To,

November 11, 2024

The MANAGING **PARTNER**,
L.S.DAVAR & Co.**,**
HEAD OFFICE - KOLKATA,
INDIA
,

Sub: Application for a suitable lead position - "Partner–Patents"/suitable senior management position that commensurate with my experience
Ref: Advertisement from your organisation in Job Groups for recruiting various positions in Patents: Associate Partner/Partner Designate and Managing/Principal Associate

Dear MADAM/HIGHER MANAGEMEN**T**,

Greetings!

It has been an incredibly enjoyable journey all through these years, transitioning from a technical expert in chemistry to a seasoned patent/IP practitioner (as **law firm** attorney, **Corporate in-house IP counsel - Chemicals, Pharmaceuticals and Agrochemicals, IP Management** in Government of India and private **IP consultancy**/patent practitioner). I have built my career in varied technical, techno-legal, legal advisory and leadership positions in varied industries, with global giants as well as mid-sized companies. That has made me to champion challenging projects, taught me time management and resource management, lead people by example and motivate the team personnel, and last of all thrive and perform in diverse work environments.

My key strengths which include meticulousness and planning skills (for instance, in drafting patent applications), detail-oriented and argumentative skills (in patent prosecution, opposition/s), analytical, legal and advisory skills (in IP Analytics, IP competitive intelligence, IP landscaping, IP due diligence, transactional IP practice and devising IP strategic business decisions), networking and collaboration (updating clients on current issues in IPR, advising on procedural aspects and legal aspects of patent laws and with trade/industry bodies/government authorities on IP protection/IP policy related matters etc.), accountability for my team performance, leadership skills in project/patent portfolio management (combined with training and development skills/IP awareness creation in Corporates, academic Universities), adaptability/responsiveness in handling complex tasks/situations (Complex patent drafting and prosecution, IP protection and Management), negotiation and networking (client counselling and IP/business negotiation), my passion for writing and Speaking Engagements has placed me as a meritorious candidate in every organization that I have served.

Having crafted a track record of concrete and successful outcomes as in-house IP Counsel and IP Consultant, I view the prospect of bringing my background to your esteemed organisation as an opportunity - I approach with deep reverence for this subject role involving promoting and harnessing IP Culture with a profound passion in utilising/expanding my proficiency in IP and legal practice in worldwide jurisdictions.

As an IP Expert and a legal professional, and a highly motivated individual with outstanding communication, organizational and time management skills, I firmly believe in my capabilities to assist your organisation **in the subject role** that involves a cross-functional role in **your organisation's** Intellectual **P**roperty initiatives, leveraging **IP**, legal and commercial acumen for competitive and business advantage and integrate proactive legal strategies with your strategic needs. **Having lived and worked in there major metropolitan cities in India – Delhi, Mumbai and Chennai, I am open to take up** PAN – INDIA role (and am fluent in English, Hindi, **T**amil, **T**elugu). My **p**reference would be in the order of Mumbai or Delhi, followed by Bangalore.

Further, I sincerely consider working with your organisation in the subject role as an unique opportunity to contribute, learn and integrate with the strategic objectives of this dynamic organisation.

Please find attached the following for your review and consideration:

1. This motivation letter (**p**age 1);
2. A Combined Document comprising my detailed CV and Annexure of Publications and Speaking Engagements in IPR/patent practice along with website links (**p**ages 1 t**o** 3);
3. Soft copies of a few magazine publications in IPR/patent practice; Certificates of National Awards in IPR/patent practice;

I sincerely appreciate your consideration and look forward to hear from you soon.

Thank you,

Yours sincerely,
Kameshwari Sridhar
Mobile:+91-**9819731390/9821276407;** PS: Please contact me in +91-9819731390, in case my +91-9821276407 is not available. Thanks.

KAMESHWARI SRIDHAR

INTELLECTUAL PROPERTY LEADER/ADVOCATE

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LinkedIn: https://www.linkedin.com/in/kameshwari-sridhar-4233a624/

CORE COMPETENCIES

- Patent Analytics
- Chemical Structure Searches
- Patent (IP) Landscaping
- Competitive Intelligence
- IP Due Diligence
- IP Agreements
- Validity/Patentability/FTO/Infringement Opinion
- Patent Portfolio Management
- Patent Drafting
- Patent Prosecution
- IP Strategy
- Opposition/Litigation Support
- Negotiation
- Corporate IP Training
- IP Awareness Training
- IP Team Mentoring
- IP Consultancy
- Client Counselling
- IP Advisory
- Patent Databases
- IP Policy
- IP/Legal Research
- IP Publications
- Speaking Engagements
- Technical Writing
- Research and Development
- Content Development
- Copy Editing
- Trusted Advisor
- Leadership/Team Building

Intellectual Property Expert in India with experience of two decades and more having held various middle/senior management positions as corporate IP counsel, law firm attorney, IP management role and IP consultancy combined with technical/research experience. Proven capabilities as Corporate in-house patent counsel/IP leader/IP consultant in patent portfolio management and transactional IP/Legal Agreements with special focus on business functions pertaining to chemicals, pharmaceuticals and agrochemical crop protection technologies, food and personal care; other technologies include mechanical engineering, chemical engineering, biochemistry, biotechnology, healthcare, ICT and medical technologies. Passionate IP Leader making presentations to the team and top management on IP Strategies and IP policy; actively involved in leadership role and team building. Significant contributor to corporate training in IPR to R&D scientists, global IP team, relevant stakeholders and IP Awareness workshops in Universities through educative IP awareness training/development. Four national Awards in Intellectual Property practice.

WORK EXPERIENCE

I) IPR CONSULTANCY (PRIVATE PRACTICE) – MUMBAI MAR 2018 TILL DATE AND JAN 2014 – SEP 2016

- Consultancy work undertaken in intellectual property (patent practice and designs) domain;
- IP portfolio management/patent practice in Technology areas of chemistry, pharmaceuticals, biotechnology, medical devices, food, personal care etc., for both national and international clients;
- IP Advisory in Drafting, reviewing and negotiating Transactional IP Agreements - Non-disclosure and Confidentiality Disclosure Agreements, Technology Transfer Agreements, Technology Service Agreements; Collaborative Research and Development Agreements
- IP Landscaping projects, conducting IP trainings, IP Advisory, IP publications, Speaking Engagements and Client Counselling (For United States, India, Europe)

II) GLOBAL INTELLECTUAL PROPERTY COUNSEL – BASF INDIA PVT LTD, MUMBAI SEP 2016- AUG 2017

- Responsible IP Counsel for Crop protection Business in India, Germany and Switzerland - Effective patent portfolio management of in-house technologies on chemicals and agrochemicals; Robust Drafting, filing and global patent prosecution of patent applications in worldwide JURISDICTIONS (FIRST FILING IN EUROPE); Rendering opinions on patentability, validity, Freedom-to-operate (FTO) studies and appropriate FTO strategies
- IP Expert and advisory role in drafting, reviewing and negotiating IP Agreements – Non-Disclosure Agreements, Collaborative Research Agreements; Assignment Agreements, Ideation Agreements in partnership with legal and business development; building templates, standard protocol and guidelines formatting internal standards;
- Ensure IP risk management and defending portfolios (global jurisdictions – US, EP, PCT, INDIA, CHINA and BRAZIL etc.)
- IP strategy advisory/counselling to business units - R&D, legal, other departments and higher management to drive IP strategic business decisions
- Team building and leadership role – training and mentoring of patent team personnel in patent practice/advisory
- Corporate IP training sessions and presentations on latest IP and relevant legal developments to global IP team, top management, R&D, marketing, legal and business units
- International business visit to Germany and Switzerland

III) PHARMACEUTICAL IN-HOUSE IP COUNSEL- PIRAMAL ENTERPRISES LIMITED, MUMBAI

SENIOR MANAGER – PATENTS MAY 2010-APR 2013

MANAGER PATENTS MAY 2007-MAY 2010

- Responsible in-house patent Attorney for company engaged in new drug discovery – (Medicinal Chemistry business units: New Chemical Entities (NCE), Small molecule drugs, API and intermediates, Formulation, Prodrugs, Natural Products (herbal) and follow-on pharmaceutical inventions); Effective Patent portfolio management of in-house pharmaceutical inventions/technologies in worldwide jurisdictions (USA, EUROPE, INDIA, AUSTRALIA, NEW ZEALAND, CHINA, JAPAN, RUSSIA, SOUTH AFRICA, KOREA etc. & FIRST FILING in US) including:
  - Patent searches, chemical structure searches (using STN/SCIFINDER), Novelty Search Reports, patentability, validity freedom-to-operate, non-infringement and other legal opinion; Complex patent drafting and global patent prosecution and filing of patent applications including PCT international applications (FIRST FILING IN US)
  - Patent due diligence analysis - active involvement in evaluation of potential in-licensing/out-licensing opportunities that drive potential strategic mergers and acquisitions
  - Managed IP and legal aspects of business development transactions including IP licensing and collaboration Agreements, Research Agreements, Internal Mergers
  - Drafting, reviewing and negotiating IP Agreements – Deed of Assignment, Research Agreements, technology Licensing Agreements in coordination with legal, regulatory, business development, clinical, R&D and Finance;
  - IP strategic advise to regulatory, business development, clinical, R&D, other departments on legal matters of IP protection
  - Competitive IP Intelligence in specific therapeutic areas of interest;
- Guidance and training to junior team personnel patent practice areas
- Corporate IP knowledge sharing, awareness and training sessions in patent practice for in-house Patents team, R&D and updates on latest IP/legal developments to higher management

IV) LAW FIRM: SENIOR ASSOCIATE – IPR, CORPORATE LAW GROUP, NEW DELHI MAR 2005 to SEP 2006

- Patent portfolio management for Indian and multinational clients (pharmaceutical giants), FMCG, Biotechnology companies, Government organizations, Universities
- Patent Searches, inventor interviews, patentability, validity, non-infringement and Freedom-to-operate opinion; Filing, drafting and prosecution of Indian and national phase patent applications
- Patent opposition work, prosecution/opposition strategies for clients/patent litigation support through claim mapping and file wrapper analysis
- Client Counselling; IP Advisory to multinational clients on periodical updates/media news reports in Indian patent laws and procedural aspects of IPR
- Team presentations to clients on IP matters and IP knowledge sharing presentations to top management/patents team; Liaison with trade/industry bodies/government authorities on IP policy related matters

ACCOLADES

I) SPEAKING ENGAGEMENTS

- ✓ Guest Speaker in Professional Forums/Law/Technical Universities on Topics related to Intellectual Property (2004 to 2020)

II) NATIONAL AWARDS IN INTELLECTUAL PROPERTY

- ✓ National Patent Drafting Competitions held in 2015 (First Prize) and International Patent Drafting Competition held in 2016 (Second Prize) : Awarded by jointly by a leading US law firm and a leading Indian law firm
- ✓ National IP Essay Competitions held in 2010 (third best entry)and 2011 (second best entry)

III) PERFORMANCE AWARDS

- ✓ Drafting most complex patent application in NCEs in 2010
- ✓ Setting trend record - Fastest track drafting and filing of NCE patent application in 2012
- ✓ Meritorious Global IP Counsel from India team selected for leadership training in Germany and Switzerland in 2017

IV) PUBLICATIONS

International publications and national level magazine publications in Intellectual Property (1999 to 2023):

- ✓ Case Review S. 3(d) – Published in Nov 2023 in Wolters Kluwer IPLaw blog
- ✓ Bt GM Technology Patent Chronicle in India (2018)
- ✓ Lead Compound Approach and pharmaceutical obviousness at US PTAB (2018)
- ✓ Pharmaceutical patent infringement and doctrine of equivalents at US CAFC (2016)
- ✓ IPO's Saxagliptin Compulsory License decision (2016)
- ✓ IPO's rejection of pharmaceutical patents under S. 3(d) of Indian patent law (2015)
- ✓ Lead Compound Approach and Structural obviousness at US PTAB (2015)
- ✓ Intersection of Structural Obviousness and Unexpected Results (BMS Baraclude patent decision) (2015)
- ✓ Inter Partes Review and formulation patent decision (2015)
- ✓ Pharmaceutical Mergers (2010); Geographical Indications (2011); Case Laws and Case Studies for IPR Bulletin (2004)
- ✓ Educational CD-ROMs in Chemistry (2000); Technical Research Publication in Personal Care Cosmetics (1999)

For further details on SPEAKING ENGAGEMENTS AND IP PUBLICATIONS, Please see, Annexure-KS-IP-Speaking – Publications.pdf attached separately.

KAMESHWARI SRIDHAR

PATENT ATTORNEY/ INTELLECTUAL PROPERTY EXPERT

LinkedIn: https://www.linkedin.com/in/kameshwari-sridhar-4233a624/

Email: dhanyakams@gmail.com; kameshwari.dhanyakamsips@gmail.com

V) SCIENTIST IPR, GOVERNMENT OF INDIA (NEW DELHI) FEB 2004- MAR 2005
(PATENT FACILITATING CENTRE, TECHNOLOGY INFORMATION FORECASTING AND ASSESSMENT COUNCIL)

- ❖ Patent searches and novelty assessment of inventions for seeking financial assistance
- ❖ Pre-drafting interviews with inventors and prosecution strategies with applicant/inventors
- ❖ Preparation of disclosure reports for management
- ❖ Liaisoning with inventors/Universities and external law firms/outside Counsel for drafting,filing and prosecution of patent Applications
- ❖ IP landscaping studies – Report for TIFAC on "Patents in hydrogen production and storage"
- ❖ Managing IPR Bulletin work and rendering articles for IPR bulletin; Organised/participated in IPR workshops/Awareness programs conducted by TIFAC in variousparts of India

VI) TECHNICAL POSITIONS/RESEARCH EXPERIENCE – POSITIONS HELD FROM 1997 TO 2003

- ➢ **COPY EDITOR THOMSON PRESS INDIA PVT, LTD, NOIDA, INDIA MAY 2003 - AUG 2003**
  AMNET SYSTEMS PVT LTD., CHENNAI, INDIA OCT 2001 - FEB 2002
- ✓ Copy Editing/Proof Reading of Scientific journals and Team Management

- ➢ **TEACHING FACULTY MAESTROS STUDY CENTRE, CHENNAI, INDIA JUNE 2001- JUNE 2002**
- ✓ Teaching Chemistry for XI and XII grade students and continuous assessment of students performance

- ➢ **CONTENT DEVELOPER (Computer Based Training)** SOFTWARE SOLUTIONS INTEGRATED LTD, CHENNAI **JULY 2000- JUNE 2001**
- ✓ Content Development for Educational CD-ROMs in Chemistry, Project Planning, Conceptualizing interactive modules and Team Management

- ➢ **SENIOR TECHNICAL EDITOR/TEAM COORDINATOR (TECHNICAL WRITING) - DOMEX TECHNICAL INFORMATION PVT LTD, CHENNAI OCT 1998- JULY 2000**
  (WORK UNDERTAKEN FOR DERWENT INFORMATION, UNITED KINGDOM)

- ✓ Patent Abstracting (Chemistry, Chemical Engineering, Pharmaceuticals, Polymer technologiesetc,);
- ✓ Editing of Patent Abstracts written by Junior Editors;
- ✓ Manual Coding of Patent Abstracts in Polymer Technology and Enhanced Polymer Indexingapplied to Polymers and Related chemicals
- ✓ Responsible for Team Production
- ✓ Coordination with DERWENT technical team, training and development of Junior Editors

- ➢ **OFFICER CHEMIST - PONDS INDIA LIMITED, CHENNAI, INDIA (SUBSIDIARY OF UNILEVER INDIA) JAN 1997 TO MAR 1997 AND JULY 1997 TO JULY 1998**

- ✓ Basic Research related to Product Development; Competitors Product Analysis
- ✓ Research on Sensory Properties of Emollients (for application in final products/cosmetic formulation)

EDUCATION

- ❖ **2009-2012 L.L.B, University of Mumbai (Final Year Topper with 66%)**
- ❖ **1995-1997 M.Sc. (Chemistry),** Queen Mary's College, **University of Madras (Topper with 80%)**
- ❖ **1995-1996 PG Diploma in Applied Chemistry,** Loyola College, **University of Madras (Topper with 81%)**
- ❖ **1992-1995 B.Sc. (Chemistry), University of Madras (Topper with 80%)**
- ❖ **2004 Diploma in Management, Indira Gandhi National Open University, Delhi**

PROFESSIONAL CERTIFICATIONS

- ❖ **Authorized Indian Patent Agent (IN/PA/1009), Government of India from 2005**
- ❖ **Registered Advocate with the Bar Council of Goa and Maharashtra**
- ❖ **Qualified Bar council of India Examinations for license to practice**
- ❖ **All India Women Scientist Scholarship sponsored by Department of Science and Technology (2004) for undergoing professional training in IPR**

KAMESHWARI SRIDHAR

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MUMBAI/CHENNAI, INDIA

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kameshwari.dhanyakamsips@gmail.com

Linkedin: https://www.linkedin.com/in/kameshwari-sridhar-4233a624/

SPEAKING ENGAGEMENTS

- ✓ **IP Trainings in Patent Practice for clients (2018-2023) and Corporate IP Awareness trainings (2005 to 2017)**
- ✓ **Intellectual Property Quiz Winner (World IP Day Conference by Sagacious IP), April 2020**
- ✓ **"Copyright Management in Educational Institutions" for Academicians in University of GOA- IP Awareness workshop conducted by Goa State Council of Science and Technology, TIFAC, GOVERNMENT OF INDIA, GOA, September 2019**
- ✓ **"Overview of IPR – Focus on Copyrights and Internet" for professors/Librarians in IP Awareness Workshop on COPYRIGHTS AND RELATED RIGHTS in SVKM's Jitendra Chauhan College of Law, September 2019**
- ✓ **"General Overview of IPR – Focus on Copyrights and Internet" for Professors/Librarians in IP Awareness Workshop in Pravin Gandhi College of Law, Mumbai, August 2019**
- ✓ **Talk on "Best Practices – Patent Prosecution at the Indian Patent Office" delivered to Global IP Team, BASF, Germany, March 2017**
- ✓ **"Intellectual Property Rights and Patents" – Experiences Sharing in IP and Patent Practice" on the Inaugural Day of Government of India's 8th Batch Women Scientist Scholarship Scheme on IPRs, at TIFAC, NEW DELHI, APRIL 2016**
- ✓ **"Intellectual Property Rights and Patents – A Perspective – Focus on Patent Searches and Patent Drafting Strategies" delivered for IP Management Students in NATIONAL INSTITUTE OF INDUSTRIAL ENGINEERING, MUMBAI, NOVEMBER 2015**
- ✓ **Guest Speaker in ORIENTATION PROGRAMME for L.L.B. students enrolled in 2012-13 in JITENDRA CHAUHAN COLLEGE OF LAW, MUMBAI, 2012**
- ✓ **General Overview of IPR" – Talk for pharma management students from GARWARE INSTITUTE OF CAREER EDUCATION AND DEVELOPMENT, 2007**
- ✓ **"Patentability of pharmaceutical inventions" – Talk for pharma management students from GARWARE INSTITUTE OF CAREER EDUCATION AND DEVELOPMENT, 2007**

ANNEXURE: SPEAKING ENGAGEMENTS (MAJOR) AND PUBLICATIONS IN INTELLECTUAL PROPERTY PRACTICE

PUBLICATIONS IN INTELLECTUAL PROPERTY PRACTICE/TECHNICAL PUBLICATIONS

Article titled "Biochemical substances and the realm of S. 3(d) (Novozymes vs The Assistant Controller of Patents and Designs) : Scope of applicability of Section 3(d) redefined by Madras High Court? Published on November 23, 2023 in Wolters Kluwer IP Law Blog - https://lnkd.in/gxp_9s-5; https://patentblog.kluweriplaw.com/2023/11/23/biochemical-substances-and-the-realm-of-s-3d-novozymes-vs-the-assistant-controller-of-patents-and-designs-scope-of-applicability-of-section-3d-redefined-by-madras-high-court/; also Available at **https://ssrn.com/abstract=4619101, October 2023**; A few **more writings/articles in IP to be published soon**

The Bt and GM Technology Patent Chronicle in India (Monsanto vs Nuziveedu): The Intricate Dynamics of Patentable Exclusions and Plant Varieties?" available at https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3185934; published in Intellectual Property: Patent Law e-Journal, Vol 9, Issue 46, June 28, 2018 and others; ranked in the top ten downloaded list for July 2018

Lead Compound Approach: An Eternal standard for chemical and pharmaceutical obviousness at US PTAB?, published in LEGAL ERA MAGAZINE, May-June 2018 (pages 58 to 61), also available at: https://ssrn.com/abstract=3135222, February 2018.

US Court of Appeals affirmation of infringement (of pharmaceutical formulation) strikes the chord withdeterminants under Doctrine of equivalents?, IPFRONTLINE, PATENTS practice paper, pgs 1-6; abridged version republished in IP ERA magazine, June-July 2016

Indian Patent Office's recent decision on SAXAGLIPTIN Compulsory License: a step towards more coherent interpretation of Indian patent law's CL provisions?, IPFRONTLINE, Patents Practice Paper, pgs1-10, February 9, 2016, also available at http://ssrn.com/abstract=2729778, ranked in the top ten downloaded list in 2016

Invasive Recap of Indian Patent Office's patent rejections based on Section 3(d): A battle cry for pharmaceutical patents? – Part I, published in IPERA (a leading national Indian IP magazine),Vol 2, Issue2,pgs 28-31, Sep-Oct 2015

Invasive Recap of Indian Patent Office's patent rejections based on Section 3(d): A battle cry for pharmaceutical patents? – Part II, published in IPERA (a leading national Indian IP magazine), Vol 3, Issue2, pgs 36-39, Nov-Dec 2015

Reliving the tradition of lead compound approach for structural obviousness evaluation of new chemical compounds: US PTAB denies inter partes review petition for Merck's prodrug patent on Emend, IP Frontline, Patents Practice Paper, pgs 1-47, July 28, 2015, also available at http://ssrn.com/abstract=2636915

Expect the Unexpected: Intersection of Structural Obviousness and Unexpected Results in Patentability Determination of New Chemical Compounds, SSRN, 1-78, January 26, 2015). Available at SSRN: http://ssrn.com/abstract=2555621, ranked in the top ten download list in the Medical-Legal Studies e-Journal and Intellectual Property Patent Law e-journal for the period Dec-April 2015

Inter partes review – a new frontier for Hatch-Waxman generics vs innovators pharma patent battles: Recent Oracea decision sets the pace!—Does inter partes review signify a death knell for pioneer patents?, IP Law Practice Paper, IP Frontline, pgs 1-16, January 15, 2015, also available at http://ssrn.com/abstract=2555681, ranked in the top ten download list in the Medical-Legal Studies e-Journal and Intellectual Property Patent Law e-journal for the period Dec-April 2015

Protecting traditional arts, handicrafts and community IPRs - India's approach on Geographical Indications protection, - IP National Award winning entry in July 2011

Pharmaceutical mergers and the Intellectual Property implications of MNCs joining hands with generic companies, IP National Award Winning Entry in 2010, published at http://iips.nmims.edu/files/2012/05/IPost_magazine_2010.pdf

Apotex loses patent battle based on Doctrine of Equivalents (Case Law), IPR BULLETIN, PFC, September 2004 (www.indianpatents.org.in); Hydrogen – The Fuel of the Future, (Case Study), **IPR BULLETIN, PFC, September 2004, (www.indianpatents.org.in)**

Cadila's combination drug loses patent battle, IPR BULLETIN, PFC, August 2004, (www.indianpatents.org.in); No more needle pricking for drug delivery, IPR BULLETIN, PFC, August 2004, (www.indianpatents.org.in)

Generic drug makers vs Innovators, Case Law, IPR BULLETIN, PFC, June - July2004, (www.indianpatents.org.in)

The CD-ROMs "**Organic and Inorganic Chemistry" and "Physical Chemistry**" developed during my association with Software Solution Integrated Limited, released in market in **June/July 2001**

Research work on "**Sensory properties of Emollients**" undertaken during my association with Ponds (India) Limited, published in an U.S. International Journal 'Cosmetics & Toiletries' (**January 1999**) creditedto my name and my senior

Kluwer Patent Blog

INDIA, LEGISLATION, PHARMA

Biochemical substances and the realm of S. 3(d) (Novozymes vs The Assistant Controller of Patents and Designs): Scope of applicability of Section 3(d) redefined by Madras High Court?

Kameshwaris Sridhar (Intellectual Property Attorney, India)/**November 23, 2023**

I) Introduction

The science of biochemicals and the realm of Section 3(d) of Indian Patents Act! Can there be a reconciliation between the two?

This question is a hot topic of discussion amongst the Indian biochemical patent community following the recent decision (Novozymes vs The Assistant Controller of Patents and Designs) pronounced by the Madras High Court on 20 September 2023. In a first-of-its-kind decision that may redefine the applicability of S.3(d) to the biochemical realm, the Court adopted a constrictive interpretation of the scope of substances that fall under the purview of S. 3(d) of the Indian Patents Act.

Invoking the doctrine of "*ejusdem generis*", the Court's interpretation of the applicability and scope of the statutory explanation provided under S. 3(d) in the context of biochemical substances has advanced a new twist to the tale – an unexpected and significant development to the inherent intricacies surrounding the interpretative framework of S. 3(d). Ultimately, the Court has ruled that S. 3(d) does apply to biochemical substances but that the Explanation to S. 3(d) does not apply to the claimed invention and that Novozymes appeal should be allowed in part. In so doing, the court relied on the Division Bench[1] and Supreme Court decision in Novartis AG[2], to arrive at its conclusion on the applicability of the substantive provision and the doctrine of "*ejusdem generis*" for the inapplicability of the Explanation to S. 3(d) to the claimed invention.

Until this case, the key determinants of S. 3(d) – "known substance" and "efficacy" have only been analysed through the lens of chemical/pharmaceutical inventions and its patent practitioners by the Indian courts. The present decision examines these key determinants in the context of biochemical substances. The scrutiny of S. 3(e) in the present case also sheds light on the standards required to be met for its applicability to composition claims.

II) Novozymes HC decision: A brief overview

1) Background of the Patent and invention at issue

In its decision dated September 20, 2023, the Court, setting aside the Indian Patent Office (IPO)'s order partly, pronounced that the substantive provision in S. 3(d) applies to biochemical substances in principle but Explanation to S. 3(d) becomes inapplicable to the claimed invention in Indian patent application 5326/CHENP/2008 – pertaining to the variants of phytase, i.e. an enzyme or a biochemical. The appellant (Novozymes) had challenged the IPO's order (of 15.11.2016) in which the claims were rejected primarily on the grounds that the claimed invention in Claims 1 and 2 pertaining to the phytase variant with improved thermostability is a known substance not patent eligible under S. 3(d) and claims 8 to 11 (the composition claims comprising the phytase variant) falls within the scope of S. 3(e) because the composition is a mere admixture of ingredients.

2) Legal tenets governing the subject matter

S. 3(d) of the Indian Patents Act is a unique "Made in India" provision that is exclusive to the Indian jurisdiction and which acts an additional barrier to patentability of incremental inventions in the field of chemicals, pharmaceuticals, agrochemicals, biochemicals, biotechnology inventions etc. S. 3(d) mandates heightened standards of patentability for these technologies with an objective to prevent evergreening. This provision mandates that minor modifications carried out to existing substances/products (for instance, the parent compound) are not patentable unless they exhibit enhanced efficacy compared to the existing substance.

Under Indian patent law, the following are not inventions within the meaning of this Act – with S. 3(d) of the Indian patent Act reading as:

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;
of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant.

Explanation – For the purposes of this clause, 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.

The Honourable Supreme Court of India, which adjudicated the landmark judgement on S. 3(d) in Novartis AG vs Union of India (Novartis SC judgement) in April 2013 concerning the chronic myeloid leukemia drug, Glivec® (active ingredient imatinib as a mesylate salt) clarified that S. 3(d) does not bar patent protection for all incremental inventions related to chemical and pharmaceutical substances, even though it rejected Novartis's patent application on the beta-crystalline form of imatinib mesylate (subject product, a polymorphic form). The Court carried out a known substance determination to hold that the subject product was a new form of a known substance, imatinib mesylate (the precursor substance, a salt) having known efficacy even though Novartis had contended that only imatinib free base was known from its earlier patent (US 5,521,184, referred to as Zimmermann patent) and not its mesylate salt form. The SC also restrictively defined the other key determinant, "efficacy" as "therapeutic efficacy" for pharmaceutical inventions.

In rejecting the patent application, SC held that that the improved physico-chemical properties of the beta crystalline form of imatinib mesylate, namely (i) more beneficial flow properties, (ii) better thermodynamic stability, and (iii) lower hygroscopicity, may be otherwise beneficial but these properties cannot even be taken into account for the purpose of the test of section 3(d) of the Act, since these properties have nothing to do with therapeutic efficacy. On increased bioavailability, SC had ruled that Novartis had not provided evidence that 30% increase in bioavailability could result in enhanced (therapeutic) efficacy. Although SC clarified that physico-chemical characteristics which are not indicative of therapeutic efficacy of a new form of a known substance may not qualify as advantages to meet the efficacy criteria, the decision did not specify as to "what

kind" of parameters or therapeutic advantages of a new form of a known substance shall suffice to meet the efficacy criteria, leaving room for further interpretation in future cases.

S. 3(e) of the Indian patent act excludes from patentability, 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. Accordingly, claims related to compositions obtained by mere admixture resulting in aggregation of the properties of the individual components are not patentable under S. 3(e) of the Act. Therefore, experimental evidence to substantiate that the combinative effect of the composition is greater than the sum of the technical effects of the individual components is mandated to rebut objections under S. 3(e).

3) Examination of key determinants of S.3(d) by the Madras High Court: "Known substance" and "Efficacy"

(A) Determination of "known substance" based on Statutory Explanation under S. 3(d)

a) Whether a "Known substance" in S. 3(d) is confined to pharmaceutical substances – The appellant contended that the key determinant "known substance" in the first limb of S. 3(d) is confined to chemical substances and more particularly, pharmaceutical substances. In addressing this question, the court referred to paragraphs 12 and 13 of Novartis Division Bench judgement and clarified that S. 3(d) is not limited in its application to pharmacology but its explanation is limited thereto and also referred to paragraphs 82, 87 and 157 of the Supreme Court publications of the Novartis judgement and pronounced that it does not follow from the determination of SC judgement that S. 3(d) applies only to pharmaceutical and agrochemical substances and not to biochemical substances.

b) Applicability of the Explanation portion of S. 3(d) to claimed invention (variants of phytase) and the doctrine of "*ejusdem generis*"- The appellant contended that that all the enumerated derivatives in the Explanation to S. 3(d) are derivatives of synthesized chemicals and not of biochemicals or chemicals found in a living organism. The court agreed with the appellant's contentions that the enumerated derivatives in the Explanation to S. 3(d) fall within the genus "derivatives of chemical substances" and invoking the doctrine of "*ejusdem generis*", the Court applied this principle to the expression "and other derivatives of known substance" to construe that the Explanation portion of S. 3(d) becomes inapplicable to the claimed invention, i.e. variants of phytase.

c) Sequitur of inapplicability of Explanation of S. 3(d) to the claimed invention – The court explained that the sequitur of the claimed invention not falling within the scope of the Explanation is that the claimed invention (variants of phytase) qualifies as a new form of a known substance even if it does not cross the filter prescribed in such Explanation; the filter being – "shall be considered to be the same substance unless it differs significantly in properties with regard to efficacy." The court further opined that that this does not mean that S. 3(d) becomes inapplicable to the claimed invention and it is the Explanation to S. 3(d) that does not becomes applicable in its entirety as underscored by its inapplicability to the third limb of S. 3(d) dealing with known processes, known machines and not known substances.

(B) "What kind" of Experimental Data is required for meeting "Enhanced Efficacy" in the context of biochemical substances?

The court referred to Novartis SC judgement and held that increased thermostability data provided by the appellant in Example 8, Table 5 of the complete specification is indicative of enhanced efficacy as contended by the appellant. The IPO (respondent) contended that enhanced efficacy can only be correlative of enzymatic activity of the variants of phytase. According to the court, increased thermostability of the variants of phytase precludes denaturation and enables production, storage and sale in pellet form. It enhances the known efficacy of the enzyme in aiding

digestion especially when used in animal feed. The court also held that there is nothing in the text or context of S. 3(d) which supports the interpretation that enhancement of known efficacy of the substance should be restricted to engineering or prospecting variants of phytase with inherently greater enzymatic activity over the reference phytase.

As to “how much” improvement in efficacy is required, the court further concluded that, as the practice guidelines also do not fix a numerical value to the margin of enhancement, the patent applicant has to establish that there is a reasonable enhancement of efficacy to the satisfaction of the Controller of Patents. The court held that as the measuring units, Improvement Factor (IF) were assigned numerical values which can be construed as a claim of efficacy and as no objections were raised to its materiality by the IPO, the claimed invention of the appellant satisfies the criteria of enhanced efficacy under S. 3(d).

4) Scrutiny of Section 3(e) requirement by the High Court

The court, referring to the Stempeutics decision[3] and contrasting with the view provided by this decision on the applicability of S. 3(e) to composition claims, held that there is nothing in S. 3(e) that limits its application to a composition claim that is obtained by aggregation of known ingredients as contended by the appellant and that the adjective “known” is used only in sections 3(d), 3(f) and 3(p) and is conspicuous by its absence in S. 3(e). Further, the court said that S. 3(e) does not appear to be limited in terms of independent claims and appears to exclude from patent eligibility any composition for a substance that merely exhibits the aggregate properties of its constituents. Therefore, the rejection of composition claims 8 to 11 by IPO is justified in the absence of evidence that the composition is more than the sum of its parts.

III) The Madras HC order: Practice pointers?

1) Scope of Explanation to S. 3(d)

In the instant case, the practice pointer is that the enumerated derivatives in the Explanation portion are all synthesised chemicals and not biochemicals. The decision therefore signposts that for future cases/reference, there may be a need to expand the scope of the Explanation portion to S. 3(d) by including in this provision possible illustrative derivatives for biochemical substances also. Alternately, the practice guidelines to S. 3(d) may be updated with possible illustrative examples for derivatives of biochemical substances also and more illustrations in respect of “other derivatives of known substances.”

2) Variants of a Biochemical substance and “other derivatives of known substance” under S. 3(d)

Given that the instant decision has made a difference in assessment between chemical/pharmaceutical vis-à-vis biochemical substances, would the future cases carve out exceptions for arriving at known substance determination under S. 3(d) for variants of biochemical substances? The instant decision despite holding that the variant of phytase, i.e. a variant of a biochemical substance, does not fit into the Explanation portion of S. 3(d) (i.e. other derivatives of a known substance) has arrived at the determination that the claimed invention, i.e. the variants of phytase is a new form of a known substance. This adds a new dimension to the interpretative framework of S. 3(d) in the context of biochemical substances.

3) Experimental data on “Enhanced Efficacy” for biochemical substances

The instant decision, despite relying on Novartis SC judgment, had contrasted with its view on experimental data requirement and pronounced that physicochemical properties like thermal stability are indeed indicative of efficacy requirement in the context of a variant of a biochemical substance (in the instant case, a variant of phytase useful as animal feed). From a practice perspective, the question that emanates is what are the other physicochemical properties of biochemical substances the improvement of which might correlate to or can inherently result in enhanced efficacy? Should that be decided on a case-by-case basis or the practice guidelines need to be built for providing more clarity in this regard?

4) Definition of the term New Biochemical Substance

The instant decision has classified the different categories of biochemical substances. In this backdrop, from a practice perspective, there may be an imperative need to define NBS or a New Biochemical Substance and also formulate separate practice guidelines for patentability determination of biochemical substances (including the interpretative framework of S. 3(d) and S. 3(e) in the context of biochemical substances).

IV) Conclusion

While the instant decision has been welcomed by the patent community, the picture is not yet clear in India as to when S 3(d) will bite on inventions to biochemical substances. Future development of case law from the Courts and decisions by the IPO will inevitably refine the practice framework and interpretative framework of S. 3(d) in the context of biochemical substances. We await further developments with interest.

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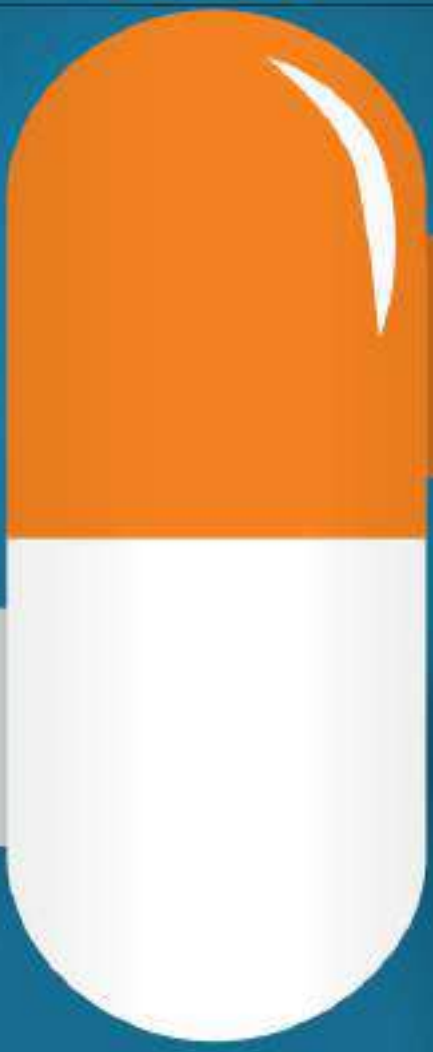


Lead Compound Approach: An Eternal Standard For Chemical And Pharmaceutical Obviousness At US PTAB?

While the generics wage an uphill battle to bust patents for new chemical compounds, with the PTAB's reliance on the US CAFC's eternal and time-tested standard of LCA framework, it may not be easy to invalidate compound patents even under the preponderance of evidence standard

Kameshwari Sridhar
Intellectual Property Lawyer

It is all about reinforcing the lead compound approach (LCA) for structural obviousness determination of new chemical compounds in chemical and pharmaceutical patents, which is trending at the United States Patent Trial and Appeal Board (US PTAB)! Synchronizing with the United States Court of Appeals for Federal Circuit (US CAFC)'s eternal and time-tested standard of LCA framework, the PTAB issued an Inter Partes Review decision (IPR 2015-0340 dated August 18, 2017) in Mylan Pharm. v. AstraZeneca AB[1], to uphold the validity of patent RE44,186 (a reissue of U.S. patent no. 6,395,767) covering claims directed to AstraZeneca's Saxagliptin (drug originally developed by BMS, the active ingredient in Onglyza and Kombiglyze XR).

The LCA framework and the characteristics of a lead compound?

In doing so, the PTAB relied on one of the CAFC's landmark pronouncements, Ostuka vs Sandoz, wherein evaluation of obviousness in new chemical compounds under the LCA framework involves a two-pronged inquiry considering first, whether one of ordinary skill would have selected one or more lead compounds for further development, and second, whether the prior art would have supplied sufficient motivation to modify a lead compound to arrive at the compound claimed with a reasonable expectation of success.

A natural outcome of LCA[2] in obviousness determination of new chemical compounds is that establishing a reason for selection of a compound in the prior art as a "lead compound"[3] *depends on the functional properties and limitations of prior art compounds. Thus, under LCA, the CAFC has laid out the requirement that a compound which has either a potent and promising activity*[4] *in the prior art* may be preferred as a "lead compound" (over other compounds in the prior art) *or a compound which has some limitations* like adverse effects to signify that this compound may not be the suitable choice (compared to other compounds in the prior art).

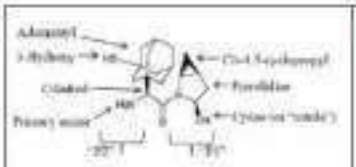
[1] The initial petition was filed by Mylan and later joined by Wockhardt Bio AG, Teva Pharmaceuticals USA, Inc., Actavindo Pharma USA Inc., and jointly by Sun Pharmaceuticals Industries, Ltd., Sun Pharma Global FZE, and Aurobal Pharmaceuticals LLC. [2] While Takanosho laid the foundation for application of "LCA" in pharmaceutical obviousness inquiry and Eli Lilly (both pre-KSR cases), implanted strongly the legal "LCA" framework, KSR's generalized obviousness doctrines made the CAFC synchronize some of these determinants (like "common sense requirement", "teaching away") with the "LCA" by mandating a reason for selection and modification of a lead compound as a sensible starting point for further development within the LCA framework to conduct the obviousness analysis of new chemical compounds. [3] In Ostuka, the CAFC augmented it with the characteristics, that a lead compound is "a natural choice for further development efforts", it can be identified by "evidence of the compound's pertinent properties," including positive properties (e.g., "activity and potency") and negative properties (e.g., "toxicity") and most importantly the proposition that, "absent a reason or motivation based on such prior art evidence, mere structural similarity between a prior art compound and the claimed compound does not inform the lead compound selection." The CAFC in *Takeda defined the lead compound as the compound in the prior art that would be "most promising to modify" to obtain better activity.* In Daiichi Sankyo decision, the CAFC *named factors helpful in identifying potential lead compounds: "it is the possession of providing useful properties in a lead compound that motivates a chemist to make structurally similar compounds."*

PTAB's Saxagliptin decision: A snapshot

The challenged patent was RE44,186, a reissue of U.S. Patent No. 6,395,767 and the challenged claims (claims 1, 2, 4, 6–22, 25–30, 32–37, and 39–42) were directed to a specific class of "cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV (DP-4)" as well as methods for treating diabetes, with Saxagliptin recited in claim 25. Initially, the Board refused to initiate the petition, but upon Mylan's petition for rehearing, the Board reversed and instituted the IPR on grounds of obviousness.

A. *Reasoned selection of a lead compound under the KSR?*

The decision focused primarily on whether the "lead compound", compound 25, the compound in Ashworth (I) reference, asserted by the petitioner would lead to a conclusion of structural obviousness. The Board highlighted the structural differences between Saxagliptin and Ashworth (I) compound with Saxagliptin having 3-hydroxyl adamantyl in place of cyclohexyl group and also having a cyclopropyl fusion in the pyrrolidine ring (respective structures are depicted below for reference)



Saxagliptin (Claim 25) | Compound 25

In addressing lead compound selection, the PTAB under the preponderance of evidence standard, rejecting the petitioners' choice of compound 25 as the lead compound, reasoned that (i) there was no substantial data provided to guide the skilled artisan to select compound 25 among the other 2-cyanopyrrolidides for further modification to develop a DP 4 inhibitor; (ii) stability data of compound 25 was based on *in vitro* tests at room temperature with no reliable information on *in vivo* stability; and (iii) evidence showing compound 25 would have presented additional concern of toxic cyanide release *in vivo* to the skilled artisan seeking to develop a DP 4 inhibitor.

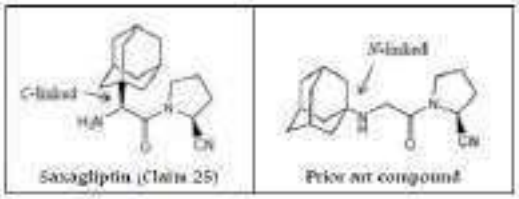
Further, the PTAB crediting Patent owner's testimony, Dr. Weber based on her contemporaneous experience when she herself performed a similar lead compound analysis while working at Merck to develop a DP 4 inhibitor at the time of the invention held that NVP DPP728 and P32/98 were recognized by one of the skill in the art as the most promising, natural starting points for further development efforts (as they avoided stability issues and advanced to clinical trials despite both being less potent than compound 25) and found that the petitioners' testimony, Dr. Rotella's lead compound selection of compound 25 was more likely to be prejudiced by hindsight bias.

B. *No reason or motivation to modify the petitioners' asserted "lead compound" and secondary considerations.*

The PTAB indicated that even if compound 25 was accepted as the lead compound, the petitioners had not established by a preponderance of evidence that the skilled artisan had sufficient reason to modify compound 25 to arrive at Saxagliptin. The three chemical modifications asserted by the petitioners were rejected by the PTAB on the basis that:

(i) a skilled artisan would have no reason to modify compound 25's proline pyrrolidine ring by adding a cyclopropyl group to create Cis 4,5-methanoproline, to increase the compound's stability with a reasonable expectation of success, because there was insufficient evidence in Hanessian's reference concerning the cyclopropanation of proline and the petitioner's own expert testimony from Dr. Rotella who admitted that there was nothing in the literature prior to invention of Saxagliptin that actually suggested that cyclopropanation of compound 25 would improve its stability; with similar considerations to conclude that there was no reasonable expectation of increased potency and these modifications were indeed surprising as supported by the patent owner's expert testimony;

(ii) replacing the cyclohexyl group for an adamantyl group was also not supported by the cited prior art as it related to N-linked and not C-linked substituents because of the differences in shape of the resulting molecules and further the secondary amine disclosed in prior art would be expected to be less available for cyclization and be more stable;



Saxagliptin (Claim 25) | Prior art compound

(iii) no reasonable expectation that the petitioner's proposed modification of hydroxylating the adamantyl moiety would improve stability or bioavailability of the molecule, based in part on petitioner's arguments being made with regard to adamantane rather than the adamantyl group in Saxagliptin;

(iv) and the petitioners' failure to show that a skilled artisan would have reasonably expected that the combined modifications would have been successful based on predictability of the individual modifications.

Further, the PTAB gave credence to the secondary considerations of non-obviousness, with the patent owner's assertions on unexpected results, failure of other DP 4 inhibitor compounds to obtain FDA approval and long-felt need despite other DP 4 inhibitor compounds known in the art being persuasive to its finding of non-obviousness.

Conclusion

The PTAB applying LCA has in the past denied to institute IPR proceedings for the patent covering drug Emend® (*Merck vs Aprotex*), because the petitioner-asserted lead compound "compound 90" failed to qualify due to absence of activity data. So is the case with *Torrent vs Merck* concerning the drug DALIRESP® (as the petitioner failed to explain how a skilled artisan would have identified two prior art compounds (DI and DJ) from the list of 147 exemplary compounds as lead compounds); Mylan vs Gilead (even assuming that an ordinary artisan would have selected the lead compound PMPA/tenofavir, the invention cannot be proved obvious owing to unpredictability of prodrug strategies); in *Ex Parte Yann Forlcher* and *Ex parte Caliguiri* (wherein the PTAB reviewed and reversed the Examiners finding of obviousness on the basis that the prior art failed to provide a reason for selection of the asserted lead compound).

While the generics wage an uphill battle to bust the patents for new chemical compounds, with the PTAB's reliance on LCA, it may not be easy to invalidate the compound patents even under the preponderance of evidence standard. LCA framework is here to stay and it may therefore be fair to conclude that LCA would continue to drive the structural obviousness analysis of new chemical compounds at CAFC and the PTAB!

LCA framework is here to stay and it may therefore be fair to conclude that LCA would continue to drive the structural obviousness analysis of new chemical compounds at CAFC and the PTAB!

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US Court Of Appeals

Affirmation of Infringement

(of pharmaceutical formulation) striking a chord with determinants under

Doctrine of Equivalents?

The key take-away for generic pharmaceutical companies is to define their non-infringement positions/arguments in alignment with their submissions to the FDA during approval of their generic formulation/product

KAMESHWARI SRIDHAR
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Intendis GmbH v. Glenmark Pharmaceuticals Inc., USA[1], concerning Finacea® gel (a patented pharmaceutical formulation) is a typical Hatch-Waxman patent battle, wherein the United States Court of Appeals for the Federal Circuit (US CAFC) affirmed the district court of Delaware's determination of infringement under doctrine of equivalents.

This judgement is a classic instance of the US CAFC's test for legal equivalency for infringement of a patented pharmaceutical formulation established on the basis of the determinants/limitations under doctrine of equivalents – namely, "functional equivalency" and "hypothetical claim construction". This is also a decision illustrating to pharmaceutical patent practitioners that infringement determination under the function-way-result test was based on establishing functional equivalence of the allegedly equivalent component/s (with the claimed element/component) and not based on whether the relevant claimed components were physically present in the generic pharmaceutical formulation.

Background of the Patent and invention at Issue

The patent (US patent no. 6,534,070) in the infringement suit and listed in the Orange book for Finacea® Gel formulation, claims azelaic hydrogel compositions, (including Finacea®), as well as methods for treating rosacea and other skin conditions. The patent assignee is Intraserv GmBH & Co., exclusively licensed to Intendis GmBH.

The independent claim 1 in US '070 patent reads as:

A composition that comprises:

(i) azelaic acid as a therapeutically active ingredient in a concentration of 5 to 20% by weight,

(iii) at least one triacylglycerides in a concentration of 0.5 to 5% by weight,

(iv) propylene glycol, and

(v) at least one polysorbate, in an aqueous phase that further comprises water and salts; and the composition further comprises

(ii) at least one polyacrylic acid, and

(vi) lecithin,

wherein the composition is in the form of a hydrogel.

US CAFC's decision

The US '707 patent covered Finacea® Gel, which contained azelaic acid as the therapeutically active ingredient, and triglycerides and lecithin as inactive ingredients, or "excipients", whereas, Glenmark's proposed generic formulation (Abbreviated new drug application) substituted isopropyl myristate for the claimed triglyceride and lecithin. Prior to Finacea® Gel, Bayer Healthcare Pharmaceuticals (the new drug application holder for Finacea®), marketed and sold a topical 20% azelaic acid cream known as Skinoren® (which is prior art to US '070 patent). Intendis, Intraserv and Bayer sued Glenmark Pharmaceuticals Inc., USA, and Glenmark Pharmaceuticals Ltd. for infringement of the US '070 patent.

The district court of Delaware held that the claims 1-12 of US '070 patent were valid. Applying function-way-result test, it further held that the generic formulation infringed US '070 patent under doctrine of equivalents.

I) <u>On Glenmark's appeal, the CAFC affirmed the district court's finding of infringement</u> based on:

a) Function-way-result test, as a determinant for infringement under Doctrine of equivalence[2]:

The district court under function-way-result test determined that the excipient **isopropyl myristate**

[1]See, *Intendis GMBH, Intraserv GmBH & Co. KG, Bayer Healthcare Pharmaceuticals Inc., vs Glenmark Pharmaceuticals Inc., USA, Glenmark Pharmaceuticals Ltd.*, Fed. Cir. Case 2015-1902 (May 16, 2016). [2] See, *Intendis GmBH supra* note 1 at page 6.Even when an accused product does not meet each and every claim element literally, it may nevertheless be found to infringe the claim "if there is 'equivalence' between the elements of the accused product or process and the claimed elements of the patented invention." Warner-Jenkinson Co. v. Hilton Davis Chem. Co., 520 U.S. 17, 21 (1997) (quoting Graver Tank & Mfg. Co. v. Linde Air Prods. Co., 339 U.S. 605, 609 (1950)). One way to show equivalence is by showing on an element-by-element basis that "the accused product performs substantially the same function in substantially the same way with substantially the same result as each claim limitation of the patented product," often referred to as the function-way-result test. Crown Packaging Tech., Inc. v. Rexam Beverage Can Co., 559 F.3d 1308, 1312 (Fed. Cir. 2009). Each prong of the function-way-result test is a factual determination. In this case, neither party objects to employing the function-way-result test as a means to determine equivalency of these chemical compounds.

in Glenmark's formulation **performs the same function** as the **claimed excipients, triglycerides and lecithin** – namely, enhancing azelaic acid's penetration of the skin; **in substantially the same way** as the claimed excipients – namely by disrupting lipids in the skin's outermost layer, stratum corneum (based on expert testimony and scientific literature); **obtained substantially the same result** – namely, a therapeutically effective azelaic acid composition able to penetrate the skin to deliver the active ingredient (relying on data from '070 patent, Glenmark's own patent application, skin penetration study and a clinical trial).

Glenmark objected to the function prong on the basis that the appellees failed to prove that the claimed excipients functioned as penetration enhancers arguing that US '070 patent itself is silent on the question of whether lecithin or triglycerides function as penetration enhancers. Glenmark also pointed to appellees Federal Drug Regulatory Authority (FDA) filings and development reports which identified lecithin and triglycerides as emulsifier and emollient, respectively, and further argued that not a single literature evidence identified lecithin or triglyceride as a penetration enhancer.

Rejecting Glenmark's argument, the CAFC reasoned:

We have never held that a patent must spell out a claim element's function, way, and result in order for the doctrine of equivalents to apply as to that element; "[t]he relevant inquiry is what the claim element's function in the claimed composition is to one of skill in the art, and a fact finder may rely on extrinsic evidence in making this factual determination," citing Zenith Labs., Inc. v. Bristol-Myers Squibb Co., 19 F.3d 1418, 1425 (Fed. Cir. 1994)."

Glenmark's arguments were further met with the CAFC's determination that

"We see no clear error in this district court fact finding. Fatal to Glenmark's argument is its own ANDA submission to the FDA, repeatedly referring to the claimed excipients (triglyceride and lecithin) as penetration enhancers".

In what can be termed as a strange turn of events, when Glenmark took an incongruous position that its submissions to the FDA about the claimed excipients as penetration enhancers should be rejected and not be construed as evidence to support district courts' finding, the court noted:

"These seemingly extemporaneous arguments do not persuade us that there is clear error in the district court's decision that isopropyl myristate in Glenmark's generic product and the claimed triglyceride and lecithin perform substantially the same function. No such arguments were made by Glenmark in any of its briefing to this court."

b) Whether doctrine of equivalents precluded by ensnarement: the hypothetical claim construction?

Ensnarement is a limitation on the doctrine of equivalents that bars a patentee from asserting a scope of equivalency that would encompass, or 'ensnare,' the prior art.Hypothetical claim analysis is a practical method to determine whether an equivalent would impermissibly ensnare the prior art. The court conducting ensnarement analysis must first (i) construct a hypothetical claim that literally covers the accused product and then (ii) assesses prior art introduced by the accused infringer and determine whether the patentee proved that the hypothetical claim was patentable over the prior art.

The CAFC in this case held that "the district court adopted **a proper hypothetical claim, one that includes triglycerides and lecithin or alternatively isopropyl myristate**. ***It correctly rejected as too broad, Glenmark's proposed hypothetical claim which would capture all penetration enhancers***. The district court's infringement finding was that the excipient in Glenmark's product (isopropyl myristate) was equivalent to the claimed excipients (lecithin and triglycerides); it was not a finding that any penetration enhancer would be equivalent to the claimed excipients".

> This judgement is a classic instance of the US CAFC's test for legal equivalency for infringement of a patented pharmaceutical formulation established on the basis of the determinants/ limitations under doctrine of equivalents – namely, "functional equivalency" and "hypothetical claim construction".

The district court further determined that the hypothetical claim was not anticipated or rendered obvious by Gasco (prior art asserted by Glenmark covering azelaic acid microemulsion with DMSO as penetration enhancer) and rejected Glenmark's argument that finding infringement under doctrine of equivalents would ensnare Gasco. Relying on expert testimony, the CAFC reasoned that a skilled artisan would not have substituted the hypothetical claim excipient (isopropyl myristate or lecithin and triglyceride) for Gasco's DMSO and would not have had a reasonable expectation of success in doing so. The CAFC thus held that Gasco does not bar the application of doctrine of equivalents to find Glenmark's generic version to infringe the asserted claims.

c) Prosecution history estoppel does not apply?

The applicants amended two dependent claims during prosecution (examiner noted that these claims in original form could include zero lecithin) to recite a lecithin "concentration of from more than 0 to 1%" and "concentration of from more than 0 to 3%," respectively, noting that they were "amended to expressly state what has already been made clear on the record."

Glenmark argued that prosecution history estoppel barred the finding of infringement under the doctrine of equivalents, because the applicants surrendered a lecithin-free composition during prosecution. In agreeing with the district court's determination, the CAFC held that:

"Argument-based estoppel only applies when the prosecution history "evince[s] a clear and unmistakable surrender of subject matter." **...Applicants' clarifying statement ... did not clearly and unmistakably disavow claim scope to distinguish prior art**. Amendment-based estoppel does not apply because the amendment was not a narrowing amendment made to obtain the patent. Rather, **this record demonstrates that the amendment to the dependent claims was a clarifying amendment ...and it does not give rise to prosecution history estoppel**".

II) Upholding the district court's determination of non-obviousness, the CAFC held that the claims were not invalid as the skilled artisan would not have been motivated to combine the asserted prior art or in finding no reasonable expectation of success based on evidence on record. The court further saw no clear error in district courts findings on objective indicia of non-obviousness.

Conclusion

This is a decision wherein scrutiny applied by the CAFC under the function-way-result prong to determine infringement under doctrine of equivalents did not mandate that the patent specification should clearly specify the function of the relevant claimed component/s in the claimed formulation in ascertaining the functional equivalence of the allegedly equivalent component/s in the generic formulation. Rather, the court emphasized that the relevant inquiry is to decipher the claimed component's function in the claimed composition from the eyes of one of skill in the art, and a fact finder may therefore rely on extrinsic evidence in making this factual determination.

This case further demonstrates as to how while determining infringement under the doctrine of equivalents, the patent owner would not be limited by prosecution history estoppel for every claim amendment made by him during prosecution (as it would not amount to disclaiming of any subject matter that is otherwise within the scope of the claim language). Finally, the key take-away for the generic pharmaceutical companies would be to define their non-infringement positions/arguments ***in alignment with*** (and not deviate from) their submissions made to the FDA during the approval of their generic formulation/product.

IP

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Indian Patent Office's recent decision on SAXAGLIPTIN Compulsory License – a step towards more coherent interpretation of Indian patent law's CL provisions?

*Kameshwari Sridhar**

I dedicate this article to my loving mother for her birthday

February 4, 2016

** The author is an Intellectual property lawyer (Patent practice) and Patent Agent, currently engaged in Intellectual Property Consultancy practice, specialised in chemical and pharmaceutical technologies, practising in Mumbai, India*

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Indian Patent Office's recent decision on SAXAGLIPTIN Compulsory License – a step towards more coherent interpretation of Indian patent law's CL provisions?

(I) Introduction

" I believe in Evidence…[1]"

Isaac Asimov

These are certainly redefining moments in the Indian pharmaceutical patent litigation landscape for the pioneer pharmaceutical companies! Reflecting Isaac Asimov's quote on evidence, *the Indian Patent Office (IPO)'s recent rejection of the compulsory license (CL) application filed by the generic pharmaceutical company, Lee Pharma, for the BMS's (assigned later to AstraZeneca) patented antidiabetic drug SAXAGLIPTIN for want of credible evidence, shall resonate so across the globe*! The decision shall also echo to the world, loud and clear, that there is no unconstrained granting of CL in India, and as to how India's approach to the grant of CL rests entirely on examining the merits of each CL application, for which certain threshold prerequisites need to be fulfilled by the CL applicant. This decision concerning the third CL application filed so far, may further aid in paving the way for strengthening the evolving Indian CL jurisprudence!

The CL application, filed in June 2015, was initially rejected by the IPO in August 2015 by a *prima facie* notification stating that although Lee Pharma had made credible attempts to negotiate a voluntary license with the patent owner Bristol Meyers Squibb (BMS), they could not establish a *prima facie* case under any of the conditions under *S. 84(1)* of the Indian Patent Act, 1970 (hereinafter referred to as the Act). On request for a further hearing by Lee Pharma, the IPO issued a subsequent order on January 19, 2016 rejecting the CL application for SAXAGLIPTIN, substantially for same reasons stated in the *prima facie* notification.

The IPO decision assumes significance as it is a yet another CL rejection after the second CL application pertaining to BDR Pharmaceutical's application for BMS's anticancer drug Dasatinib, which was rejected at the threshold itself by the IPO for the applicants failure to demonstrate a *prima facie* case for the grant of CL. The IPO decision holds further significance as it provides newer dimension to the CL jurisprudence by setting a higher threshold for the CL applicants to fulfill the conditions under *S. 84(1)* of the Act, in circumstances such as the present one, where alternative patented drugs are also available for treatment of type II diabetes mellitus (along with the patented drug SAXAGLIPTIN, the subject matter of the present CL application discussed here). The decision also reinforces the importance of garnering credible evidence and providing appropriate supporting data, by the CL applicant to substantiate their contentions and fulfilling each of the conditions under *S. 84(1)*, for a CL to be granted.

[1] "**I BELIEVE IN EVIDENCE. I believe in observation, measurement and reasoning, confirmed by independent observers. I will believe anything no matter how wild and ridiculous, if there is evidence for it. The wilder and more ridiculous something is, however, the firmer and more solid the evidence will have to be." – *Isaac Asimov***

(II) Background on Compulsory Licensing in India

Compulsory license is a non-voluntary authorization imposed by a government between the patent holder and a third party, by which the latter is allowed to use the patented invention without the patent owner's consent. Doha declaration, 2001, the declaration of Trade Related Aspects of Intellectual Property Rights (TRIPS) signed by the members of the World Trade Organisation (WTO) TRIPS in Doha, including India, pertained to include public health considerations for the first time and provided a strong negotiating tool to developing countries by allowing them to issue compulsory licensing of pharmaceuticals, with an aim to improve access of essential drugs[2].

The provisions relating to CL are provided under *S. 84 to S. 92* in Chapter XVI of the Act, 1970 with specific conditions for granting of CL laid out in *S. 84 and S. 92*. In terms of *S. 84* of the Act, after the expiration of 3 years, from the grant of a patent, it is open to any person to apply to the Controller for grant of a CL from the original patent holder. Such an application for grant of CL would be granted by the Controller, if any, of the following circumstances under *S. 84* (which reads as below) with regard to the patented invention (drug) exist:

(1) At any time after the expiration of three years from the date of the grant of a patent, any person interested may make an application to the Controller for grant of compulsory licence on patent on any of the following grounds, namely:—

(a) that the reasonable requirements of the public with respect to the patented invention have not been satisfied, or

(b) that the patented invention is not available to the public at a reasonably affordable price, or

(c) that the patented invention is not worked in the territory of India.

However a condition precedent for the grant of CL licence to any person making an application under S. 84(6) is the refusal and/or failure of the patent holder to grant the applicant a voluntary license. The aforesaid refusal by the patent holder to such an applicant must be in spite of applicant's efforts to obtain the same. While granting CL, the IPO shall also take into account other considerations laid out in S. 84(6), such as the nature of the invention, measures already taken by patentee or licensee to make full use of the invention, the ability of the applicant to work the invention to public advantage, time elapsed since the grant of patent, i.e. worked or not worked[3].

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[2] *See, Charitini Stavropoulou and Tommaso Valletti*, "Compulsory licensing and access to drugs", Eur J Health Econ, January 2014, DOI 10.1007/s10198-013-0556-2.

[3] *See*, *S. 84(6)* of the Act which reads as: *(6) In considering the application field under this section, the Controller shall take into account,—(i) the nature of the invention, the time which has elapsed since the sealing of the patent and the measures already taken by the patentee or any licensee to make full use of the invention; (ii) the ability of the applicant to work the invention to the public advantage; (iii) the capacity of the applicant*

India, in the post TRIPS complaint era, followed by, Doha Declaration in 2001 and the patent amendments in 2002, 2003 and 2005, issued the first CL under *S. 84* of the Act for the generic pharmaceutical company, Natco Pharma which made a CL application for Bayer's patented drug, Nexavar. The IPO granted CL for Nexavar, a first-of-its-kind drug available in the treatment of patients suffering from renal cell carcinoma (kidney cancer) and hepatocellular carcinoma in March 2012, for satisfying all the three conditions for invoking a CL under *S. 84(1)*. When the Controller granted the first CL for Nexavar, this case assumed worldwide significance and had landed India in a spate of controversies in the international arena, particularly that the judgement/s will hit innovation in the pharmaceutical sector in India and investors were wary that Indian patent law would not adhere to international standards. On the other hand, many of the developing countries welcomed this decision as this would enable highly expensive life-saving drugs to be manufactured at a very low price and make them easily accessible to the public.

On Bayer's appeal to the Controller's order, the Intellectual Property Appellate Board (IPAB)[4] upheld the IPO's decision and revised the royalty rate fixed by IPO from 6% to 7% and also provided certain important pronouncements in terms of what constitutes "working of the invention" under *S. 84(1) (c)* of the Act. The IPO's decision had the Controller stating that the patented product shall be considered to be worked in India only if the patentee manufactures the patented product in India within a reasonable time. The IPAB, in this case, agreed with the Controller's decision that the "working of the invention" was not satisfied as the appellant Bayer had not proved working. However, the IPAB gave a flexible interpretation to the term "worked" and held that the 'working' could mean local manufacture entirely and 'working' in some cases could mean only importation. It would depend on the facts and evidence of each case. The IPAB further held that the word 'worked' must be decided on a case to case basis and it may be proved in a given case, that 'working' can be done only by way of import, but that cannot apply to all other cases. However, the IPAB also indicated that the patentee must show why it could not be locally manufactured. A mere statement to that effect is not sufficient there must be evidence. Bayer challenged the IPAB's order before the Bombay High Court by way of a writ petition.

to undertake the risk in providing capital and working the invention, if the application were granted; (iv) as to whether the applicant has made efforts to obtain a licence from the patentee on reasonable terms and conditions and such efforts have not been successful within a reasonable period as the Controller may deem fit: Provided that this clause shall not be applicable in case of national emergency or other circumstances of extreme urgency or in case of public non-commercial use or on establishment of a ground of anticompetitive practices adopted by the patentee, but shall not be required to take into account matters subsequent to the making of the application. Explanation.—For the purposes of clause (iv), "reasonable period" shall be construed as a period not ordinarily exceeding a period of six months.

[4] *See*, *Bayer Vs Union of India and others*, IPAB, OA252012/PTMUM, March 4, 2013, MANU/IC/0016/2013.

The HC[5] upheld the IPAB's order and affirmed the CL granted to Natco for Bayer's Nexavar. The HC also made certain significant assertions in its judgement, particularly,

(i) the most important one being *on the "working of the invention*"; applying the provisions of *S. 83* which provides the legal framework for interpretation of "worked in the territory of India" - the HC agreed with IPAB's decision that the matter should be considered on a case by case basis and manufacturing in India would not constitute the only method for satisfying the requirements of working under *S. 84(1) (c)*. *However, the HC also insisted that "working by importation" can be an acceptable proposition only if the patentee provides satisfying reasons for not manufacturing the patented product in India*;

(ii) *it held that in respect of medicine, the term "adequate extent", for meeting the demand of the drug has to be 100%* and the medicine should be made available to every patient. The term "adequate extent" has relevance to *S. 84(7)*[6] of the Act, which lays down that where the supply of the patented invention is not to an adequate extent and where the patent holder has refused to grant a voluntary license to the applicant it would be deemed that the reasonable requirements of the public for the patented invention has not been met;

(iii) further held *that dual pricing (having differential pricing for people from different economic strata for those who don't have the capacity to pay the drug) can be adopted* to meet the reasonable requirement of the public; this concept of dual pricing having relevance to *S. 84(7)* of the Act requiring that the patented article be available to an adequate extent or on reasonable terms;

(iv) also held that the *sales made by (Cipla Ltd) a patent infringer can be considered to meet reasonable requirements of the public only when the patentee has not filed a patent infringement suit* against the alleged infringer.

Further, in December 2014, Supreme Court of India rejected Bayer's Special Leave Petition (SLP application) that challenged a July, 2014 order of the Bombay HC that upheld the grant of the CL to Natco.

The second CL application had been filed by BDR Pharmaceuticals International Private Limited, for anti-cancer drug Dasatinib covered in Indian patent no 203937, patented by BMS and useful in the treatment of chronic myeloid leukemia. The CL application was rejected by the IPO in October 2013, since BDR had failed to make out a *prima facie* case for grant of a

[5] *See*, *Bayer vs Union of India and others*, In the High Court of Judicature at Bombay, Writ Petition No. 1323 of 2013.

[6] *See*, *S. 84 (7) (a), of the Act, which reads as: For the purposes of this Chapter, the reasonable requirements of the public shall be deemed not to have been satisfied— (a) if, by reason of the refusal of the patentee to grant a licence or licences on reasonable terms- (i) an existing trade or industry or the development thereof or the establishment of any new trade or industry in India or the trade or industry of any person or class of persons trading or manufacturing in India is prejudiced; or (ii) the demand for the patented article has not been met to an adequate extent or on reasonable terms; or(iii) a market for export of the patented article manufactured in India is not being supplied or developed; or (iv) the establishment or development of commercial activities in India is prejudiced;*

CL, as according to the Controller, BDR had not made sufficient attempts to procure a voluntary license from the patentee, for reasons that BDR failed to respond to BMS' letter asking them to provide them with details as to how BDR would work the patent in contention.

(III) SAXAGLIPTIN CL case

1. Background

Coming back to the recent IPO order[7] under discussion, SAXAGLIPTIN, is a dipeptidyl peptidase-IV (DPP-IV) inhibitor, covered by the Indian patent number 206543 (and titled "A cyclopropyl-fused pyrrolidine-based compound" granted in 30.04.2007), a drug useful in the treatment of type II diabetes mellitus, by achieving glycemic control without accompanying weight gain. The original patent holder, Bristol-Meyers Squibb (BMS) made an assignment to AstraZeneca AB on April 3, 2014. SAXAGLIPTIN is used in the treatment of type II DM, sold under the brand name ONGLYZA in dosages of 2. 5 mg and 5 mg and also sold in combination with metformin under brand name KOMBIGLYZE XR in dosages 5/500 mg and 5/1000 mg.

A CL application was filed by Lee Pharma, a Hyderabad based Indian generic company, under *S.84 (1)* of the Act, on June 29, 2015 seeking the grant of a CL for the manufacture and sale of the compound SAXAGLIPTIN, under all the three grounds, as follows:

(a) that the reasonable requirements of the public with respect to the patented invention have not been satisfied, or

(b) that the patented invention is not available to the public at a reasonably affordable price, or

(c) that the patented invention is not worked in the territory of India.

(A) Efforts to negotiate Voluntary license:

For a CL to be granted, it is a precondition to establish whether adequate efforts were made for negotiating a voluntary license. In this regard, the CL applicant, Lee Pharma maintained that it requested BMS for a license *vide* letter dated May 2014, to which BMS, sought certain clarifications *vide* its email response in June 2014. Lee said it had not received BMS's response for reasons unknown and thereafter sent reminders to BMS, whose counsel sent a response in November 2014. Lee replied to BMS's response, further to which there was no communication from BMS in this regard.

(B) IPO's preliminary notification:

The IPO, issued a preliminary notice on August 12, 2015, in which it stated that the CL applicant had indeed made credible attempts to negotiate the voluntary license with BMS, however, they could not establish a *prima facie* case under any of the conditions under *S. 84(1)* of the Act, for reasons stated hereunder:

[7] *See*, IPO's order no C.L.A.No.1 of 2015, *In the matter of Lee Pharma Ltd vs AstraZeneca AB*, dated January 19, 2016.

(i) The applicant made submissions on statistics that 60.1 million people suffer from diabetes, more than 90% of diabetic people suffer from type II DM, with more than 99% of shortage of SITAGLIPTIN in the market, Form 27 data (stating that patentee imported 8,23,855 tablets in 2013) suggesting that only 0.23% of the requirements were met by the patentee (AstraZeneca) and also insisted that there exists a demand for SAXAGLIPTIN despite the available substitutes (LINAGLIPTIN, SITAGLIPTIN, VILDAGLIPTIN). The Controller however, determined that because no sufficient detail regarding the quantum of substitutes were provided, it was not possible to arrive at any conclusion regarding the demand for SAXAGLIPTIN. **As the demand could not be viewed in isolation when the substitutes were available in the market, the Controller held that a *prima facie* case has not been made out by the applicant on the applicants ground under reasonable requirements of public not being satisfied *(S. 84(1(a))***.

(ii) The applicant's submissions that the respondent/patentee's selling price for ONGLYZA and KOMBIGLYZE XR in the range of Rs. 41 to 49 per tablet, although they imported these medicines at the cost of Rs. 0.80 and 0.92, were countered by the Controller stating that even the applicants selling price for these medicines (Rs. 27 to 31.50 per tablet) were several times the alleged importation cost. Further, **from the price variance between the applicants pricing and the respondents pricing not being high, the Controller held that the applicant failed to make a *prima facie* case on the grounds that the patented invention is not available to the public at a reasonably affordable price (*S. 84(1)(b)*)**.

(iii) The applicant submitted that even after 7 years of grant, the patentee had not made adequate efforts to working of the invention. The Controller referring to the Bombay HC judgment and IPAB decision in *Bayer vs Natco*, pointed out that manufacturing in India is not a necessary precondition, however, the patentee is required to provide reasons that make it prohibitive for not manufacturing the patented invention, particularly only in those cases having manufacturing facilities in India. **Further, the Controller, rejecting applicants submissions, held no *prima facie* case was made out under the grounds of the patented invention not being worked in India, as the applicant did not supplement its submissions with data concerning whether AstraZeneca had manufacturing facilities in India.**

2. IPO's order issued on January 19, 2016[8]

Further to the notification, the applicant's counsel requested for a hearing under rule 97(1), therefore, hearing was held on December 15, 2015 and supplementary submission filed on December 29, 2015.

(A) Person Interested and Capacity of the Applicant

The IPO held that prima facie the applicant is a person interested (as a Pharmaceutical company involved for 17 years in research and development, production, manufacture, distribution and sales of pharmaceutical products, APIs etc.) and has the capacity to supply SAXAGLIPTIN to the market if the CL is granted. Further, in line with its finding in the

[8] *See*, IPO's order no C.L.A.No.1 of 2015, *supra* note 7.

preliminary notification, the IPO did find that Lee Pharma made a reasonable attempt to negotiate a voluntary license with the patentee.

(B) Grounds of CL

(i) No *prima facie* case made under the grounds of "reasonable requirements of the public" (*S. 84(1) (a)*) for lack of concrete evidence/authentic data:

Placing reliance on an International Diabetes Federations (IDF) report, the applicants contended that there were 60.1 million type II DM patients in India and even if 1 million of them were prescribed SAXAGLIPTIN, whereas, according to the Form 27 data (8,23,855 tablets per year as in 2013) provided by the patentee AstraZeneca, only 0.23% of the actual requirement of tablets in an year were being met by the patentee. The Controller put forth to the applicant certain important enquiries concerning (i) the reason for diabetes was higher sugar levels or reduction in sugar levels?; (ii) number of type II DM patients being prescribed medicines vis-à-vis life style changes; (iii) how many of them were prescribed SAXAGLIPTIN and how many could not get it because of its non-availability?. None of these enquiries were answered by the applicants Counsel who also made no such data available.

The Controller's order placed reliance on Bombay HC's *Bayer vs Union of India* & *others discussed supra*, and highlighted that reasonable requirements of the public have to be quantified, therefore shifting the burden of quantifying the requirements of SAXAGLIPTIN in India and establishing that the patentee did not meet the demand, on the CL applicant. In this respect, the Controller further pointed out that the CL applicant had also not shown the comparative requirements of SAXAGLIPTIN vis-à-vis the alternative antidiabetics of the same class of DPP-IV inhibitors (LINAGLIPTIN, SITAGLIPTIN AND VILDAGLIPTIN) or any authentic data/statistics of prescriptions establishing the preference of SAXAGLIPTIN over the other DPP-IV inhibitors.

The Controller opined that the evaluation under *S. 84(1) (a)* should be done based on *S. 83, S. 84(1) and S. 84(7)* of the Act and Bombay HC's *Bayer* decision discussed *supra*, and further insisted that the burden lies on the applicant:

a) to provide authentic data/statistics to substantiate their submissions on quantifying the number of patients requiring SAXAGLIPTIN and other DPP-IV inhibitors;

b) to establish through authentic data or concrete evidence, that there is an inadequacy or shortage of supply of SAXAGLIPTIN, which were applicants submissions based on patentee's Form 27 data;

c) to support their counsels argument that SAXAGLIPTIN is the latest and best option of treatment compared to other DPP-IV inhibitors having side effects, with comparative study or authentic evidence, i.e. in the form of clinical data or any other experimental evidence or expert evidence of a medical practitioner.

As the applicant failed to demonstrate through authentic data or concrete evidence, any of their assumptions, submissions or their contentions, the Controller held that there is no way to understand the exact requirements of SAXAGLIPTIN in the market and no *prima facie* case to the effect that the reasonable requirements of the public had not been satisfied under S. 84(1) (a), was not made out by the applicant.

(ii) No prima facie case under the grounds of "reasonably affordable price" (S. 84(1) (b)) due to insufficient evidence

The Controller relied on Bombay HC's Bayer's decision (*supra*) to pronounce that the Act does not bestow any powers upon him or any authorities to work out **a reasonably affordable price and it is rather arrived on the basis of the evidence led by the parties**.

The Controller arrived at his determination that no *prima facie* case to the effect that the ground of "reasonably affordable price" was not satisfied under *S. 84(1) (b)*, was not made out by the applicant, due to insufficient evidence for reasons stated hereunder:

(a) **the applicants failure to provide any comparative study or authentic evidence to establish that SAXAGLIPTIN is the best and latest option of treatment available and priced unreasonably high** (Rs. 41-49 per tablet), **when the three other DPP-IV inhibitors**, LINAGLIPTIN, SITAGLIPTIN AND VILDAGLIPTIN (sold at large volumes) **were also sold at similar prices** (Rs. 42 to 58) in India;

(b) the applicants revised selling prices during the hearing of Rs. 11 to Rs. 16 for SAXAGLIPTIN (after indicating in the notice that the price variance between the applicant and the importation cost was also high) were not considered persuasive enough to constitute a reasonably affordable price, because the applicant could not provide the Controller with the details as to how many poor people were prescribed but could not afford the patented drug because of its high price;

(c) the applicants failure to provide authentic data pertaining to the exact quantum of requirements of SAXAGLIPTIN or the comparative requirements of SAXAGLIPTIN with the other three DPP-IV inhibitors or the doctors prescription showing preference of SAXAGLIPTIN over others, the Controller held it may not be possible to conclude that the drug is not available to the general public at a reasonable affordable price (when the other three DPP-IV inhibitors were sold at similar prices).

(iii) No case made under the grounds of "worked in the territory of India" (S. 84(1)(c)) as a consequential implication of not satisfying grounds under S. 84(1) (a) and S. 84(1)(b)

The Controller arrived at this finding that no case was made out by the applicant under the grounds of "worked in the territory of India" for reasons stated hereunder:

(a) quoting Bayer's HC decision that manufacturing in India is not a necessary precondition for establishing "working requirement", the Controller **highlighted the applicants failure to provide authentic data or evidence or report or comparative study to establish clearly the**

exact requirement/demand for SAXAGLIPTIN and justifying the necessity of a manufacturing facility in India;

(b) further the applicants failure to make out a *prima facie* case under *S. 84(1) (a)* (by not furnishing the quantum of requirements of SAXAGLIPTIN with authentic data) or under *S. 84(1) (b)* (as pricing of patentees medicines were similar to other three DPP-IV inhibitors), questioning whether the necessity of its manufacture in India should apply to this case;

(c) the applicants data pertaining to sales % of SAXAGLIPTIN and world diabetic statistics, pointing to the fact that despite high incidence of diabetes the sales figures of SAXAGLIPTIN were low in India as compared to United States (having higher share of sales % despite lower incidence of diabetes patients) and lack of evidence that shortage of SAXAGLIPTIN is due to importation only, led the Controller to conclude that the case does not mandate the necessity of its manufacture in India.

The Controller for the aforesaid reasons, finally held that, due to applicants failure to provide evidence and satisfy any of the grounds under *S. 84(1)* of the Act, a *prima facie* case has not been made out for making an order under S. 84 of the Act and therefore rejected the application for grant of CL.

(IV) Conclusion

The IPO's order rejecting the grant of CL to Lee Pharma for SAXAGLIPTIN professes certain pertinent telling points from pharmaceutical patent practice perspective:

1. the Bombay HC's Bayer's decision on Nexavar CL stands as the precedent, relied upon in the IPO order to arrive at its determination of rejecting the CL and provides guiding principles for evaluating the merits of a CL application under *S. 84(1)* of the Act;

2. that whether the reasonable requirements of public ground is satisfied by the CL applicant has to be determined in a case like the present one,

a) **by not merely making general assertions** or providing general data regarding (i) the number of patients requiring the patented drug (SAXAGLIPTIN), (ii) the demand that exists for the patented drug or (iii) that the patented drug would make the best possible treatment for the disease condition when alternative drugs of the same class are available to the patients, **but by substantiating these assertions with authentic supporting data or concrete evidence in the form of experimental data, clinical trials or expert evidence/opinion of a medical practitioner**

b) **deviating from the Bombay HC's Bayer decision**, where the interpretation of 'adequate extent' to meet the demand (for reasonable requirements of public) was provided in case of medicine as 100%, this IPO order suggests that for 'adequate extent' to be interpreted as the "fullest extent", it may require the CL applicant to garner data and evidence on a case by case basis, depending on (i) the kind of patented invention (whether medicine and life saving drug? as Nexavar?), (ii) the nature and severity of the disease condition (life threatening?),

(iii) how many patients need the patented drug for treatment and whether alternative therapies are available and are of same class? (iv) whether by way of doctors prescriptions or opinion of a medical practitioner the CL applicant can establish the preference of the patented drug over the alternative therapies?

3. in terms of meeting the requirements of a reasonably affordable price, the decision sets a high threshold for the CL applicant to be able to establish **through authentic data** that **the patented drug is the most preferred option of treatment (compared to the alternatives) and cannot be afforded by the poor because it is unreasonably priced high**

4. in terms of meeting the requirements of "worked in the territory of India", aligning with the Bombay HC's Bayer decision (that working may not amount to manufacturing in India in all cases, but the burden is upon the patentee to provide reasons as to why the patented drug was not manufactured particularly those having manufacturing facility), **the pertinent takeaway for the CL applicant would be to establish through evidentiary data that the patented drug is in great demand in order to justify the necessity of a manufacturing facility in India**

The IPO's order of rejection of CL for SAXAGLIPTIN reinforces the guiding principles laid out in the Bombay HC's Bayer decision (discussed *supra*) and the importance of garnering credible evidence and providing authentic supporting data, by the CL applicant to substantiate their contentions and fulfilling each of the conditions under *S. 84(1)*, for a CL to be granted. **While this order may be a quick rejoice to the pioneer pharmaceutical companies, may be subject to appeal and/or there may be more to come in the near future in the CL space (in the form of IPO orders/ IPAB appeals/court decisions), presently, the order certainly signifies a step towards a more coherent interpretation of the CL provisions and does strengthen the evolving CL jurisprudence!**

Invasive Recap Of Indian Patent Office's Recent Patent Rejections Based On *Section 3(d)*: A Battle Cry For Pharmaceutical PATENTS?–Part I

The influence of SC's NovartisAG ruling and its constricted definition of the term "efficacy" (to "therapeutic efficacy") - is being increasingly felt in some major decisions by IPAB in 2013/2014, and some recent patent application rejections this year by the IPO, pertaining to drugs Sofosbuvir (marketed as Sovaldi®), Roche's Valganciclovir and Pfizer's Tofacitinib, all of which have referred to and/or applied the SC's reasoning in refusing them to proceed for grant.

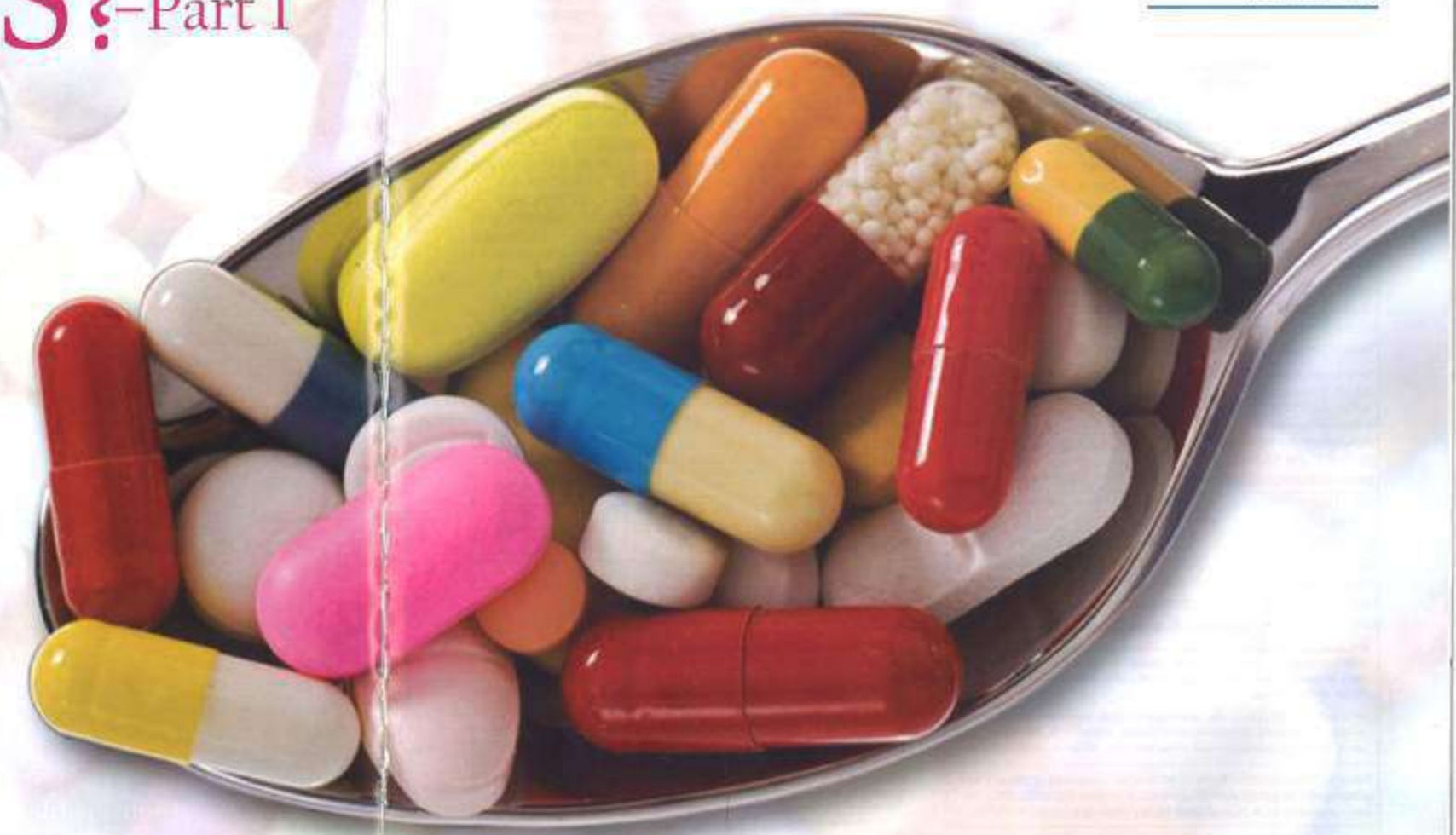
KAMESHWARI SRIDHAR
Intellectual Property Lawyer
(Patent Practice)

The Indian pharmaceutical patent landscape is witnessing turbulent times, principally due to the inherent complexities within the interpretative framework of Section 3(d) of the Indian Patent law! The decade-long journey of product patent regime under Indian patent law is still in the state of unplugging the ambiguities and contradictions presented by S. 3(d) of the Indian Patent Act, 1970 (Act, 1970). The keywords that emerge from some of the recent decisions of the Indian courts, the Intellectual Property Appellate Board (IPAB) and the Indian Patent Office (IPO) concerning S. 3(d) are "efficacy" and "known substance".

The Honorable Supreme Court of India, which adjudicated the landmark judgment in *NovartisAG* v Union of India[1], decided in April 2013, concerning the Chronic myeloid leukemia drug, Glivec (rejecting Novartis's patent application on beta-crystalline form of imatinib mesylate), did resolve partially the complexities inherent within *S. 3(d)* by restrictively defining the standard and scope of one of its substantive elements, "efficacy", which also determines the scope of protection of incremental inventions in the technology areas of chemicals and pharmaceuticals in India.

In so doing, the SC circumscribed the term "efficacy" to define it as "therapeutic efficacy", clarifying to a certain degree as to "what kind" of properties of a "*new form of a known substance*" ***may not be considered*** to meet the requirements of "enhanced efficacy", leaving room for further interpretation in future cases. As to "how much" difference in degree of properties of a "new form of a known substance" vis-à-vis the "known substance", would be required to surpass the test of "enhanced efficacy", is imbibed in the statute itself which reads as ***"significantly differ in properties with regard to efficacy"***.

[1] *See, NovartisAG vs Union of India & Others*, Civil Appeal Nos. 2706-2716 of 2013 and Civil Appeal No. 2728 of 2013 and Civil Appeal Nos. 2717-2727 of 2013 Supreme Court of India Order dated 01 April 2013, http://judis.nic.in/supreme court/imgst.aspx?filename=40212, August 6, 2013.

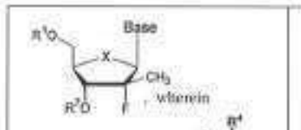


The influence of SC's *NovartisAG* ruling and its constricted definition of the term "efficacy" (to "therapeutic efficacy") – is being increasingly felt in some major decisions by IPAB in 2013/2014, and some recent patent application rejections this year by the IPO, pertaining to drugs Sofosbuvir (marketed as Sovaldi®), Roche's Valganciclovir and Pfizer's Tofacitinib, all of which have referred to and/or applied the SC's reasoning in refusing them to proceed for grant.

IPO's Sovaldi® Patent Order

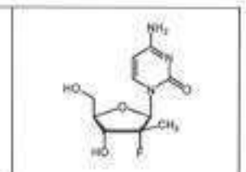
IPO's order rejecting the Indian patent application number 6087/DELNP/2005 filed by GILEAD PHARMASSET, INC, USA, pertaining to drug Sovaldi® useful in the treatment of Hepatitis C virus (HCV), and its reversal by the Delhi High court for fresh consideration of IPO's orders, raises concerns on procedural laxities in the order as well as the IPO's interpretation of substantive provisions, particularly *S. 3(d)* of the Act, 1970.

The claimed invention under contention pertained to 2´-fluoro (down)-2´-methyl (up) nucleosides and their corresponding mono-, di-, and tri-phosphate forms, and the specific compound 5. The IPO order found that the claimed compounds[2] were novel and inventive, but the patent application was not allowable under *S. 3(d)*by:



Base is represented by;
X is O; R1and R7are independently Hydrogen, a monophosphate, a diphosphate or a triphosphate; R3 is Hydrogen; and R4 is NH2 or OH;

Nucleoside compound of claim 1



Sofusbavir or (2´-R)-2´-deoxy-2´-fluoro-2´-C-methylcytidine

(Compound 5)

(XI)

Compound XI of prior art D1

Table A: Chemical structures of nucleoside compound of claim 1 and compound 5 in Indian patent application number 6087/DELNP/2005 and compound XI in closest prior art D1 (WO2001/192282)

a) rejecting applicants arguments that the claimed compounds were completely novel and inventive and are not merely new forms (salt, ester, derivative, etc.) of "known substances";

b) determining that ***the evidentiary pharmaceutical test data in Table 1[3] of the patent specification*** (referred to by the patent applicant during hearing) demonstrating that unexpected high activity against HCV and low toxicities of the claimed compounds, particularly, compound 5 were attributed to the unique substitution pattern of 2´-fluoro (down), 2´-methyl(up) in the nucleoside ring, ***was not indicative of enhancement of therapeutic efficacy***;

c) ***referring to SC's NovartisAG decision (for efficacy determination)***, determined that clinical trial data would be required to satisfy the requirements of therapeutic efficacy;

d) observing that ***what was pertinent to S. 3(d) analysis lies in establishing enhancement of therapeutic efficacy of the claimed compounds over "structurally and functionally similar" compounds in the closest prior art (compound XI in D1)***, and not in arriving at a 'known substance' as argued by the applicant.

The uncertainties posed by this order and inquiries that confront the pharmaceutical patent applicants/practitioners, are:

[3] *See*, Table 1 of the Indian patent application number 6087/DELNP/2005 reproduced in IPO ORDER, in the matter of Indian patent application number 6087/DELNP/2005 (January 13, 2015)

Table 1. Activity and Cytotoxicity Comparison of 2'-substituted cytidine analogs

No.	Compound	HCV Activity EC_{50} (μM)	Cytotoxicity Clone A CC_{50} (μM)	Huh-7 CC_{50} (μM)	BxPC3 CC_{50} (μM)	CEM CC_{50} (μM)
1		<1	>0.1	<1	<1	<1
2		5.66	>100	100	10	6
3		Cannot determine; Toxic to cells	>50	100	5	5
4		9.71	10.47	40	<1	<1
5		4.5	>100	>1000	>1000	>1000

"C" represents cytosine

I) Determination Of "Known Substance" Based On Structural Similarity

(1) Can a generic or implicit disclosure of a prior art substance be construed as a substance known to have close structural similarity (with the claimed new form)"? or may it even include a hypothetical substance which may be constructed from the generic/implicit disclosure of a prior art substance, for the purposes of *S. 3(d)* analysis?

The controller arrived at the determination that while the claimed compounds have 2´-fluoro(down), 2´-methyl(up) substitution pattern, compound XI differing only in the orientation of the fluorine atom, is structurally and functionally close to the claimed compounds, because it generically discloses compounds that may have 2´-fluoro(up), 2´-methyl (down) substitution pattern. Even though the disclosure of D1 is broad (85 compounds listed for compound XI) and there is no specific compound having the fluoro (up) substitution pattern in D1, the determination that the claimed compounds have close structural and functional similarity with compound XI for *S. 3(d)* analysis, raises questions as to whether a generic disclosure of a prior art substance or a hypothetical substance can be construed as a substance of close structural similarity with the claimed compounds, for *S. 3(d)* analysis?

(2) Disregard of factual considerations required for *S. 3(d)* analysis also raises ambiguities in identifying the "precursor substance":

The order highlights that what is pertinent to *S. 3(d)* analysis lies in whether the claimed compounds exhibit properties indicative of 'enhanced therapeutic efficacy' vis-à-vis structurally and functionally close prior art compound/s and in not making a "known substance" determination, as contended by the applicant. Does this stance not indicate a deviation from earlier decisions of IPAB *(for instance, in TYKERB case[4], identifying lapatinib tosylate, a specific compound disclosed in the respondent Glaxo's earlier prior art patent IN 221017 as the predecessor substance for S. 3(d) analysis)* or IPO's order/s *(for instance, Takeda vs Controller of patents[5], wherein one of the prime requirements specified for S. 3(d) analysis was to identify the closest prior art compound as a 'known substance', which in this case was pantaprazole)*, wherein, IPAB/IPO ***had zeroed in on a predecessor substance of close structural similarity, whose physico-chemical and therapeutic properties*** were well defined.

II) "What kind" of pharmaceutical test data for enhanced efficacy determination under *S. 3(d)*?

The order discredits the evidentiary pharmaceutical test data provided by the applicant on the premise that the data is insufficient and not appropriate to fulfill the requirements of 'significant increase in therapeutic efficacy' for it: (1) mandated clinical trial data and discredited cytotoxicity data as not indicative of 'significant increase in therapeutic efficacy'; (2) mandated comparative test data of the claimed compounds vis-à-vis structurally and functionally close compound XI of prior art D1. The thrust on clinical data may be burdensome on the patent applicant as the clinical trial data are generated by the pharmaceutical companies much later and not at the time of filing of the patent application. The requirement of comparative test data vis-à-vis compound XI, without identifying a specific compound or a class of compounds falling within the generic disclosure of compound XI having the specific substitution pattern of fluoro(up) in the sugar moiety, and discrediting cytotoxicity data, presents greater complexities to patent applicants in terms of "what kind" of pharmaceutical test data would suffice for "comparative enhanced efficacy determination" under *S. 3(d)*?

On Gilead's appeal, of IPO's non-compliance with principles of natural justice, the HC[6] has set aside the IPO's order on procedural grounds and remanded the case back to IPO for reconsideration of its order rejecting the patent application concerning Sovaldi®. While the pharmaceutical community would eagerly await the outcome of the IPO decision, is it not time to revisit the pharmaceutical guidelines for revising/drawing the practice framework for *S. 3(d)* analysis, (particularly in light of post *NovartisAG* decisions by IPAB/IPO), in order to aid the chemical and pharmaceutical patent practitioners and for *S. 3(d)* to stand, tall and strong?

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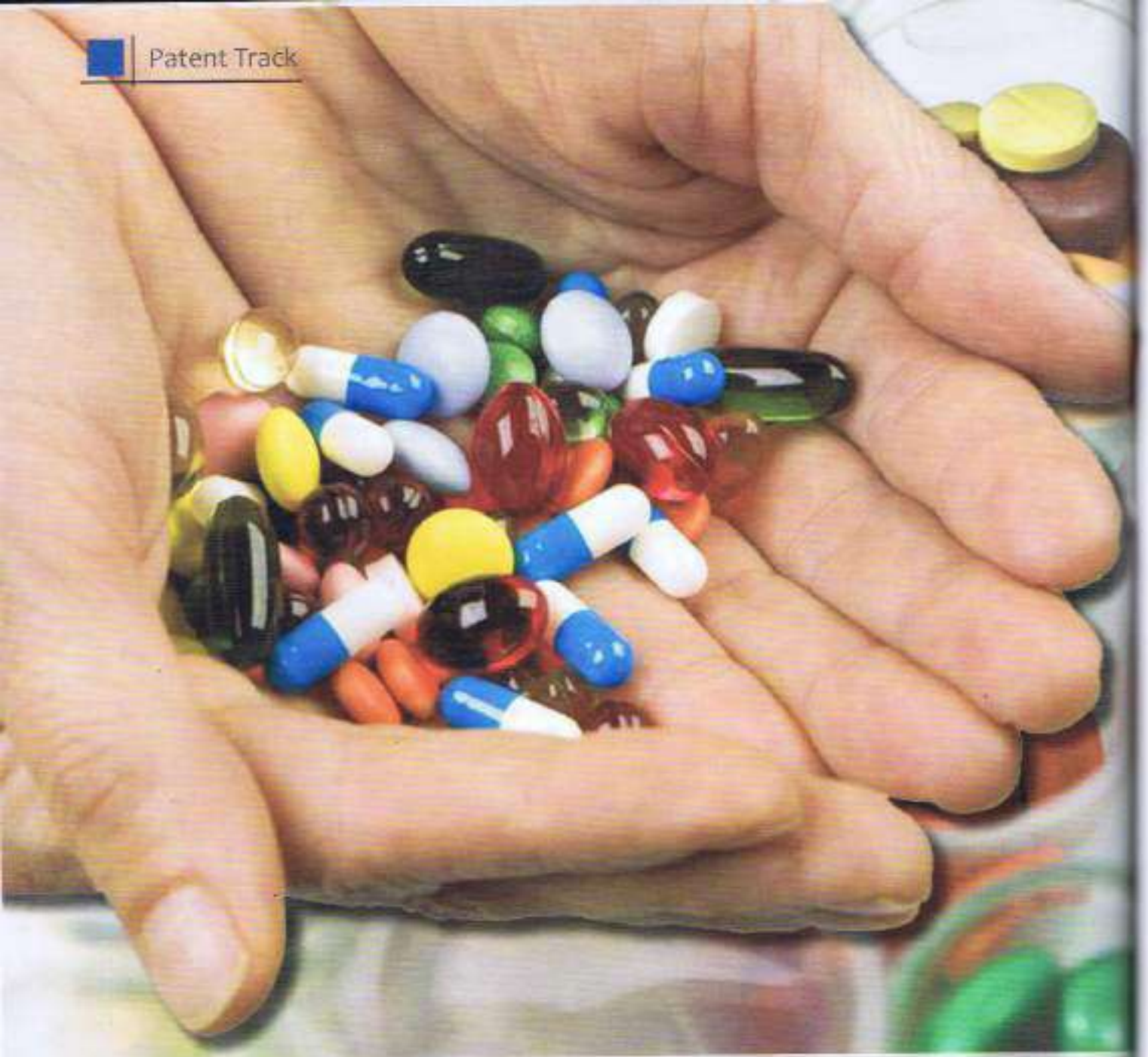
Disclaimer *– The views expressed in this article are the personal views of the author and are purely informative in nature.*

[4] *See, Frecenius Kabi Oncology Limited v. Glaxo Group Limited and The Controller of Patents* (ORDER NO. 161 OF 2013), ORA/22/2011/PT/KOL and M.P. NO.140/2012 IN ORA/22/2011/PT/KO, IPAB, July 27, 2013. [5] *See, Takeda GmBH vs Controller of patents*, in the matter of an application for an Indian patent 243/MUMNP/2008. [6] *See, Gilead Pharmasset LLC, vs. Union of India & ANR*, Delhi HC, case no. WP (C) 687/2015 and CM No. 1222/2015, January 30, 2015. The court sided with Gilead in holding that the impugned order suggests the possibility or potential that IPO would have been influenced by the material placed on record (pregrant representations filed) by NATCO and IMAK and therefore, it would have been more appropriate for the IPO to have issued notice to Gilead in respect of applications filed under S. 25. The court remanded the case back to IPO for fresh decision and fixing a date of hearing for both S. 14 and S. 25 proceedings.



While the interpretative framework of S. 3(d) is evolving on a case by case basis, future development of case laws from courts and decisions from Indian Patent Office and Intellectual Property Appellate Board shall unearth the applicable standards for patentability of new forms of known substances under S. 3(d). At present, each decision has the potential to create a precedent on its own accord and provide guidance in respect of the applicable patentability standards with greater clarity from patent practice perspective

Invasive recap of Indian Patent Office's recent patent rejections based on S. 3(d): A battle cry for Pharmaceutical PATENTS? –Part II

These are times in the Indian pharmaceutical patent landscape when the "Made in India" provision, S. 3(d) of the Indian patent law, an important weapon in the armoury of the generics challenging the validity of the originator's patents, has been put to test through a continuing spate of pharmaceutical patent rejections at the Indian Patent Office (IPO). These are also times to reflect upon the inherent complexities surrounding the patentability of "new forms of known substance" under S.3(d), which is not just restricted to the interpretative framework of its substantive constituent terms "efficacy" and "known substance", but also extends to the auxiliary constituent, pertaining to the evidentiary standard required to meet the tests of efficacy for patenting new forms of known substances.

KAMESHWARI SRIDHAR
Intellectual Property Lawyer
(Patent Practice)

Part I of this article published in the previous edition of IP ERA, highlighted as to how the *influence of the Supreme Court's landmark decision of Novartis vs Union of India[1], concerning the chronic myeloid leukemia drug, Glivec, and its* constricted definition of the term "efficacy" (to "therapeutic efficacy") is being increasingly felt in some recent patent application rejections by IPO this year, concerning Gilead's Sofosbuvir (marketed as Sovaldi®), Roche's Valganciclovir and Pfizer's Tofacitinib, all of which have referred to and/or applied the SC's reasoning in refusing them to proceed for grant.

Part I which delved into the IPO's Sovaldi® order of rejecting the patent application on grounds of *S. 3(d)*[2] and its determination that the interpretation of the substantive elements of *S.3(d), inter alia, a) the heightened threshold requirements laid out for "enhanced efficacy" and b) its construing of what qualifies as the "known substance"*, may be considered as contentious, leaving the pharmaceutical patent community grappling with more incongruities, with regard to patentability of 'new forms of known substances', than ever.

Another pertinent inquiry that confronts the pharmaceutical patent practitioner is regarding the auxiliary element of *S. 3(d)*, i.e. as to ***"What kind"*** of parameters or properties of a "new form of a known substance" and ***"How much"*** of difference in properties between the claimed new form (of known substances)

[1] *See, Novartis AG vs Union of India & Others, Civil Appeal Nos. 2706-2716 of 2013 and Civil Appeal No. 2728 of 2013 and Civil Appeal Nos. 2717-2727 of 2013 Supreme Court of India Order dated 01 April 2013, http://judis.nic.in/supreme_court/imgs1.aspx?filename=40212, August 6, 2013.* [2] *See, Gilead Pharmasset Inc. USA vs Controller of Patents, In the matter of Application no. 6087/DELNP/2005. IPO rejected the Indian patent application number 6087/DELNP/2005 covering drug Sovaldi® useful in the treatment of Hepatitis C virus (HCV). On appeal, the Delhi High Court has set aside the IPO's order and has remanded the case back to the IPO for fresh reconsideration on procedural grounds and principles of natural justice.*

and the known substance (compound/s of the closest prior art) shall qualify **to meet the standard of proof or experimental evidence required to meet the tests of "enhanced efficacy" under *S. 3(d)***. While the substantive provision (S. 3(d)) mandates an "enhanced efficacy" requirement, the explanation portion to the substantive provision specifies that these new variants (of a known substance) should differ "significantly in properties with regard to efficacy".

In *Novartis AG*, although SC clarified that **physicochemical characteristics or characteristics which are not indicative of therapeutic efficacy of a new form of a known substance/drug may not qualify as advantages to meet the efficacy criteria, the decision did not specify as to "what kind" of parameters or therapeutic advantages of a new form of a known substance shall suffice to meet the efficacy criteria**. Furthermore, the term "significantly" is neither defined in the Indian Patent Act, 1970, nor in the Manual of Patent Office Practice and Procedure or in the Pharmaceutical Guidelines for one to construe as to "how much" difference in properties would suffice for meeting the "enhanced efficacy" criteria?

What is germane to the context, in part II of this article, is therefore to take a look at the recent patent rejections by the IPO pertaining to Roche's Valganciclovir and Pfizer's Tofacitinib, for any telling points on the interpretative framework of *S. 3(d)*, from patent practice perspective.

I) IPO's Valcyte® Order:

The claimed invention under contention in Roche's Indian patent number 207232 (granted in 2007) pertained to Valganciclovir (a prodrug in the form of mono L-valine ester of ganciclovir), an anti-retroviral drug useful for the treatment of active cytomegalovirus retinitis (CMV) infection, which if not treated, could cause blindness in persons affected with Human Immunodeficiency Virus (HIV). The patent was revoked for the second time by the IPO order dated July 1, 2015, in a matter where Intellectual Property Appellate Board (IPAB) (in December 2014), set aside the IPO's earlier order[2] of revoking the patent and remanded it back to IPO for a fresh reconsideration of expert evidences and recommendations of the Opposition Board.

The instant order held that the prodrug Valganciclovir (designed to improve the oral bioavailability of ganciclovir) and the only process claim remaining in the patent relating to its preparation was found to be anticipated due to the teachings of the prior art EP patent no. 0375329A (which disclosed bis L-valine ester and its preparation) and obvious based on the combined teachings of US patent no. 4957924 (which disclosed L-valine ester of acyclovir prepared to improve oral bioavailability over acyclovir, a molecule differing with ganciclovir only by –CH2OH group) and EP '329.

The order identified ganciclovir as the known substance and revoked the patent on the grounds of not satisfying the requirements of *S. 3(d), for reasons stated as hereinunder*:

A) "What kind" of pharmaceutical data for enhanced efficacy determination?

a) Oral bioavailability not correlative of efficacy and "enhanced efficacy" criteria not satisfied– The "enhanced efficacy" criteria was not satisfied as improvement of oral bioavailability data presented by the applicant in Examples 9 and 10 of the complete specification had been construed as not indicative of "efficacy". Referring to *Novartis AG*[3], it was reasoned that although esterification of ganciclovir might improve oral bioavailability and may be advantageous in preparation of oral dosage forms, it cannot however be considered as correlative of efficacy.

b) "Pharmaceutical test activity" not forming part of the patent specification cannot be regarded as indicative of "significantly differ in properties with regard to efficacy" – *The order highlighted that any unforeseen property observed in new form, unless such property directly relate to efficacy* ***will be considered as inherent property*** *of such substance. Since no direct relation was shown for the improved bioavailability* ***of new form of ganciclovir in the description of the complete specification with*** *regard to significant difference in the efficacy, enhanced efficacy was not established and the* ***new form of the present case, i.e. monovaline ester of ganciclovir was considered as a same substance (i.e. ganciclovir).***

II) IPO's Xeljanz® order:

The order rejected the Indian patent application number 991/MUMNP/2003, filed by Pfizer Inc., on September 3, 2015, covering the drug Tofacitinib (marketed as Xeljanz®) useful for the treatment of rheumatoid arthritis, for the second time, in a matter where the IPAB set aside its earlier order for violating principles of natural justice and remanded the case back to the IPO for a fresh reconsideration.

The claimed invention under contention pertained to an enantiomer, 3-{(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo [2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl}-3-oxo-propionitrile and the base compound, 3-{4-Methyl-3-[methyl-

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[2] The IPO in its earlier order in May 2010, when dealing with the Oppositions filed by the patient groups, the Indian Network of Positive People (INP+), the Tamil Nadu Network of Positive People (TNNP+), the Delhi Network of Positive People (DNP+) and generic companies (Ranbaxy Laboratories Ltd, Cipla Ltd, Matrix Laboratories, Bakul Pharma Pvt Ltd), had revoked the patent on the grounds of obviousness and for not satisfying the requirements under S. 3(d).
[3] Site, NovartisAG, supra note 1. The decision did not provide any concrete ruling or guidance as to whether 'bioavailability' could be regarded as indicative of 'therapeutic efficacy' under S. 3(d) — limiting its ruling on facts, the court held that Novartis had not filed evidence that a 30% increase in bioavailability would result in enhanced therapeutic efficacy.

(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl)-3-oxo-propionitrile disclosed in claim 20 and Example 14 of the closest prior art document D1 (IN 241773), Pfizer's own patent filed earlier.

The IPO order found the claimed invention to be anticipated by prior claiming in D1, which had an earlier filing date (November 23, 2000) and priority date (December 10, 1999) than the claimed invention (filed on May 29, 2002, claiming priority date of May 31, 2001), but published later on June 14, 2001. The IPO's finding of anticipation by prior claiming raises questions as to how the prior art claiming the base compound (with generic disclosure that the compound/s exist in different stereoisomeric and enantiomeric forms) could be construed to be anticipating the claimed enantiomeric form (3R, 4R) of the base compound.

The order also rejected the patent application on grounds of S. 3(d), for reasons discussed hereunder:

A) Known substance determination:

The applicant argued that *S. 3(d)* was not applicable because the base compound was not in public domain, as D1 was not published at the date of filing of IN'991 patent application, and therefore there was no known compound with known efficacy. The order however, held that because the prior art D1 was filed earlier and the applicant being common for both D1 and '991 application, the applicant cannot deny that that the compound was not known to them.

B) "What kind" of pharmaceutical test data for "enhanced efficacy" determination?

a) Comparative kinase selectivity test data of the claimed enantiomer vis-à-vis other enantiomers not indicative of "enhanced efficacy" - The order mandated that the comparative data for enhanced efficacy determination under *S. 3(d)* should be between the claimed enantiomer and the base compound in the prior art D1, whereas the applicant relying on a 2008 publication of the inventors submitted data demonstrating that Tofacitinib, the claimed (3R, 4R) enantiomer exhibited high stereoselectivity for Janus kinase family of receptors vis-à-vis the rest of enantiomers (i.e. 3S, 4S; 3R, 4S; 3S, 4R).

b) "Pharmaceutical test activity" not forming part of the patent specification and reliance on a later filed publication not demonstrative of significant efficacy – The order held that the failure of the disclosure in the specification to provide any clue or data demonstrating significant efficacy of the claimed compound and the reliance of a later filed publication to correlate the invention to the said document cannot be considered as demonstrative of significant efficacy. Further, the order highlighted that enhancement of therapeutic efficacy of the claimed enantiomer over D1 be established by substantive research data, which the applicant did not provide despite plethora of opportunities.

Both the IPO orders provide significant practice pointers, in terms of "what kind" of pharmaceutical test data shall not suffice for proving "enhanced efficacy" criteria, with the IPO's Tofacitinib order mandating that "enhanced efficacy" be established by substantive research data. Both IPO orders also insist on the pharmaceutical test data to be forming part of the disclosure in the specification, i.e. at the time of filing of the invention, with the IPO's Tofacitinib order rejecting the data relied upon on a later filed publication.

While the Indian patent law is in the state of unplugging the ambiguities prevailing in the interpretative framework of S. 3(d), evolving on a case by case basis, future development of case laws from courts and decisions from IPO and IPAB shall unearth the applicable standards for patentability of new forms of known substances under S. 3(d). At present, while each decision has the potential to create a precedent on its own accord and provide guidance in respect of the applicable patentability standards with greater clarity from patent practice perspective, is it not time to revisit pharmaceutical guidelines to revise the practice framework of S. 3(d) to aid the pharmaceutical patent practitioners and for S. 3(d) to stand, tall and strong?

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