oppositions

- After the publication of the Application and before the grant of the patent any person can oppose by written application to the Controller
- Any person means anyone and includes NGOS and other public interest bodies
- After application and before grant misconstrued
- IPO has accepted pre grant oppositions after grant but before patent certificate stamped

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Pre Grant

- July 2010 judgement by Delhi High Court on six writ petitions
- Patent deemed to be granted when Controller makes the order for grant
- A mere letter that the application has been accepted for grant is not a grant

Grounds for Pre Grant Opposition

- Invention wrongfully obtained
- Prior publications of the claims
  - Indian patent applications after January 1912
  - Any other document
- Public knowledge or use in India
- Obviousness
- Excluded inventions
- Fails 3(d) 3 (e) requirements

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Grounds

- Insufficiency
- Section 8 requirements failure
- Convention application not within 12 months from date of first application
- Specification fails to disclose origin of biological material used for invention
- The claimed invention known or available within any local or indigenous community in India

Post Grant Oppositions

- At anytime after the grant but before expiry of a period of one year from the date of the publication of grant of the patent any interested party may oppose
- Any interested party will not include the NGOS and public interest bodies

Post Grant

- Grounds the same as pre grant
- No appeal from pre grant
- Appeal from post grant to the IP Appeal Board

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Opposition Procedure

- Opposition to be heard by appointed examiner/Assistant Controller
- Opposing party to file statement containing grounds of opposition and experts report
- Applicant can file reply and produce its own expert report
- Oral hearing

Section 8 Compliance

- An applicant prosecuting a patent in India is required to file with the Indian application details of all applications filed outside of India for the same or substantively similar inventions:
  - Statement setting out detailed particulars of the applications
  - An undertaking to keep the Controller informed in writing, from time to time, provide detailed particulars of each of these applications

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Section 8

- The Controller may also require the applicant to furnish details relating to the processing of the foreign applications
- Failure to comply could lead to rejection, opposition or revocation

Chemutra v Union of India

- Applicant failed to furnish details of its foreign applications
- Failed o comply with express requests to provide search and examination reports pf the US, EPO and Japanese applications
- Supressed relevant information
- Application rejected

Working the Patent

- Inventions should be worked in India on a commercial scale and to the fullest extent that is reasonably practicable
- Mere monopoly for the importation of the patented article not allowed
- Promote public interest and balance rights and obligations

Working the Patent

- Not impede public health or prohibit Central Government to take measures to protect public health
- Patentee not resort to practices that unreasonably restrain trade or adversely affect technology transfer
- Patented inventions are available at reasonably affordable prices to the public

Section 146

- A statement setting out the extent to which an invention has been worked in India has to be filed by 31 March each year or within two months of being notified by the Controller
- If not worked the reasons for it and the steps taken

Section 146

- Information to include
  - Quantum and value of goods produced
  - Licences and sub licences granted
  - Whether public requirement has been met
  - Whether available at a reasonable price

Compulsory Licences

At any time three years after the grant of the patent any interested person can apply to the Controller for a compulsory licence

Grounds

- Reasonable requirements of the public have not been satisfied
- The patented invention is not available to the public at a reasonable or affordable price
- The patented invention is not worked in India

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Procedure

- Application to contain a statement setting out nature of interest and particulars and facts
- Prima facie case to be made out

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Considerations

- Nature of the invention
- The time elapsed since grant and the measures taken by the patentee or licensee to make full use of the invention
- Ability of the applicant to work the invention to the public advantage
- Capacity of the applicant to invest capital and work the invention
- Effort made by the applicant to obtain licence on reasonable terms and conditions

Reasonable Requirements

- An existing trade or industry or development or establishment of these in India is prejudiced
- Demand for the patented article has not been met to an adequate extent or on reasonable terms
- A market for export of the patented article manufactured in India is not supplied or developed

Reasonable Requirements

- Establishment or development of commercial activities in India is prejudiced
- The patentee imposes conditions on the licensee that prejudices establishment or development of any trade or industry in India
- The patentee imposes conditions such as exclusive grant back and prevention of challenges to the validity
- If working of the patent in India is prevented or hindered by import of the patented article

Natco/Bayer

- Nexavar / sorafenil tosylate
- Nexavar is not available to the general public
- Bayer does not manufacture, it only distributes
- Nexavar is not available at a reasonably affordable price

Indian Biological Resources

- Plants, animals, micro-organisms or parts thereof, their genetic material and by products with active or potential use but does not include human genetic material
- Bio-survey, bio-utilisation includes species, sub species, genes, components and extracts of biological surveys

Prior written approval of NBA

- Any foreign company intending to do following needs approval :
- Obtain the Resource
- Obtain any knowledge relating to the Resource for research or commercialisation
- Transfer the results of any research relating to a Resource for monetary consideration
- Apply for a patent or other IP right

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Exclusions

- Collaboration research for transfer or exchange of Resource

Conditions that may be imposed

- Benefit sharing fee/royalty
- Benefits from commercialisation

Approval is not transferable

- Criminal offence
- 5 years imprisonment
- Rs 10 lakhs fine or both and damages

Licences

- Registration with the Patent office
- Information on change of licence
- Dispute resolution clauses
- Protection of technology/exit strategy

Licences

- Licences have to be registered with the Controller to validate entitlement
- Controller will need to be satisfied of the title
- In event of a dispute Controller will take no action

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THANK YOU