The Guide to Life Sciences: Key issues for senior life sciences executives

2024

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The fourth edition of the Guide to Life Sciences delivers key analysis designed to help senior life sciences executives better understand the strategic and legal IP challenges that they face around the world. This specialist intelligence will help them to protect, enforce and monetise the IP rights that are so crucial to businesses in the space.

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How to navigate the biosimilar and biologic markets amid challenging US litigation trends

Gerard P Norton, Jonathan R Lagarenne, Jianming Jimmy Hao, Howard S Suh and Jonathan Madara

Fox Rothschild LLP

Summary

A slew of recent litigation in the biologics and biosimilars space (including a high-profile decision in Amgen Inc v Sanofi by the US Supreme Court) has drastically changed the landscape of this space and made it more challenging for biopharma companies and IP professionals.

The biologics market was valued at US$264 billion in 2021 and is expected to reach US$596.65 billion by 2029. The first biosimilar was approved by the US Food and Drug Administration (FDA) nearly eight years ago. A biosimilar is a biologic treatment (ie, made from living cells) that is just as safe and effective as an existing FDA-approved biologic, also referred to as the 'reference product'. As of 15 May 2023, there are 40 FDA-approved biosimilars, 27 of which are available in the US market and four of which are interchangeable biosimilars. These FDA-approved biosimilars are as follows (denoting interchangeable biosimilars):

Biosimilar product information | FDA		
Biosimilar name	Approval date	Reference product
Idacio (adalimumab - aacf)	December 2022	Humira (adalimumab)
Vegzelma (bevacizumab - adcd)	September 2022	Avastin (bevacizumab)
Stimufend (pegfilgrastim - fpgk)	September 2022	Neulasta (pegfilgrastim)
Cimerli (ranibizumab - eqrn)	August 22	Lucentis (ranibizumab)
Fylnetra (pegfilgrastim - pbbk)	May 2022	Neulasta (pegfilgrastim)
Alymsys (bevacizumab - maly)	April 2022	Avastin (bevacizumab)
Releuko (filgrastim - ayow)	February 2022	Neupogen (filgrastim)
Yusimry (adalimumab - aqvh)	December 2021	Humira (adalimumab)
Rezvoglar (insulin glargine - aglr)	December 2021	Lantus (insulin glargine)
Byooviz (ranibizumab - nuna)	September 2021	Lucentis (ranibizumab)
Semglee (Insulin glargine - yfgn)	July 2021	Lantus (Insulin glargine)
Riabni (rituximab - arrx)	December 2020	Rituxan (rituximab)
Hulio (adalimumab - fkjp)	July 2020	Humira (adalimumab)
Nyvepria (pegfilgrastim - apgf)	June 2020	Neulasta (pegfilgrastim)

Avsola (infliximab - axxq)	December 2019	Remicade (infliximab)
Abrilada (adalimumab - afzb)	November 2019	Humira (adalimumab)
Ziextenzo (pegfilgrastim - bmez)	November 2019	Neulasta (pegfilgrastim)
Hadlima (adalimumab - bwwd)	July 2019	Humira (adalimumab)
Ruxience (rituximab - pvvr)	July 2019	Rituxan (rituximab)
Zirabev (bevacizumab - bvzr)	June 2019	Avastin (bevacizumab)
Kanjinti (trastuzumab - anns)	June 2019	Herceptin (trastuzumab)
Eticovo (etanercept - ykro)	April 2019	Enbrel (etanercept)
Trazimera (trastuzumab - qyyp)	March 2019	Herceptin (trastuzumab)
Ontruzant (trastuzumab - dttb)	January 2019	Herceptin (trastuzumab)
Herzuma (trastuzumab - pkrb)	December 2018	Herceptin (trastuzumab)
Truxima (rituximab - abbs)	November 2018	Rituxan (rituximab)
Udenyca (pegfilgrastim - cbqv)	November 2018	Neulasta (pegfilgrastim)
Hyrimoz (adalimumab - adaz)	October 2018	Humira (adalimumab)
Nivestym (filgrastim - aafi)	July 2018	Neupogen (filgrastim)
Fulphila (pegfilgrastim - jmdb)	June 2018	Neulasta (pegfilgrastim)
Retacrit (epoetin alfa - epbx)	May 2018	Epogen (epoetin - alfa)
Ixifi (infliximab - qbtx)	December 2017	Remicade (infliximab)
Ogivri (trastuzumab - dkst)	December 2017	Herceptin (trastuzumab)
Mvasi (Bevacizumab - awwb)	September 2017	Avastin (bevacizumab)
Cyltezo (Adalimumab - adbm)	August 2017	Humira (adalimumab)
Renflexis (Infliximab - abda)	May 2017	Remicade (infliximab)

Amjevita (Adalimumab - atto)	September 2016	Humira (adalimumab)
Erelzi (Etanercept - szzs)	August 2016	Enbrel (etanercept)
Inflectra (Infliximab - dyyb)	April 2016	Remicade (infliximab)
Zarxio (Filgrastim - sndz)	March 2015	Neupogen (filgrastim)

CURRENT STATE OF US BIOSIMILAR MARKET

Biosimilar advancements in the United States began when the Biologics Price Competition and Innovation Act (BPCIA) was enacted in 2010, which established an abbreviated pathway to FDA approval for biosimilars under section 351K, with the aim of enabling greater patient access to lower cost, high-quality products. The approval process requires biosimilar manufacturers to submit data that demonstrates there is no clinically meaningful difference from the reference biologic. Although the approval pathway for biosimilars is abbreviated, the FDA requires biosimilars to meet equally rigorous approval standards, which means patients and healthcare professionals can be assured of their safety, efficacy and quality – just as they would the reference products.

TO DANCE OR NOT TO DANCE: BIOSIMILAR STRATEGIES

The patent dance is a part of the biosimilar approval pathway that allows both the originator company and the biosimilar company to exchange information relevant to the patents on the reference product that might be infringed by marketing of the proposed biosimilar.

The patent dance is intended to streamline and formalise the exchange of information and cut down on needless litigation that might delay the introduction of cost-saving biosimilars. The steps in the patent dance are:

- the FDA accepts a biosimilar application;
- the biosimilar applicant has 20 days to notify the reference product sponsor (RPS) that the FDA has accepted the biosimilar application;
- within 60 days of notification, the RPS must provide the biosimilar applicant with a list of patents that might be infringed;
- within 60 days of receiving that list, the biosimilar applicant must provide a list of potential patents for resolution and its defence;
- the RPS must respond within 60 days with an infringement analysis for those patents;
- both parties then have 15 days to negotiate patents to be included in the first round of litigation; and
- the RPS may file a patent infringement lawsuit within 30 days asserting the agreed patents.

In 2017, the Supreme Court of the United States issued a unanimous (9–0) opinion in Sandoz v Amgen, 137 S Ct 1664 (2017), a highly anticipated case concerning key provisions of the BPCIA, part of the larger Patient Protection and Affordable Care Act of 2009.

At the heart of this decision lay a fight between two major biopharmaceutical manufacturers over claims of patent infringement brought by Amgen Inc against Sandoz Inc on a blockbuster drug representing hundreds of millions of dollars in sales each year. Amgen

has marketed filgrastim, a synthetically produced therapeutic protein, under the trade name Neupogen since 1991, when it was approved for use by the FDA. In 2014, Sandoz sought FDA approval for a compound biosimilar to filgrastim, dubbed filgrastim-sndz, under the trade name Zarxio.

Notably, Sandoz sought FDA approval for Zarxio under the BPCIA, which sets forth regulations concerning an abbreviated approval pathway for FDA approval of biosimilar compounds, as well as the procedural framework concerning patent litigation that arises from the filing of an application for a biosimilar compound. These patent regulations are often referred (as above) to as the 'patent dance' due to the back-and-forth nature of sharing patent lists, confidential information and resolution negotiations between the biosimilar applicant (termed 'subsection (k) applicant' in the statute) and the patent holder (reference product sponsor or RPS in the statute).

The two provisions of the BPCIA at issue in Sandoz v Amgen involved the mandatory nature (or lack thereof) of participating in the patent dance and what remedies exist for failing to participate, as well as the timing of obtaining licensure (approval) by the FDA for the biosimilar, involving issues of providing notice of commercial marketing by the biosimilar applicant. Regarding the patent dance, the BPCIA provides in part that the biosimilar applicant shall provide to the patent holder 'a copy of the [biosimilar] application' and 'such other information that describes the process or processes used to manufacture the biological product' (42 USC § 262(l)(2)(A)). Regarding the notice of commercial marketing, the BPCIA provides that the biosimilar applicant shall provide notice to the patent holder 'no later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k)' (42 USC § 262(l)(8)(A)). The BPCIA is silent as to whether the notice of commercial marketing may occur prior to FDA approval, or if it may only occur after.

On the issues of the patent dance and commercial marketing, the Supreme Court held that participating in the patent dance is optional. The applicant has the option of participating in the patent dance, but if they do not, the only negative consequence is that the applicant loses the right to file a declaratory judgment action on invalidity and the sponsor now can sue the applicant where and when for infringement and pursue damages the sponsor could not get if the applicant pursues the dance. Notice of commercial marketing may be given prior to, or after, FDA approval. Thus, the incentive given the potential sales is to just go to market.

Overall, the Supreme Court handed biosimilar applicants a major and decisive victory by siding with Sandoz. The biggest benefit to biosimilar applicants is almost certainly the holding that notice of commercial marketing may be given prior to FDA approval. As previously noted, had the Supreme Court sided with Amgen, the regulatory exclusivity for biologics, such as filgrastim, would have been extended by an extra half year (180 days), which could have meant tens to hundreds of millions of dollars in lost revenue for the biosimilar applicant.

For example, after the first four months on the market, Zarxio had taken nearly a quarter share of the market. Regarding the patent dance, the biosimilar applicant may decide not to engage in a framework that invariably delays FDA approval of their abbreviated biologics licence application (BLA) while the parties litigate patents before a bench trial in the Phase I. Even if the biosimilar applicant prevails in Phase I litigation, the RPS can still file a second lawsuit (Phase II) with any remaining patents not litigated in Phase I, potentially further delaying the launch of the abbreviated BLA. The patent dance usually provides benefits to

abbreviated BLA applicants who face many multitudes of potential patents because the exchange of information provided by this mechanism allows the applicant to have a better understanding of the potential patent challenges. However, for abbreviated BLA applicants who already believe they have a sophisticated understanding of the RPS's patents, the patent dance may have less appeal. By allowing the patent dance to be optional, the Supreme Court essentially allows biosimilar applicants to direct the course of patent litigation. They may choose to either follow the framework and receive some of the benefits involved, such as controlling patent lists and gaining potentially greater regulatory exclusivity for the biosimilar (if interchangeable) or ignore the framework entirely and either defer or speed up the patent litigation, or seek alternate venues such as an inter partes review (IPR), depending on the circumstances.

IMPACT OF INTER PARTES REVIEWS, POST-GRANT REVIEWS AND THE BIOLOGICS PRICE COMPETITION AND INNOVATION ACT

Patent protection is a significant consideration for biosimilars entering the US market. There are a variety of ways patent disputes proceed in the United States, including IPRs and post-grant reviews (PGRs) at the United States Patent and Trademark Office (USPTO), and litigation under the BPCIA, often referred to as the patent dance, where biosimilar manufacturers and reference product sponsors exchange patent validity and infringement information prior to filing a lawsuit in district court. All these mechanisms have the goal of an early resolution of patent disputes prior to biosimilars coming on the market.

As of 15 May 2023, there have been 144 biosimilar-related IPRs encompassing 70 patents and 14 reference products and there have been 46 BPCIA litigations related to 12 reference products. PGRs have not been a preferred way of resolving biosimilar-related patent disputes, with only three biosimilar-related PGR filings to date, possibly because of the far-reaching risks of estoppel based on final decisions that are based on PGRs and the fact that PGRs need to be instituted within nine months of issuance of the patent. While many of the reference product sponsors have faced both IPRs and litigation related to their patents, some biologic patents have only faced one type of challenge.

Each biosimilar reaches the market through a different path, be it through IPRs, litigation, settlements or a combination of the above. Only a few biologic patents have been invalidated in the USPTO through IPR and PGR proceedings, as well as district court litigation. Also of note, the BPCIA dispute resolution process has not been a significant barrier for many biosimilars.

US BIOSIMILAR LITIGATION TRENDS

There have been nine BPCIA cases involving five reference products that have concluded either with infringement or validity determinations by the court (seven) or through stipulated judgments of non-infringement by the parties (two). Of these nine cases, three were resolved in the RPS's favour with resulting damages (one) and permanent injunctions (two), with the remaining six resulting in a finding that the patents remaining at issue were not infringed by the biosimilar.

The fact that the favourable outcomes for biosimilars typically did not find patents invalid is interesting, particularly because some have suggested that weak drug patents are keeping biosimilars off the market. That has not proven to be true in the BPCIA litigation context based on the outcomes to date.

IPRs are a less expensive alternative to litigation and avoid resource-intensive litigation for biosimilars. To date, seven biosimilars of six reference products have successfully negotiated settlements after bringing IPRs, prior to any litigation being filed. This includes the Humira biosimilar Yusimry, Neulasta (pegfilgrastim) biosimilars Stimufend and Fylnetra, Rituxan (rituximab) biosimilar Ruxience, Herceptin (trastuzumab) biosimilar Ogivri, Soliris (eculizumab) proposed biosimilar ABP 959 (not yet approved) and Actemra (tocilizumab) proposed biosimilar MSB11456 (not yet approved).

While at least 11 of the 27 launched biosimilars (40.7 per cent) launched at-risk to at least some degree, to date, none of them have been ordered to pay any damages. While there has been one BPCIA litigation resulting in a damages award, it dealt with pre-launch manufacturing batches that were not found to be covered by 35 USC § 271(e)'s safe harbour and was not the result of an at-risk launch into the US market.

Some of the at-risk launches took place after an initial decision in the biosimilar's favour before appeals were exhausted, but some took place earlier in litigation. Ultimately, at-risk launches have eventually resulted in settlements in most cases.

While IPRs are a potential way to bring about an early resolution to patent disputes, some biosimilars have avoided patent disputes altogether by settling prior to the filing of any IPRs or litigation in the United States. To date, there have been at least nine biosimilar settlements without a patent dispute in the patent office or district court, including: Humira biosimilars Hadlima, Abrilada, Hulio, Idacio and Yuflyma; Lucentis (ranibizumab) biosimilars Byooviz and Cimerli; Rituxan biosimilar Riabni; and Avastin (bevacizumab) biosimilar Vegzelma. There have been two additional biosimilars launched without patent disputes or announcements of a settlement agreement, including Avastin biosimilar Alymsys and Remicade (infliximab) biosimilar Avsola.

It is possible that some of these biosimilars began the patent dance and negotiated settlements during the process, which is a benefit to the early back-and-forth between the RPS and biosimilar manufacturer and has potentially led to deals between these companies that has kept them out of court.

Overall, 18 biosimilars have launched or negotiated a future launch without litigation. One company in particular, Fresenius Kabi, has negotiated settlements for all of its three approved or pending biosimilars (Stimufend, MSB11456 and Idacio) without facing litigation in the United States.

PENDING AND RESOLVED PATENT LITIGATION

This past year, there were four new patent lawsuits. The cases ranged in how much the parties took part in the patent dance: two of the cases went through all steps of the patent dance process (Regeneron Pharmaceuticals, Inc v Mylan Pharmaceuticals, Inc (1:22-cv-00061), West Virginia Northern District Court and Genentech, Inc v Tanvex BioPharma USA, Inc et al (3:22-cv-00809), Southern District of California; one case went through some of the steps (Biogen Inc and Biogen MA Inc v Sandoz Inc, Sandoz GmbH, Sandoz International GmbH and Polpharma Biologics SA (1:2022-cv-01190), District of Delaware) and one went through none (Janssen Biotech, Inc v Amgen Inc (1:22-cv-01549), District of Delaware).

The Regeneron v Mylan case resulted in a scheduled trial for June 2023. The current standing of the Biogen v Sandoz/Polpharma Biologics case is that the parties have jointly requested

an expedited preliminary injunction proceeding. In the Genentech v Tanvex case, the parties settled in January 2023. The Janssen v Amgen case was filed in November 2022 and the parties settled on 22 May 2023.

PATENTING BIOLOGICS: REQUIREMENTS

To obtain a patent, an inventor must meet a number of requirements. For biologics, three of these can be particularly tricky to meet: patent-eligible subject matter, enablement and written description.

PATENT ELIGIBILITY

Laws of nature and natural phenomena are fundamentally not patent eligible, such as physical, chemical and biological principles and naturally occurring compounds. First, the court looks to whether the claims are directed to patent-ineligible subject matter, such as laws of nature, natural phenomena or abstract ideas. See Alice Corp Pty Ltd v CLS Bank Int'1, 134 S Ct 2347, 2354 (2014). Second, the court must determine whether the application is patent eligible by considering 'the elements of each claim both individually and 'as an ordered combination' to determine whether the additional elements 'transform the nature of the claim' into a patent-eligible application' (Alice, 134 S Ct at 2355). Put another way, there must be a further inventive concept to take the claim into the realm of patent eligibility.

'Prometheus' patents set forth laws of nature – namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harmful side effects' (Mayo Collaborative Servs v Prometheus Labs, Inc, 566 US 66, 77 (2012)). The Supreme Court then asked, 'do the patent claims add enough to their statements of the correlation to allow the processes they describe to qualify as patent-eligible processes that apply natural laws?' (Mayo Collaborative Servs v Prometheus Labs, Inc). The Supreme Court held that the claimed steps of administering, determining and wherein did not sufficiently transform the nature of the claims to render them patent eligible.

'Myriad discovered the precise location and sequence of human genes, mutations of which can increase the risks of breast and ovarian cancer' (Association for Molecular Pathology v Myriad Genetics, Inc, 569 US 576, 582-83 (2013)). The Supreme Court queried whether the naturally occurring DNA was patent eligible, 'by virtue of its isolation from the rest of the human genome?' (Myriad, 569 US at 580). The Supreme Court held that it was not. What about synthetically created DNA, such as complementary DNA or cDNA? The Supreme Court held that it was patent eligible. 'cDNA cannot be isolated from nature, but instead must be created in the laboratory . . . because the introns that are found in the native gene are removed from the cDNA segment' (Myriad, 569 US at 588).

ENABLEMENT

Under 35 USC § 112(a), first paragraph, the specification must describe how to make and how to use the invention. Why is this necessary? To weed out inventions that cannot be made or used. The test is 'whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation' (United States v Telectronics, Inc, 857 F 2d 778, 785 (Fed Cir 1988)), considering the Wands factors (In re Wands, 858 F 2d 731, 737 (Fed Cir 1988)).

The Wands factors include:

- the breadth of the claims;
- the nature of the invention;
- the state of the prior art;
- the level of one of ordinary skill in the art;
- the level of predictability in the art;
- the amount of direction provided by the inventor;
- the existence of working examples; and
- the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Genentech, Inc v Novo Nordisk A/S, 108 F 3d 1361 (Fed Cir 1997) involved a patent directed to a method for cleavable fusion expression of human growth hormone (hGH). In the claimed process, hGH is produced in cleavable conjugate form, wherein the conjugate is cleaved enzymatically outside the cell. The Federal Circuit ruled that claim was not enabled for cleavable fusion expression. 'To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without "undue experimentation"' (Genentech, Inc v Novo Nordisk A/S at 1365).

Bio-Technology Gen Corp v Genentech, Inc, 267 F 3d 1325 (Fed Cir 2001) involved a patent directed to a method for producing hGH using the recombinant techniques of bacterial production and gene expression. In the claimed process, hGH is produced with a methionine leader amino acid, resulting in a 192-amino-acid sequence 'met-hGH'. According to the '980 patent, the methionine sequence is thought to be cleaved within bacteria, resulting in the native 191-amino-acid sequence or 'mature hGH'. According to evidence submitted in BTG's ANDA to the FDA, hGH made by the process of the '980 patent contains 93.8 per cent met-hGH and 6.2 per cent mature hGH. At the district court, a jury had found that the claim was enabled. However, the district court granted judgment as a matter of law (JMOL) for invalidity, setting aside the jury's ruling. The Federal Circuit ruled that claim construction did not require that mature hGH would need to be produced in a substantial amount or in exclusion of met-hGH for claim two to be enabled. Moreover, the Federal Circuit found that the jury's verdict had been supported by substantial evidence and could have been reached by a reasonable jury. As such, the Federal Circuit vacated the JMOL and reinstated the jury verdict.

In Amgen Inc v Sanofi (2023), at issue was whether a valid patent can cover all the members of an identified group or if it is limited to only those members of the group specified by the patent owner. Amgen sued Sanofi and Regeneron in 2014 for patent infringement over Praluent. Both drugs use laboratory-made antibodies to block a protein called PCSK9 that inhibits the removal of bad cholesterol from the blood, but they achieve this result through different chemical combinations. Bad cholesterol, known as LDL, can cause a build-up of plaque in blood vessels and increase the risk of heart disease and stroke.

Relying on rulings from the turn of the 20th century related to the telegraph, incandescent lamp and wood veneer, the court reinforced the applicability of section 112 of the Patent Act's longstanding enablement requirement in the modern context of antibody development. The court reiterated that section 112(a) 'requires a specification to include "a written description of the invention, and of the manner and process of making and using it, in such full, clear,

concise, and exact terms as to enable any person skilled in the art . . . to make and use the same"'. This requirement that a patent application be sufficiently enabled is essential to secure for the general public 'its benefit of the patent bargain by ensuring that, "upon the expiration of [the patent], the knowledge of the invention [i]nures to the people, who are thus enabled without restriction to practice it"'.

The court summarised its longstanding enablement jurisprudence succinctly: '[i] other words, the specification must enable the full scope of the invention as defined by its claims. The more one claims, the more one must enable'.

The court then applied these principles in the modern context of antibody development. Both Amgen and Sanofi hold patents that describe relevant PCSK9-targeting antibodies by their amino acid sequences; these patents were not at issue here. What was at issue were particular claims of two additional patents held by Amgen that 'did not seek protection for any particular antibody described by amino acid sequence. Instead, Amgen purported to claim for itself "the entire genus" of antibodies that (1) "bind to specific amino acid residues on PCSK9" and (2) "block PCSK9 from binding to [LDL receptors]"'.

Although the court readily found that Amgen's specification enabled 26 exemplary antibodies it identified by their amino acid sequences in these two patents, the court rejected Amgen's arguments that it had enabled its broad functional claims 'because scientists can make and use every undisclosed but functional antibody if they simply follow [Amgen's] "roadmap" or its proposal for "conservative substitution"'. The court held these two approaches described by Amgen to 'amount to little more than two research assignments . . . fail[ing] to enable all that [Amgen] has claimed, even allowing for a reasonable degree of experimentation'. The court further rejected Amgen's additional arguments that the Federal Circuit had applied a different enablement standard in the context of antibody patents than in other contexts and that such a narrow interpretation would risk 'destroy[ing] incentives for breakthrough inventions'.

On the other hand, the court also clarified '[a]ll this is not to say a specification always must describe with particularity how to make and use every single embodiment within a claimed class. It may suffice to give an example if the specification also discloses "some general quality . . . running through" the class that gives it "a peculiar fitness for the particular purpose". . . Nor is a specification necessarily inadequate just because it leaves the skilled artist to engage in some measure of adaptation or testing"'.

This high-profile ruling applies long-standing principles of patent law to the modern context of antibody development. As such, the implications of this case are of immense significance for the US biopharmaceutical industry.

WRITTEN DESCRIPTION

Under 35 USC § 112(a), first paragraph: the specification must ensure that the inventor had possession of the specific subject matter later claimed as of the filing date of the application. This is required to give others incentive to continue to invent. The test is whether the disclosure of the application 'reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter'. Ralston Purina Co v Far-Mar-Co, Inc, 772 F 2d 1570, 1575, 227 USPQ 177, 179 (Fed Cir 1985). The specification must show either representative species or structural features. Relevant cases are recited as follows:

- *Fiers v Revel et al, v Sugano, 984 F 2d 1164 (Fed Cir 1993);*

- *Regents of the Univ of California v Eli Lilly & Co, 119 F 3d 1559 (Fed Cir 1997);*
- *Univ of Rochester v GD Searle & Co, 358 F 3d 916 (Fed Cir 2004);*
- *Ariad Pharms, Inc v Eli Lilly & Co, 598 F 3d 1336 (Fed Cir 2010) (en banc));*
- *Centocor Ortho Biotech, Inc v Abbott Laboratories, 636 F 3d 1341 (Fed Cir 2011);*
- *AbbVie Deutschland GmbH & Co, KG v Janssen Biotech, Inc, 759 F 3d 1285 (Fed Cir 2014); and*
- *Juno Therapeutics, Inc v Kite Pharma, Inc, 10 F 4th 1330, 1342 (Fed Cir 2021), cert denied.*

Fiers was a lengthy and highly publicised US patent interference proceeding involving the patent rights to the DNA sequence coding for Interferon-beta, in which the Federal Circuit affirmed the application of the principle of simultaneous conception and reduction to practice to genetic material. An adequate description of DNA requires a description (structure or nucleotide sequence) of the DNA itself.

In Lilly, the Federal Circuit held that University of California's patents failed to meet the written description requirement for a claimed broader genus of vertebrate and mammal insulin cDNAs since they only described a rat proinsulin cDNA. A genus is not adequately described by simply describing a species of that genus, but 'a description of a genus of cDNAs may be achieved by means of recitation of a representative number of cDNAs' (Lilly, 119 F 3d at 1569).

In Searle, the University of Rochester sued for patent infringement based on anti-inflammation drugs Celebrex and Bextra targeting COX-2, a type of cyclooxygenase, by GD Searle & Co, Inc, Monsanto Co, Pharmacia Corp and Pfizer Inc. The University of Rochester developed a screening assay for determining whether a particular drug selectively inhibited the activity of COX-2 and obtained a US patent covering methods for selectively inhibiting COX-2 activity in a human host by administering a non-steroidal compound that selectively inhibits the activity. The University of Rochester's patent was invalidated for failing to comply with the written description requirement.

In Ariad, a claim was directed to a method for reducing, in eukaryotic cells, the level of expression of genes that are activated by extracellular influences that induce NF-κ-B-mediated intracellular signalling, the method comprising reducing NF-κB activity in the cells such that expression of said genes is reduced, carried out on human cells. Ariad had not described any molecules that could do the many things the claims said. The vague functional descriptions were essentially just invitations for skilled artisans to conduct further research and therefore were not sufficient to meet the written description requirement. The specification disclosed three classes of compounds that could be used in the claimed methods; however, it only disclosed examples of one of the classes of compounds and did not disclose any examples of the described compounds actually linked to use in the claimed method.

In Centocor, Centocor identified a murine antibody to human TNF-α and then modified the murine antibody to make it look like a human antibody. The resulting product was a chimeric antibody that was not fully human, but Centocor nevertheless obtained US Patent 7,070,775 with claims covering fully human antibodies. Abbott constructed a fully human antibody from scratch using a phage display library containing a spectrum of human variable regions. The Federal Circuit stated 'the fact that a fully human antibody could be made does not

suffice to show that the inventors of the '775 patent possessed such an antibody . . . The specification at best describes a plan for making fully human antibodies and then identifying those that satisfy the claim limitations. But a "mere wish or plan" for obtaining the claimed invention is not sufficient' (Centocor, 636 F 3d at 1350-51).

In AbbVie Deutschland GmbH, AbbVie filed suit against Janssen Biotech, Inc and Centocor Biologics, LLC for infringement of claims directed to a neutralising isolated human antibody or antigen-binding portion thereof that binds to human IL-12 and disassociates from human IL-12 with a koff rate constant of 1x10-2 s-1 or less, as determined by surface plasmon resonance. The Federal Circuit held that claims were invalid for lack of written description. There are eight isotypes of variable heavy chains (VH1-8) and two isotypes of variable light chains (VL κ or λ) in any antibody. The antibodies AbbVie disclosed all had VH3 heavy chains and λ light chains and at least 90 per cent amino acid sequence similarity in their variable regions. Centocor's hIL-12 antibody (Stelara) had VH5 heavy chains and κ light chains and about 50 per cent sequence similarity in the variable regions to Abbivie's.

In Juno, the patent to Juno at issue related to chimeric antigen receptor (CAR) T-cell therapy. Juno sued Kite for infringement of claims directed to a nucleic acid polymer encoding a chimeric T cell receptor. The chimeric T cell receptor comprises, among others, 'a binding element that specifically interacts with a selected target'. One type of the binding element disclosed by Juno is single-chain antibody variable fragments (scFvs). Following a trial in the Central District Court of California, a jury found no issue of written description and found Kite wilfully infringed the patent. The district court agreed and awarded Juno a damage of about US$1.2 billion and an ongoing royalty of 27.6 per cent. However, on appeal, the Federal Circuit reversed and invalidated Juno's patent claims for lack of written description. Noting the Juno patent disclosed two scFvs while 'the claims cover an enormous number (millions of billions) of scFv candidates,' the Federal Circuit concluded the Juno patent 'does not disclose representative species or common structural features to allow a person of ordinary skill in the art to distinguish between scFvs that achieve the claimed function and those that do not'.

These court decisions regarding enablement and written description have reshaped the landscape of the biologics and biosimilars space drastically. While they provide biosimilar applicants with more opportunities and ammunition to challenge RPS patents, they have also made it more challenging for bio-pharma companies and IP professionals.

CONCLUSION

President Biden signed the Inflation Reduction Act (IRA) into law on 16 August 2022. With a robust set of funding, the Act incorporates several of President Biden's domestic policy priorities and sweeping reforms to many areas, including healthcare reform. In that regard, it is the federal government's ability to negotiate pharmaceutical prices for Medicare. The negotiation methodology has many aspects, but at interest on this topic is that biologics that have been on the market for at least 13 years will be subject to negotiation starting in 2026 for Medicare Part D drugs and 2028 for Part B drugs. Of note, however, is that certain branded reference products may petition to be excluded from negotiation if a biosimilar is anticipated to come to market within two years. The cases discussed above emphasise the variability in potential estimates of timelines for biosimilar market availability. The question remains, will the IRA succeed as intended and protect and foster the growing biosimilar market? Time will tell.

Gerard P Norton gnorton@foxrothschild.com
Jonathan R Lagarenne jlagarenne@foxrothschild.com
Jianming Jimmy Hao jhao@foxrothschild.com
Howard S Suh hsuh@foxrothschild.com
Jonathan Madara jmadara@foxrothschild.com

2000 Market Street, 20th Floor, Philadelphia PA 19103 3222, United States

Tel: +1 215 299 2000

https://www.foxrothschild.com/

Leveraging injunctive relief in pharmaceutical patent disputes in China

Hans She, Tingting Liao and Doris Dong
Fangda Partners

Summary

INTRODUCTION

Pharmaceutical patent infringement cases navigate a complex terrain marked by prolonged litigation processes, significant economic stakes and the pressing need for judicial intervention amidst the delicate balance between original pharmaceuticals and generics, impacting public health and well-being. This intricate landscape necessitates a swift interim relief mechanism to forestall infringement actions pending a final judgment.

Injunction relief, encompassing terms such as 'pre-litigation injunctions', 'preliminary injunctions', 'interim measures' and 'precautionary measures' constitutes a pivotal aspect of this legal landscape. In China, injunction relief entails the court's issuance of temporary compulsory measures, at the behest of one party, compelling the opposing party to undertake specific actions or refrain from certain behaviours until the case concludes. In exigent circumstances, such relief can be sought pre-trial, with rulings rendered within 48 hours, and the mandated actions immediately enforced. Primarily geared towards halting infringement, injunction relief acts expeditiously, fostering dispute resolution, averting irreparable harm through precautionary measures and streamlining judicial processes. In the realm of pharmaceutical patent infringement, injunction relief emerges as a potent and indispensable recourse.

GENERAL PROCEDURE FOR APPLYING FOR PRELIMINARY INJUNCTION

OVERVIEW OF THE PROCESS

Under the People's Republic of China law, a patentee or interested party can seek a preliminary injunction from the court if they provide evidence of current or anticipated patent infringement or actions impeding their rights, with potential irreparable harm. In urgent cases, the court must rule within 48 hours and if granted, the injunction is immediately enforced.

During the assessment of a preliminary injunction application, the court considers various factors, including the legal and factual basis, stability of the IP's validity, potential harm to the applicant's rights, balance of harms, public interests and other relevant factors. While most injunctions are granted ex parte, inter partes hearings may occur if necessary.

The court may grant a preliminary injunction based on the applicant's submission, potentially limiting the alleged infringer's chance to present evidence or defence. Unlike Europe, Chinese laws lack a 'protective letter' doctrine. However, the alleged infringer can request reconsideration post-decision, with a claim for damages in the case of preservation errors.

CASE STUDY: AN INSIGHT INTO THE CASE BETWEEN ASTELLAS AND ZHEJIANG HAIZHENG

The case of AstraZeneca v Zhejiang Haizheng is a typical example of how courts examine and issue preliminary injunctions in pharmaceutical patent litigation. In this case, the court presumed that the validity of AstraZeneca's invention patent, which had undergone substantive examination and was still within the protection period, was stable. Furthermore, based on a litigation preservation guarantee issued by the Beijing Branch of China People's Property Insurance Company, valuing 15 million yuan, the court ruled to adopt preservative measures. Following the ruling, both parties swiftly reached a settlement. In this case, the court thoroughly analysed whether the plaintiff's application for preservative measures met the statutory requirements.

Condition	Reasoning for court's support of preservative measures
Factual basis and legal grounds	The involved patent is valid, stable and underwent substantive examination, resulting in an authorised invention patent within the protection period. The stability analysis report on the patent, commissioned by the respondent, does not sufficiently prove the patent's invalidity.
Possibility of success for the applicant	The applicant provided evidence such as the product instruction manual and label of the accused infringing product, test reports from the Beijing Municipal Institute of Physical and Chemical Analysis, registration approval for generic drugs, consistency evaluation results and quality standards for the accused infringing product.
Urgency of the case and potential irreparable harm	Failure to take preservative measures may result in the respondent continuing to infringe during the remaining patent protection period, further exacerbating the consequences of the damage. Failure to take immediate preservative measures may lead to the product being sold in more pharmacies or imitated by other manufacturers, causing more infringement and increasing the applicant's damages and enforcement costs. Given the accused infringing products' significant price advantage, the infringement may significantly reduce the applicant's market share or force price reductions, resulting in irreparable damage to the applicant.
Balancing of interests of both parties	Ordering the respondents to cease the infringing activities only involves suspending production and sales during the remaining protection period of the involved patent, which can be resumed afterward. Their losses are foreseeable.
Consideration of public interest	Prohibiting the respondent from providing the accused infringing products still allows consumers to purchase the applicant's corresponding products; there are other drugs with similar therapeutic functions available, preserving public interests. There is no evidence to suggest that ordering the respondent to cease the accused infringing activities would disrupt the social and economic order.
Other factors to consider	The applicant submitted a litigation preservation liability insurance guarantee

	from the China People's Property Insurance Co., Ltd., Beijing branch, for 15 million yuan.

UNDERSTANDING OFFER FOR SALE IN THE CONTEXT OF PATENT INFRINGEMENT AND PRELIMINARY INJUNCTION

The determination of 'offer for sale' of generic drugs has long been a contentious issue in practice. As there are no exhaustive legal provisions regarding the elements of offer for sale, judicial precedents generally analyse and determine based on whether the drugs are on the market for circulation and the expressed intention of the operators to sell the drugs.

For instance, in the case of Eli Lilly v G&L Pharmaceutical, the defendant G&L Pharmaceutical submitted a registration application for the drug Insulin Injection 75/25 to the Chinese authority. Lilly argued that the active ingredient in G&L's drug fell within its patent's scope. However, the Beijing Second Intermediate People's Court issued a judgment (2005) Beijing Second Intermediate People's Court Civil Initial No. 6026, indicating that the defendant's conduct of conducting clinical trials and applying for production permits was aimed at meeting the needs of the state's administrative approval for drug registration, rather than directly for the purpose of sales, and did not constitute the act of implementing another person's patent for production and operation purposes as stipulated in China's patent law. Additionally, since the drug involved was still in the registration approval stage and did not meet the conditions for listing, the relevant promotional content on the defendant's website did not constitute offer for sale.

By comparison, in the case of Qilu Pharmaceutical v Beijing Sihuan Pharmaceutical, the original plaintiff Beijing Sihuan Company filed a lawsuit against Qilu Pharmaceutical based on the jurisdictional basis of offer for sale, claiming that Qilu participated in drug centralised procurement bidding within the jurisdiction of the first instance court. Qilu Pharmaceutical raised an objection to jurisdiction, which was rejected by the first-instance court. Dissatisfied, Qilu Pharmaceutical appealed. Eventually, the Inner Mongolia High People's Court issued a ruling (2016) Inner Mongolian Civil Jurisdiction Final No. 16, finding that offer for sale refers to a product meeting all the conditions for entering the market circulation domain and the operator expressly indicating an intention to sell the product to the public. In this case, the involved injection product had already obtained good manufacturing practice certification and the approval number from the National Medical Products Administration, indicating its qualification for sale on the market. Moreover, Qilu's participation in drug centralised procurement, according to the ruling, demonstrated its intention to sell the involved product in the market, thus constituting offer for sale under the patent law.

Additionally, in the case of Jiangsu Haosen v Sanofi, Sanofi accused Haosen of participating in drug centralised procurement activities, claiming it constituted offer for sale. Haosen argued that it had not expressed an intention to sell the allegedly infringing products to unspecified medical institutions in Fujian Province. The Supreme People's Court issued a ruling (2020) Supreme People's Court Civil Jurisdiction Final No. 290, determining that Haosen's action of listing the alleged infringing products for online procurement constituted an expression of willingness to sell the alleged infringing products to medical institutions. Given that the alleged infringing acts occurred in Fuzhou, Fujian Province, according to the relevant reply from the Supreme Court, the first-instance intellectual property civil cases related to patents occurring in Fujian Province are under the jurisdiction of the Fuzhou Intermediate People's Court. Therefore, the original court had jurisdiction. The Supreme Court evaded discussing the definition of offer for sale in the ruling, essentially indicating that

the act of listing the alleged infringing products online itself should constitute infringement through offer for sale.

Through summarising the viewpoints of the judgments in the above cases, it can be concluded that two conditions must be met for the establishment of offer for sale of pharmaceuticals, which will potentially be subject to preliminary injunction: first, the product must meet the conditions for listing and circulation (ie, it has obtained a market approval number, rather than a clinical trial approval number); and second, the operator must clearly express an intention to sell the product to the public (for example, by participating in centralised procurement bidding).

REMEDIES FOR WRONGFUL PRESERVATION

Wrongful preservation incidents are not uncommon occurrences within pharmaceutical patent infringement lawsuits in China. The determination of wrongful preservation primarily hinges upon article 105 of China's Civil Procedure Law. According to this provision, if an application is deemed erroneous, the applicant is obligated to compensate the respondent for any ensuing losses incurred due to the preservation. The judicial interpretation by China's Supreme People's Court further delineates four scenarios constituting errors in application: failure to initiate litigation or arbitration within 30 days of taking preservative measures; the preservative measures becoming inappropriate due to the invalidated intellectual property; a final judgment declaring the actions not constituting infringement; or other situations deemed as erroneous application.

Moreover, the judicial interpretation stipulates that withdrawing a preservative application or requesting the removal of preservative measures does not absolve the applicant of liability for wrongful preservation.

Both legal statutes and judicial interpretations adopt an objective accountability principle, where failure to prevail leads to liability. This provision aims to prevent the abuse of injunction systems, prompting parties not only to assess the litigation risks of their claims when applying for preservative measures but also to consider the potential legal liabilities for erroneous applications. For respondents, it provides a means of recourse for losses incurred due to the applicant's erroneous preservation application.

The determination of wrongful preservation and liability can be illustrated through a classic case. In the case of Li Quan Xi Qin and Xianyang Xi Qin v Rohm and Haas, involving preliminary injunction, Rohm and Haas obtained an exclusive license to implement the patent in dispute in China. Alleging that Li Quan Xi Qin and Xianyang Xi Qin had offered to sell or sold a kind of chemical preservative, Rohm and Haas applied for preliminary injunction in September 2008. The trial court for the infringement lawsuit issued a preliminary injunction order and subsequently rejected Li Quan Xi Qin and Xianyang Xi Qin's reconsideration application. Subsequently, the patent at issue was declared entirely invalid in July 2010. The two defendants to the infringement lawsuit then sued Rohm and Haas in a separate proceeding, seeking compensation for wrongful preservation. The Shanxi High People's Court rendered a second instance judgment ruling that although Rohm and Haas was the licensee of the patent at issue from AgroFresh Corporation, the invalidation of the patent rendered their exclusive implementation license non-existent. Consequently, Rohm and Haas's application for preliminary injunction in September 2008 was deemed erroneous. Therefore, the court held Rohm and Haas liable for wrongful preservation. In this case, the court deemed the invalidation of the protected intellectual property as falling under article

105 of the Civil Procedure Law, constituting an inappropriate preservation measure and thus held the applicant responsible for wrongful preservation liability, without delving into whether Rohm and Haas had an intention of malice when enforcing the patent.

CONCLUSION

To sum up, preliminary injunctions play a pivotal role in pharmaceutical patent infringement lawsuits, serving as a crucial procedural tool for patentees to protect their intellectual property rights. These injunctions enable patentees to swiftly halt potential infringements, preventing irreparable harm and preserving their market position. However, while preliminary injunctions offer significant advantages, patentee pharmaceutical companies must exercise caution due to the risks associated with wrongful preservation.

The case studies highlighted both the importance of preliminary injunctions in swiftly addressing patent infringement allegations and the inherent risks of wrongful preservations. In the case of AstraZeneca v Zhejiang Haizheng, the court granted preliminary injunctions based on the strength of the patentee's case and the urgency to prevent further harm. The example underscores how preliminary injunctions can effectively safeguard patent rights and maintain market exclusivity in the face of potential infringements. Nevertheless, the risk of wrongful preservations also looms, as demonstrated in the above cases. While seeking preliminary injunctions, patentee pharmaceutical companies must carefully assess the validity of their patents, the likelihood of success in litigation and the potential consequences of wrongful preservation. The decision to pursue preliminary injunctions should be strategic and well considered, balancing the need to protect intellectual property rights with the potential risks of erroneous applications.

In conclusion, preliminary injunctions are a vital tool for patentee pharmaceutical companies in defending their intellectual property rights against infringement. However, the risks associated with wrongful preservation highlight the importance of careful deliberation and strategic decision-making in utilising this procedural mechanism. By navigating the complexities of pharmaceutical patent litigation with prudence and foresight, patentee pharmaceutical companies can effectively safeguard their innovations and maintain their competitive edge in the market.

Hans She hshe@fangdalaw.com
Tingting Liao Tingting.liao@fangdalaw.com
Doris Dong Doris.dong@fangdalaw.com

27th Floor North Tower, Beijing Kerry Centre, 1 Guanghua Road, Chaoyang District, Beijing 100020, China

Tel: +86 10 5769 5600

http://www.fangdalaw.com/

What rights holders need to know about patent-term extensions in Europe

Arwed Burrichter, Natalie Kirchhofer and Romina Kühnle
COHAUSZ & FLORACK

Summary

Patent term extensions via supplementary protection certificates (SPCs) play a key role in the protection of drugs and plant protection products in Europe. Understanding their complex legal framework is just as crucial.

As the European Court of Justice (ECJ) has seen an overwhelming number of referrals regarding patent term extensions in recent years, the interpretation of the law in this area has become increasingly complex. This article provides up-to-date answers to the most frequently asked questions on SPCs and elucidates the impact of the entry into force of the Agreement on the Unified Patent Court (UPC) on SPCs.

WHAT IS AN SPC?

SPCs can provide a patent term extension of up to five years and compensate patent owners for the regulatory delays caused by marketing authorisation procedures for medicinal and plant protection products.

FOR WHICH COUNTRIES CAN SPCS BE OBTAINED?

SPCs for medicinal products in the European Union are governed by EU Regulation 1768/92, which came into force on 2 January 1993 and was codified and replaced by EU Regulation 469/2009. A similar legislative framework is in place for SPCs for plant protection products. These regulations apply in all EU member states. Of the non-EU countries for which European patents can be granted, only some (eg, Switzerland but not Turkey) have SPC legislation in place. Only SPCs within the European Union are discussed here.

WHAT IS THE DURATION OF AN SPC?

SPCs extend the patent term for a period that is equal to the time that elapsed between filing the patent application and the first EU marketing authorisation, minus five years. The overall term of an SPC may not exceed five years. In calculating the duration of SPCs, the first marketing authorisation in the European Economic Area (EEA) (ie, the European Union plus Iceland, Liechtenstein and Norway) is important (article 13). In Seattle Genetics (C-471/14) the ECJ clarified that the date of the first marketing authorisation is the date of notification of the decision granting the marketing authorisation. SPCs can be corrected accordingly on request, as clarified by the ECJ in Incyte (C-492/16). A first marketing authorisation in non-EEA country Switzerland can also count as a first authorisation in the EEA because, up to 1 June 2005, it automatically extended to Liechtenstein (an EEA member) on the same day (see AstraZeneca, C-617/12). Today, this extension applies only with a certain delay but may still be important for calculating the SPC term.

According to EU Regulation 1901/2006, the SPC term can be further extended by six months if the marketing authorisation preparations included clinical trials specifically addressing paediatric use of a drug. The ECJ clarified in Merck (C-125/10) that an SPC can also be granted with a zero or negative term. This can be desirable, as paediatric extensions are possible only if an SPC is in place. A six-month extension of a six-month negative-term SPC will result in a positive term extension.

WHAT SUBJECT MATTER IS ELIGIBLE FOR SPC PROTECTION?

For pharmaceutical SPCs, only active ingredients (including derivatives thereof – eg, salts or esters (Farmitalia/Idarubicin, C-392/97)) or (fixed-dose) combinations of active ingredients

protected by a basic patent and having marketing authorisation as a medicinal product can be the subject of an SPC. 'Basic patent' means (article 1):

- a patent protecting the active pharmaceutical ingredient as such;
- a process to obtain the product; or
- an application of the product.

In Boston Scientific (C-527/17), the ECJ confirmed that medical devices, even if they comprise active ingredients, cannot be the subject of an SPC. In Abraxis Bioscience (C-443/17), the ECJ held that an SPC cannot be granted for a new formulation of an old active ingredient in case that active ingredient has already been the subject of a marketing authorisation. Finally, according to Santen (C-673/18), an SPC cannot be granted for a different therapeutic application of an active ingredient. In particular, the ECJ ruled that a marketing authorisation cannot be considered to be the first marketing authorisation, for the purpose of article 3(d), where it covers a new therapeutic application of an active ingredient, or of a combination of active ingredients, and that active ingredient or combination has already been the subject of a marketing authorisation for a different therapeutic application.

WHAT ARE THE CONDITIONS FOR OBTAINING AN SPC?

SPC applications must be filed with each national intellectual property (IP) office on a country-by-country basis (article 9). The filing deadline is six months from receiving the marketing authorisation for that country (nationally or centrally via the European Medicines Agency) or within six months of obtaining the basic patent, whichever is later (article 7). Calculation of the SPC filing deadline takes into account the notification date of the first market approval in the country of filing, not the first market approval in the EEA. If the marketing authorisation is granted only after expiry of the basic patent, this leads to an irremediable deficiency, as confirmed in MSD (C-567/16). In addition to the regular SPC term, a six-month paediatric extension is possible. Paediatric extensions can be applied for together with the SPC application or up to two years before expiry of the SPC. An SPC may be granted only to the basic patent owner or its successor in title (article 6) if the following conditions are met at the SPC application filing date (article 3 (a) to (d)):

- the product is protected by a basic patent in force;
- a valid marketing authorisation has been granted;
- the product has not already been the subject of an SPC belonging to the same person; and
- the marketing authorisation is the first to have been granted for this product in the country for which the SPC application is filed.

WHAT CRITERIA SHOULD BE USED TO DETERMINE WHETHER A PRODUCT IS PROTECTED BY A BASIC PATENT?

What is meant by the product needing to be 'protected' by the basic patent in article 3(a) is one of the most highly debated and open questions in SPC law, despite the many ECJ decisions on the matter. In November 2011 in a quintet of landmark decisions led by Medeva BV (C-322/10), the ECJ put an end to the fight between advocates of the infringement test and the disclosure test. The ECJ took the middle ground by setting out a unique criterion – namely, that the product must be 'specified [or identified] in the wording of the claims'.

However, what degree of 'specification/identification in the wording of the claims' is necessary and sufficient remained unclear and is still a major matter of dispute. In Eli Lilly (C-493/12), the ECJ provided some guidance, stating that the active ingredient need not be identified in the claims of the patent by a chemical name or structural formula, but that functional claim language (in that case an antibody binding to a specific target) may also suffice. Claims would not have to expressly mention, but would need to 'relate, implicitly but necessarily and specifically' to the active ingredient in question.

A general question on the interpretation of article 3(a) was again referred to the ECJ in the Teva UK case (C-121/17), which was heard and decided by the Grand Chamber in 2018. The ECJ held that for combination products that article 3(a) required, at the filing or priority date of the basic patent:

- the combination of active ingredients must necessarily, in the light of the description and drawings of the patent, fall under 'the invention covered by that patent'; and
- each of the active ingredients must be 'specifically identifiable'.

For the latter, all information disclosed by the basic patent and the prior art (ie, not only the common general knowledge) at the filing or priority date of the basic patent can be taken into account.

Regarding the first criterion, the ECJ in Teva UK again emphasised the primacy of the claims and their interpretation as governed by article 69 of the European Patent Convention for determining what is protected under article 3(a). That this is a matter of national or European patent law (ie, non-EU law) and must be decided by the national courts, was already the ECJ's position in its first judgment on article 3(a) (Farmitalia (C-392/97)). In Royalty Pharma Collection Trust (C-650/17), the ECJ decided that a product is not protected by a basic patent in force, within the meaning of article 3(a), if, although it is covered by the functional definition given in the claims of that basic patent, it was developed after the filing date of the application for the basic patent, following an independent inventive step.

When prosecuting patent applications for new active pharmaceutical ingredients, it is highly advisable to ensure that all potential products (individually and in combination) are expressly mentioned in the claim language to avoid any later article 3(a) discussions.

WHAT IS THE SCOPE OF PROTECTION AFFORDED BY AN SPC?

The protection conferred by an SPC should – within the limits of protection conferred by the basic patent – extend only to the product covered by the marketing authorisation and for any medicinal use of the product authorised before expiry of the SPC (article 4). In Novartis (C–442/11 and C–574/11), the ECJ confirmed that an SPC provides the same protection as the basic patent against unauthorised use of the product in the form of any medicinal product that contains that product. Accordingly, sale of a combination product A+B infringes an SPC for A. SPCs also cover derivatives if they have the same medical effect and are also included in the scope of protection of the basic patent. Paramount is the scope of protection provided by the basic patent.

HOW MANY SPCS PER PRODUCT AND PER PATENT?

As a rule, an SPC can cover only a single product. The ECJ addressed the question of whether a patent protecting different products can also serve as a basis for more than one SPC in Actavis I (C-443/12), Actavis II (C-577/13) and Georgetown II (C-484/12).

In Actavis I, the ECJ considered that, in principle, it is possible to obtain several SPCs on the basis of a patent protecting several different products, provided that each (combination) product presents a core inventive advance and is protected as such by the basic patent. The additional core inventive advance criterion that the ECJ introduced in its assessment of article 3I makes it necessary to evaluate each case individually. In Actavis I and II, patents claiming an active ingredient A as the subject matter of the invention, and for which an SPC had already been obtained, were found to contravene article 3(c) and therefore could not serve as the basis for a second SPC on the combination of this active ingredient with another substance.

In Georgetown II, the ECJ allowed a basic patent claiming a combination of active pharmaceutical ingredients A+B for which a combination SPC had already been obtained to serve as a basis for a second SPC for one of those active pharmaceutical ingredients if this was also individually protected as such by that patent.

In Royalty Pharma Collection Trust (C-650/17), it was found that the core inventive advance criterion set out in Actavis I does not apply to article 3(a). This opened the question whether a reassessment of the prior ECJ case law on article 3(c) would be needed. Two currently pending referrals before the ECJ (Teva BV (C-119/22) and Merck Sharp & Dohme (C-149/22)) both of which concern the interpretation of article 3(c) in light of the interpretation of article 3(a) in Teva UK and Royalty PharmaCollection Trust, may help to shed light on this question.

Article 3(c) as interpreted by the ECJ prohibits the grant of a second SPC for the same product only in case of identity of the applicants. Multiple SPCs for the same product based on the same marketing authorisation are possible when the underlying patents are owned by different parties, which is known as a 'third-party SPC' (see ARP Manufacturing (C-482/07) and Biogen (C181/95)). To avoid any article 3(c) discussions, it is worth exploring the option of splitting up subject matters (eg, mono and combination products) into patent applications owned by different legal entities.

HOW CAN SPCS BE FORFEITED OR LOST?

SPCs can be invalidated if they were granted contrary to the provisions of article 3. In addition, SPCs are linked to the validity of the basic patent for which they were issued. Therefore, an SPC becomes invalid if the underlying basic patent prematurely lapses or is revoked, or if it is limited to an extent that it no longer protects the product for which the SPC was granted (article 15). Depending on the nature of the basic patent and on the opt-out status thereof, SPCs can be invalidated by third parties in national nullity proceedings before the competent national courts or in nullity proceedings before the UPC at least during a transitional period of seven years.

WHAT IMPACT WILL THE ENTRY INTO FORCE OF THE UNIFIED PATENT CONVENTION HAVE ON SPCS?

An SPC can also be granted on the basis of a European patent with unitary effect (unitary patent) if the unitary patent is effective in the respective EU member state in which the SPC application is filed. The SPC applications based on unitary patents must be filed with each national IP office on a country-by-country basis. The territorial scope of protection of such an SPC is limited to the EU member state that granted the SPC, although the underlying unitary patent is uniformly valid in all participating member states. An SPC with unitary effect in

all participating member states does not yet exist (although there are plans to introduce a unitary SPC in the future).

SPCs that have been granted or are being applied for on the basis of a European patent or a European patent with unitary effect fall under the jurisdiction of the UPC, while national courts retain jurisdiction for SPCs that have been granted or are being applied for on the basis of national patents. During a transitional period of at least seven years for SPCs based on classical European bundle patents there will be a competing jurisdiction of both the UPC and the national courts. During this period, it will be possible to opt-out of the jurisdiction of the UPC by filing an opt-out declaration for the respective European patent (thereby automatically including granted or future SPCs based on this patent) as long as no legal action with regard to this European patent is pending at the UPC. Opting out is not possible for unitary patents and, therefore, SPCs granted on the basis of unitary patents fall under the exclusive jurisdiction of the UPC.

PROPOSALS FOR A UNITARY SPC AND CENTRALISED SPC EXAMINATION

Significant changes to the SPC system have been proposed in a draft SPC regulation published on 27 April 2023. The new proposal serves two main goals: (1) to establish a centralised review procedure and (2) create a unified SPC. The new examination procedure is intended to simplify the existing SPC system, reduce fragmentation between member states and provide more legal certainty with regard to the granting and refusal of SPCs.

It is proposed to establish a new SPC unit within the European Union Intellectual Property Office (EUIPO). The examination would be carried out by a new panel composed of one member of the EUIPO and two qualified examiners from the national patent offices of the member states.

The centralised procedure may become mandatory if the basic patent is a European patent (standard EP or unitary patent (UP)) and the marketing authorisation has been granted through the centralised procedure.

Contrary to the present system, the proposal provides the possibility of filing third party observations within three months from the publication of the SPC application and third-party oppositions within two months from the grant of the SPC. Decisions may be appealed (before an EUIPO Board of Appeal) and further contested before the General Court of the EU and ultimately the Court of Justice of the European Union. After grant, a declaration of invalidity may be filed with the EUIPO.

For obtaining the proposed new unitary SPC, the basic patent would need to be a UP and the marketing authorisation a centralised one. The unitary SPC would be effective in all member states where the basic patent has unitary effect. Since the unitary SPC would not cover territory outside the unitary patent system, there may be an option to file a combined SPC application, including a request for grant of a unitary SPC and national SPCs.

Although significant changes to the examination procedure are proposed, the provisions governing the grant, duration and effects of the unitary SPC are proposed to be identical to the existing SPC regime. The proposals for amending the SPC system will be discussed by the European Parliament and the Council and may therefore be subject to change before final adoption.

CONCLUSION

The low number of SPC applications filed annually, coupled with the tremendous economic importance of SPCs and the complexity of parallel filings in potentially all EU member states, calls for appointing an experienced lead counsel in Europe to manage, coordinate and oversee the diverse national SPC examination proceedings.

Although having been in force for more than 20 years and the subject of a plethora of ECJ decisions, the SPC regulation is still one of the most unsettled and controversial areas of European IP law. Many users of the SPC system have been disappointed by the guidance given by the ECJ, which often seems to open up more new questions than it answers.

In regard to the unitary patent system, the currently envisioned legal framework already provides for SPCs derived from European patents to fall under the jurisdiction of the UPC if no opt-out is declared.

On 27 April 2023, the European Union's draft legislation for a reform of the existing legal regime on SPCs was published including the establishment of a centralised SPC filing and examination procedure before the EUIPO as well as the introduction of a unitary SPC. This draft regulation is not yet in force. If adopted into legislation, the proposed reforms will have far-reaching implications for the practicalities of obtaining SPCs in Europe and may also affect the substantive aspects of SPC law.

COHAUSZ & FLORACK

Arwed Burrichter aburrichter@cohausz-florack.de
Natalie Kirchhofer nkirchhofer@cohausz-florack.de
Romina Kühnle rkuehnle@cohausz-florack.de

Bleichstrasse 14, Dusseldorf D-40211, Germany

Tel: +49 211 90 490 0

http://www.cohausz-florack.de/en

Comparison of Canadian and US approaches to patentability and infringement issues

Nicholas J Wong, Belle Van and Rae Daddon
Blaney McMurtry LLP

Summary

INTRODUCTION

The United States and Canada are deeply integrated on many levels, from their shared international border to commonalities in culture and language, as well as intertwined economic relationships. The US and Canada also share common roots in their legal systems, with many overlapping rules and principles, as particularly evident in patent law. However, potential inventors, patent holders, stakeholders, industry professionals and legal experts should also be aware of fundamental differences that may have practical implications on intellectual property (IP) strategy.

This article will explore how the US and Canadian regimes differ on three patentability and patent infringement-related issues: (1) whether a prior sale of a product bars patentability, (2) the question of how similar a product could be without infringing on a patented invention and (3) infringement in the context of the skinny label pathway for drugs.

ON-SALE BAR

In the US, the statutory on-sale bar precludes an inventor from obtaining a patent if the invention was commercially sold or offered for sale before the effective filing date.

Specifically, 35 USC § 102(a) of the America Invents Act (AIA) provides that a person shall be entitled to a patent unless 'the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention'.

This bar applies when the invention is found to be the subject of a commercial offer for sale and is ready for patenting. A commercial sale agreement with a third party who is under an obligation of confidentiality, or a secret sale, is still encompassed by the catchall phrase 'otherwise available to the public' and thus triggers the on-sale bar.

In Canada, there is no standalone on-sale bar provision under the Canadian Patent Act. Rather, the concept of a prior sale barring patentability arises in the context of public sale or use and is relevant to the doctrine of novelty.

The requirement that an invention be novel is rooted in the definition of 'invention' in section 2 of the Patent Act: 'any new . . . art, process, machine, manufacture or composition of matter, or any new . . . improvement in any art, process, machine, manufacture or composition of matter'.

Whether a claimed invention is new (novel) is grounded in subsection 28.2(1) of the Patent Act, which requires that the claimed subject matter must not have been previously disclosed before the applicable disclosure deadline. If this subject matter has been previously disclosed before the applicable deadline, the claim is invalid for being anticipated.

Anticipation is assessed by determining whether the single prior disclosure, when understood by the skilled person, provides both (1) a description of the claimed invention (disclosure) and (2) sufficient instructions to enable the invention to be practised (enablement).

The prior sale or use of an invention in Canada does not function as an automatic bar. Instead, it can only bar patentability if it provides an enabling disclosure of the claimed subject matter prior to the applicable disclosure deadline for the pending application. To have disclosed the claimed invention, the prior sale must provide the skilled person with

information sufficient to comprehend the invention. The ability to reverse engineer the product without inventive effort may also be relevant to the consideration of enablement.

In the US, a secret sale of an invention will invalidate a US patent irrespective of where it happened because the AIA removed the geographic limitation of the prior art disclosure. In Canada, however, if an invention is disclosed to a third party who is expressly or impliedly obliged to keep the invention confidential, it is not considered a public disclosure to bar patentability.

Both jurisdictions provide a one-year grace period for inventor-derived disclosures. If the prior sale or use of the invention has occurred directly or indirectly through the inventor, such disclosures originating from the applicant occurring during the grace period will be excluded as prior art. In Canada, the grace period is one year before the filing date of the Canadian patent application or within 12 months of the earliest patent filing date (section 28.2, Patent Act). In the US, the patent application must be filed within one year of public use or sale of the invention or any public disclosure of the invention (35 USC § 102(b)).

Given that differences impact commercial dealings over the prior sale of unpatented IP in Canada and the US, companies that own potentially patentable subject matter and are planning to engage in commercial dealings with third parties over these assets should meet with patent counsel in advance to obtain advice. Circumstances may require early patent filings to avoid a potential bar to patentability.

AT WHAT POINT WOULD A SIMILAR COMPETITOR PRODUCT BE FOUND INFRINGING?

In the US, patent holders can prevent competitors from the use, sale or manufacture of products or processes or may pursue patent infringement even if the competitor's product or process lacks elements of the patented invention or is not identical to it. This right is based on the legal principle known as the 'doctrine of equivalents'. The doctrine of equivalents expands the scope of patent protection beyond the literal claim language to encompass minor variations and substitutions that do not alter the underlying patented invention.

The modern formulation of the doctrine of equivalents in the US asks: does the accused product or process contain elements identical or equivalent to each claimed element of the patented invention? (Warner-Jenkinson Co. v Hilton Davis Chemical Co., 520 US 17, 29 (1997) at p. 40 (Warner-Jenkinson)). In determining equivalence, the role of each element in the claim must be analysed in the context of the specific patent claim. A substitute element must match the function, way and result of the claimed element or be substantially similar to the claimed element (Warner-Jenkinson at p. 40).

In Canada, the same concerns apply with respect to 'a copycat device that simply switched bells and whistles to escape the literal claims of the patent' (Free World Trust v Électro Santé Inc., 2000 SCC 66 at paragraph 55 (Free World)). Instead of the doctrine of equivalents, the analysis in Canada starts with a consideration of the language in the claims using a purposive construction.

Purposive construction aims to distinguish the essential from the non-essential to define the scope of the claims. Some elements in a claim are intended to be essential to the working of the patented invention, while other elements are non-essential and substitutable or omitted entirely without affecting the working of the invention (ie, had the skilled worker at that time been told of both the element specified in the claim and the variant and asked whether the variant would obviously work in the same way, the answer would be yes (Free World

at paragraph 55)). There is infringement if there have been substitutions or omissions of non-essential elements, but no infringement if essential elements are absent in a competitor product or process.

The following table summarises the differences between the US and Canada when assessing infringement.

	US	Canada
Test	Each element in a patent claim is deemed material to define the scope of the patented invention and is subject to the essential inquiry: does the accused product or process contain elements identical or equivalent to each claimed element of the patented invention?	Some elements are considered to be essential while other elements are not essential. Substitution of an essential element affects infringement.
Date	The relevant date for considering the patent is the filing date of the patent. The knowledge of the interchangeability or equivalence is considered as at the date of the infringement, not the date of the patent.	The relevant date for considering the patent is the date of publication of the patent.
Amendments during prosecution	The amendment of the claims during prosecution may, but not always, preclude the patent holder from claiming infringement. For example, if the scope of the claims were narrowed during the prosecution of the patent application, the scope of the patent may be restricted to the exact or literal wording of the claims. The burden of proof is on the patent holder to establish the reason for the amendment during the prosecution of the application (Festo v Shoketsu, 535 US 722 (2002)).	The amendment of the claims during prosecution may bar the patent holder from asserting a contrary position from that taken during prosecution; however, the determinative issue is the construction of the claims themselves.

Before deciding to manufacture, sell or implement a product or process, it is crucial to assess the patent landscape to determine if there are potential similarities with existing patented inventions. Whether the product or process might infringe upon a patent will vary from one jurisdiction to another and will depend on the specific test applied.

GENERIC DRUGS AND SKINNY LABELS

Understanding jurisdictional differences is crucial in the pharmaceutical sector, which is notorious as a hotbed for patent infringement lawsuits on both sides of the US–Canada border.

The US and Canada both provide pathways for generic companies to obtain approval for generic versions of previously approved brand drug products, provided they contain the same active ingredients and are bioequivalent to the brand. However, the United States Food and Drug Administration (FDA) and Health Canada will not approve a generic product that would infringe an active patent listed against the brand drug.

A generic company that files an Abbreviated New Drug Application (ANDA) (in the US) or Abbreviated New Drug Submission (ANDS) (in Canada) and compares its drug to an approved brand (innovator) drug must address all patents listed in the Orange Book (for the US) and Patent Register (for Canada) in respect of the brand drug.

In the US, if a generic applicant wishes to enter the market before the expiry of a method of use patent listed in the Orange Book, one option is to propose a label that carves out any patented indications (referred to as a 'skinny label') and file a section viii statement. Skinny labelling permits a generic company to market its drug but only for approved non-patented indications (21 USC § 355(j)(2)(A)(viii); 21 CFR § 314.94(a)(8)(iv); 21 USC § 355(j)(2)(A)(viii); see also Caraco Pharmaceutical Laboratories, Ltd. v Novo Nordisk A/S, 566 US 406 (2012) (Caraco)).

Assuming the other requirements are met, the Hatch-Waxman Act instructs the FDA to approve an ANDA filed with a section viii statement when it proposes to market a drug for only unpatented methods of use (see Caraco at 419; H. Lundbeck A/S v Lupin Ltd., 87 F 4th 1361, 1371 (Fed Cir 2023) (Lundbeck)).

In contrast, Canada does not have a statutory regime that expressly permits skinny labelling or specifically instructs Health Canada to approve a skinny label ANDS, but that is not to say that the practice is prohibited. If properly carved out, skinny labelling is a legitimate strategy within the framework of Canadian patent law and regulatory approval processes.

In both jurisdictions, the central question is whether the generic's activities with respect to a skinny label drug constitute a direct or induced infringement of the patented indications.

US	Canada
Induced infringement requires knowledge that the induced acts constitute patent infringement. The knowledge requirement can be met by a showing of either actual knowledge or wilful blindness (-Global–Tech Appliances, Inc. v SEB S.A., 563 US 754, 766 (2011)).	The test of induced infringement is a three - part test: • the acts of infringement must have been completed by the direct infringer;

	• the completion of the acts of infringement must be influenced by the acts of the alleged inducer to the point that, without the influence, direct infringement would not take place; and • the influence must be knowingly exercised by the inducer – in other words, the inducer knows that this influence will result in the completion of the acts of infringement. (Corlac Inc. v Weatherford Canada Ltd<., 2011 FCA 228.)

Recent developments suggest that the availability of skinny labelling as a path to early generic entry is more established in the US than in Canada. For example, in its 2025 Legislative Proposals (FY25), the US FDA proposed that legislation, including the Hatch-Waxman Amendments, be amended 'to create a safe harbor for applicants who market skinny label drugs'. The FDA recognised skinny labelling as an 'important statutory marketing pathway' and expressed concern that a decision of the US Court of Appeals for the Federal Circuit had cast skinny labelling into uncertainty, potentially affecting the timely availability of generic drugs (GlaxoSmithKline LLC v Teva Pharmaceuticals USA, Inc., No. 18-1976 (Fed Cir 2022) (GSK)).

More recently, however, the US Court of Appeals for the Federal Circuit in Lundbeck distinguished GSK on the facts and confirmed that the skinny label pathway remains a viable strategy for generic applicants in the US. Lundbeck confirmed that in the Hatch-Waxman context, mere knowledge of possible infringement by others does not amount to inducement; specific intent and action to induce infringement must be proven. According to the court, '[t]his is so because a central purpose of the Hatch-Waxman Act is to allow, through the section viii carve out process, the sale of drugs for unpatented uses even though those sales result in some infringing uses' (Lundbeck at 1372). To find induced infringement, the accused infringer must have taken active steps to encourage, recommend or promote infringement (eg, through advertising an infringing use or instructing how to engage in an infringing use) (Lundbeck at 1370).

The Canadian Federal Court of Appeal has recently suggested that although an absence of explicit instruction (eg, of patented use in a generic company's product monograph) and of intention that direct infringement should result may be relevant to the issue of influence, they may not be sufficient to establish absence of influence under the second prong of the inducement test. The court's analysis also appears to suggest that other factors, such as standard of care, may form the basis for a finding of inducement (see Apotex Inc. v Janssen Inc., 2023 FCA 220).

In both the US and Canada, whether a carved-out label is 'skinny enough' to avoid a finding of infringement should be evaluated on a case-by-case basis. Generic companies should

continue to monitor legislative updates concerning skinny labelling and the development of case law surrounding this important topic.

CONCLUSION

The differences in the US and Canadian regimes described above underscore the complexity of navigating patent law across jurisdictions and the importance of having effective legal counsel on both sides of the border. Stakeholders should remain vigilant of developments in US and Canadian patent law and adapt their IP strategies as they identify opportunities and challenges in each jurisdiction.

Nicholas J Wong nwong@blaney.com
Belle Van bvan@blaney.com
Rae Daddon rdaddon@blaney.com

2 Queen Street East, Suite 1500, Toronto, Ontario, M5C 3G5, Canada

Tel: +1-416-593-1221

https://www.blaney.com

A closer look at the latest PTAB estoppel developments

Brian M Gummow, Karen Mangasarian and James F Haley Jr
Haley Guiliano LLP

Summary

INTRODUCTION

More than a decade ago, the America Invents Act (AIA) changed US patent law, including establishing post-grant proceedings, post-grant review (PGR) and inter partes review (IPR), allowing third parties to challenge the validity of patents before the Patent Trial and Appeal Board (PTAB). PGRs, available for patents with a priority date of 16 March 2013 or later, must be filed within nine months of issuance and may assert any ground of invalidity. IPRs, by contrast, can be filed nine months or more after issuance and are limited to prior-art invalidity grounds. In both cases, the prior art can only be patents or printed publications.

Congress established PTAB proceedings to provide a 'quick and cost effective [sic] alternative to litigation' (HR Rep No. 112-98, Part 1, at 45 (2011)). Accordingly, they included estoppel provisions that affect the rights of third parties challenging the validity of a patent both before the PTAB and in litigation.

Specifically, 35 USC 315(e)(2) provides that:

> [t]he petitioner in an [IPR] of a claim in a patent . . . that results in a final written decision . . . or the real party in interest or privy of the petitioner, may not assert . . . in a civil action . . . that the claim is invalid on any ground that the petitioner raised or reasonably could have raised during that [IPR].

35 USC 325(e)(2) has identical estoppel provisions for PGRs.

In the biotechnology and pharmaceutical industries, billion-dollar products can be protected by just one or a handful of US patents. Accordingly, life science patent owners should aggressively assert these estoppel provisions after prevailing in a post-grant proceeding in abbreviated new drug application and biosimilar infringement litigation. By contrast, patent challengers should carefully consider the estoppel risks as they develop their overall litigation strategy, including the filing of any IPRs or PGRs.

US PTAB ESTOPPEL CASES

Various Federal Circuit, district court and PTAB decisions have shaped the contours of these estoppel provisions. While the cases were decided in the context of IPR estoppel, they should apply equally to PGR estoppel because the statutes are identically worded, although the courts may develop different tests for whether non-prior-art invalidity grounds (eg, lack of utility, written description or enablement) that are only available in PGRs could have reasonably been raised. Additionally, while these cases relate to technology patents, they provide useful lessons for life sciences patent practitioners.

DURING THE INTER PARTES REVIEW

In Apple, Inc v California Institute of Technology, the Supreme Court denied certiorari leaving in place a Federal Circuit decision that Apple was estopped to raise in litigation prior-art obviousness combinations it 'reasonably could have raised' in concurrent PTAB proceedings.

In Caltech, the university sued Apple and Broadcom (collectively Apple) for patent infringement. Concurrently with the litigation, Apple filed multiple IPR petitions challenging the validity of Caltech's patents. The PTAB instituted the IPRs and issued final written decisions holding that Apple had not shown that the patents were unpatentable.

Apple then raised new obviousness defences before the district court. It was undisputed that Apple was actually aware of the art that formed the bases of the new defences when filing the IPR petitions but chose not to include the specific combinations, subsequently relied on in the litigation, in those petitions. The district court granted summary judgement of no invalidity holding that Apple was estopped to raise the obviousness defences on the basis of the IPR decisions.

Before the Federal Circuit, Apple argued that estoppel only applied to invalidity grounds that were 'raised or reasonably could have raised during' the IPR. In support, Apple pointed to Shaw Industries Group, Inc v Automated Creel Systems, Inc, which held that an IPR 'does not begin until it is instituted'. In Shaw, the Federal Circuit opined that a party was not estopped in litigation from raising invalidity grounds on which the PTAB declined to institute an IPR. Apple then went one step further, arguing that because new grounds cannot be added after institution, only the grounds on which the IPR was instituted could reasonably have been raised during the IPR and be the basis of estoppel.

The Federal Circuit disagreed, distinguishing Shaw as being decided when the PTAB often instituted IPRs on fewer than all of the grounds raised. Post-Shaw, however, the Supreme Court held in SAS Institute, Inc v Iancu that the AIA does not authorise institutions on fewer than all of the petitioned grounds. The petition, not the institution decision, therefore, defined the scope of the IPR. As a result, the Federal Circuit in Caltech held that 'any ground that could have been raised in a petition is a ground that could have been reasonably raised 'during inter partes review'. Because Apple was aware of the new defences before filing its IPR petitions and chose not to raise them, the Federal Circuit affirmed the district court's estoppel decision.

ESTOPPEL STANDARD AND BURDEN

The Federal Circuit has also clarified whether patentee or petitioner carries the burden of establishing estoppel in litigation and the standard that should be used to determine whether prior art could reasonably have been raised in the IPR.

In Ironburg Inventions Ltd v Valve Corp, the Federal Circuit partially vacated a district court decision that Valve was estopped to raise invalidity grounds included in the IPR petition but not in the final written decision as a result of a pre-SAS partial institution (ie, non-instituted grounds, as well as new invalidity grounds not included in the petition).

Regarding the non-instituted grounds, the Federal Circuit affirmed the district court's estoppel holding. Valve admitted that in view of SAS, it could have asked the PTAB to reconsider the partial institution and the other invalidity grounds raised in the petition. Valve did not do so. The Federal Circuit, thus, held that Valve's choice resulted in estoppel with respect to the non-instituted grounds.

In the context of the new grounds, the Federal Circuit first addressed what grounds 'reasonably could have been raised' during the IPR and adopted a skilled searcher standard: a party reasonably could have raised any ground that 'a skilled searcher conducting a diligent search reasonably could have been expected to discover'. Under this standard, the party would not be estopped to assert an invalidity ground that could only be discovered, for example, by a scorched-earth search. While the skilled searcher standard would likely apply to prior-art-based invalidity grounds in PGRs, it may not apply to non-prior-art-based invalidity grounds available in PGRs (eg, utility, written description and enablement). Accordingly, courts will likely need to establish standards for determining when such grounds reasonably could have been raised in a PGR – perhaps 'a skilled IP attorney' standard.

Next, the Federal Circuit held that the patent owner bears the burden of proving, by a preponderance of the evidence, that a skilled searcher, exercising reasonable diligence, would have identified the new invalidity ground (ie, consistent with the general practice that a party asserting an affirmative defence bears the burden of proving it). That said, a petitioner would be well advised to document the reasonableness of its search and investigation of all grounds of potential invalidity.

On this allocation of the burden, the Federal Circuit vacated the estoppel as to the new grounds of invalidity:

> [b]ecause the district court improperly placed the burden of proof on Valve, to show that it could not 'reasonably . . . have raised' the ['new' grounds] in its petition, when instead the burden of proof rests with [the patentee] to prove that these were grounds Valve 'reasonably could have raised' during the IPR.

Indeed, in EIS, Inc. v IntiHealth Ger GmbH, the petitioner was able to avoid PTAB estoppel in a litigation by providing the court with two prior-art searches performed by skilled search firms: one performed prior to filing the IPR petition and the other before serving invalidity contentions in the litigation. Neither contained the art at issue (Yang). While the patent owner also provided two searches, which purportedly identified Yang, the court held that those searches were 'plagued by hindsight bias' because the searchers were provided a copy of Yang before conducting their searches. Indeed, the patent owner's search strings included terms present in Yang but missing from the challenged patents. When those terms were excluded from the search strings, Yang was not identified. Accordingly, patent owners must take care to avoid such hindsight bias when attempting to meet their burden under the skilled searcher standard.

UNAVAILABLE PRIOR ART

IPR invalidity grounds (and any prior-art-based PGR invalidity grounds) must be based on patents or printed publications. Because PTAB invalidity grounds cannot be based on prior sales or use, patent challengers often contend that they are not estopped to raise such invalidity defences in litigation because they could not have been reasonably raised during the PTAB proceeding. District courts applying Ironburg's skilled searcher test have split in addressing this issue, especially when a printed publication (eg, a user manual) describing the prior-art product or use exists.

On one hand, in Carolyn W Hafeman v LG Electronics Inc, the district court held that LG was estopped form relying on two alleged prior-art products (ie, the products themselves, not publications describing them). Even though the products could not have been included as invalidity grounds in the IPR, the court held that 'estoppel still applies when the allegedly new references have 'materially identical' disclosures as the IPR art'. The IPRs relied on prior-art patents and based on LG's admissions, the court found that the products practise those patents because there was 'no substantial difference' between the products and the patents and LG was estopped.

By contrast, in Singular Computing LLC v Google LLC, the court held that Google was not estopped to raise invalidity defences based on prior-art CPU systems after losing on its 'patents and publications' invalidity grounds before the PTAB. The court noted that the AIA:

> says nothing about estopping invalidity claims that are 'cumulative' or 'duplicative' of those raised in an IPR proceeding. Nor does it specify that evidence outside of patents or publications is permissible only when that evidence provides the sole support for a claim limitation.

Accordingly, the court held that:

> an accused infringer who receives a final written decision in an IPR proceeding may challenge the validity of a patent in … district court, but only to the extent that the challenge is based on prior-art evidence that it could not have presented in a petition for IPR.

Interestingly, the court also held that Google could only raise invalidity grounds based solely on prior-art evidence that it could not have presented in the IPR (the CPU systems) but was estopped from arguing obviousness based on a combination of the CPU systems with a prior-art patent or printed publication (ie, that could have been raised in an invalidity ground in the IPR), even though such a combination would not have been permitted in the IPR.

In Prolitec Inc. v Scentair Techs., LLC, Federal Circuit Judge Bryson (sitting by designation in D Del) held that 'IPR estoppel does not apply to device art, even when that device art is cumulative of patents and printed publications that were or could have been asserted in a prior IPR'. Judge Bryson focused on the Federal Circuit's use of 'ground' 'to mean a legal argument based on a specific combination of references' and, therefore, 'as the specific pieces of prior art that are the bases on which a petitioner challenges a claim'. Because the prior-art product could not have been raised in the earlier IPR, the estoppel provisions of 35 USC 315(e)(2) did not apply. The court in EIS, Inc. v IntiHealth Ger GmbH similarly held that 'IPR estoppel does not apply to products covered by the actual prior-art reference underlying the IPR where the actual prior-art reference discloses the same claim limitations as the product'.

ESTOPPEL IN OTHER PATENT OFFICE PROCEEDINGS

IPRs also have estoppel effects on invalidity challenges in other patent office proceedings. Similar to the estoppel in litigation, defendants who fail in their patent challenge in an IPR are estopped in subsequent invalidity challenges in the Patent Office from pursuing grounds, which they raised or could have raised in the earlier IPR. Indeed, the United States Patent and Trademark Office (USPTO) recently held that Salesforce, which, as a real-party-in-interest in prior IPRs, had unsuccessfully challenged two AIT patents, was estopped from challenging the patents in ex parte re-examinations (see Ex parte Reexamination 90/019,069, Decision on Petitions (USPTO, 25 May 2023) and Ex parte Reexamination 90/019,070, Decision on Petitions (USPTO, 25 May 2023)). In the IPRs, the PTAB issued final written decisions finding that several claims were unpatentable. The Federal Circuit vacated those decisions, and the PTAB terminated the IPRs on remand.

In the re-examinations, AIT argued that Salesforce was a real-party-in-interest in the earlier IPRs, which had resulted in final written decisions and, therefore, was estopped to request ex partere-examination on invalidity grounds that were raised or could have been raised in the IPRs. Salesforce argued, on the other hand, that estoppel should not apply given the Federal Circuit's vacatur. Citing Intuitive Surgical, Inc v Ethicon LLC, the USPTO held that the vacatur did not negate the statutory estoppel effect of the final written decisions. In

particular, the USPTO noted that in Intuitive Surgical, the Federal Circuit held that the estoppel occurs upon the issuance of the final written decisions. Vacatur does not change that fact. The re-examination requests also relied on additional art as compared to the IPRs. As to that art, the USPTO applied the skilled searcher test and determined that the art reasonably could have been raised in the IPRs. The USPTO, therefore, terminated the re-examination proceedings.

COMMON LAW ISSUE PRECLUSION DOES NOT EXPAND INTER PARTES REVIEW OR POST-GRANT REVIEW ESTOPPEL

The court in the Central District of California held that common law issue preclusion (an earlier final judgment binds the parties as to issues actually litigated in the prior action) cannot be used to bar a challenger's invalidity grounds that could not have been reasonably raised in a related IPR. In DMF, Inc v AMP Plus, Inc, DMF moved to estop AMP from raising invalidity grounds that were raised or could have been raised in an earlier IPR, which resulted in a final written decision finding that most of the challenged claims were not unpatentable. The district court granted the motion with respect to invalidity grounds that were based on prior-art patents and printed publications but denied the motion with respect to invalidity grounds based on a prior-art product, which could not have been raised in the IPR and which it found to be substantively and germanely different from a catalogue relied on in the IPR because the catalogue did not disclose every feature of the product.

DMF then argued that common law issue preclusion barred AMP's product-based invalidity grounds. The district court denied the motion, finding that 35 USC 315(e)(2) 'embodies an evident statutory purpose to apply the specified framework in lieu of common law issue preclusion'. Accordingly, common law issue preclusion was not appropriate '[b]ecause Congress enacted a specific framework with respect to the issue preclusive effect of IPR proceedings'.

CONCLUSION

As courts continue to shape and refine the metes and bounds of PTAB estoppel on subsequent invalidity challenges in the district courts and the Patent Office, patent challengers should carefully consider their strategies for invalidating biotechnology and pharmaceutical patents. The lower burden of proof in a PTAB proceeding (preponderance of the evidence) as compared to a district court infringement litigation (clear and convincing evidence) and the availability of technically trained administrative patent judges still makes the PTAB an attractive venue for challenging patents. Petitioners in the generic and biosimilar industries, however, should be sure to present all of their arguments and not to hold any back in reserve, because they likely will be estopped to raise them in subsequent proceedings directed to patent claims upheld in the IPR or PGR. Further, until the Federal Circuit weighs in on how estoppel applies to prior-art products or non-prior-art invalidity grounds in PGRs, challengers should have these uncertainties in mind as they develop their strategies in the PTAB and subsequent litigation. Many generic or biosimilar producers may file 'clear the path' PTAB proceedings ahead of their FDA submissions. If such clear the path PTAB challenges are unsuccessful, the generic or biosimilar producer may have to either wait for the patent to expire before commercially launching their product or design around the unsuccessfully challenged patent. Therefore, these potential clear the path challenges should be carefully evaluated in view of any subsequent product development or litigation strategies.

Haley ▪ Guiliano

Brian M Gummow brian.gummow@hglaw.com
Karen Mangasarian karen.mangasarian@hglaw.com
James F Haley Jr james.haley@hglaw.com

75 Broad Street, Suite 1000 , New York NY 10004, United States

Tel: +1 646 973 2500

https://www.hglaw.com

Why introduction of patent term extensions in China is good news for rights holders

Na Wang
CCPIT Patent and Trademark Law Office

Summary

China has developed rapidly in the pharmaceutical industry in the past few years and has become one of the largest and most active pharmaceutical markets in the world. To further encourage innovation in drug development, China has initiated a series of regulatory and patent reforms in the pharmaceutical industry in recent years, including the implementation of patent term extension (PTE).

BACKGROUND

The pharmaceutical industry is highly dependent on patent protection due to the high cost, long cycle and high risk of researching and developing new drugs. Without patent protection, it would be difficult for innovative drug companies to recover their research and development costs and achieve reasonable profits, thereby negatively affecting their enthusiasm for research and development of new drugs. However, drug marketing requires strict approval by the drug regulatory authorities, including a series of studies like non-clinical safety evaluation and clinical trials. This means that even if a patent application is granted, it cannot be implemented for a considerably long period until it obtains a marketing approval, resulting in a greatly shortened protection period of the patent.

Patent term extension originated in the United States under Drug Price Competition and Patent Term Restoration Act in 1984, also known as the Hatch-Waxman Act. Then, several countries or regions, such as Japan, South Korea, the European Union and Canada have also established similar systems to compensate for the loss of patent protection period caused by the lengthy approval process for innovative drugs.

China has been exploring the patent term extension in recent years. On 15 January 2020, China agreed to provide patent term extension to compensate for unreasonable delays that occur in granting the patent or during pharmaceutical product marketing approvals under the Economic and Trade Agreement between the Government of the People's Republic of China and the Government of the United States of America. On 17 October 2020, China passed the amendments to the Chinese Patent Law. Since 1 June 2021, the new Chinese Patent Law has come into effect and patent term extension has been available in China. The new Implementing Regulations and Patent Examination Guidelines came into effect on 20 January 2024 and further detailed the implementation of PTE in China.

OVERVIEW OF PTE

The new Chinese Patent Law stipulates in paragraph 3 of article 42 that to compensate for the time taken for review and approval of a new drug for marketing, the China National Intellectual Property Administration (CNIPA) will extend the term of the patent for invention related to the new drug for which a marketing approval is obtained in China, at the request of the patentee. The patent term extension should not exceed five years and the resulting total effective patent term should not exceed 14 years from the approval for marketing of the new drug.

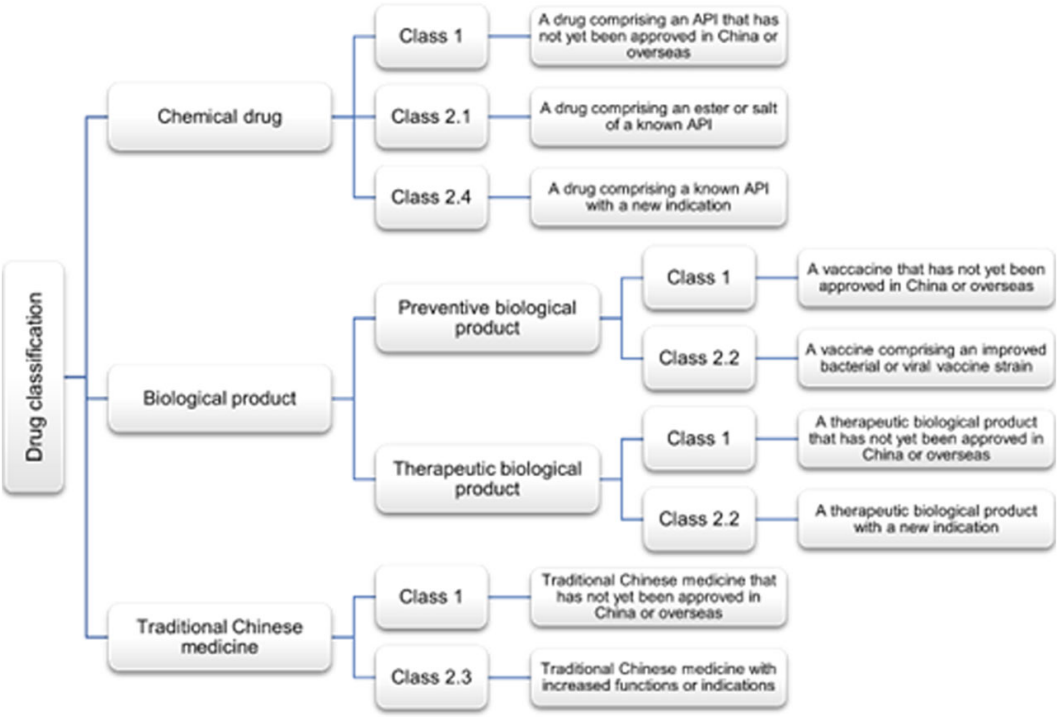
ELIGIBLE DRUGS OF PTE

PTE is available to product patents, preparation method patents and medical use patents of the active pharmaceutical ingredient (API) contained in a 'new drug'. The term 'new drug' here is interpreted to mean innovative drugs and certain improved new drugs defined in drug regulatory laws and provisions of National Medical Products Administration (NMPA). For a pharmaceutical product to qualify as a 'new drug' that is eligible for PTE in China, the

pharmaceutical product must be new to the world, meaning that the new drug application (NDA) of the product must be filed in China before the product is approved for marketing in any other countries. However, it is not a requirement for the NDA to be approved in China before it is in other countries.

- Innovative drugs eligible for PTE: according to the current drug classification provisions of NMPA, innovative drugs refer to class 1 drugs and must be new to the world. Innovative drugs include the following drugs that have not yet been approved in China or overseas: (i) a chemical drug; (ii) a preventive biological product – vaccine; (iii) a therapeutic biological product; and (iv) traditional Chinese medicine.
- Improved new drugs eligible for PTE: improved new drugs eligible for PTE must be new to the world as well and are limited to the following drugs according to the NMPA's drug classification:
- an ester or salt of a known API in Class 2.1 of chemical drugs;
- a drug comprising a known API with a new indication in class 2.4 of chemical drugs;
- a vaccine comprising an improved bacterial or viral vaccine strain in class 2.2 of preventive biological products;
- a therapeutic biological product with a new indication in class 2.2 of therapeutic biological products; and
- traditional Chinese medicine with increased functions or indications in class 2.3 of traditional Chinese medicine.
- 'Imported drugs' are not eligible: according to the above definition of 'new drug', the 'imported drugs' in class 5.1 of chemical drugs, classes 3.1 and 3.2 of preventive biological products and classes 3.1 and 3.2 of therapeutic biological products, which have been marketed overseas when seeking marketing approval in China, are excluded from PTE.

Drug classification eligible for PTE is summarised in the following chart.



TIME LIMIT FOR FILING OF A PTE REQUEST

A PTE request should be filed by the patentee or its agent upon authorisation of the marketing authorisation holder within three months from the date of approval of the drug, together with the payment of the official fee.

REQUIREMENTS FOR OBTAINING A PTE

To obtain a PTE in China, the following requirements should be met:

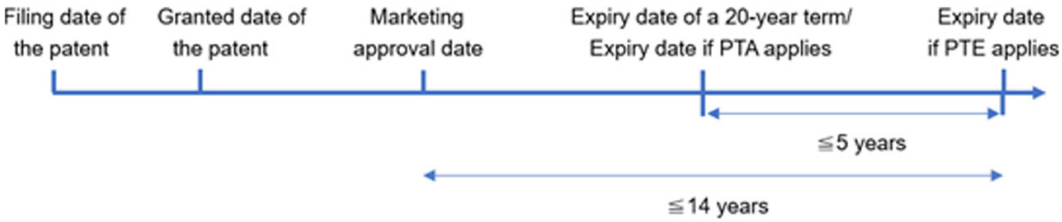
- the issue date of the patent shall be earlier than the approval date of the drug;
- the patent is valid when the PTE request is filed;
- the patent has not been granted a PTE yet;
- the claims of the patent include the drug-related technical solutions; the drug-related technical solutions refer to the structure, components and amount thereof and the approved manufacturing process and indications of the approved new drug;
- if the drug is covered by multiple patents, the term of only one patent can be extended; and
- if a patent covers multiple drugs, PTE of the patent is possible for one drug only.

CALCULATION OF PTE

PTE is applied in addition to any patent term adjustment (PTA) and the calculation of PTE shall be done after the decision of PTA is made. Due to different reasons for compensation, the compensation periods involving PTA and PTE can be accumulated.

PTE is calculated by subtracting five years from the number of days between the filing date of the Chinese patent application and the marketing approval date in China. Meanwhile, PTE should meet the following two requirements: the maximum PTE is five years and the resulting total effective patent term after drug approval for marketing should not exceed 14 years.

The following line chart and equations show the two requirements regarding the extension period for PTE.



PTE = (marketing approval date in China – filing date of the Chinese patent application) five years (f5 years)

Total effective patent term after drug approval for marketing = (the expiry date of a 20-year patent term – marketing approval date in China) + PTA (if any) +PTE (f14 years)

EXAMINATION OF THE PTE REQUEST AND CHALLENGE TO CNIPA'S DECISION

Before making an unfavourable decision, the examiner will give the patentee at least one opportunity to make observations or amendments. If PTE requirements are met, the CNIPA will grant PTE, notify the number of days by which the patent term is extended and publish information such as drug name, approved indications and the original and new expiry dates of the patent in the patent gazette.

The CNIPA's decision is challengeable by the patentee and an interested third party by applying for an administrative reconsideration at the CNIPA.

SCOPE OF PROTECTION DURING PTE

Since the purpose of PTE is to compensate for the time taken for the market approval of the new drug, it is necessary to directly associate the approved new drug with the technical solutions of the drug patent that requests PTE. The technical solutions related to a new drug would serve as the bridge connecting the marketed new drug with the drug patent that requests PTE.

The protection scope of PTE is narrower than the patent and limited to the new drug for the indication as approved, which is interpreted to mean that the protection scope of PTE is: (i) new drug product used for the approved indications for product claims; (ii) the approved indication of the new drug for medical use claims; and (iii) manufacturing process recorded with NMPA for the new drug used for the approved indications for preparation method claims.

A new indication can support a new PTE, but the scope of PTE obtained only covers the new indication underlying the PTE but not any earlier or later approved indications.

Therefore, the patentee when filing a request for PTE, should provide materials for determining the protection scope of PTE, such as materials showing the composition of the approved drug, materials showing the indication of the approved drug, materials showing the drug manufacturing process approved by NMPA and the like.

TAKEAWAYS

For innovative drug companies, due to the lengthy process from the discovery of 'hit' compounds, to the optimisation of lead compounds, to preclinical and clinical trials of

candidate drugs and to marketing, patent applications are often filed long before the drug is marketed. The implementation of PTE in China has positive effects for innovative drug companies, since it can provide extended protection of patents of innovative drug companies, if PTE is granted by the CNIPA. Under PTE, the protection of the legitimate rights and interests of innovative drug companies is strengthened to incentivise continuous innovation in new drug research and development.

Therefore, the innovative drug companies should actively seek for extension of patent term by utilising PTE in China. When requesting for PTE, the innovative drug companies should take into account all the factors, such as the type of the claims, scope of the claims, stability of the patent, enforcement of patent, PTE scope and 'one PTE per drug per patent' rule so as to maximise and rationalise the extension of patent term of one or more patents. For example, the patentee may choose one patent to file a PTE request based on the new drug and its approved indication and then choose another patent to file a PTE request based on a newly approved indication. Therefore, patents filing strategy may also need to adapt to the NDA approvals such as indication expansion.

As mentioned earlier, imported drugs that have been marketed overseas when seeking marketing approval in China, including class 5.1 of chemical drugs, classes 3.1 and 3.2 of preventive biological products and classes 3.1 and 3.2 of therapeutic biological products, are not eligible for PTE. Therefore, innovative drug companies should consider submitting the NDA in China before the new drug is marketed in other countries.

For generic drug companies, extending the patent term of innovative drugs will inevitably delay the entry of generic drugs into the market, resulting a significant impact on numerous generic drug companies in China. The generic drug companies should closely monitor the patent term of innovative drug companies, pay attention to whether a PTE has been obtained and whether CNIPA's decision for PTE is challengeable and plan for the Abbreviated New Drug Application progress strategically. If necessary, the generic drug companies may also consider filing a request of invalidation against the patents of innovative drug companies.

The resulting delayed entry of generic drugs into the market is likely to increase patients' pharmaceutical expenses in China. Therefore, seeking for a balance between the profit of innovative drug companies and generic drug companies is significant. When formulating patent laws and implementing regulations regarding PTE, this has already been taken into consideration and could be reflected in several requirements for obtaining a PTE. For example, the requirements include that only patents for which a PTE has not been granted are eligible to receive a PTE; if the drug is covered by multiple patents, the term of only one patent can be extended; and if a patent covers multiple drugs, PTE of the patent is possible for one drug only. Besides, it is also stipulated that the maximum PTE is five years and the resulting total effective patent term after drug approval for marketing shall not exceed 14 years. These requirements not only effectively avoid repeated compensation of the patent term of innovative drug companies, but also prevent excessive extension of a patent term.

CCPIT PATENT & TRADEMARK LAW OFFICE

Na Wang wangn@ccpit-patent.com.cn

10/F Ocean Plaza, 158 Fuxingmennei Street, Beijing 100031, China

Tel: +86 10 6641 2345

http://www.ccpit-patent.com.cn

How to take advantage of both EPO prosecution and German enforcement

Markus Grammel, Sebastian Ochs and Elena Biselli
Grünecker Patent Attorneys and Attorneys-at-Law

Summary

Europe is one of the most important markets for the life sciences and pharma industry and Germany is one of its key jurisdictions. As in the rest of Europe, the legal landscape in Germany in patent matters is highly complex, due to different degrees of harmonisation between European countries and a wide range of different options to protect intellectual property on a national and European level.

Until recently, two options were available for obtaining patent protection in Germany: the national route through the German Patent and Trademark Office (GPTO) (in accordance with Germany's national laws) and the European route through the European Patent Office (following the European Patent Convention). Filing a patent application with the European Patent Office (EPO) meant to file and prosecute a single patent application, which after grant could be validated in any of the member states of the European Patent Convention (EPC), including Germany.

Since 1 June 2023, as a third option, applicants can file a patent application with the EPO; however, after grant, applicants can request the grant of a unitary patent, which, at the moment, provides unitary protection in 17 states, based on a single patent right, including Germany, without needing validation in each member state separately. Similarly, with the creation of the Unified Patent Court (UPC), right holders can enforce unitary patents in a single action in all 17 states that are party to the Agreement on a Unified Patent Court (UPCA), including Germany.

Accordingly, there are now essentially three routes to patent protection in Germany:

- filing a national German patent application (or a national phase from an international patent application);
- filing a European patent application with the EPO and validating in Germany; or
- filing a European patent application with the EPO and requesting a unitary patent after grant.

The majority of patents in the life sciences and pharma sector are filed with the EPO and not the GPTO; therefore, we focus this article on the life sciences practice at the EPO.

As in other parts of the world, patenting life science inventions in Germany can be a tricky business as some biological subject matter is excluded from patent protection and careful patent drafting is required to obtain allowable claims. Furthermore, it is crucial to consider how much and what data should be included in a life sciences patent application, as this may determine the ultimate fate of the application, more so than in other technical areas.

THE HUMAN BODY AND ITS ELEMENTS

The EPO does not grant patents for processes for cloning human beings and modifying the genetic identity of the germ line of human beings. The EPO also does not allow patenting uses of human embryos for industrial or commercial purposes. However, this does not affect inventions for therapeutic or diagnostic purposes, which are applied to the human embryo and are useful to it. The mere discovery of a human gene is also not a patentable invention. However, if the gene is isolated from the human body or otherwise produced by means of a technical process, it may be patentable, especially if such a gene has industrial application and this application is demonstrated and described in the patent.

In the EPO, patent claims involving human embryonic stem cells are generally patentable as long as the claimed subject matter does not necessarily involve the destruction of human embryos. In particular, patent claims on this matter are usually allowable if the patent application has a filing date on or after 5 June 2003 and its technical teaching can be put into practice using human embryonic stem cells derived from parthenogenetically activated human oocytes. Culture media, supports and apparatuses 'suitable for' use with human embryonic cells, or even 'specifically designed' for this purpose, may also be patentable, since their production normally does not require the use of human embryos as base material. Foetal and post-natal human cells are also, in principle, not excluded from patentability.

ANTIBODIES

Antibody technology is a rapidly developing field in the context of biotechnological and pharmaceutical research. Considering the extensive, time-consuming and expensive research in this field, ensuring appropriate patent protection for inventions based on antibodies is very important. Therefore, a large body of case law has formed concerning the patentability of antibody claims. In the EPO, composition of matter claims directed to antibodies can be defined by the antibody structure, by nucleic acid sequences encoding the antibody, by reference to the target antigen or the epitope that they bind to, by the production process, or by reference to their functional and structural features.

If an antibody is defined by primary sequence information, examiners typically require that the claim recites all complementarity-determining region sequences. If broad functionality is used in the claim, which in the EPO is still possible in certain instances, it has to be carefully assessed whether the application provides an enabling disclosure across the whole scope of the claim and whether the functional definition allows the skilled person to clearly determine the limits of the claim. In particular, the patent application must enable the person skilled in the art to produce further antibodies having the claimed functional property without undue burden. The claim should therefore normally include the relevant characteristics of the method used to determine and define the functional property.

Recently, the EPO has made clear that, in claims directed to antibodies defined by their ability to compete with a reference antibody that is disclosed for the first time in the application, this ability will not normally be considered sufficient to identify antibodies in the state of the art. In these cases, a complete search cannot be carried out and the applicant will be invited to provide more details with respect to the subject matter to be searched.

Furthermore, in all cases relating to antibodies defined by their target antigen, epitope and further functional features, in the absence of any indication to the contrary, a prior-art antibody binding the same target antigen is considered to have the claimed functional properties, thereby leading to an objection of lack of novelty with respect to the claimed antibodies.

PLANTS AND ANIMALS

Patenting of plants or animals that have been modified by genetic engineering or other technical processes is generally possible. The fruits of plants and subsequent generations of animals can also be covered by patent protection. However, processes for modifying the genetic identity of animals, which are likely to cause these animals suffering without any substantial medical benefit to humans or the animal, as well as animals resulting from such processes, are not patentable. For example, a claim directed to a pharmaceutical preparation, which involves a certain amount of animal suffering and does not have different

mechanisms of action or targets different pathways from other widely available compounds of the prior art may be considered not patentable, since there may be plenty of alternative medicaments on the market that achieve the same or a comparable therapeutic effect without involving the same amount of animal suffering. Plant and animal varieties are not patentable; neither are essentially biological processes for the production of plants and animals. Likewise, plants and animals that are obtained exclusively by means of an essentially biological process are also excluded from patentability, on the national level as well as in the EPO.

MEDICAL USE CLAIMS

In Germany and the EPO, methods of treatment of the human or animal body are not patentable. However, claims directed to a substance or composition for use in the treatment of a subject are amenable to patent protection. These claims provide purpose-limited product protection for any therapeutic application (first medical use) or for a specific medical use (second or further medical use). For example, an acceptable claim could be directed to compound X for use in the treatment of a disease, providing purpose-limited product protection for compound X, limited to its use in the treatment of the recited disease. The treatment of more than one disease can be covered by a single claim, provided that the treatment of those diseases forms a single general inventive concept. As long as the prior art does not teach the use of compound X for treating the recited disease or diseases, the claim would be novel, even if compound X itself is known in the art. This principle applies only to substances and compositions and cannot be extended to other products, such as a device for an intended medical use (eg, pacemaker or implantable chemical sensor for use in . . .). Recently, the Boards of Appeal of the EPO held that the question of whether a material or an object is a 'substance or composition' should be decided, in the first place, on the basis of the claimed material or object as such. No additional restrictions relating to its mode of action are derivable from the EPC.

PLAUSIBILITY AND POST-PUBLISHED DATA

A hotly debated topic over the past few years in Germany, and in particular at the EPO, has been the 'plausibility' requirement or test, which often comes up in life sciences cases. While there is no express regulation in the law that requires plausibility for the grant of a European or German patent in particular, the Boards of Appeal of the EPO have held that a relevant technical effect of the claimed invention (eg, a treatment of a particular disease) must have been credible to the skilled person at the time of filing of the application based on the disclosure of the application as filed.

In principle, experimental data are not always required for there to be a plausible teaching of a technical effect. However, in most cases, at least some relevant experimental data (eg, relevant in vitro data) will be necessary in the patent application. It may still be possible to file supplementary experimental data to support the presence of a technical effect after the filing date of the patent application, for example, for convincing the EPO that the claimed invention involves an inventive step. This possibility can be of critical importance in the life science sector, where patent applications are often filed before clinical trials start. Under which circumstances post-published data may be taken into account by the EPO for support of an inventive step has been the subject of decision G 2/21 of the Enlarged Board of Appeal of the EPO in 2023. The Board held that the applicant or proprietor may rely upon a technical effect for inventive step if the skilled person, having common general knowledge in mind, and based on the application as originally filed, would derive this effect as being encompassed by

the technical teaching and embodied by the same originally disclosed invention. However, the debate regarding post-published data remains open. Indeed, on 17 January 2024, the appellant/opponent in the appeal proceedings that led to decision G 2/21 filed a petition for review against this decision. The outcome of this petition may push for a further clarification in the use of post-published data to support inventive step.

ENFORCEMENT

Germany has been a preferred venue for right holders to enforce their patents for quite some time. In addition to the very experienced judges, the structure of German proceedings and the available remedies provide an ideal set-up to enforce patents both extensively and quickly. Right holders can, for example, seek injunctive relief, recall and destruction of infringing products and accounting and damages and claim cost reimbursement to a certain degree. German law still provides for an 'automatic injunction'. If the court establishes that there is infringement, it is common for injunctive relief to be granted. Although the disproportionality defence established by the German courts has since been codified in law, it still remains rather the exception than the rule. However, it can become relevant in particular with respect to pharmaceutical patents when considering third parties' interests (eg, patients who need to be treated, etc).

Germany has a bifurcated patent litigation system. Matters of infringement and matters of validity are dealt with by different courts in separate proceedings (post-grant oppositions are handled by the EPO or GPTO). Typically, the infringement courts of first instance issue a decision within 12 to 15 months and are rather reluctant to stay the proceedings in light of a separate invalidity action before the German Patent Court. Furthermore, provisional measures, such as preliminary injunctions, are possible too. On the other hand, the proceedings before the German Patent Court tend to take much longer. In connection with the automatic injunction, this can result in the injunction gap (ie, the period between the first instance infringement decision, which can be enforced against a security deposit and the decision by the German Patent Court on the validity of the enforced patent). Depending on which side you are, this can be a great advantage.

A notable topic when dealing with pharmaceutical patents is the enforcement of second medical use claims. German law provides for protection against illegitimate use of second medical use inventions by third parties. The requirements for showing infringement of second medical use claims used to be stricter in the past. German courts generally required that the patent owner showed that the product was manufactured and 'purposefully arranged' for the claimed use. With the Pemetrexed decision (Case No. X ZR 29/15), the Federal Supreme Court increased the level of protection for the owners of second medical use patents.

Now, second medical use claims are construed as purpose-limited product claims. This claim type provides for protection against any offering or distribution of the product for the patent protected purpose (ie, the medical use). The actual use of the product for the specific (second medical) use is no longer required to find infringement.

The Court of Appeals Dusseldorf, applying this new case law, developed this further in its decisions on Oestrogenblocker (Case No. I-2 W 6/17) and Fulvestrant (Case No. I-2 U 27/18). Accordingly, a second medical use claim can be infringed if: (i) the product in question is suitable for the claimed use; or (ii) the infringer makes use of circumstances, which lead – in a similar way to the purposeful arrangement – to the claimed use of the product. The latter

is the case if the product is not only used accordingly in individual cases and the infringer knows about this or should know about this.

Since 1 June 2023, the UPC has also been an option for right holders to enforce patent rights. Its decisions will cover all the contracting member states, including, in particular, Germany. Four Local Divisions (LDs) of the UPC have been established in Germany. They are staffed with experienced German litigation judges. This makes Germany a very good option as a venue for right holders litigating patents before the UPC. The remedies available before the UPC are almost identical to what German patent courts offer. The UPC can grant provisional and protective measures and injunctions as well. Looking at the first decisions to date (all of which were issued in preliminary proceedings), a trend might be that the German LDs stick to German practice. Automatic injunctions are possible – even without a prior oral hearing (eg, LD Dusseldorf, UPC_CFI_177/2023). At the same time, one can hardly deduce implications for proceedings on the merits from this – in preliminary injunction proceedings it is usually a matter of whether injunctive relief is granted, rather than to what extent. With the first decisions on the merits still pending, it remains to be seen how the UPC will handle proportionality considerations. This applies particularly considering that a uniform supranational case law will have to be established. German case law will likely have a certain impact on that, given that, until April 2024, about 75 per cent of the pending infringement actions have been filed before the German LDs. At some point in time, the UPC Court of Appeals will provide guidance. The first landmark decisions can be expected fairly soon and may well be rendered in the life science sector – well-known companies such as Amgen, Abbott and Sanofi are already involved in infringement proceedings. Overall, life science companies seem to be welcoming the UPC with the sector accounting for approximately 30–40 per cent of the pending infringement cases.

From the current status, one can take that Germany remains a favourable venue, in particular considering biotech and pharmaceutical patents – be it the German national courts or the UPC's LDs.

SUPPLEMENTARY PROTECTION CERTIFICATES

In Germany, supplementary protection certificates (SPCs) are available for effectively extending the patent term of pharmaceutical patents. The legal basis for German SPCs is Regulation (EC) No. 469/2009, which has direct effect in all member states of the European Union. Obtaining an SPC requires a granted European patent and a market authorisation. The maximum term of the SPC is five years. Even though the SPC is based on a granted European patent, as of now, and for the near future, the request for grant of a SPC has to be filed on the national level with the GPTO. However, based on recently published draft legislation, the EU may establish a centralised SPC filing and examination procedure and a unitary SPC at some point in the future.

SUMMARY AND OUTLOOK

With the UPC just getting underway and further IP legislation on the horizon, the IP landscape in Germany is currently undergoing fundamental changes. Given the peculiarities of protecting and enforcing life sciences inventions in Europe, particularly in Germany, high-quality IP management is decisive for commercial success. This is all the more the case as in the life sciences, different from other technical fields, individual products are often only covered by a small number of patent rights.

GRÜNECKER
PATENT ATTORNEYS AND ATTORNEYS-AT-LAW

Markus Grammel grammel@grunecker.de
Sebastian Ochs ochs@grunecker.de
Elena Biselli biselli@grunecker.de

Leopoldstrasse 4, Munich 80802, Germany

Tel: +49 89 21 23 50

https://grunecker.de/fr/

A deep dive into patent law and exclusivity in the United States

Robert J Paradiso
Lowenstein Sandler

Summary

INTRODUCTION

The pharmaceutical industry is critical to the progress of science in researching, developing and introducing new therapies that improve the health and quality of life for patients around the globe. This continued progress requires an extensive amount of funding and financial risk due to the complexity and unpredictability of basic research, clinical trials and the approval process, which result in many failed drugs for every success. It is estimated that it takes about 10 to 15 years, with an average cost of US$1–2 billion, for each new drug product to be approved for therapeutic use (D Sun, W Gao, H Hu, S Zhou, Why 90% of clinical drug development fails and how to improve it?Acta Pharm Sin B 2022, 12(7):3049–62). Accordingly, exclusivity – provided by a robust patent portfolio and regulatory statutes – is essential in order to recoup the massive investments incurred during research, development and regulatory approval of pharmaceutical products. These exclusivities are also critical in providing and maintaining resources for the further development of other therapies in a company's pipeline.

Unlike many other industries, the filing and development of a pharmaceutical patent portfolio with the United States Patent and Trademark Office (USPTO) most often occurs concurrently with a long and protracted process before commercialisation can occur. The process includes initial research and development and pre-clinical and clinical trials and culminates with the filing of an application for regulatory approval with the United States Food and Drug Administration (FDA). A US patent expires 20 years from the earliest filing date, not including certain statutorily available extensions. Therefore, it is not uncommon for a patent to be in force and losing valuable patent term while the subject matter of the patent is being developed and under regulatory review. It is also not uncommon that, upon drug approval, the underlying patent has expired or has only a fraction of its available term available.

Unfortunately, this often results in the discontinuation of programmes that could have otherwise provided great benefit to many patients. These inequities, among others, were mitigated by passage of The Drug Price Competition and Patent Term Restoration Act, better known as the Hatch-Waxman Act. The Hatch-Waxman Act provides incentives for the development of new innovative pharmaceutical products, as well as an abbreviated pathway for generic manufactures to bring lower-cost versions to market.

The timelines of both patent prosecution and regulatory approval should never be viewed as two separate and distinct exercises. Statements made to the FDA should always be consistent with statements made to the USPTO as unintentional inconsistencies could result in difficulties with the eventual enforcement of a patent. Likewise, the dates related to patent filing and patent term expiration intertwine with actions and exclusivities related to regulatory approval as promulgated by The Hatch-Waxman Act.

There are many pitfalls in the developmental timeline of a pharmaceutical product, from initial identification of a candidate to post-marketing launch. Not having a well-thought-out strategy can make a significant difference in the result: the approval of a beneficial medicine with strong exclusivity as opposed to an aborted launch or a relatively short exclusivity with quick generic entry. Having a keen understanding of the intricacies of US patent law and its interplay with regulatory provisions is key to navigating the many minefields inherent in the ultimate commercialisation of a successful product.

PECULIARITIES OF US PATENT LAW

When a pharmaceutical company first identifies and designates a new molecular entity as a developmental candidate for the pursuit of regulatory approval, immediate consideration must be given to filing a patent application in order to initiate the process to secure exclusivity. This is particularly important in light of the conversion of the US patent system from a 'first to invent' system to a 'first to file' system in 2013 under the Leahy-Smith America Invents Act (AIA). In the highly competitive landscape of the life sciences industry, sometimes filing a patent application even one day earlier can prove to avoid 'prior art' such as a journal publication or a patent application of a competitor being citable against the application, which could negatively impact the possibility of obtaining meaningful patent claim scope.

When filing an initial patent application for a new molecular entity, all in-vitro and in-vivo studies have not yet been performed. In many cases, these studies provide important data to support a comprehensive patent application. In this situation, the filing of a provisional patent application with the USPTO under 35 US Code § 111(b) may help to mitigate this issue. This type of filing – unique to the US patent system – provides a low-cost way to establish an earlier filing date with less formal requirements. A US provisional application does not get examined, nor does it issue as a patent; rather, it is a placeholder to obtain a filing date that acts as the cut-off for the availability of prior art that could be available for citation against the subject matter of the application. To maintain the filing date of the provisional application, a non-provisional or 'utility' application with a claim of priority to the earlier date must be filed within 12 months. The utility application then undergoes formal examination with the hope of issuance as a US patent.

Beyond offering lower cost and less preparation time than a utility application, a US provisional patent application provides other benefits, such as the ability to add further disclosure, examples and data to the application while preparing the non-provisional application claiming priority to the provisional application. The provisional application also allows the establishment of a priority date before the generation of all data that may be desired to be included in the application.

A common misconception when claiming priority to a provisional application is that all of the subject matter in a later non-provisional patent application is entitled to the provisional filing date. However, a provisional application only provides priority support for the disclosure that is actually contained in the document. Any additional disclosure that is included in a non-provisional application is only entitled to the non-provisional filing date and will not enjoy the benefit of the provisional filing date. For instance, if a provisional application discloses that Compound X is suitable for the treatment of asthma but does not include a dosing range for human subjects, the later disclosure of the dosing range in a later non-provisional application would not have the benefit of the earlier date. A claim to the dosing range in the non-provisional application would be susceptible to intervening prior art that was known after the provisional filing date but before the non-provisional filing date. Therefore, it is always good practice to prepare and file as robust a provisional patent application as possible based on the knowledge and data available at that time. This maximises the probability that the provisional application will provide a strong priority date.

The other benefit of utilising provisional patent applications is maximising patent term. The statutory patent term of a US patent is 20 years from the earliest non-provisional filing date. Provisional patent applications are not part of the patent term calculation. Therefore, a priority date can be established with the filing of the provisional patent application but the

patent term will not start to run until after the non-provisional application is filed up to one year later. This allows up to a 21-year period from the provisional filing date to the end of the patent term. If a utility application is filed without first filing a provisional application, the 20-year term will expire up to one year earlier. Utilisation of provisional applications will necessarily delay the examination and grant of the patent application. However, as pharmaceutical products are subject to regulatory approval and are not being marketed at early periods of the patent process, this delay in examination and grant will not typically have any commercial effect and is outweighed by the later expiring patent term provided by the utilisation of provisional applications.

Another important distinction between US patent law and many other jurisdictions is the availability of a 12-month grace period under 35 US Code § 102 for prior public disclosures by the inventors (or by another party who obtained the disclosed subject matter from an inventor). This allows for the filing of a US patent application up to one year after inventor-related disclosures, including publication of the invention, public use of the invention or a sale or offer to sell the invention, without the public disclosure being available for citation against the patent application as prior art. This differs from many other jurisdictions, which have either (1) a six or 12-month grace period under specific circumstances as prescribed by each jurisdiction or (2) an absolute novelty bar that negates patentability even if the application was filed the next day after any public disclosure related to the inventor. Regardless of the 12-month grace period, patent applicants in the US that plan on filing patent applications outside the US must be conscious of public disclosures in order to preserve their foreign filing rights. At the very least, a US provisional patent application should be filed prior to any inventor-related public disclosures, as most industrialised countries recognise US filing dates in their own countries based on the Paris Convention for the Protection of Industrial Property (1883).

PRODUCT LIFE CYCLE MANAGEMENT STRATEGIES

The identification of a new molecular entity as a developmental candidate is the first step in the development and approval of a pharmaceutical product containing the same. Likewise, the filing of a patent application directed to the new molecular entity should be the first step in a series of newly filed patent applications, with staggered filing dates for each milestone during the developmental process.

It is undoubtably the case that during research and development of a pharmaceutical product, there will be challenges and obstacles that will need to be overcome. Many of the solutions will not be obvious to one of ordinary skill in the art and have the potential to become the subject of a new patent application.

Example fact patterns include the following.

- In-vivo testing demonstrates that a drug has affinity for a particular human receptor and is applicable to treat a disease state. However, the drug is insoluble and has poor or variable absorption, leading to low bioavailability and lack of efficacy. Identification of a new and unobvious polymorph or nano-sized version of the drug that leads to increased solubility and bioavailability is patentable subject matter.
- A drug exhibits a short half-life, is quickly excreted by the body and must be frequently dosed, leading to decreased patient compliance and poor therapeutic outcomes. Identification of a novel twice daily or once daily controlled release dosage form

that overcomes the limitations of the short half-life of the drug is patentable subject matter.

- An acid labile drug cannot be orally administered as it breaks down in the gastro-intestinal system. The identification of a novel and unobvious formulation that can effectively deliver the drug by an alternative route of administration (eg, transdermal or nasal) is patentable subject matter.
- A drug is shown to lack stability and breaks down after short term storage. The identification of a novel and unobvious formulation that includes an inactive excipient that stabilises the formulation (eg, as shown by accelerated storage conditions at high humidity and temperature) is patentable subject matter.
- In-vivo studies showing novel and unobvious pharmacokinetic parameters (eg, maximum plasma concentration (Cmax) or time to maximum plasma concentration (Tmax)) that provide a positive therapeutic plasma drug concentration over time is patentable subject matter.
- In-vivo studies demonstrating a novel and unobvious dose of a drug (eg, mg amount) or dosing regimen (eg, ascending or descending dose) providing an unexpected positive therapeutic outcome is patentable subject matter.
- Research and development showing that a drug initially exhibiting therapeutic use for one indication (eg, nausea) has therapeutic use for an additional indication (eg, antineoplastic) is patentable subject matter.

The series of multiple patent filings provides additional obstacles that a competitor must overcome in the development of an equivalent or similar product and increased value to the company for potential licensing, acquisition or other transaction. However, the greatest benefit of tiered patent filings (ie, a patent filed for each stage of development) is staggered patent term. Each new filing will provide the product with a new 20-year patent term for a longer exclusivity time.

This path must be very strategic as it is possible that the initial or prior filings will have published more than 12 months before the new filing and will have to be overcome as prior art so the new filing can issue as a patent. This is where presentation of the patentability story and how the applicant overcame previously described obstacles can have a great impact on the successful issuance of new patents providing valuable extended term. Data and working examples can be very valuable in establishing patentability (eg, by showing unexpected or surprising results). Thus, it is best practice to include this data in the application. However, under the rules of the USPTO, the data can sometimes be presented by way of an expert declaration, if the new data is based on the teachings of the disclosure present in the application.

When drafting a patent application, in addition to showing utility (ie, use), novelty and non-obviousness, care must be taken that the patent application presents the invention to meet the written description and enablement requirements as codified in 35 US Code § 112, as well as directed to patentable subject matter as codified in 35 US Code § 101.

The written description requirement requires that the patent application be sufficient to demonstrate that the inventor had possession of the invention being claimed at the time of the application was filed. This is most often tested when amendments are made to the claimed subject matter during the examination process. Amendments or new claims that

are made during prosecution that are not supported by the patent specification as originally filed will violate the written description requirement. Accordingly, the application when filed should include disclosures such as alternative embodiments of the invention, materials and components that can be interchanged in the invention and working numerical ranges and parameters that can be varied (eg, percentages of components in a mixture or processing temperature ranges).

The enablement requirement demands that the patent application teaches one of ordinary skill in the art of how to make and use the invention without undue experimentation. In the pharmaceutical arts, this typically takes the form of examples and data. The patent laws also require that broad patent applications must be enabled for the entire breadth of the claims and will typically require more enabling disclosure as compared to a narrower patent claim.

Patentable subject matter is another obstacle an applicant may face when applying for a patent. Patentable subject matter is continuously evolving based on new case law. This is particularly pertinent to natural products and diagnostics. In Alice Corp. v CLS Bank Int'l-, 573 US 208 (2014), the US Supreme Court set forth a two-part test to determine patent eligibility under 35 US Code § 101. Under the test, a patent claim is ineligible if (1) it is directed to a law of nature, natural phenomena or abstract idea and (2) lacks elements sufficient to transform the claim into a patent-eligible application. One example of a transformation of a natural phenomenon to a patent eligible application is a method of treating a disease with a pharmaceutical formulation containing a plant component (ie, a natural product). Although a patent claim to the plant component itself would violate the first step, a claim to the pharmaceutical formulation (ie, the natural product combined with additives) or a claim to a method of treatment would likely overcome the second prong of the test.

NON-PATENT EXCLUSIVITY

Separate and distinct from patent exclusivity is clinical exclusivity granted by the FDA upon approval of new drug applications that rely upon clinical studies. The effect of clinical exclusivity is certain non-patent time limited delays and prohibitions on the FDA approving competitive products. This non-patent exclusivity is granted by the FDA as an incentive to the development of pharmaceutical products that may otherwise not have patent protection (eg, due to patent expiration or statutory bars to patentability), although the FDA will grant clinical exclusivity even if there is patent protection for the approved product or approved method of treatment. The clinical exclusivity term starts to run from the approval date of the pharmaceutical product; therefore, when there is an existing in-force patent encompassing the drug product when the clinical exclusivity is granted, the two terms run concurrently. The clinical exclusivity is not tacked on to the end of the patent term.

Various non-patent exclusivities include New Chemical Entity Exclusivity (five years), New Clinical Investigation Exclusivity (three years), Orphan Drug Exclusivity (seven years) and Pediatric Exclusivity (six months added to existing patents or exclusivity).

Before discussing each exclusivity, it is important to understand various types of drug applications that are filed with the FDA.

- A new drug application (NDA) is an application submitted under section 505(b)(1) and approved under section 505(c) of the Federal Food, Drug and Cosmetic Act (the FD&C Act) that contains full report of safety and effectiveness.
-

An abbreviated drug application contains a reference to the clinical studies of the innovative product and takes the form of either an abbreviated new drug application (ANDA) or a 505(b)(2) application.

- An ANDA is an application submitted under section 505(j) of the FD&C Act for a drug product that is considered to be bioequivalent to a previously approved innovator product. The ANDA references the FDA's previous findings that the drug product is safe and effective without the ANDA filer having to provide clinical studies to prove the same. The ANDA needs to show that the submitted product has the same active agent, dose, route of administration, dosage form and conditions for use and is bioequivalent (showing similar blood concentration levels that produce the same effect as the comparator product).
- A 505(b)(2) application is an NDA submitted under section 505(b)(1) and approved under section 505(c) of the FD&C Act that contains full report of safety and effectiveness but references certain findings of a previously approved product. A 505(b)(2) application has the same active ingredient as the innovator product but typically differs by one or more of dosage form, dose or route of administration.
- New chemical entity (NCE) exclusivity is granted based on clinical studies conducted on a compound that was not previously the subject of FDA approval either alone or in combination. The five-year term runs concurrent with any existing patent exclusivity and expires five years starting from the date of approval of the drug product. During this time, the FDA will not accept the filing of an ANDA or 505(b)(2) application referencing the approved product, except that such abbreviated applications may be submitted after four years if they contain a certification of patent invalidity or non-infringement (see below).
- New clinical investigation exclusivity provides a three-year term that the FDA will not approve an ANDA or 505(b)(2) from the date of the exclusivity, for a drug product that contains an active moiety that has been previously approved, when the application contains reports of new clinical investigations (eg, directed to new formulations, new routes of administration or new therapeutic indications) that were essential to approval of the application. This type of exclusivity does not block the submission of the abbreviated applications.
- Orphan drug exclusivity is associated with rare diseases that effect fewer than 200,000 people in the US. The increased term is an additional incentive for the development of drugs for these rare disease states. It is a seven-year term that the FDA will not approve any application for the same drug for the same orphan disease, regardless of whether it is a full NDA or an abbreviated application. Orphan drug exclusivity does not bar the FDA from approving the same active agent for a different disease state than the orphan disease.

Paediatric exclusivity does not run from the approval date. Rather it adds term to existing patents and non-patent clinical exclusivity. The term is six months based on the submission of paediatric studies on the active agent in response to a request from the FDA.

Biologicals have a longer term based on the AIA. Upon approval of a biological product, the FDA will not grant the approval of a bioequivalent product for 12 years after approval.

PATENT TERM EXTENSION

Under 35 US Code § 156, there are circumstances when an unexpired patent may receive a patent term extension (PTE) based on regulatory delay of a pharmaceutical product that is the subject of the patent. PTE may only apply to a pharmaceutical product that has never been the subject of FDA approval in any other application. PTE is based on the following calculation:

- PTE = RRP – DD – ½ TP
- RRP is the portion of the regulatory review period that occurs after the issue date of the subject patent. The RRP includes a testing phase (TP) and an approval phase (AP) as defined below.
- DD is the time period during the RRP that the applicant did not act with due diligence.
- TP is the time period during the RRP between the effective filing date of an Investigational new drug application (IND) and the initial submission of a New Drug Application (NDA) (only one-half of this time is eligible for PTE).
- AP is the time period during the RRP between the initial submission of the NDA and the approval of the product.
- An application for PTE must be submitted within 60 days of the approval of the pharmaceutical product by the FDA. A maximum of a five-year term can be restored to a patent under this process, which is subject to the limitation that the total patent life cannot exceed 14 years from the approval date of the product.
- PTE can only be applied to one patent (although PTE applications can be filed for multiple patents and the applicant can then choose the patent that has the most favourable outcome).
- When a PTE application has been made but the patent will likely expire before a final determination is made, the applicant may request one or more extensions of the patent for periods up to one year.

ORANGE BOOK AND HATCH-WAXMAN TIMELINES

A critical strategic goal in portfolio development is the grant of one or more patents that can be listed in the publication Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the Orange Book). The Orange Book lists drug products that have been approved on the basis of safety and efficacy by the FDA and lists patents that cover the approved product or method. Composition of matter and method of treatment patents are eligible for listing in the Orange Book. Method of manufacturing patents are not eligible to be listed in the Orange Book.

When a competitor files an ANDA or 505(b)(2) application seeking approval of a generic product, a certification must be made against the patents listed in the Orange Book for the innovator product under 21 US Code § 355. The available certifications are as follows (referred to by the numbered paragraph in the statute):

- Paragraph 1 certification: there are no patents listed in the Orange Book.
- Paragraph 2 certification: the patents listed in the Orange Book are expired.
- Paragraph 3 certification: the generic applicant will wait to market its product until the Orange Book patents expire.
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Paragraph 4 certification: the Orange Book listed patents are invalid, unenforceable or will not be infringed by the manufacture, use or sale of the drug product for which the abbreviated application is submitted.

If a Paragraph IV certification is filed, the generic applicant is required to contact the NDA holder. After notification, the NDA holder has 45 days to initiate a patent infringement lawsuit against the generic applicant under 35 US Code § 271(e)(2)(A).

With initiation of the patent infringement suit, the FDA will initiate a 30-month stay provision. Under this provision, the FDA will not approve the abbreviated application for 30 months. The stay can be shortened by the court in the event that a court finds 'a failure of either the plaintiff or defendant to cooperate reasonably in expediting the action' or a court issues a final order ruling that the patent is invalid, non-infringed or unenforceable.

The 30-month stay is automatic and does not rely upon the NDA holder showing a likelihood of success on the merits. Therefore, obtaining Orange Book listable patents is an important strategy in delaying generic entry.

CONCLUSION

Life Science patent law entails many nuances that must be navigated to create a patent portfolio that enables an innovative company to recoup its investment in bringing new drugs to market and to allow further investment into their new product pipeline. With the proper strategy and implementation of a holistic approach, a valuable patent portfolio can be created to advance human health and wellness.

Robert J Paradiso RParadiso@lowenstein.com

2200 Pennsylvania Avenue, N.W., Washington, D.C. 20037, United States

Tel: +1 202 753 3800

https://www.lowenstein.com/

Building a robust trade secret strategy in China

Benjamin Bai, Miao (Mia) Qu and Jia (Jane) Wu
King & Wood Mallesons

Summary

INTRODUCTION

As one of the largest markets in the world, China offers significant opportunities for multinational life sciences companies, including access to the Chinese market, world-leading research facilities, institutional and private Chinese investors and partners with manufacturing, distribution and other supply chain expertise. Trade secrets can be worth tens or hundreds of millions of dollars. With today's interconnectedness in the biotechnology and pharmaceutical fields, more collaborations, joint ventures and outsourcing arrangements among firms and increased employee mobility, it is imperative that life sciences companies have robust policies and procedures for protecting trade secrets.

As far as China is concerned, life sciences companies have relied upon patents to protect their innovation. Trade secrets, however, are often the overlooked sibling. This is, in part, because trade secrets litigation in China had historically been less common than patents and more challenging for plaintiffs, with lower win rates. The difficulty was largely due to the heavy burden of proof placed on IP owners and the lack of a discovery or disclosure process in the Chinese legal system.

The 2019 amendment to China's Anti-Unfair Competition Law and a 2020 Supreme Court judicial interpretation have brought about positive changes. Of significance are the reversal of the burden of proof from IP owners to alleged infringers under certain circumstances and the availability of punitive damages up to five times for wilful infringement. Additional changes include lowering the threshold for criminal liability such that it becomes easier to prosecute trade secret crimes. Thus, Chinese courts are now increasingly inclined to provide meaningful redress for trade secret wrongs and render record-setting damages awards. A trade secret strategy refresh for China is therefore warranted and, more fittingly, the time to repair the roof is when the sun is shining.

TRADE SECRETS AND MISAPPROPRIATION DEFINED

China's Anti-Unfair Competition Law defines 'trade secret' as:

- technical, operational or other commercial information that is unknown to the public;
- that has commercial value; and
- for which the trade secret owner has taken measures to maintain its confidentiality.

Examples of trade secrets include technical drawings, production processes, design specifications, test results, toxicity information, dosing research, source code, marketing strategies and compiled lists of customers and suppliers. Misappropriation includes the following acts:

- acquiring trade secrets by theft, bribery, fraud, coercion, electronic intrusion or other illicit means;
- disclosing, using, or allowing others to use trade secrets acquired by the above means;
- disclosing, using, or allowing others to use trade secrets in breach of an agreement or a confidentiality obligation imposed by a legal owner;
-

encouraging, inducing, or helping others to violate confidentiality obligations or violate a rights holder's requirements to keep secrets, obtain, disclose, use or allow others to use the rights holder's secrets; and

- acquiring, using, disclosing or allowing others to use trade secrets when a third party knows or should have known that the trade secret has been misappropriated in any of the above ways.

Therefore, liability can attach to individuals or entities that are involved in the above five acts of misappropriation. In particular, third-party liability arises where a third-party acquires, uses, discloses or allows others to use trade secrets that they knew or should have known to have been misappropriated.

Acts of trade secret misappropriation can be criminal if such misappropriation causes an economic loss of at least 300,000 yuan. Criminal prosecution should always be considered as an enforcement option because Chinese police have the power to seize any relevant evidence, which can be used in subsequent civil litigation. It is an excellent discovery tool to aid civil litigation.

CHANGING JUDICIAL TIDES

Before 2020, it was uncommon to see multimillion dollar damages awards for trade secrets misappropriation. US$50,000 was considered as an average. Starting in 2020, however, courts have consistently applied an approach that is more favourable to trade secret owners, resulting in high damages awards.

On 24 November 2020, the Chinese Supreme Court handed down the first decision on punitive damages for intellectual property infringement. The case concerned misappropriation of trade secrets for manufacturing Carbomer products. The Court awarded quintuple punitive damages of 30 million yuan. A few months later, on 26 February 2021, the Court affirmed the award of 159 million yuan in compensatory damages to a vanillin maker, which was the largest trade secret damages award at the time. This, however, was quickly surpassed by a Supreme Court judgment on 27 December 2023, which affirmed a trade secret damages award of 201.54 million yuan in favour of Sennics Co, Ltd, whose trade secrets involved rubber additives technology. This now stands as the largest trade secret damages award in China.

Subsequent to the Sennics case, a combined patent and trade secret enforcement strategy ultimately led to a total recovery of 658 million yuan. The plaintiff in the case is Sichuan Golden-Elephant Sincerity Chemical Co Ltd, a foreign-invested entity. Golden-Elephant, a leading melamine producer, owns proprietary pressurised gas phase quenching melamine production technology. The lead offender, a Mr Yin, was a former chief engineer of Golden-Elephant. He resigned from Golden-Elephant in 2012 and took their trade secrets to a state-owned listed company, Shandong Hualu-Hengsheng Group Co, Ltd, Ningbo Chemical Research and Design Institute and Ningbo Houcheng Consulting Company. They worked together to design and build Hualu-Hengsheng's melamine production lines using the trade secrets. In March 2016, Golden-Elephant filed a trade secrets lawsuit against all the involved parties. To complement the trade secret enforcement, Golden-Elephant also filed a patent infringement suit. The first-instance damages award for the patent case was 80 million yuan and the first-instance damages award for the trade secret case was 50 million yuan. Notably, a temporary injunction was issued concurrent with the judgment in the trade secret case.

On appeal, the Supreme Court rendered simultaneous judgments in the two cases, which granted all the relief that Golden-Elephant sought. In addition to the first instance judgment of stopping the infringement, the Supreme Court also added the destruction and dismantling of the production equipment involved in the infringement in a verifiable manner in both cases. More importantly, the damages were increased to the amounts originally sought in the first instance. In the end, the two cases resulted in damages of 218 million yuan in favour of Golden-Elephant. Subsequently, Golden-Elephant launched a follow-on melamine-related trade secret lawsuit against the same defendants, demanding 600 million yuan in damages. A settlement amounting to 440 million yuan was reached in a couple of months. As a listed company, Hualu Hengsheng had to make public disclosure of the court judgment and settlement.

On 22 February 2024, the Supreme Court announced China's Top Ten Most Influential IP Cases for the past five years. The Golden-Elephant case tops the list as it demonstrates strong judicial protection of IP rights and stands for the equal treatment principle – all litigants are treated equally regardless of whether they are Chinese state-owned companies, Chinese private companies, foreign-invested companies or foreign companies.

PREVENTION IS THE BEST MEDICINE

Litigation is the last resort for trade secrets protection. Prevention should always be the first priority. Trade secrets protection strategies should aim to stop leaks happening and to maximise the chances of success in legal actions should misappropriation occur. One of the key elements for a protectable trade secret is that the trade secret owner has taken measures to keep the trade secret confidential; therefore, is important to establish and enforce a company-wide confidentiality policy. Establishing a confidentiality and trade secret policy and creating a corporate culture for trade secret protection is critical.

Industry best practices should be implemented in China. Utilising encryption, multi-factor authentication and intrusion detection systems can fortify digital walls and safeguard sensitive data. Regular security audits and vulnerability assessments aid in identifying potential weak points. Employment contracts, non-disclosure agreements and vendor agreements play a crucial role in explicitly spelling out rights, responsibilities and consequences related to trade secrets. Clear contractual provisions can mitigate disputes and facilitate enforcement. For China, implementation of a heightened trade secret policy is essential. For example, written acknowledgment must be obtained when an important trade secret or confidential information is passed onto a recipient. The following is considered the minimum necessary to protect trade secrets in China.

ESTABLISHING A CONFIDENTIALITY POLICY

The necessary steps of any effective confidentiality policy should include at least the following:

- identifying what information the company deems confidential and how its employees should handle such information;
- clearly spelling out the consequences of any unauthorised, improper use, or disclosure of confidential information; and
- clearly stating that improper use or disclosures can and will be grounds for employment termination or even criminal prosecution.

ENFORCING A CONFIDENTIALITY POLICY

The following are the recommended practices on how to enforce a company confidentiality policy and effectively protect the company's trade secrets:

- require all key personnel who have knowledge of trade secrets to sign confidentiality agreements;
- conduct regular training on the company's confidentiality policy to cultivate a culture of awareness and responsibility regarding trade secrets;
- verify that all employees have received a copy of the confidentiality policy in their employee handbook and have signed a statement acknowledging that they have read, understood and will comply with the policy as a condition of their employment;
- keep confidential information in restricted areas and in clearly marked binders or storage media. Items should be marked as 'confidential', 'do not disclose', 'do not copy' or other appropriate methods particular to the company's business;
- restrict access to confidential information and disclose it only on a need-to-know basis; adopt a physical locking system or electronic access control to confidential information, such as a check-in and check-out system; and use encryption or passwords on confidential information;
- impose confidentiality requirements on all visitors to the company's factories and premises;
- to the extent possible, require all employees to sign a written acknowledgement prior to receiving important company information. If not, a subsequent written acknowledgement must be obtained. For a consultant, subcontractor or any other third party, a written acknowledgement must be obtained in advance;
- conduct exit interviews of departing employees to ensure that they are not taking to their new jobs any information that the company would not want to disclose to a competitor. This also serves to remind all key employees that their obligation not to disclose trade secrets extends beyond their employment with the company. Departing employees must also provide written acknowledgment that they had access to certain confidential information and attach a list of such information. It is advisable to have departing employees return all electronic storage devices, such as USB drives, upon resignation. More importantly, image the hard disk of the computer of departing employees before such computer gets reassigned to other employees and save such files;
- terminate electronic access for departing employees immediately prior to termination. Alternatively, closely monitor electronic access in accordance with company computer policies because one of the most common avenues for loss of trade secrets is disclosure through electronic means. It is also advisable for the company to have computer policies in place that permit monitoring of electronic transmissions, such as regular imaging of an employee's computer, in a manner that would alert the company if confidential files are being transmitted outside the company without the company's consent. It should also trigger an alarm if an unusual amount of sensitives files are downloaded;
- to the extent possible, keep the key computers or servers bearing critical confidential information off the network;

- to the extent possible, limit unauthorised downloading or installation of software that is not work-related;
- to the extent possible, but without invading personal privacy and in compliance with data protection laws, monitor employee web surfing and email communication both in and out of the company computers;
- obtain reference and background checks on all managers, key employees and persons who will have regular access to critical confidential information;
- build and maintain good relationships with the local police and Chinese government agencies, such as the State Administration for Industry and Commerce; and
- use technology to protect trade secrets. Companies should use state-of-the-art data loss prevention and cloud access security broker tools to monitor and protect confidential data.

If all the above recommendations are followed, a trade secret owner should be able to minimise the risks of misappropriation and enhance the chance of enforcing its trade secret rights in China. Keep in mind that these are necessary to prove that the trade secret owner has taken adequate confidentiality measures to effectively pursue any type of enforcement action against misappropriation.

It should be noted that an overwhelming majority of trade secret misappropriation cases involves former employees taking trade secrets to new employers. Therefore, if an employee has departed and taken employment with a new employer, the first step for the company to take is to give immediate notice to the new employer of the employee's continued obligation to not disclose the company's trade secrets. This can be accomplished by sending a letter to the new employer indicating that the new employee has knowledge of the company's trade secrets. The letter should include an explanation of the legal basis for the employee's confidentiality obligation. If this is done, the trade secret owner may have a cause of action against the new employer should the employee disclose the trade secret to their new employer. The notice may prompt the new employer to take steps to ensure that its new employee will not disclose or use their former employers' trade secrets. The letter must be carefully drafted so that it would not become a basis for a claim of defamation or unfair competition.

BALANCED CHINA IP STRATEGY

Recent successful stories of trade secret enforcement in China are encouraging. Trade secrets constitute a critical component of the R&D fruits in the life sciences industry. Trade secrets protection complements patent protection for life sciences innovation. For example, a diagnostic device having a unique combination of biomarkers that is patent protected may only provide a meaningful diagnosis when paired with proprietary software. In addition, information captured by a diagnostic device could be kept confidential and used to further evaluate and fine-tune analytical methods. Hence, a combination of patent protection on unique arrays of biomarkers and trade secret protection over analytical software could provide comprehensive protection of IP assets. Therefore, the best strategy is to have a balanced approach to protecting trade secrets and patents in China. Life sciences companies should look to China's recent legislation and court decisions as a framework to build a robust China IP strategy that integrates both patents and trade secrets.

KING&WOOD MALLESONS

Benjamin Bai benjamin.bai@cn.kwm.com
Miao (Mia) Qu qumiao@cn.kwm.com
Jia (Jane) Wu wujia1@cn.kwm.com

18th Floor, East Tower, World Financial Center, 1 Dongsanhuan Zhonglu Chaoyang District
Beijing 100020, China

Tel: +86 10 5878 5588

http://www.kwm.com

Australia: a toolkit for prosecution and enforcement amid patentability barriers

Mark Wickham, Danielle Burns, Neil Ireland, David Longmuir, Annabella Newton and Jessica Chadbourne

Phillips Ormonde Fitzpatrick

Summary

LEGAL FRAMEWORK

Australia remains an in-demand jurisdiction for patent protection in the life sciences, with strong growth and opportunities in areas including pharmaceuticals, RNA therapeutics, gene editing, immune- and cell-based therapies and vaccines. The Australian patent system supports applicants and patentees with a legal framework closely harmonised with major jurisdictions, as standards for novelty, inventive step, support and enablement, for example, have increasingly tended to follow a European or UK law approach.

Support and enablement must be across the full breadth of the claims, with examiners and the courts closely scrutinising examples in the specification and considering the actual contribution to the art. One interesting consequence of this, which distinguishes Australian practice from other jurisdictions, is that claims to any medical uses of novel therapeutics are not automatically allowable. Medical use claims – even of novel therapeutics – are assessed against the standard one might expect for a second medical use claim, with evidence of target or pathway or in vitro or in vivo data for a disease or disease group typically required.

In another interesting departure from Europe, Australia's version of the 'added subject matter' rule states that amendments are not allowable if they would claim or disclose matter that extends beyond the specification as filed. That amendments made during prosecution were not allowable, however, is not a ground for revocation in Australia. Any validity attack on this ground needs to be launched during prosecution of the application, such as through ex parte third-party observations before acceptance or by launching an inter partes procedural (amendment) opposition prior to grant. Parties therefore need to maintain a close watch over applications of interest as they are amended during examination and be prepared to take early action if needed.

Additionally, unlike Europe, where an invention must be 'directly and unambiguously derivable' from a priority document and therefore a valid priority claim requires the same level of disclosure as an allowable amendment, a priority document need only provide an enabling disclosure of the invention, which is a different and arguably lower threshold to meet than that of allowability of amendments.

PATENTABLE SUBJECT MATTER AND PATENTABILITY ISSUES

There are a few express exclusions from patenting. The most significant is for human beings and the biological processes for their generation.

To be patentable, the claimed invention must be a 'manner of manufacture' – it must result in an artificially created state of affairs and the invention claimed must have economic utility. Judicial interpretation has recognised several categories of subject matter that fail to satisfy this test, including mere discoveries, ideas, scientific theories and laws of nature.

Subject Matter	Patentability
Naturally occurring	Isolated polypeptides (eg, antibodies, hormones), cells including stem cells, bacteria, fungi, viruses and chemical molecules, are patent eligible.
Nucleic acids	Isolated naturally occurring nucleic acid sequences, particularly DNA, RNA and cDNA are generally not patent

	eligible. However, codon - optimised genes, interfering RNA (RNAi), antisense oligonucleotides (in some circumstances) and transgenes where the naturally occurring gene sequences are operably connected to heterologous sequences such as a promoter vectors are.
Antibodies	For a new antibody to a known antigen, it is usually necessary to define the antibody by its six complementarity - determining regions (CDRs) unless it is experimentally shown that one or more of the CDRs do not interact with the target epitope or the antibody format allows epitope recognition with less than six CDRs. It is rare for claims that permit variation in the CDRs to be allowed, though this is possible if it can be shown that some variation can be tolerated and a functional criterion (affinity, specificity, therapeutic effect) is included to exclude inoperative variation. The specification will need to put the skilled person in a position to be able to predict with some certainty which of the CDR residues can be mutated while maintaining the technical effect.
Methods of medical treatment	Methods of medical treatment are patent eligible. Swiss - type or second - medical - use - type formats are also permitted. If using the EPC2000 format for second - medical - use claims, the 'for' will not be considered limiting with the claim construed as only requiring that the compound be suitable for the recited use. If novelty is derived from the use, the claim will need to be written as '[compound] when used for…', or, alternatively, 'Use of [compound] for…'.
Swiss - type claims provide additional protection being directed to a method or process of manufacturing a medicament using the compound recited and not to a product or to the use of the medicament for treating the disease recited in the claims. Advantageously, they can be enforced directly against the manufacturer of an infringing product.	
Courts have held that 'a reasoned hypothesis' detailed in an overview of a	

clinical trial study that is publicly available before the priority date can deprive a later patent application of novelty even if the 'reasoned hypothesis' has not yet been validated. This is particularly relevant for claims to new dosage regimes.	
Diagnostic methods	Diagnostic methods are patent eligible.
Software	Diagnostic methods, methods of medical treatment, medical devices that use software are patent eligible. However, it can be challenging to get claims to the software or software implemented by a generic computer. Patent specifications should be drafted carefully to emphasise technical features of the invention or technical outcomes resulting from the invention. Thought must be given to the 'actors' (eg, servers, processors) within a claim and where they are located to avoid divided infringement.
Artificial intelligence (AI)	AI is increasingly being used to identify new targets, validate candidate drug compounds, predict drug properties, for de novo drug design, candidate drug prioritisation and generating synthesis pathways. Diagnostic methods, methods of medical treatment, therapeutic compounds made with the help of AI or that incorporate AI are patent eligible. Inventions made with the help of AI will likely meet the present inventive step requirements. But as artificial intelligence becomes part of the normal toolkit for the person skilled in the art, the bar for inventiveness will likely increase.

STRATEGIES FOR ENFORCEMENT (INCLUDING WHETHER INJUNCTIONS ARE NECESSARY OR EASILY AVAILABLE)

Patent infringement proceedings are generally commenced by a patentee or exclusive licensee in the Federal Court of Australia and conducted before a single judge with experience in patent matters. Infringement proceedings are often accompanied by a cross-claim for revocation and it is usual for issues of liability or validity to be bifurcated from issues of quantum.

The parties can appeal a first instance decision to the Full Court of the Federal Court.

Typically, proceedings begin with an exchange of pleadings and determination of any application for a preliminary injunction (PI) following which there will be discovery, exchange

of evidence (generally through independent experts), necessary pretrial steps and a final hearing. The time from commencement to trial is typically 18–24 months and further 6–12 months for judgment.

While PIs are available, it is uncommon for them to be sought or granted outside of pharmaceutical litigation.

To obtain a PI, the patentee must establish that there is a serious question to be tried on infringement, that damages will not be an inadequate remedy and that the balance of convenience favours the grant of the injunction. The Court retains a broad discretion and delay on the part of the patentee can be significant. A patentee must act quickly after becoming aware of the potentially infringing conduct or threat thereof to be granted a PI, a patentee must also give the 'usual undertaking as to damages', an undertaking to pay compensation to any person (whether a party or not) affected by the undertaking if it is ultimately overturned.

Historically, PIs were routinely granted to originators in pharmaceutical cases where the mandatory price reduction resulting from the first generic listing of a pharmaceutical substance on Australia's Pharmaceutical Benefits Scheme has been considered a factor weighing strongly in favour of granting an injunction preventing a generic entry. More recently, the Court has taken a different approach, and recent cases indicate the balance has shifted away from the granting of an injunction. This shift follows the realisation of the difficulty in calculating damages suffered by a generic restrained by a PI granted in a respect of a patent found invalid. Ultimately, it is easier for an originator to prove its loss from a generic entry.

A further development relevant to the granting of a PI in pharmaceutical cases has been the Commonwealth of Australia's pursuit of compensation under the 'usual undertaking as to damages'. The Commonwealth has made several claims on the undertaking for loss suffered as a result of delayed generic entry. While a number of these claims have settled, the Commonwealth's A$325 million claim against Sanofi in respect of the drug clopidogrel will be heard by the High Court in 2024 following the Full Federal Court's rejection of its claim on the basis that it has not been proven that the generic (Apotex) would have launched at risk.

While originators no doubt face increased hurdles and risks to obtaining PIs, they are still available to patentee in appropriate cases. A patentee can now rely simply on the mandatory price reduction and must give considerations to the calculation of compensation, the strength of its prima facie case on infringement and, importantly, invalidity and the potential effect on third parties such as the Commonwealth.

STRATEGIES FOR EXTENDING PROTECTION

A patent that claims a pharmaceutical substance (or a process using recombinant DNA technology to produce the pharmaceutical substance) contained in a drug that is either registered or will be registered on the Australian Register of Therapeutic Goods (ARTG) may be eligible for an extension of term of up to five years. Medical use claims, such as methods of treatment, cannot be extended.

'Pharmaceutical substance' includes not only novel active agents but also includes new formulations and combinations of active agents.

Patent term extension (PTE) is calculated by reference to the date of the patent that substantially claims and discloses the pharmaceutical substance and the first regulatory approval date of the pharmaceutical substance on the ARTG. In other words, the regulatory approval of the pharmaceutical substance that is the subject of the PTE must mark the first time that the pharmaceutical substance has been approved for marketing and use in Australia.

When a patent covers two pharmaceutical substances, a PTE application must be based on the pharmaceutical substance having the earliest regulatory approval date. So, where a patent application covers two or more potentially registerable products (eg, a single active product and combination product), applicants should strongly consider filing divisional applications to quarantine these substances. In that way, an earlier registration in respect of one product will not preclude a PTE for the later registered product.

Regulatory approval is often sought later in Australia, resulting in trailing PTE protection in a global context.

Protection	PTE
Legislation	Patent Act (sections 70–79, 79A and schedule 1).
Guidance	Patent Manual of Practice and Procedure (section 7.12).
Covered	Pharmaceutical substances.
Term	Up to five years.
How to calculate the term	PTE = ([date of first regulatory approval] – [date of filing of corresponding patent]) – five years.
Paediatric/orphan extension	No.
Eligible patent for drug products	Patent must in substance disclose and claim a pharmaceutical substance per se, or a pharmaceutical substance when produced by recombinant DNA technology.
Goods containing or consisting of the substance must be included in the ARTG.	
Scope of protection	Entire claim scope, applies to any pharmaceutical substance claimed but limited to the therapeutic use.
Assertable under linkage regulations	Yes.
Authority to grant	IP Australia.
Deadline for filing application	Six months or later of the first inclusion of goods containing the substance in the ARTG or patent grant date.
Protection by patent in force requirement	Yes, patent must be in force on the date the PTE application is filed.

First authorisation requirement for drug products	PTE application must be based on the first regulatory approval (human) for goods containing or consisting of the pharmaceutical substance.
Active agent	Pharmaceutical substance per se is not limited to the active agent and includes a compound, an active metabolite, a composition or a mixture of substances for therapeutic use whose application involves either a chemical or physicochemical interaction, with a human physiological system, or action on an infectious agent, or on a toxin or other poison, in a human body, but does not include a substance that is solely for use within in vitro diagnosis or in vitro testing (the Act, Sch 1).
Number of patents extendible based on one approval	Multiple patents can be extended based on the same regulatory approval date.
Number of extensions	One (can cover multiple products; shorter term awarded).
Third - party filing	Yes, the patentee does not need to be the holder of ARTG registration.
Consideration of third - party observations during pendency of application review	No indication yet that IP Australia will consider any such observations.
Declaration of invalidity of application	Determined by patent office (re - examination or opposition) or on application to the federal court.
Infringement proceedings	The patentee and exclusive licensee have the right to start infringement proceedings (section 120) unless the PTE is granted after expiry of the patent, in which case only the patentee has standing to sue for infringement that occurred during the PTE period (section 79). This could be an issue where party that suffers loss is an exclusive licensee.

NON-PATENT EXCLUSIVITIES

Australia also provides an automatic five-year data exclusivity period for therapeutic goods containing a new active component, where no other therapeutic goods consisting of or containing that active component were included in the ARTG (first registration or export listing).

An 'active component' is defined as a substance that is, or substances that together are, primarily responsible for the biological or other effect identifying the goods as therapeutic goods.

GENERICS TO MARKET

Section 26B of the Therapeutic Goods Act requires a generic applicant to certify to the Therapeutic Goods Administration (TGA) that it is either:

- not infringing a valid patent; or
- proposes to market a product before the expiry of a patent and has given the patentee notice of its application.

In practice, generic applicants do not notify originators of their anticipated market entry. Originators become aware of market authorisation of a generic competitor only on the inclusion of the generic in the register.

Notification after entry of generics on the register leaves little time for originators to consider whether its patents are infringed and, consequently, to prepare for infringement litigation.

However, given the difficulties now faced by originators in obtaining PIs, consideration should be given to pre-emptive revocation actions to clear the way. We also suggest placing a watch on the register to identify any generic entrants as soon as possible to start infringement proceedings and obtain final judgement prior to the generic's launch, avoiding the need for interlocutory relief.

Relevantly, following consultation in 2019–2020, the TGA proposed a patent notification scheme for a first generic to address originator concerns. The scheme was intended to provide greater opportunity for early negotiation and resolution of patent disputes before first generic entry. While keenly anticipated by originators, as at December 2023, the change had not been progressed and, disappointingly, now appears in doubt.

Mark Wickham Mark.wickham@pof.com.au
Danielle Burns danielle.burns@pof.com.au
Neil Ireland Neil.ireland@pof.com.au
David Longmuir david.longmuir@pof.com.au
Annabella Newton annabella.newton@pof.com.au
Jessica Chadbourne Jessica.chadbourne@pof.com.au

Level 16, 333 Collins Street, Melbourne VIC 3000, Australia

Tel: +61 3 9614 1944

https://www.pof.com.au/

Brazil: Navigating patenting challenges in the pharmaceutical landscape

Gustavo de Freitas Morais, Pedro Moreira and Rodrigo Augusto Oliveira Rocci

Dannemann Siemsen Advogados

Summary

This article attempts to provide a summarised guide on intellectual property protection in Brazil for pharmaceuticals, particularly patents of invention, shedding light on the complexities and challenges faced by stakeholders in the Brazilian pharmaceutical landscape.

LEGAL AND REGULATORY FRAMEWORK

The dynamics of the Brazilian pharmaceutical market are directly related to the health regulatory landscape, the patent system and the means of access to healthcare. Drugs are known for providing innovative solutions to improve efficacy in the treatment of many diseases. To ensure that increasingly effective therapies continue to be developed and that inventors of innovative pharmaceuticals can be rewarded for the large investments in R&D, it is essential that such inventions be protected by a reliable patent system. Pharmaceuticals are governed by a comprehensive and complex regime of legislation and regulations spanning many different areas of law. The legislative and regulatory landscapes are also very active, as patent laws are constantly under review and government authorities constantly update regulatory processes and policies.

Intellectual property (IP) rights are considered to be fundamental rights and entrenched clauses in the Constitution of Brazil, whereby the authors of industrial inventions are guaranteed temporary privilege for their use, as well as protection for industrial creations, taking into account the social interest and the technological and economic development of the country (article 5 (XXIX) of the Brazilian Constitution of 1988).

The Brazilian patent system is ruled by the Brazilian Patent and Trademark Office (BRPTO), which was created by Law 5,648/1970. The BRPTO is the only autarchy legally entitled to receive, examine and grant IP rights, an authority established by Brazilian IP Law 9,279/1996, currently in force.

Brazil is a strategic market for many local and foreign pharmaceutical companies due to its demographics and protective legislation regarding access to healthcare. In the past decade, the Brazilian market has witnessed the expiration of patents for many relevant drugs and the entry of competitors. Also, due to recent and significant changes in patent laws, some companies are facing a scenario of uncertainty regarding the patent term of relevant products, which may raise concerns for both patent holders and new competitors.

The protection of rights relating to IP is effected by means of the grant of patents of invention, utility model patents and industrial design registrations (article 2 (I and II) of the IP Law). The following chart summarises the corresponding patentability requirements and scope and terms of protection (articles 8, 9, 40, 42 and 108 of the IP Law):

	Patents	Utility models	Designs
Patentability requirements	Novelty Inventive activity Industrial application	Novelty Inventive act Industrial application	Novelty Originality Being a type of industrial manufacture
Scope of protection	To prevent third parties from manufacturing, using, offering for sale, selling or importing for such purposes, without authorisation, the patented or registered subject matter.		

Terms of protection	20 years counted from the filing date	15 years counted from the filing date	10 years counted from the filing date; renewable for three successive periods of five years each

PATENT TERM ADJUSTMENT, PATENT TERM EXTENSION AND SUPPLEMENTARY PROTECTION CERTIFICATES

The IP Law does not provide for patent term extension, patent term adjustment (PTA) or a supplementary protection certificate. Until 2021, article 40 of the IP Law provided a 20-year term from the filing date or a 10-year term from the granting date, whichever is the longest. In 2021, the Supreme Court declared the sole paragraph of said article that provided for the 10-year term as unconstitutional. The main interpretation for the declaration of unconstitutionality was the alleged lack of definition of the final term of a patent in Brazil, which was allegedly uncertain until it was granted.

Regarding the pharmaceutical sector, the Supreme Court decision – issued during the covid-19 pandemic – stated that commercial leverage provided by patents for very long periods has an impact on the population's access to public health services, since it would burden the system by eliminating competition and imposing the acquisition of pharmaceutical items at a price unilaterally stipulated by the patent holder. Due to this perception, a different treatment has been established for the effects of the decision on pharmaceutical patents, which is clearly against the Trade-Related Aspects of Intellectual Property Rights Agreement. Non-pharmaceutical patents granted with a 10-year term until the decision are to be considered valid until the original term. In the case of pharmaceutical patents, the terms were automatically changed to 20 years from the date of filing and, as a result, many patent holders lost a significant amount of time in the patent exclusivity period, regardless of whether the delay in analysing the patent was attributable to the patent holder or the BRPTO. Here, it is important to remember the huge backlog of examination faced by the BRPTO in the past, due to its enormous delay on examination.

Consequently, many patent holders initiated legal actions against the BRPTO seeking recognition of the administrative delay and the returning of the period of exclusivity unduly taken from the patent holders to the extent of the delay caused by the BRPTO. Up to this moment, an estimation of 57 actions – usually addressed as 'PTA actions' – has been lodged so far and is currently under the analysis of the judiciary.

SKINNY LABEL

On 11 December 2023, the Brazilian Health Regulatory Agency (ANVISA) issued new rules to authorise skinny labelling in Brazil, which came into force on 6 February 2024. ANVISA's previous rules established that labels of generic medicines should have all and the same therapeutic indications and uses of the reference-listed medicine, with no exceptions permitted, being in line with Law 9,787/1999 that created the generic drugs system in Brazil. This law establishes that a generic medicine must 'have the same . . . therapeutic indication as its reference drug'. Once ANVISA's new rules entered into force, skinny labeling should be authorised in Brazil, meaning that pharmaceutical companies should be able to market their generic medicines with labels with one or several – but not necessarily all – of the therapeutic uses of the corresponding reference medicine when there is a Brazilian patent or patent application covering the excluded uses.

The new rules establish that (1) ANVISA's approval is not necessary for the carving out a therapeutic use from the generic medicine's labels; (2) any skinny label under the new rule must contain a note informing that patented therapeutic uses have been carved out; and (3) once the patent expires or if the application is rejected, the carved-out use must be included in the label. The new rules, besides encouraging off-label use, could be used by infringers to undermine the enforceability of medical use patents. Pharmaceutical companies could argue that their generic medicines would not infringe a medical use patent because they have carved out from the label the patented therapeutic use.

Before the new rules, generic companies could not use this argument to avoid infringement of a medical use patent as they had to include all therapeutic uses of the reference medicine (including the patented therapeutic use). However, it is most apparent that skinny labeling alone is insufficient to avoid infringement of a medical use patent. Based on constitutional principles, such as good faith, a pharmaceutical company (1) has the burden of proving that they only marketed the generic medicine for non-patented uses; and (2) must take solid actions to discourage off-label use for the patented therapeutic indication or use. Without these actions, exploiting a generic medicine with an excluded label infringes a medical use patent.

As a further option to secure exclusivity, a patentee can challenge a skinny label before the courts, grounded on the argument that ANVISA's new rules authorising skinny labeling are illegal. This is because (1) Law 9,787/1999, which created the generic drugs system in Brazil, establishes that a generic medicine must 'have the same therapeutic indication as its reference drug' and (2) the Brazilian Constitution states that a governmental entity – such as ANVISA – is entitled to issue internal rules provided that they comply with the federal laws.

STRATEGIES FOR PROTECTION OR PRE-ENFORCEMENT

PATENTABILITY ISSUES

Among other matters, the following are not considered to be inventions or utility models or not patentable (articles 10 (I, VIII and IX) and 18 (III and Sole Paragraph) of the IP Law):

- discoveries, scientific theories;
- operating or surgical techniques and therapeutic or diagnostic methods, for use on the human or animal body;
- natural living beings, in whole or in part, and biological material, including the genome or germ plasm of any natural living being, when found in nature or isolated therefrom, and natural biological processes; and
- living beings, in whole or in part, except transgenic micro-organisms complying with the patentability requirements of novelty, inventive activity and industrial application, and which are not mere discoveries.

Moreover, the claim languages disclosed below are usually objected by the BRPTO, although their official regulations foresee interpretations and possibilities to attempt acceptance thereof (BRPTO's Resolutions 124/2013, 169/2016, 208/2017 and 118/2020):

- Markush formulae;
- selection matters (selection patents);

- new medical uses;
- dosage regimen;
- polymorphs;
- product-by-process claims;
- omnibus claims;
- salts, N-oxides, esters and ethers;
- prodrugs;
- stereoisomers;
- solvates, clathrates and co-crystals;
- product defined by the results to be achieved;
- product-for-use claims; and
- sequence identity percentage and homology.

The following exemplified embodiments usually find no bar in the IP Law:

- compounds;
- compositions or formulations;
- kits;
- processes of manufacture;
- 'Swiss-type' uses; and
- equipment and devices.

BACKLOG OF EXAMINATION

The initiative implemented by the BRPTO from 2019 to 2022 to address the backlog of examination yielded favourable outcomes and it is still reducing it. The average time from effective filing to grant in Brazil has decreased from about 10 years (2018) to approximately five years (2023). In this regard, the BRPTO offers possibilities to expedite examination of patent applications (BRPTO's Normative Instruction 02/2020 and Ordinances 78/2022 and 79/2022) as, for instance, the Patent Prosecution Highway – PPH and inventions related to cancer, AIDS and neglected and rare diseases, 'green' technologies and subject matter reproduced by third parties without authorisation, among others, which are quite effective; it takes about five to seven months to have a first official action issued. The following could be applied to pharmaceutical inventions:

- patent applications covering a subject matter considered patentable and allowed or granted by a partner Patent Office – Patent Prosecution Highway (PPH) – and patent application having at least one claim considered patentable in the International Preliminary Report on Patentability (IPRP) by the partner Patent Office acting as the PCT international Authority (PPH-PCT) in Austria, Canada, China, Denmark, Finland, France, Europe, Japan, Portugal, Singapore, South Korea, Spain, Sweden, the UK, the US and PROSUL (Chile, Colombia, Dominican Republic, El Salvador, Ecuador, Nicaragua, Panama, Paraguay, Peru and Uruguay);
-

patent applications covering a therapy to the following diseases: cancer, AIDS and neglected and rare diseases;

- patent applications to be used in public health emergency of national or international importance according to Law 7,616/2011 and the WHO;
- patent applications covering a technology available in the Brazilian market;
- patent applications covering subject matter reproduced by third parties without authorisation;
- patent applications covering an invention derived from activities funded by the government and applications filed by governmental-supported entities;
- patent applications claiming a Brazilian priority;
- patent applications containing subject matter of interest to drug policies of the Ministry of Health and the Sistema Único de Saúde; and
- patent applications containing a subject matter of interest to national emergency or public interest.

CHECKING LOCAL PORTFOLIO INCLUDING SUBSEQUENT INNOVATION PATENTS

Subsequent innovation patents (SIPs – sometimes also referred to as secondary patents) are important for a comprehensive strategy of IP protection. Brazilian courts accept SIPs for enforcement purposes and they tend to be respected locally.

PRE-EMPTIVE MEASURES

Once a generic drug obtains regulatory approval, and there exists third-party ownership of a patent that restricts the drug's manufacture and sale, the exclusivity rights of this third party become vulnerable. Even before a publicised infringement takes place, this third party has the legal right to take pre-emptive judicial action to safeguard their IP rights through what is known as an inhibitory lawsuit.

REQUESTING INFORMATION FROM AUTHORITIES

Considering that article 5 (XXXIII, XXXV) of the Constitution establishes that all people are entitled to receive information concerning their private, collective or general interest from government bodies, except for that information whose secrecy is essential to the security of society and of the state and that the law shall not exclude any injury or threat to a right from review by the judiciary, respectively, and article 42 of the IP Law states that the patent confers on its proprietor the right to prevent third parties from manufacturing, using, offering for sale, selling or importing for such purposes without their consent a product that is the subject of a patent, the patentee is allowed to request authorities to provide information to support full protection of patent rights.

Information related to possible (1) M&A applications submitted by third parties to ANVISA and (2) possible importation of patented products is very important for patentees to assess potential threats to patent rights and to take actions seeking to prevent patent infringement.

Until 2019, ANVISA disclosed information about M&A application submitted by pharmaceutical companies, including the name of the active pharmaceutical ingredients (API) related to the relevant application. However, after some questions raised by part of the pharmaceutical sector – mainly arguing that the disclosure of such information could result

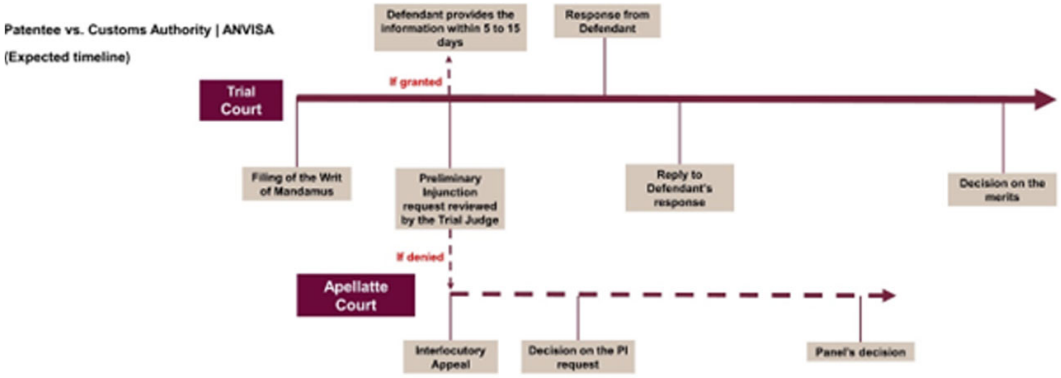
in unfair competition actions by third parties against the applicants – ANVISA refrained from disclosing ex officio any information that could connect M&A applications to API names.

Although it seems that ANVISA does not have a firm position that information relating M&A applications to their API names could not be disclosed – ANVISA submitted a formal consultation to the Brazilian Competition Authority in 2023 questioning it on whether disclosing such information could or not allow unfair competition, which is still pending analysis – requests for information concerning the matter tend to be denied by ANVISA.

The Customs Authority also considers that information regarding importation is confidential – protected by the tax secrecy established by article 198 of the National Tax Code – and therefore could not be provided to third parties, including the patentee, even in the case of importation of patented products by third parties. Similarly to ANVISA, the Customs Authority tends to deny requests for information concerning the matter.

In both cases, the patentee is allowed to file writ of mandamus before the federal courts seeking to compel ANVISA and the Customs Authority to provide the requested information. For reference, the following timeline reflects the expected course of the referred writ of mandamus at the first judicial instance before the federal courts:

Writ of Mandamus



Even though there is no consolidated position of the federal courts about the matter, most decisions rendered – mainly by the Federal Court of Brasília – granted a patentee's claims in order to compel the authorities to provide them with the requested information.

DJ VALIDITY ACTION

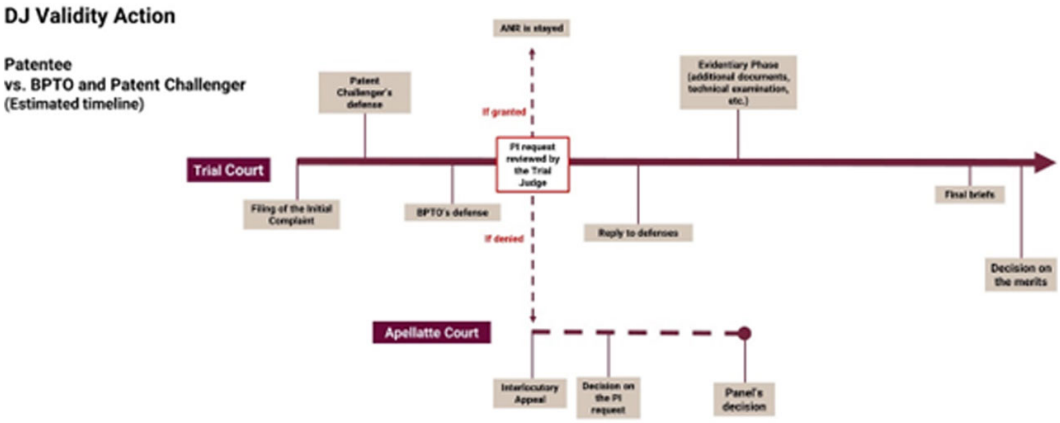
Pursuant to article 51 of the IP Law, administrative nullity request (ANR) may be filed by any interested party or ex officio by the BRPTO within six months from the date of a patent's granting. Furthermore, a patent may be challenged during its term before the federal courts by means of an invalidity action, which has erga omnes effects, or before the state court, as an argument of defence in a patent infringement action, which has inter partes effects.

Whenever an allegation of patent invalidity is raised, the patentee is allowed by the aforementioned article 5 (XXXV) of the Constitution to file a declaratory judgment validity action requesting a federal court to deny such invalidity allegation.

Considering that Brazil applies the principle of unicity of jurisdiction, according to which (1) court decisions prevail over administrative decisions and (2) only court decisions become res judicata, declaratory judgment validity action should be considered by the patentee as an important measure to obtain a definitive decision dismissing invalidity allegations through a

court proceeding that allows the performance of a technical examination by an independent court-appointed expert.

For reference, the following timeline reflects the expected course at the first judicial instance of the referred writ of mandamus before the federal courts.



The most common venues for declaratory judgment validity actions are the Federal Courts of Brasília (the legal domicile of the BRPTO) and Rio de Janeiro, where the main headquarters of the BRPTO are physically located.

STRATEGIES FOR ENFORCEMENT

Brazil is a civil law country with no jury trial for patent litigations and has an effective legal system to guarantee IP protection and enforcement, mainly because of a highly effective preliminary injunction (PI) system. Requests for PI in Brazil are typically processed approximately 7–15 days after submission.

The IP Law foresees literal or direct patent infringement, infringement under the doctrine of equivalents and contributory infringement. Said law also establishes that the patentee is entitled to recover damages due to any unauthorised exploitation that occurred while the application was pending. The Brazilian judiciary's independence empowers judges to take swift action to prevent patent violations, including granting an ex parte restraining order to immediately stop the patent infringement. The Brazilian legal system not only safeguards the right of individuals to pursue legal action when they have suffered actual harm but also extends this protection to situations where there is a threat of harm, as stipulated in Federal Constitution (article 5, item XXXV).

In Brazil, there are no discovery proceedings and specific procedure for claim construction. Patent rights are fully enforceable in Brazil. Measures aimed at preventing or ceasing infringements of pending patent applications and granted patents are available through both extrajudicial means and the judicial system.

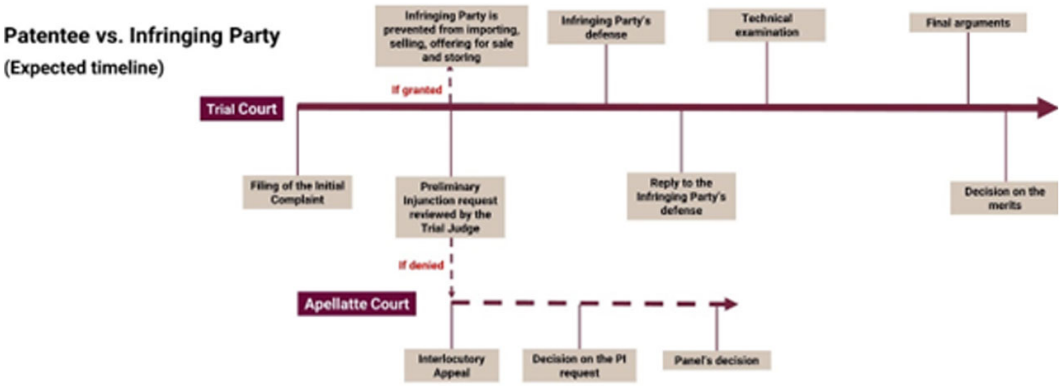
In possession of pieces of evidence that indicate that a competitor is taking concrete measures to launch a product in the Brazilian market while a related patent is in force – such as confirmation of the importation of an API or finished product in an amount that goes beyond the necessary to support the preparation of an M&A application dossier or in the case an M&A is granted by ANVISA – the patentee is allowed to file an inhibitory action with PI request before a state court, requesting an urgent court order to prevent the competitor from launching the infringing product in the market.

If patent infringement has already occurred, the patentee may request (1) the infringing party to be compelled to recall infringing products from the market and (2) compensation for damages caused by patent infringement, which should be calculated by the most favourable to the patentee of the following criteria:

- the benefits that would have been gained by the patentee if infringement had not occurred;
- the benefits gained by the infringing party; or
- the remuneration that the infringing patent would have paid to the patentee for a granted licence.

For reference, the following timeline reflects the expected course of the inhibitory or infringement action at the first judicial instance before the state courts.

Infringement / Inhibitory Action



Patent inhibitory or inhibitory actions must be filed before the state court where the infringing party is located or where patent infringement takes place. The most common venues are the state courts of São Paulo and Rio de Janeiro, which have specialised IP courts at the trial and the appellate levels.

The statute of limitations for filing an action seeking to collect damages is five years as of the occurrence of patent infringement (article 225 of the IP Law).

CONCLUSION

Navigating the Brazilian pharmaceutical landscape requires a comprehensive understanding of the legal framework governing intellectual property protection. Stakeholders in this complex ecosystem, from drug manufacturers to patent holders, must be fully aware of the legal prohibitions, patent litigation and the current discussions on PTA. This comprehensive analysis aims to equip those operating within the Brazilian pharmaceutical market with an enhanced understanding of the legal processes and intellectual property considerations that shape the industry. This understanding contributes to the delivery of safe and innovative pharmaceutical products to the Brazilian population, fostering public health and pharmaceutical innovation in the region.

DANNEMANN SIEMSEN

Gustavo de Freitas Morais gustavo@dannemann.com.br
Pedro Moreira pmoreira@dannemann.com.br
Rodrigo Augusto Oliveira Rocci rrocci@dannemann.com.br

https://www.dannemann.com.br

Mexico: regulatory certainty for biosimilars on the horizon

Alejandro Luna F and **Ingrid Ortiz**
OLIVARES

Summary

REGULATORY SCENARIO

The first time that biologics were officially recognised in the applicable legislation, the General Health Law, was in June 2009, with the inclusion of article 222-bis defining a 'biologic/biotechnological product' as any substance that has been manufactured by molecular biotechnology; has therapeutic, preventive or rehabilitative effects; is provided in a dosage form; and is identified as such by its pharmacological activity and physical, chemical and biological properties.

In October 2011, the Health Law Regulations were amended to establish the requirement to approve biologics and biocomparables (also known as biosimilars) – an area that was previously poorly regulated.

In 2012, a Mexican Official Standard Rule (NOM) was enacted to provide further clarity and certainty on the related regulatory process: Mexican Official Emergency Standard Rule NOM-EM-001-SSA1-2012.

After several amendments and other versions of the NOM, the main legislation for this type of product, besides the General Health Law and its regulations, is currently NOM-257-SSA1-2014 concerning biologics (NOM 257), which was published by the Federal Commission for Protection against Sanitary Risk (COFEPRIS) in the Official Gazette. NOM 257 essentially outlines key points to ensure that the safety, efficacy and quality of biologics are already regulated in other NOMs, such as those concerning clinical trials and pharmacovigilance.

Prior to the entry into force of the amendments to the General Health Law that gave recognition to biotechnological drugs, and during the subsequent period in which the legal framework was not yet defined or completed for the regulation of those medicines, COFEPRIS granted some marketing authorisations for non-innovative biotechnological medicines that were not properly classified as biosimilars according to the relevant criteria to guarantee their quality, safety and efficacy when compared to the reference medicine requirements and international health standards. Hence, non-innovative biotechnological drugs that were processed or granted prior to the formation of the corresponding legal framework and pending classification as biosimilars were known colloquially as biolimbos.

Owing to the above, one of the main objectives of NOM 257 was that all the non-innovative biotechnological drugs identified as biolimbos would be submitted to a new review process that would prove that those drugs have the required quality, safety and efficacy characteristics.

However, this regularisation procedure was not duly observed, so today there are some biocomparables that have never met the quality, safety and efficacy requirements established by current health legislation, in the terms indicated by NOM 257, and that consequently fail to comply with the new specifications for biocomparability studies and tests and the pharmacovigilance processes necessary to protect and guarantee the health of patients.

On 31 May 2021, the Ministry of Health issued a decree in the Official Gazette amending several articles of the Health Law Regulations. Among other things, the most relevant points of this decree for biologics were the following:

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regarding the approval of biocomparable medicines, the participation of the Subcommittee for the Evaluation of Biotechnological Products was eliminated and an opinion of the New Molecules Committee is now sufficient; and

- clinical studies in the country of origin of biocomparable medicines can be submitted as evidence for the marketing authorisation application. When applying for a renewal of the marketing authorisation, clinical studies in Mexico must be submitted.

In general, these amendments to the Health Law Regulation are focused on improving the analysis and resolution of various processes.

The Health Law Regulations define 'biocomparables' as products that must be comparable to reference products regarding safety, quality and efficacy. Innovative biological products are considered as the reference products for the approval of non-innovative products.

The Health Law Regulations and NOM 257 provide that an approved biocomparable may be a reference product for another follow-on if there is no longer an approved innovative product.

COFEPRIS divides marketing authorisation applications for biocomparables in accordance with the manufacturing of the product (national manufacturing or foreign manufacturing). Legally speaking, the review process and timeline for approval is the same for national manufacturing and foreign manufacturing.

COFEPRIS makes this classification to identify the requirements that applicants must meet. For example, for foreign manufacturing, applicants must submit official documents, such as good manufacturing practice certificates, which must be apostilled or legalised and translated into Spanish by an authorised translator.

In general terms, the standard dossier submission requirements for marketing authorisation applications for all medicines usually comprise: legal and administrative information; summaries; chemical, pharmaceutical and biological information; non-clinical reports; and trial reports.

The additional dossier requirements for biological products include describing the manufacturing process, providing information concerning the starting and biological origin materials and describing the manufacturing facilities and equipment.

The essential dossier submission requirements for biocomparables are almost the same as those for innovative biological products, except for additional requirements to prove safety, efficacy and quality comparable to the reference biological product.

To prove safety, efficacy and quality, biocomparable applicants must submit:

- in vitro studies or comparative non-clinical studies;
- comparative pharmacokinetic test reports, if requested by the Ministry of Health, to show pharmacokinetic comparability on key parameters between both the biocomparable and the reference biological product;
- pharmacodynamics test reports; and
- comparative efficacy and safety clinical tests to show comparability between both the biocomparable and the reference biological product.

Once approved, close pharmacovigilance should be followed.

The average time to obtain approval is one to three years; however, this depends on each case.

In this context, the legal framework applicable in Mexico for biological medicines provides the basic requirements and allows certain directionality to the sanitary authority to act based on a case-by-case regulatory scheme of criteria, tests and requirements applicable to a given biosimilar product, which are determined by the specific molecule with which comparability is intended.

In addition to the above, the case-by-case scheme indicates that once a biosimilar has demonstrated its biosimilarity, the indications that the reference biological medicine has approved will be authorised as long as the biosimilar medicine is presented in the same pharmaceutical form and dose as the reference biologic and these indications share the same mechanism of action or the biosimilar drug has the same pharmacodynamic effect. In other words, extrapolation of clinical data to other indications of the reference product could be acceptable but must be scientifically justified.

If it is unclear whether the safety and efficacy confirmed in one indication would be relevant for another indication or whether additional data will be required. Extrapolation should involve inclusion of the totality of the data (ie, the quality of non-clinical and clinical data). It is expected that safety and efficacy can be extrapolated when biocomparable biotechnological product comparability has been demonstrated by thorough physico-chemical and structural analyses as well as by in vitro functional tests complemented with clinical data in one therapeutic indication.

This procedure is carried out between the applicant and the health authority so that the owner of the innovative drug does not have the recognised right or legal standing to assert before the authority technical and scientific elements of safety and efficacy related to the biologic medicine.

The lack of transparency in the process of evaluation and the granting of marketing authorisations for biosimilars by the health authorities means that it is unclear whether the authorities are observing the correct fulfilment of the applicable regulatory requirements and mechanisms and, consequently, whether they are observing the industrial property rights related to those products.

REGULATORY CERTAINTY FOR BIOSIMILARS IN MEXICO

This year, the Ministry of Health issued a document that proposes a 'Regulatory Certainty Strategy for the Pharmaceutical Sector: Biosimilars'.

This Strategy is mainly intended to promote the development of biocomparable biotechnological medicines, establishing an institutional and regulatory framework that is aligned with international standards, with the aim of promoting the industry's capacity in all phases of research and production of these products, in Mexico.

The installation of a Biocidal Products Regulation Committee is proposed – its main tasks would include developing recommendations for regulatory adjustments, and changing management activities and support and evaluation mechanisms to ensure the integration of biosimilar biotechnological medicines in the system.

COFEPRIS will establish the Specialized Unit in Biosimilars (UEBio), which will focus on eliminating the current fragmentation of processes and will promote an enriching interaction between specialists in the field and manufacturers in Mexico.

Also, a collegiate body of experts will be established, which will give recommendations that consider aspects of product development. This committee will evaluate all the evidence presented by a biosimilar to determine if it is comparable to the corresponding reference medicine. The opinion of CODEBio will be considered when obtaining health registration of a biosimilar.

The agenda of regulatory harmonisation and certification of national capacities raised in the Regulatory Certainty Strategy for the Pharmaceutical Sector 2023–2030 has been resumed, to raise national regulation to the standards of the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S), as well as the adoption of WHO guidelines, among other memberships in the field.

Following up on the adoption of the ICH standards, COFEPRIS plans to adopt safety practices through the issuance of Mexican standards, replacing the issuance of Mexican standards after the publication of the Quality Infrastructure Law. This was implemented in the first quarter of 2024 by the Standards Subcommittee, which will create the National Advisory Committee for Standardization of Health Regulation and Promotion.

One of the main commitments of the Strategy emphasises the comprehensive updating of the regulatory framework for the conduct and recognition of bioequivalence and biocomparability studies, focusing on:

- adoption of WHO guidelines on the matter;
- clarification of criteria in biocomparability tests, with clinical, non-clinical and quality aspects;
- allowing biosimilar medicines to be compared with biotechnological medicines that come from abroad;
- eliminating the mandatory requirement to conduct studies in the Mexican population and adopting the development of robust risk management plans; and
- improving the recognition mechanisms of biocomparability studies carried out in countries with health authorities recognised by the WHO as a regional reference, with standards similar or superior to those in Mexico, seeking harmonisation, homologation and mutual recognition.

The aim is to define a regulatory framework for risk analysis applicable to biosimilar biotechnological medicines, through a guide that will be developed.

A regulatory update is sought for good manufacturing practices (GMP) and promotion of recognition of GMPs issued by Mexico through the establishment of GMPs for the manufacture of biopharmaceuticals. This entails a modification to NOM-059-SSA1-2015, including new criteria issued by PIC/S and ICH in terms of quality (first semester of 2026), with a reasonable time of entry into force to allow in-depth adaptability within the sector.

Regulatory support is also required, through technical sessions and goodwill verification visits at manufacturing sites for raw materials and finished products (first quarter of 2024).

The scope of this support will be implemented from the review of manufacturing site plans, prior to construction, through to on-site visits throughout construction and equipment.

The Strategy provides for comprehensive restructuring of the Committee on New Molecules, reactivation of the Subcommittee for the Evaluation of Biotechnological Products, homologating it with the operating criteria of CODEBio and establishing criteria that link technical opinions issued by the Subcommittee for making decisions in the product evaluation process. There is also a commitment to standardise criteria for the evaluation of finished products with a training plan aimed at the UEBio.

There is a plan to intensify pharmacovigilance work with general criteria and case-by-case evaluation methodologies, which includes regulatory support for the development and updating of risk management plans for biosimilars.

In addition, there is a proposal to implement a continuous training plan for distributors and points of sale in good storage and distribution practices, including the enactment of new criteria for dispensing medicines in hospitals and pharmacies.

Finally, the participation of the Ministry of Economy and the National Council of Humanities, Sciences and Technologies (Conahcyt) is proposed to create a Council for National Pharmaceutical Development that encourages investment in scientific projects and the inclusion of courses in universities or research institutes focused on the development of biotechnology for pharmaceutical purposes.

Concerning the IP field, among the proposals, the Strategy points out the need to clarify the scope of the 'Bolar Clause'. This patent exception allows unauthorised parties (ie, pharmaceutical companies) to use patented matter (ie, pilot production and tests to be performed) to eventually obtain a marketing approval for a specific (follow-on) health-related product. Currently, the Health Law Regulations provide that such use can be conducted only within eight years before the expiration date of the patent; the clarification proposed in the document is focused on eliminating this time frame and allowing the use of patented matter under such exception at any time during the lifetime of the patent. It is worth mentioning that any exception to the rule should have limits and it should be well established; therefore, if such time frame is eliminated and eventually the applicable provisions lack clarity, it may result in abusive practices.

The document that contains the strategy also mentions that the linkage system should be reviewed. Also, a legal framework for clinical data protection should be created. To achieve such objectives, COFEPRIS proposes to specify the limits and applicability of each legal instrument, implement more effective mechanisms to appeal and request clarification for the interested companies.

In this regard, it seems that the proposal is purposeful and is intended to consider the provisions and standards indicated by international treaties. In this sense, we must be attentive to the urgent need to promulgate a Regulation to the Federal Law on the Protection of Industrial Property, as well as the modification of health legislation.

The 'Regulatory Certainty Strategy for the Pharmaceutical Sector: Biosimilars', in fact, includes relevant topics related to industrial property rights and innovation that apparently aim to observe the international standards indicated in international treaties; however, it is necessary to consider that it has a diverse approach that is far from promoting and protecting innovation.

Nevertheless, Mexico is holding elections in 2024 and the strategy proposed by the current administration may be impacted by the plans of the new one. Thus, while this document provides an idea of what the trends are regarding the regulatory field for biologics and biosimilars in Mexico, so far it does not provide any certainty.

In brief, the hurdles in the Mexican system do not look so different from those faced in other jurisdictions; the challenges that are faced by innovators to enforce and defend their exclusive rights depend on the level of development of the regulatory framework in connection with the approval processes and policies by the authorities and the criteria by the courts and the administrative authorities in charge of analysing patent cases, as well challenges of uncertainty that are faced by the biosimilar industry.

Alejandro Luna F alejandro.luna@olivares.mx
Ingrid Ortiz ingrid.munoz@olivares.mx

Pedro Luis Ogazon 17, Col San Angel, Mexico City 01000, Mexico

Tel: +52 55 5322 3000

http://www.olivares.com.mx

South Africa: Winning strategies to keep pace with evolving pharma sector

Chyreene Truluck and **Tyron Grant**

Spoor & Fisher

Summary

LEGAL FRAMEWORK

The South African pharmaceutical industry has evolved into a robust sector, witnessing notable growth in recent years. While the industry has traditionally been focussed on formulation and packaging products for the domestic market, in the wake of the covid-19 pandemic, there has been increased interest in active pharmaceutical ingredient production and export, particularly to other African countries.

In the healthcare landscape, the public sector plays a pivotal role in pharmaceutical distribution, while the private sector dominates revenue generation, supported to a large extent by private medical aid schemes. The government's primary focus in the sector is to expand healthcare access, particularly in rural areas, and promote the use of generic medications and safe traditional medicines.

Noteworthy was South Africa's joint proposal with India presented to the World Trade Organization's (WTO) Trade-Related Aspects of Intellectual Property Rights (TRIPS) Council on 16 October 2020, advocating for a patent waiver to facilitate equitable access to covid-19 products. The proposal shone a spotlight on the gap between developing and developed countries regarding access to medicines.

South African patent legislation, with its origins in British law, has undergone significant divergence as legal principles have developed and evolved. The current legal framework is embodied in the Patents Act 57 of 1978 (the Patents Act) and the regulations thereto. Judicial decisions, extensively documented in the South African Law Reports, contribute significantly to shaping patent law in the country.

PATENTABILITY ISSUES

One of the most important features of the South African patent system is that there is no substantive examination of patent applications on their merits. The South African Patent Office merely examines patent applications for conformity with formal requirements and, once these are met, a patent is granted.

The other side of this equation is that the Patents Act provides that if, in infringement proceedings, a single claim is held to be invalid, even where other claims are found to be valid and infringed, then no relief can be obtained on the valid and infringed claims until the invalid claim has been amended or deleted. Thus, the patent is unenforceable until such time as the invalidity is cured by amendment. Any application for amendment after grant to amend or delete the invalid claims may only be narrowing in scope and can be opposed, which can obviously further delay the obtaining of relief for infringement. Thus, the onus is on the patentee to ensure that its patent is granted in a valid form to have the best chance of succeeding in an infringement action.

The Patents Act grants exclusive rights to patent holders to control the use, sale or disposal of their inventions within South Africa. However, a common challenge faced by pharmaceutical and medical device products is determining their eligibility for patent protection. In accordance with international standards, novelty and inventiveness of an invention are crucial considerations for patentability, with an absolute novelty requirement and well-established principles for determining non-obviousness.

Section 25(2) of the Patents Act outlines exclusions from patentability, such as methods of treatment and diagnostic methods. However, the Patents Act also provides that second and

subsequent medical uses of a known product may be regarded as patentable subject matter, provided the requirements of novelty and inventiveness are met.

In terms of decided South African case law, a claim directed to a first medical use should be drafted in the 'for use-type' claim format, similar to the EPC 2000 claim format, and a claim directed to a second medical use should be drafted in the 'Swiss-type' claim format.

New dosage regimes and inventions targeting selected patient populations may also qualify as patentable subject matter, provided they satisfy the requisite patentability criteria.

There is no decided case law on acceptable formats for claiming biologics and antibodies. However, given the commonality between South African law and British law, the South African courts tend to follow the guidance of the European courts and particularly the British courts. Thus, it is likely that South African courts will require antibody claims to include at least the six complementarity-determining regions (CDRs) or the variable fragment heavy chain (VH) and variable fragment light chain (VL) domains.

STRATEGIES FOR ENFORCEMENT (INCLUDING WHETHER INJUNCTIONS ARE NECESSARY OR EASILY AVAILABLE)

As mentioned above, if in any litigation a claim is found to be valid and infringed but another claim is found to be invalid, then no relief can be obtained on the valid and infringed claim until the invalid claim has been amended or deleted. For this reason, most applicants for pharmaceutical patents in South Africa adopt a strategy whereby they keep their patent application pending, by filing one or more requests for an extension of the acceptance deadline, until prosecution of corresponding patent applications in examining jurisdictions has progressed sufficiently for them to determine a valid claim scope. At that time, they amend the claims of their South African patent application to conform them to a valid scope and allow it to proceed to grant. In this way, the patentee has a reasonable assurance that the patent claims are valid, so that they can enforce their rights.

Unauthorised infringement of a pharmaceutical patent encompasses the actions of making, using, exercising, disposing (eg, selling), offering to dispose (eg, advertising) or importing the patented product.

Patent infringement proceedings may be brought by the patentee or, in some instances, by a licensee operating under a licence of right, where the patentee has refused to institute proceedings after being called upon by the licensee to do so.

A successful plaintiff in infringement proceedings may obtain an interdict (injunction), delivery up of patented goods, damages or a reasonable royalty instead of damages and they may recover legal costs.

Patent infringement proceedings are usually instituted by way of an action procedure, which is commenced by issuing a combined summons, together with a particulars of claim setting out the cause of action. The defendant has an opportunity to defend the action by delivering a plea to the particulars of claim, and a counterclaim, if any. The plaintiff is then provided with an opportunity to reply to the defendant's plea and to plea to the counterclaim. Thereafter, the defendant may offer a final reply to the plea. This is followed by discovery and expert summary evidence, and any other interlocutory proceedings, whereafter a trial date is requested and allocated.

Invalidity of the patent is available as a defence in an infringement action and is instituted by way of counterclaim for revocation.

Applying for marketing authorisation does not constitute patent infringement per se. However, in specific cases, when coupled with other factors, such application may raise concerns about potential infringement upon product launch following authorisation. In such cases, an interim interdict (injunction) may be sought, pending final resolution by the court. For the applicant for an interdict to be successful, it must be demonstrated that there is urgency and a well-founded apprehension of irreparable harm if interim relief is not granted pending final resolution.

STRATEGIES FOR EXTENDING PROTECTION

South African law lacks provisions or mechanisms for extending the term of a patent. Indeed, there is no linkage between the South African patent and regulatory laws. In fact, section 69A of the Patents Act, provides for a Bolar provision, which specifically exempts non-commercial scale activities reasonably related to obtaining and submitting regulatory information required under law from patent infringement. However, this section also stipulates that it is not permissible to stockpile products for sale in anticipation of patent expiration.

NON-PATENT EXCLUSIVITIES (EG, BIOLOGICS EXCLUSIVITY OR REGULATORY DATA EXCLUSIVITY)

South African legislation does not incorporate data exclusivity measures for pharmaceuticals or medical devices as is the case in Europe, the United States and elsewhere. Instead, the regulatory framework emphasises early market access and includes provisions aimed at facilitating the affordability of medicines. Beyond the above-mentioned section 69A of the Patents Act, the Medicines and Related Substances Act No. 101 of 1965 outlines a mechanism allowing for potential parallel importation of medicines registered in South Africa by entities other than the registration certificate holder under specific conditions. Such importation is exempt from patent infringement.

Further, parallel importation has been the subject of a South African-decided case, where it was held that 'where a patentee himself sells or disposes of the patented article, that article is freed from all restraints which the patentee's monopoly had imposed on it and where the patented article is disposed of by the patentee's assignee or his agent, acting within the scope of his authority, it is similarly freed from such restraints.'

LAUNCH-TO-MARKET STRATEGIES – HOW TO ENSURE A CLEAR PATH TO MARKET

Launching a product in the South African market requires a keen understanding of the intellectual property framework and regulatory framework. Ensuring a successful product launch may involve the key strategies outlined below.

Where patent protection is concerned, obtaining enforceable rights in South Africa, while relatively cheap and fast, requires an understanding of the complexities of the patent lifecycle all the way from filing to infringement proceedings, due to the non-examining nature of South African law. An understanding of appropriate claim format for a valid patent is important, especially where the onus is on the patentee to ensure that the patent is in a valid form.

As mentioned, delaying acceptance of a South African patent application until such time as there is an indication of valid rights in an examining jurisdiction is one such strategy for ensuring that the patent will pass muster.

Another strategy may include the filing of one or more divisional applications. It is possible to obtain a granted patent with a claim set that is known to be valid but is narrow in scope and to pursue a divisional application with a claim set of wider scope in the hope that this claim set will also be found to be valid.

If the patentee desires early grant of a patent, possibly with a view to instituting infringement proceedings or to deter competitors, it is also possible to request expedited acceptance of a patent application. If the request for expedited acceptance is made within the first 12 months (for PCT National Phase) or 18 months (for any other application, including a divisional application) of filing, the request must be accompanied by a search report or opinion of the international searching authority or an examining patent office, showing that the office has considered the subject matter of at least one claim of an equivalent application to be both novel and inventive, or an affidavit by the applicant, providing the reasons that expedited acceptance is required for the specific patent application.

Conducting a freedom-to-operate (FTO) analysis is important to understand whether there is potential risk of infringing existing patents. Conducting an FTO in South Africa can be a challenge, as the online records of the South African patent office only include patent numbers and titles. Thus, conducting equivalent searches for known relevant patents is one strategy for ensuring freedom to operate in South Africa. The South African patent system provides for revocation proceedings for invalidating a patent.

Finally, regulatory compliance is a cornerstone of bringing a pharmaceutical product to market. Necessary approvals may be obtained from the regulatory authority, the South African Health Products Regulatory Authority (SAHPRA). The period of marketing authorisation for approved pharmaceuticals varies depending on the product and its characteristics. The initial period of validity is ordinarily five years, but this can be shorter or longer depending on the specific product and its intended use.

Marketing authorisation can be renewed for a further period of five years if the product continues to meet the necessary requirements for safety, efficacy and quality. On the other hand, the SAHPRA can revoke a marketing authorisation on the grounds that the product is unsafe, ineffective or of poor quality, that the holder of the authorisation failed to comply with the conditions of the authorisation or that the holder failed to place the product on the market within a certain time frame.

For biologic medicinal products, there are specific obligations that must be fulfilled in South Africa for granting a marketing authorisation. Specific guidelines and requirements have been put in place to ensure that biologic medicinal products are safe, effective and of high quality. It is also worth noting that authorisation for biologic medicinal products may be more complex and take longer than for other pharmaceutical products due to their nature and the need for extensive data on their safety and efficacy.

GENERICS TO MARKET

As previously mentioned, section 69A of the Patents Act provides an exemption from patent infringement for non-commercial scale activities reasonably related to obtaining and submitting regulatory information required under law. This exemption applies equally to

generic products and it is permissible for a generic manufacturer to obtain registration of generic equivalents of patented products in South Africa, prior to the expiration of the relevant patent provided such generics are not allowed to be stockpiled for commercial sale prior to the expiration of the South African patent.

South African patent law also makes provision for a declaration as to non-infringement should an applicant wish the courts to adjudicate on the question of whether or not there is or will be patent infringement. However, this is not a requirement for generic market entry or for obtaining marketing authorisation. In fact, the medicines registration authority (SAHPRA) does not take patent protection into account at all. Furthermore, the applicant for the registration of a generic equivalent product can rely on data that is of public record in support of the application.

The SAHPRA has previously announced its intention to harmonise some of its policies and procedures with those of the European Medicines Agency and has endorsed and adopted the European Medicines Agency guidelines for quality and bioequivalence requirements. In accordance with these guidelines, the SAHPRA has adopted reliance-based evaluation procedures and evaluation may follow one of the following pathways: full review, abridged review, verified review or recognition. Thus, approval of a generic version of a previously approved drug would likely be subject to an abridged review or a verified review.

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Chyreene Truluck c.truluck@spoor.com
Tyron Grant t.grant@spoor.com

13 Highgrove Office Park, Oak Avenue Centurion, Pretoria 0157, South Africa

Tel: 27 126 761 111

http://www.spoor.com