The Life Sciences Lawyer

Issue 1 2020

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Patents are not the way to fix drug pricing issues

Bob Stoll of Drinker Biddle & Reath LLP explains why drug pricing bills may not be the answer to public concern over pharmaceutical costs

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Editor's welcome

Welcome to the first issue of our new publication, *The Life Sciences Lawyer*. The field of life sciences is a fast-moving and heavily regulated sector. It covers a wide range of subject areas, some of them highly controversial, and many of which will prove to be of critical importance to the human race as a whole, no less, as we move into what can feel like a strange and uncertain future. The possibilities and opportunities offered by, to give but a few examples, CRISPR gene editing, genetically-modified crops, personalized medicine, and therapeutic CBD, are far-reaching, but so too are the ethical debates that these topics provoke. It's no surprise, then, that the life sciences continue to present jurisdictions across the globe with uniquely complex legal and regulatory challenges.

Almost any discussion of life sciences in a legal context involves a consideration of intellectual property. To that end, *The Life Sciences Lawyer* is written and advised by a panel of international life science and intellectual property experts and guest writers, who will ensure that we provide up-to-date information on the most important international developments.

For this, our inaugural issue, the topic at the forefront of our minds is pharmaceuticals. Bob Stoll of Drinker Biddle tells us why patents are not the way to fix drug pricing issues. MacKenna Roberts GC asks whether the door is opening or closing on market abuse litigation for the pharmaceutical industry. And James Kinnaird and Tim Headley of Marks & Clerk Singapore look at the impact of Singapore's patent linkage scheme on generic drug approval.

Elsewhere, we have an update on CBD regulation in Europe, plant patent protection in Mexico, and the protection of inventions in India.

All this and much, much more can be found in this debut issue of *The Life Sciences Lawyer*. We sincerely hope you enjoy our first issue and look forward to receiving your feedback.

Matt Seex
Editor

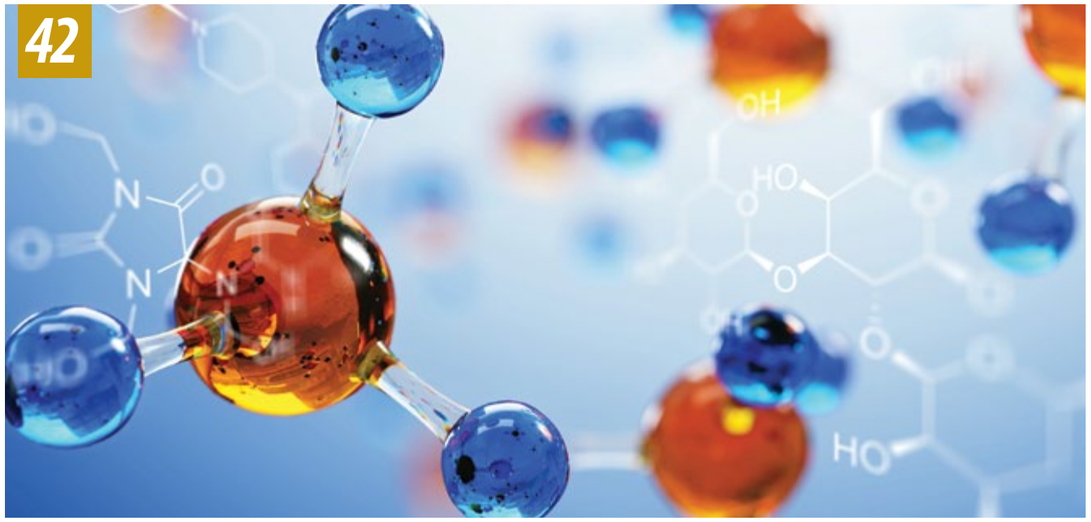
For information on our sister publications please visit www.patentlawyermagazine.com and www.trademarklawyermagazine.com

Mission statement

The *Life Sciences Lawyer* educates and informs professionals working in the industry by disseminating and expanding knowledge globally. It features articles written by people at the top of their fields of expertise, which contain not just the facts but analysis and opinion. Important judgments are examined in case studies and topical issues are reviewed in longer feature articles.

Contents

Issue 1 2020



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MacKenna is a life sciences litigation and regulatory lawyer who has worked in private practice, academia and in-house as General Counsel and DPO to Choice Telemed Ltd. MacKenna is an experienced strategic adviser assisting clients in the commercialization of medical innovation at the frontiers of medicine, specializing in cell and gene therapies/tissue engineering, genetic testing and digital health technologies.

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The Life Sciences Lawyer Magazine is advised by a distinguished panel of international patent experts. Members of our editorial board are detailed on this page.

The Life Sciences Lawyer Magazine wishes to take this opportunity to thank the editorial board for their time and support.

News

Ocasio-Cortez and Sanders challenge HIV drug patent extension

REPRESENTATIVE ALEXANDRIA OCASIO-CORTEZ and Senator Bernie Sanders have written an open letter to the US Patent and Trademark Office (USPTO) accusing US pharmaceutical giant Gilead Sciences Inc of "corporate misconduct" over its actions relating to the development of its anti-HIV drug "Descovy".

The pair are demanding that the USPTO reject Gilead's request for a patent extension for the drug. They allege that Gilead intentionally delayed developing the medication in order to maximize profit generated by its predecessor, Truvada (which was also made by Gilead, and which, it has been alleged, caused damage to patients' teeth, bones and kidneys) despite knowing that Truvada's successor "was likely to be safer". Sanders and Ocasio-Cortez contend that Gilead had been aware for years that Descovy would carry fewer health risks, but "failed to fulfil its legal obligation to disclose its true reason for halting the development of [Truvada] … to the USPTO" because it told the USPTO only that it ceased Truvada development only because it was "unlikely to be differentiated from existing drugs".

The letter continues, "If Gilead's monopoly is allowed to continue, it will reap a profit while Americans suffer needlessly. Gilead's behavior was deceitful and amoral. Corporate misconduct must not be rewarded by the U.S government through extending a government-granted monopoly on this medicine that is likely worth tens of billions of dollars".

The matter now lies with the USPTO and, by extension, the Trump Administration itself.

Shanks triumphs against Unilever

IN A DECISION that has surprised many, given earlier decisions to the contrary by the Patent Office, the High Court and the Court of Appeal, Professor Ian Shanks has won his case in the Supreme Court against his former employer, Unilever.

Whilst working for a Unilever subsidiary in the 1980s, Professor Shanks invented technology – the electrochemical capillary fill device (ECFD) – for measuring glucose levels in blood samples. However, having been told that Unilever owned his invention, the company patented it and made millions from licensing it around the world. Professor Shanks did not receive any payment or compensation beyond his usual salary.

After a thirteen-year legal battle for compensation, Professor Shanks has finally achieved victory in the Supreme Court, winning a £2 million payout.

Bethan Hopewell, Partner at IP law firm Powell Gilbert, comments:

"The decision had been eagerly anticipated, as few cases of this type ever make it to trial (most are settled before they come to judgment) and fewer still are appealed all the way to the country's highest court.

Upending expectations, the Supreme Court … [found] that Professor Shanks was entitled to £2 million in additional compensation from his former employer, Unilever, over and above his regular earnings when he was previously employed by their research and development arm. The normal rule under UK law is that where an employee is employed to invent as part of their job description, any inventions that arise during their employment will be the property of their employer. However, where an invention has been of 'outstanding benefit' to their employer, the inventor is entitled to apply for additional compensation, with the legislation setting out the rules and procedures for establishing when such additional compensation is owed.

Although exactly how much money Professor Shank's inventions generated was hotly disputed by the parties, it was common ground that they produced a large profit for Unilever, with the Court of Appeal upholding the first instance judge's valuation of £24 million. The main issue which the Supreme Court had to decide was whether such a sum could truly be called 'outstanding', when compared to the immense annual revenue and profits of a multinational corporation like Unilever. Although the legislation provides that due regard should be paid to the size and nature of the employer when deciding whether a benefit is 'outstanding', this is not a deciding factor but just one aspect to be taken into account, alongside others. The crux of this appeal therefore went to how much relative weight it should be afforded, when the overall picture is mixed.

While it is too early to say what effect this surprising decision will have on the wider field of employee inventor compensation, the success of what many observers regarded as a hopeless case raises the prospect that many more cases will now be brought by disgruntled inventors seeking additional compensation."

California stops pharmaceutical "pay-for-delay"

CALIFORNIA HAS INTRODUCED a pioneering new law designed to stop large pharmaceutical companies settling claims of patent infringement by generic drug manufacturers by paying those manufacturers to delay launching their products – the so-called "pay-for-delay" practice.

California hopes that Bill AB 824 will, in effect, block pharmaceutical companies from keeping cheaper generic medicines off the market. In doing so, it is hoped that prescription drug costs will be significantly lowered. According to the Federal Trade Commission, "pay-for-delay" deals cost consumers and taxpayers $3.5 billion in higher drug costs every year. The bill prohibits such agreements between branded and generic drug manufacturers by making them anticompetitive by presumption.

According to California Governor Gavin Newsom, "California will use our market power and our moral power to take on big drug companies and prevent them from keeping affordable generic drugs out of the hands of people who need them. Competition in the pharmaceutical industry helps lower prices for Californians who rely on life-saving treatments".

With plans for similar legislation underway at a federal level, it is expected that this first step by California will mark the beginning of a new battle between the powerful pharmaceutical industry and legislators seeking to reduce the cost of medicines for all US citizens.

Organizations demand African pharmaceutical patent reform

A COLLECTIVE OF more than ninety organizations has called for urgent reform of the Harare Protocol of the African Regional Intellectual Property Organization (ARIPO) in order to ensure that people across Africa have access to affordable medicines. The organizations are demanding that Ministers representing ARIPO Member States — change how they grant medicinal patents, in order to promote cheaper, generic competition.

ARIPO is a regional mechanism that administers the filing, examination, and grant of pharmaceutical patents for 18 African countries that have signed up to the Harare Protocol. The Protocol sets out the rules for the administration of patents, utility models and industrial designs.

"To combat growing epidemics such as drug-resistant tuberculosis, diabetes and cancer — where a single drug can cost hundreds or thousands of dollars to treat just one person — ARIPO's rules for granting patents, laid out in the 'Harare Protocol', must be changed in order to facilitate access to more affordable generics, rather than granting undeserving patent monopolies to multinational pharmaceutical companies," said Lotti Rutter from Health GAP, a global HIV advocacy organisation, "ARIPO Member States have some of the highest burdens of disease in the world.

The price of medicines in these countries determines whether the government will be able to provide treatment for these diseases to its people or not. When medicines are unaffordable, people pay with their lives".

According, to the group, ARIPO has, to date, failed to utilize many of the key public health safeguards allowed under international law and championed by national and regional bodies throughout Africa.

Instead, the organizations claim that ARIPO continues to grant unworthy pharmaceutical patents, making certain medicines unaffordable to patients and governments.

Says Allan Maleche of the Kenya Legal and Ethical Issues Network on HIV and AIDS (KELIN):

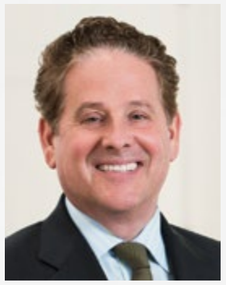
"Now is the time for urgent action. This is not just about legal technicalities — ARIPO's decisions affect the lives of many people living across the region.

In particular, we call on Ministers and Heads of Patent Offices attending the ARIPO Governing Body meetings in Liberia to ensure that ARIPO establishes a credible and transparent 'TRIPS Flexibilities Working Group' to discuss and develop proposals to implement public health safeguards in the Harare Protocol, including those recommended by civil society.

Patents are not the only way to fix drug pricing issues

Bob Stoll of Drinker Biddle & Reath LLP explains why drug pricing bills may not be the answer to public concern over pharmaceutical costs.

There is broad consensus in the patent community that the patent system could be markedly improved by both legislative fixes and the enactment of rules to better protect innovation in the biotech and pharmaceutical industries. However, very little in the way of patent legislation is expected any time soon. While we have had important decisions in *Athena Diagnostic Inc v Mayo Collaborative Services* focused on claims relating to diagnostic methods, we are far from certainty on the larger question of patent subject matter eligibility. The denial for a rehearing *en banc* of the Athena case at the Court of Appeals for the Federal Circuit this summer resulted in eight separate opinions, all of which sought clarity on subject matter eligibility, but collectively, added confusion to the applicability of the subject matter eligibility test and distress to those who must operate without clear guidelines. Even with a clarion call for action by the judges for a usable standard, we are unlikely to see a legislative remedy soon. The clamber in the patent community to obtain legislative relief from the overly-broad application by lower courts of patent subject matter ineligibility tests emanating from the Supreme Court will not easily overcome the lack of consensus on any proposed language for a legislative solution. The lack of agreement is sure to doom any Congressional action on patent eligibility this term.



Bob Stoll

Affordability should not prevent Americans from getting life-saving medicines.

It is possible that we may see legislation that would cure the "constitutionality problem" with Patent Trial and Appeal Board (PTAB) judges. The recent *Anthrex Inc. v. Smith & Nephew* case upended the Inter Partes Review process, which is used as a quick and relatively inexpensive way to invalidate patents at United States Patent and Trademark Office (USPTO). The case held that PTAB judges must be appointed by the President and confirmed by the Senate to vest them with the necessary authority to invalidate patents. However, the constitutional problems associated with their appointment by the Secretary of Commerce can be remedied by having PTAB decisions reviewed by the USPTO director, who is appointed by the President and confirmed by the Senate. Another viable alternative is to establish a small panel of judges who meet the constitutional requirements to review all PTAB decisions. Either of the proposed solutions would work to cure the problem. The need for a fix to this problem is likely to result in legislation that could move through the Congress and become a "Christmas Tree" for other legislation referred to as "ornaments" on a moving bill.

One such potential ornament has enthralled both the public and the Hill above all other patent issues and has resulted in a series of bills, which have high betting odds for quick action; these relate to drug pricing patents which some claim are a main contributor to high drug prices. The most likely provisions for addressing drug pricing through patents are contained in a couple of bills that have already seen some action. The House Judiciary Committee recently moved H.R. 5133, the Affordable Prescriptions for Patients Through Promoting Competition Act of 2019, and H.R. 3991, the Affordable Prescriptions for Patients Through Improvements to the Patent Litigation Act of 2019. The bills contain provisions that are intended to help reduce prescription drug prices by increasing access to generic and biosimilar products.

H.R. 5133 would establish that "product-hopping" is anti-competitive behavior in violation of the Federal Trade Commission Act. The bill describes "product hopping" as a practice of incrementally reformulating a drug after receiving notice that an applicant has submitted an abbreviated new drug application or biosimilar biological product license application. This would include subsequent innovation that would extent the time release of the active component or the reformulation of the product to an oral administration from an intravenous delivery.

H.R. 3991, attempts to address something called "patent thicketing". Patent thicketing is a web of overlapping patents that would require a licensee to take many licenses to be able to clear a potential conflict. The bill would cap at 20 the number of patents a brand-name biologic drug manufacturer can assert in litigation against a biosimilar infringer.

Almost everyone with a heartbeat recognizes that we shouldn't keep life-saving drugs from anyone in need. Affordability should not prevent Americans from getting life-saving medicines. And there is a large consensus that drug-prices are too high in the United States.

But are these patent drug pricing bills the way to go?

I don't think so.

"Product hopping" arguments fail to acknowledge that innovation does not stop when an active ingredient useful in treatment is

The most likely provisions for addressing drug pricing through patents are contained in a couple of bills that have already seen some action.

Résumé

Bob Stoll

Bob is a partner on the Patent team at Drinker Biddle & Reath LLP and Co-Chair of the Intellectual Property Group. In October of 2013, he was appointed, by Chief Judge Rader, to a three-year term on the CAFC Advisory Council, was reappointed for another three-year term in 2016 by Chief Judge Sharon Prost, and reappointed in 2019 for an additional three-year term. He is also serving a three-year term (2018-2021) on the Board of Directors for the American Intellectual Property Law Association. As the former USPTO Commissioner for Patents, he was instrumental in the passage of landmark patent legislation, the America Invents Act, and lauded for his efforts to reduce patent pendency and improve patent quality. He has spent his career improving the intellectual property system and educating the public, applicants, corporations and foreign governments on the criticality of intellectual property to economic growth and job creation.

developed. The different phases of trials for the original drug are extremely expensive and can take years to complete. Most drugs fail and never come to market. But for those that are successful, innovative improvements during that period can provide for a more efficacious product or reduce side-effects or any number of other developments. As a society, we want to encourage developers to continue to improve their products toward a better treatment. Patented drugs, like other patented innovations, are protected for a limited time, and, after expiration of that period, are in the public domain freely available for any company to manufacture. There are special rules that allow companies to bring generic versions to market early. But the problem might be that the patented improvements made on the original drug are so significant that the original drug or its generic version are significantly less desirable than the improved drug.

"Patent thicketing" is a different issue. In this case, patentees seek several patents which overlap with the original invention and form a web, or "thicket", of interwoven protection. But it should be recognized that each element in this family of patents must each be novel to receive a full term. If a family member is obvious over an earlier invention with a common inventor and the same entity, the USPTO will require a terminal disclaimer, so that the term of the obvious over the original drug modification does not extend beyond the term of the original invention. Patents that are not obvious over the originally patented drug or process have a presumption of validity and do not have a reduced term as they are new innovations. Capping the ability of a branded company to use the patents in its portfolio denies the company the ability to assert valid patents against competitors and violates the concept that in exchange for providing the public with the information on how to make and use the invention, the inventor will be provided with a limited period to exclude others from making and using the invention.

It is critically important that we reduce drug costs in the United States but using the patent system to do so would have many unintended consequences. The United States is by far the most innovative country in the world in the development of new drugs and biosimilars. There must be significant investigation into what effects bills such as these would have on research and development in this country for investment in the next cures for cancer and other diseases. We are already hearing about research and venture capital moving overseas because of our recent treatment of diagnostic methods related to patent subject matter eligibility. Do we want to further harm the impetus that is driving our drug research? And what are foreign countries going to do when we limit enforcement in the United States for drug-related patents? Will they consider further limitations on the patents of our drug companies in their countries?

We might create a research spiral as efforts flow into other areas where returns on investment are more certain; and we might lose our leadership in the innovation of healthcare products and cures.

Are these bills on drug "product hopping" and "patent thicketing" the proverbial "camel's nose under the tent"? There are significantly fewer patents associated with the development of a drug than those related to a telecom innovation. Smart phones and standards like 5G can have hundreds of patents associated with them. Will the bills we are reviewing now spill over into other industries?

High drug prices in the US are caused by a complex group of players, including providers, insurers, doctors, drug companies among others. Fixing the problem is critical, but the solution is not properly tied to patents. Society should distribute the burden of making sure that life-saving drugs are available to all. The costs of drug development are enormous, and most efforts are not successful. We want to continue to stimulate research in the next cures by providing funds and a collaborative atmosphere to undertake the research to find them. It does not make sense to hurt innovation by limiting the enforcement of patents.

Our patent system is so important that its basis is found in the Constitution. It has driven our economic expansion for two centuries and led to job creation and economic growth. Before we tinker with it, we should do some research to understand what the drug patent pricing changes would likely do to the system and to our leadership in a critical area of human endeavor.

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Life sciences meets competition law

MacKenna Roberts, General Counsel and DPO to Choice Telemed Ltd, asks whether courts will become an accepted forum to challenge exploitative drug pricing practices in the pharmaceutical industry, and explains why it matters.

Antitrust regulators worldwide have targeted pharmaceutical companies for investigation of alleged anticompetitive practices. The ensuing litigation has spotlighted industry practices to secure market dominance and profit margins. In the UK alone during 2019, eleven investigations into pharmaceutical companies were ongoing by the Competition and Markets Authority (CMA).

Traditionally, these investigations have scrutinized alleged anti-competitive collusion around "pay for delay" to market agreements between branded drug manufacturers and the manufacturers of generic drugs. These abuse of market claims are pursued in contravention of Article 101 of the Treaty on the Functioning of the European Union (TFEU) and Chapter I of the Competition Act 1998.

As the dynamics of pharmaceutical markets shift from blockbusters to rare disease "orphan" designations and pharmacogenetics, therapies are more specific and less likely to have substitutable competitors. Meanwhile, prices increasingly exceed production costs. Public pressure has led regulators to expand the legal toolbox and attempt alternative ways to hold pharmaceutical companies legally accountable for exploitative drug pricing practices.

Since 2013, a previously unusual legal basis for market abuse litigation has become more prevalent: the prohibition of "unfair purchase or selling prices" (Article 102 TFEU and Chapter II CA 1998). Its application to drug pricing has been keenly contested and courts are reluctant to intervene in markets in this manner.

These cases are triggered by exploitative behaviors often combined with exclusionary or deceptive conduct. Recent investigations include 12,000% price hikes for packs of hydrocortisone (£0.70 April 2008 to £88.00 March 2016) prompting three separate investigations into Actavis and others. Concordia International has been investigated for buying the license to a hypo-thyroidism drug, Liothyronine, de-branding it and raising prices by up to 1,600% (from approximately £4.46 when branded to £258 per pack). An EU example includes the Danish competition authority sanctioning the pharmaceutical distributor, CD Pharma, for increasing the price of the drug Syntocinon, given to women during childbirth, by 2000%. It has also submitted a case to the Danish state prosecutor for serious economic crime.

MacKenna Roberts

> ***Courts are extremely cautious not to become tantamount to a price regulator.***

Whether competition law is the correct remedy for excessive pricing is controversial but public appetite is fueled by outrage when old drugs become expensive almost overnight. This article examines the evolution of unfair and excessive pricing law in the pharmaceutical sector while it is on the brink of seminal decisions that will shape its development.

Potential legal turning points ahead for a divergence in EU and UK approaches

The case, *Pfizer and Flynn*, has taken center stage having been heard before the English Court of Appeal in November 2019. Its judgment is much anticipated internationally to set the parameters for how judicial jurisprudence may regulate unfair and excessive drug pricing in the courtroom. It will also impact conduct by competition agencies in a string of ongoing cases in the UK and EU.

Of particular interest will be to compare the UK approach in *Pfizer and Flynn* with the European approach in the Italian excessive pricing decisions against *Aspen Pharmacare* ("Aspen") and its pending European Commission investigation.

Résumé

MacKenna Roberts

MacKenna is a life sciences litigation and regulatory lawyer who has worked in private practice, academia and, most recently, in-house as General Counsel and DPO to Choice Telemed Ltd, a medical imaging company that supports clinical trials. MacKenna is an experienced strategic adviser assisting clients in the commercialization of medical innovation at the frontiers of medicine, specializing in cell and gene therapies/tissue engineering, genetic testing and digital health technologies.

Pfizer and Flynn

In this case, Pfizer was the seller of a capsule form of an epilepsy treatment, phenytoin sodium, previously sold under the brand Epanutin. Pfizer transferred its marketing authorization to sell the drug in the UK to Flynn without its associated trademark, effectively "debranding" and "genericizing" the drug so that it falls outside the voluntary pricing scheme for branded drugs, the Pharmaceutical Price Regulations Scheme (PPRS). Pfizer continued to be the sole manufacturer and exclusively sell the same drug to Flynn at a price increase (between 780-1,600%) and Flynn then supplied it onto wholesalers and pharmacies at an even more dramatically increased price (between 2,300-2,600% increase) with the NHS a captive market. The NHS expenditure increased from 2 million in 2012 to 50 million in 2013 with 10mg packs increasing from £2.83 to £67.50 per pack, much to the chagrin of the Department of Health.

After a three-year investigation, in 2016, the CMA found unfair pricing and abuse of dominance for both Pfizer and Flynn, ordering them to lower prices and imposing fines of almost £90 million.

On appeal, in 2018, the finding was in part set aside by the Competition Authority Tribunal (CAT) for having misapplied the relevant legal test and remanded the matter back to the CMA to be reconsidered. The CAT's judgment was a significant blow to the CMA which has multiple ongoing excessive pricing investigations.

The Court of Appeal granted leave to conjoined appeals and its decision is expected imminently.

CMA approach

In reaching its decisions, both lengthy and complex, the CMA and CAT applied the legal test from the leading case, *United Brands*. In *United Brands,* the European Court of Justice (ECJ) confirmed that it is unlawful for a dominant firm to charge a price which is excessive because it has "no reasonable relation to the economic value of the product supplied", under what is now Article 102 TFEU.

It set out a two-stage analytical framework: is the price "excessive" and, if so, is it "unfair". A price may be "unfair" either in itself or when compared to competing products. *United Brands* suggests one appropriate methodology in establishing an economic benchmark is a determination of cost and selling price thereby revealing 'the amount of the profit margin', a so-called price-cost analysis. The Court emphasized that other possible methodologies may be more suitable and should be decided on a case-by-case basis.

> ***Public pressure has led regulators to expand the legal toolbox.***

In *Pfizer and Flynn,* due to the economic complexity of drug pricing, the CMA applied a so-called "cost-plus" analysis. The CMA compared the cost and price of the medicine with reference to a "return of sales" across a portfolio of products used in the PPRS scheme, yielding a benchmark profit margin of 6% against which it compared the margin for the target drugs.

In finding unfairness, the CMA found the price to be unfair "in itself" because there was no reasonable relationship between the economic value and price of the drug. The CMA did not see it necessary to continue to the second limb. It did note for "completeness" anyway that Pfizer continued to supply the drug at much lower costs in other Member States that had different regulatory regimes and provided no justification for these differences. Given the disparity was so large, the CMA noted that it is unlikely an objective basis could justify such differences.

CAT decision

The CAT agreed with narrowly defining the markets to find that both *Pfizer and Flynn* were dominant within their respective markets. However, it overturned how *United Brands* was applied in reaching its findings.

The CAT criticized the cost-plus analysis for being an "idealized" notion of market competition. The CAT felt the CMA should have established a benchmark price or range by reference to other economic methodologies likely to apply in normal market competition, although it could not suggest one that would have provided this clearly. In particular, it felt the CMA should not have dismissed comparing the higher price of the tablets with the capsules despite agreeing that the tablet form cannot be substituted for the capsules, so it is not a comparator product.

Importantly, the CAT did not find that the prices were not "excessive" but that the single method used by the CMA was incorrect and not sufficient. This finding is in direct contrast to the Aspen decisions.

Two significant points to note in regard to the CAT's decision: Firstly, the basis for overturning the CMA's finding of "unfair" and "excessive" was largely adopted from the European Attorney General Wahl's opinion as opposed to the ECJ decision in the *Latvian Copyright* case in 2017. That is to say that the "multiple methodology" approach AG Wahl proposed was not adopted by the ECJ but endorsed nonetheless by the CAT. The CAT acknowledged that the opinion did not have the same authoritative weight as the *decision* but found it "persuasive" and "eminently sensible".

Second, the opinion and decision in the *Latvian Copyright* case was handed down after the CMA's

decision, so it was not within the contemplation of the CMA.

Ultimately, the CAT decision requires multiple economic methodologies to be utilized before determining "excessive" pricing. Also, unfairness must be found only if all possible arguments under both separate limbs of the test have been considered, including similar but non-comparator drugs. For CAT, either limb could be relied on to find unfairness, but overall analysis must account for both limbs and must evaluate any *prima facie* convincing argument that pricing is fair. This approach, if upheld by the Court of Appeal, significantly increases the evidentiary burden of the CMA, increasing the time and costs allocated from limited resources to investigations.

> ***At the heart of this litigation, a jurisprudence debate rumbles.***

Aspen

In the EU, the situation has potentially evolved differently. In 2016, the Italian competition agency (AGCM) fined Aspen Pharma for abusing its dominance to artificially inflate prices of cancer medicines it licensed from GlaxoSmithKline. The decision was upheld on appeal. In 2017, the EC commenced proceedings against Aspen for unjustified "price gouging" stating: *"Companies should be rewarded for producing these pharmaceuticals to ensure that they keep making them into the future. But when a price of a drug suddenly goes up by several hundred percent, this is something the Commission may look at".*

Aspen's anticompetitive conduct encompassed its price negotiation conduct. It sought to have its leukemia treatments re-classified so as to escape regulated price controls. It threatened to pull the drugs, for which there is no alternative treatment, from market unless a price increase (of approximately 1,500%) was agreed. Aspen caused a shortage in the drug supply and eventually its demands were agreed.

Both the AGCM and administrative appeal tribunal found unfair and excessive pricing on the basis that the price increase did not reflect increased manufacturing costs. Aspen defended that the reason for the price increase was to bring Italian drug prices into alignment with European prices. This reason was held to be insufficient and the only justifications for a price increase could be: R&D costs, innovation costs or increases in manufacturing or distribution costs.

The EC is now investigating whether Aspen has unfairly priced these same cancer drugs across Europe.

The administrative appeal of the Aspen case found that the cost-plus analysis to calculate a profit margin was sufficient to make a determination of excessive pricing. This is in stark contrast to the CAT's decision in *Pfizer and Flynn.*

Depending on the Court of Appeal ruling and the EC's Aspen investigation into unfair pricing across Europe, this contrast could demark a divergence in approach to exploitative drug pricing cases in the UK and EU.

Market intervention debate

At the heart of this litigation, a jurisprudence debate continues to rumble. Courts are extremely cautious not to become tantamount to a price regulator. AG Wahl, like many sceptics, cautioned against price interventions, discussing his concern for a tendency towards false positives. He warned of the greater difficulty to correct errors in rulings than commerce to correct for errors in the market.

He also expressed concern for the legal uncertainty for dominant firms to be able to assess when a price might be deemed to be excessive and the need not to set the threshold too close to the benchmark price. Drug pricing is a result of often highly complex economic algorithms, wider commercial factors and opaque reimbursement policies.

Some argue this prosecution will detract investment into R&D of innovative medicines in an industry that suffers high attrition rates and exceedingly costly and lengthy pipelines to market. Others argue that social policy dictates a remedy when market abuses distort access and negatively impact public health while relying heavily on public investment. Indeed, the OECD Competition Committee convened hearings on "Excessive Prices in Pharmaceutical Markets" in November 2018.

Conclusion

Despite the economic complexity of bringing unfair and excessive pricing claims in the life sciences sector, it is unlikely to stem the tide. There have been complaints of excessive pricing by, for example, Biogen in Belgium and Italy for its orphan drug Spinraza to treat spinal muscular atrophy. Future cases, therefore, are anticipated and clarity on the application of EU law would be welcome by industry and regulators alike.

However, the awaited determination on the calculus required for competition authorities with limited resources to discharge its burden of proof likely will influence the enthusiasm with which this strand of litigation is pursued in future. It remains to be seen if the UK will diverge in its approach from the EU which may serve to offer jurisdictional preferences that either open or close the door on this emerging body of case law.

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The CBD regulatory landscape in Portugal and in the EU

Ricardo Costa Macedo and Diana Mâncio da Costa of Caiado Guerreiro look at Portugal's approach to CBD.

All across the world, the interest in Cannabidiol (CBD) products is on the rise, which is attested by the millions of searches being made online each month about CBD. Also, shops selling CBD products are springing up like mushrooms in various locations.

CBD, which is a non-psychoactive chemical compound from the cannabis plant, can be incorporated in a number of products, from food to medicinal products and cosmetics.

In Europe and elsewhere, the legal cannabis industry is rapidly developing and an exponential growth in this area is expected in the upcoming years. Various EU countries have passed new legislation on the matter, Portugal being one of those countries.

The question remains as to how CBD should be handled from a regulatory point of view, and doubts arise as to how these CBD products can be marketed in the EU and in Portugal.

CBD as a medical product

In Portugal, Law 33/2018, of 18 July 2019, approved the legislative framework for the use of products, preparations and substances based on the cannabis plant for medicinal purposes. This recent approval is perceived as a significant step to encourage scientific and pharmaceutical investments in this area. Further legislation, namely Decree-Law 8/2019, of 15 January, has detailed the legal regime applicable to these medical products.

According to the INFARMED (the Portuguese Drug Authority), the intent of enacting regulation on cannabis was to enhance the availability of medical treatments based on the cannabis plant. The INFARMED is responsible for guaranteeing that these products meet all the mandatory requirements concerning their quality and safety. Pursuant to this, the entire production chain, from

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Résumés

Ricardo Costa Macedo

Ricardo Costa Macedo joined Caiado Guerreiro in 2000 and has been a partner since 2006. He heads the intellectual property and life sciences groups of the firm. His practice covers a wide range of contentious and non-contentious patent, trademark and other IP-related rights, such as trade secrets and unfair competition, in particular in the pharmaceutical, home care, food and insurance sectors. Moreover, he has vast knowledge in regulatory matters in these sectors. He is considered by Chambers and Partners as a "leader in their field" in the area of IP.

Diana Mâncio da Costa

Diana Mâncio da Costa is a Junior Lawyer at Caiado Guerreiro. She is a member of the Intellectual Property and Life Sciences department of Caiado Guerreiro, and she has provided legal assistance regarding various aspects of the pharmaceutical and health sector, including the provision of advice on the advertising of medical products and medical devices, home care services, regulatory aspects of new medical products and drug prescription. She has also concentrated her practice on the enforcement of Intellectual Property rights in these sectors.

cultivation of the plant to its preparation and distribution, shall be controlled by the INFARMED.

As for the availability of these medical products, they may only be dispensed in pharmacies, upon medical prescription, issued by a physician. Another important remark to be made is that on account of Resolution n. 11/CD/2019 of the INFARMED, there is a closed list of therapeutic indications deemed appropriate for the prescription of cannabis-based products, substances and preparations for medicinal purposes. This list will be periodically revised, and such revision will be based on the evolution of the technical and scientific knowledge in this field.

Due to the novelty of the legal framework of medical cannabis in Portugal, there are still some essential questions that remain unanswered, for instance, the legal classification of one of the components of cannabis, the well-known Cannabidiol (CBD), thought to have an extensive range of therapeutic properties and a fairly safe, tolerable and non-addicting use. Moreover, unlike Tetrahydrocannabinol (THC), cannabidiol does not portrait any (relevant) intoxicating or psychotropic effect in humans. Consequently, consumers and industries, not only in Portugal but also at a European level, are paying attention to the many utilizations of CBD.

Upcoming changes in the classification of CBD

The winds may be changing regarding the classification of CBD. In a public letter, dated 24 January 2019 from the Director-General of the United Nations' World Health Organization (WHO), Mr. Tedros Ghebreyesus, to the United Nations Secretary-General, Mr. António Guterres, there is a recommendation to review the classification of cannabis in the context of the 1961 Single Convention on Narcotic Drugs. These recommendations are oriented towards removing cannabis and cannabis resin from Schedule IV of the mentioned Convention, removing cannabis extracts and tinctures from Schedule I and adding a footnote on cannabis and cannabis resin in Schedule I in the lines of: *"Preparations containing predominantly cannabidiol and not more than 0.2% of the delta-9-tetrahydrocannabinol are not under international control."*

The insertion of a substance both on Schedule I and Schedule IV is considered as the most restrictive level of control to be applied. Indeed, the cannabis (plant) is currently indicated in both Schedule I and IV of the UN Single Convention of 1961. Consequently, removing the indication of cannabis from Table IV, as suggested in the letter from Mr. Tedros Ghebreyesus, would present itself as a game changer in the legal framework of cannabis.

> ***In Europe and elsewhere, the legal cannabis industry is rapidly developing and an exponential growth in this area is expected in the upcoming years.***

For the purpose of exploring the legal framework of this cannabis component in Portugal, Decree-Law 15/93, of 22 January, on the fight against drugs, enacted as a result of the United Nations Convention Against Illicit Traffic In Narcotic Drugs And Psychotropic Substances of 1988, should be considered. This piece of legislation made it clear that the INFARMED is the competent authority to supervise the activities of cultivation, production, manufacture, use, wholesale, distribution, importation, exportation, transit, acquisition, sale, delivery and holding of the plants, substances and preparations listed in Tables I to IV. As such, Table I-C lists the following substances:

- **Cannabis** - flowering or fruiting leaves and flowering matter of the Cannabis sativa L. plant from which no resin has been extracted, whatever its designation.
- **Cannabis** - separate raw or purified resin obtained from the Cannabis plant.
- **Cannabis oil** - Crude or purified separated oil obtained from the Cannabis plant.
- **Cannabis** - Seeds not intended for sowing Cannabis sativa L7.

Additionally, Table II-B lists THC as a substance subject to INFARMED's control. As for CBD, it is not possible to find a reference to this cannabis component neither in Decree-Law 15/93 nor in the UN Convention. As such, the question arises regarding the legal classification of CBD as a prohibited substance or not, particularly since THC is specifically foreseen (and regulated) in the abovementioned legislation.

The implementation of Mr. Tedros Ghebreyesus' recommendations may have less far-reaching effects in Portugal. First of all, in Portugal, cannabis is only listed in Table I-C and not in Table IV (thus, not being subject to the strictest form of control). As for the remaining recommendations, the proposal of not including preparations containing predominantly cannabidiol with no more than 0.2% THC in the international drug control conventions will certainly have a tremendous effect in the pharmaceutical industry. In fact, not scheduling a substance in these Tables determines that they are not subject to strict international control, including for the purpose of their production and supply.

Likewise, Article 81 of the Portuguese Road Traffic Code foresees a general prohibition of driving under the influence of narcotic or psychotropic substances. Nevertheless, the drug-screening tests that will be performed, aimed at detecting whether the driver has a concentration value of cannabinoids equal to or greater than the concentration of 50 ng/ml, do not foresee CBD as a component to be measured (indeed, THC, 11-OH-THC and THCCOOH will be the searched substances), possibly due to its classification as a non-intoxicating substance.

This leads to the conclusion that there may be a different legal regime to be designed specifically for CBD.

It could be argued that the footnote set to be included in the Convention does not concretely alter the legal status of CBD, since this cannabis component was already not scheduled in the international conventions. Nevertheless, the case should be made for this simple footnote to bring clarity to the legal regime surrounding CBD, due to its consignation as a non-controlled substance under the referred conventions. As a matter of fact, even though this component is not listed in the schedules of the 1961, 1971 or 1988 United Nations International Drug Control Conventions, CBD that is produced as an extract of cannabis remains included in Schedule I of the 1961 Convention and, as such, is prohibited. In general, these modifications will most likely translate into a development of the distribution of medical cannabis products as a whole.

Food containing CBD

The Novel Food Catalogue states that extracts of cannabis sativa L. and derived products containing cannabinoids are considered novel foods. The Catalogue lists foods that were not significantly consumed within the Union, prior to 15 May 1997, thus requiring further risk assessment and authorization before they are sold and marketed within the EU. Even though this Catalogue is not legally binding, it is still considered relevant for national authorities. As such, producers willing to sell food products with CBD will have to follow the due process set out in Regulation (EU) 2015/2283.

> ***Relevant concerns are also raised regarding the legal framework of food containing CBD.***

Accordingly, a recent German decision confirmed that products containing CBD will be classified by the competent authorities as either a prescription-only medicine or a novel food, meaning they shall not be marketed to the general public without additional safety concerns and research being followed.

As for the regulatory framework of food containing CBD in Portugal, it should be acknowledged that the competent authority for these matters is the DGAV (the Food Quality and Safety Agency). Nevertheless, there has been a struggle in determining which one is the competent authority to handle matters related with cannabis. In this sense, the distinction to be made here relies on the purpose to be attributed to the product, for instance, if it will be a medical product vs. food and food supplement.

In this regard, it should be noted that the entity that intends to bring the product to the market will have to make a choice between marketing it as a medical product or as food or food supplement. As such, and as already clarified by the INFARMED, if we are dealing with a product that has been extracted from the cannabis plant and that will be used for medical purposes, then said product will be subject to the INFARMED's supervision. The inverse reasoning applies to the products used as food or food supplements, which will fall within the scope of responsibility of the DGAV.

CBD in cosmetics

When reflecting on the recent interest for CBD products, one should take into account the increased use of CBD in cosmetic products.

Regulation (EU) No. 1223/2009 (the Cosmetics Regulation) contains in Annex II a list of substances prohibited in cosmetic products. Entry 306 of this list includes any substance referred to in Tables I and II of the Convention on Narcotic Drugs of 1961, in which cannabis is included. Once again, the question is raised regarding the use of CBD in cosmetic products, since CBD is not directly mentioned in the UN Single Convention. The European Commission has clarified that *"Cannabidiol (CBD) as such, irrespective of its source, is not listed in the Schedules of the 1961 Single Convention on Narcotic Drugs. However, it shall be prohibited from use in cosmetic products (II/306), if it is prepared as an extract or tincture or resin of Cannabis in accordance with the Single Convention"*. Future developments may also be looming, especially with the recommendations for the modifications to be introduced in the UN Convention.

Conclusions

The recommendation made by the WHO on the rescheduling of cannabis and cannabis-related substances in the UN Single Convention may be an important step to enhance the legal discussion on the cannabis framework, which ties up with the momentum that is currently felt across the word in relation to cannabis and CBD.

The legal framework surrounding CBD is currently in a grey state, being that some CBD products are used as medicinal products, with the associated marketing authorization and clinical testing, whereas other products may be regarded as food & food supplements or cosmetics.

A push for regulation of CBD products seems to be in order, being that the sectors of medicinal, food and cosmetic products will most likely benefit from the harmonization of the legislation and from less puzzling regulatory regimes, as will patients and consumers.

Portugal in particular, having passed interesting legislation on medicinal cannabis and having attracted a number of companies and start-ups in this sector, would certainly benefit from clear CBD regulation and clarity as to which authority is responsible for what in this domain.

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Singapore's patent-linkage scheme and its effects on marketing approval for generic drugs

James Kinnaird, Partner, and Tim Headley, Associate, Marks & Clerk Singapore, discuss the aims and operation of Singapore's patent-linkage scheme.

Singapore's stated ambition is to be an IP-hub for South-East Asia and part of this plan involves a robust patent-linkage scheme that was originally introduced to meet its obligations under the US-Singapore free-trade agreement. This patent-linkage scheme allows the patent proprietor to delay (or halt) the approval process for a generic drug. In addition, the scheme places a significant burden on a company looking to launch a generic version of a drug in Singapore, and failure to comply could result in criminal sanctions.

The marketing approval and "patent-linkage" system in Singapore

The marketing approval process is governed by the Singapore Health Sciences Authority (HSA), under the Health Products (Therapeutic Products) Regulations 2016 (TPR), which also sets out the applicant's obligations under the patent-linkage scheme and provides legal basis for regulatory data exclusivity.

An applicant for approval of any drug must declare to the HSA whether there are any patents in force that relate to the product in question. The applicant must also declare to the HSA that:

(a) the patent owner has given consent (to the launch of the generic version);
(b) the patent is invalid; or
(c) the patent will not be infringed by acts relating to the therapeutic product.

The consequence of filing a declaration that contains false information include a fine and/or imprisonment of up to 12 months, so it is important for a generic competitor to diligently list any and all patents (including process patents) that may be relevant to the product they wish to launch.


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Résumés

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Tim Headley
Tim is a Chartered (UK) and European Patent Attorney, qualifying in 2018. He graduated with a First-Class Honors for his MSci in Natural Sciences from the University of Cambridge. Before joining Marks & Clerk Singapore, Tim worked at a leading London-based UK Patent Attorney firm working for clients ranging from multinational pharmaceutical companies to local start-ups. Tim specializes in patent matters relating to chemistry and has particular experience in patents relating to small molecule pharmaceuticals and polymers. Tim has experience handling large patent families covering all of the major IP offices around the world.

If the generic company applies for marketing authorisation in the last 18-months of the patent's life, with an indication that the approval should be dated after the patent has expired, then the marketing approval process will continue unabated. In any other case where the existence of a patent is declared and patentee has not consented to the marketing authorisation application, the HSA will issue a notice requiring the generic company to serve notice on the patentee, stating that they have applied for marketing approval.

Upon service of notice to the patentee, the marketing approval process is halted for a period of 45 days to allow time for the patentee to apply to the court to block the approval or to obtain a declaration that the patent is valid and would be infringed. If no application to the court is made during the 45-day period, the marketing approval process continues unabated. However, the registration process will be suspended for up to 30-months (total delay of up to 31.5 months) if the patentee challenges the proposed registration. This delay in proceedings is intended to provide sufficient time for the courts to consider the facts and arrive at a conclusion. In the unlikely event that a decision has not been reached by the courts within 30 months, the generic company can then continue with the approvals process while awaiting the conclusion of the court case. If the court case concludes in the favour of the generic company within 30-months, then they can apply to the court to overturn the stay in proceedings. However, if the patentee wins, then the generic will need to wait until closer to the expiration date of the patent before trying to register their product.

The procedure above can lead to uncertainty for both the generics company, as well as the patentee. For example, should the patentee apply to the court if they cannot determine whether a generic product falls within the scope of their patent within the 45-day period? On the other hand, does a generics company have to declare the existence of a process patent when they will manufacture the drug by a different process? Both of these issues are discussed below with reference to case law in Singapore.

Identity of generic product unclear

Can a patentee use the patent-linkage scheme to block a generic competitor when they are unsure of infringement? This issue was considered by the Singapore High Court in *AstraZenaca AB v Sanofi-Aventis Singapore Pte Ltd* [2012] SGHC 16.

This case was decided under the old Medicines Act, which was replaced by the TPR in 2016. However, the provisions of the Medicines Act that were relied upon are essentially identical to those in the TPR and so it appears highly likely that the same outcome would occur under the TPR.

Sanofi-Aventis (Sanofi) sought marketing approval for certain film-coated tablets comprising rosuvastatin and a stabiliser. They declared that the products would not infringe AstraZeneca's Singapore Patent No. SG 89993 ('993) because their proposed composition did not comprise an *"inorganic salt in which the cation is multivalent"*, as set out in the patent claims.

AstraZeneca had two important decisions to make in 45 days. First, did they have sufficient basis to apply to the court when they did not have enough information to know whether Sanofi's product would infringe their patent? Secondly, what should they rely on for "infringement" – the Patents Act or the Medicines Act?

AstraZeneca applied to the court within the specified 45 days under the Medicines Act for a declaration that the '993 patent would be infringed by Sanofi's product, and sought an injunction to restrain Sanofi from performing acts that would infringe the '993 patent. AstraZeneca chose the Medicines Act as the basis for their suit due to concerns that the Patents Act requires an infringing act to have been committed before infringement proceedings can begin. In contrast, the Medicines Act only requires that a prospect of future infringement needs to be established for their case to succeed (i.e. approval would result in the launch of an infringing product). The court approved the use of the provisions of the Medicines Act in this context.

AstraZeneca argued that they did not believe that the Sanofi product fell outside the scope of the patent. This is because AstraZeneca did not believe it possible to produce a stable formulation of rosuvastatin that fell outside their patent claims. They also argued that their application to the court was reasonable given that they only had 45 days to bring proceedings to benefit from the 30-month stay on the marketing approval and that it was not possible to obtain all of the evidence in this time-frame, especially as Sanofi had not disclosed full details of their product. Sanofi sought to have the claim struck out on the basis that AstraZeneca were unable to provide evidence of infringement.

While mere belief of infringement would probably not be sufficient to bring proceedings under the Patents Act, the court held that the Medicines Act was intended to cover this scenario and so the level of information provided in the initial claim was acceptable. AstraZeneca sought discovery in respect of Sanofi's specific products, on the basis that it needed this information to properly assess infringement. Discovery was granted and Sanofi had to disclose the composition of their product, although appropriate confidentiality provisions were put in place.

As is clear from the above, the patentee can start proceedings without a clear idea of whether the product will infringe the patent(s) in question. However, further evidence will need to be obtained during the proceedings, which could be through the voluntary sharing of information by the generic to exclude infringement or by discovery. This appears to be a balanced approach, given the short period of time available to the patentee to start proceedings under the TPR (or formerly, the Medicines Act).

What constitutes a "relevant" patent that must be disclosed?

Certain issues relating to marketing approval and when a patent is relevant are dealt with in *Millennium Pharmaceuticals, Inc. v Drug Houses of Australia Pte Ltd* [2018] SGHC 149 (first instance) and the subsequent appeal [2019] SGCA 31. The full trial has not been heard, and both of these judgements relate to applications to strike out certain claims.

Millennium Pharmaceuticals (Millennium) are the proprietor of Singapore patent nos. SG 151322 and SG 182998 (the patents), both of which relate to processes for the manufacture of the anti-cancer drug bortezomib.

Drug Houses of Australia (DHA) obtained marketing approval in Singapore for a product containing bortezomib. Although the declaration filed as part of DHA's application process was never made available, the Court of Appeal concluded that, *"...it can be fairly implied that the Respondent did not declare the existence of the Appellant's two patents to the Health Sciences Authority..."*. This meant that Millennium was not served notice that DHA had applied for marketing approval and were not able to halt the approval process by commencing litigation under the TPR. DHA asserted that they did not use the processes disclosed in the patents, and accordingly that there was no need to declare their existence to the HSA.

Millennium applied to the High Court for a number of remedies, including:

(i) an order that by failing to declare the existence of the patents, DHA had filed a declaration containing a material falsehood (obtaining such an order would enable Millennium to apply for the granted marketing approval to be revoked);
(ii) a declaration that DHA's performance of the acts for which their products had been registered would constitute infringement of the patents; and
(iii) an injunction to restrain DHA from infringing the patents.

DHA applied to have these claims struck out. As they had not been notified by DHA, Millennium could not rely on the provisions discussed above. Instead, they based their claim on a different provision in the TPR, which allows any interested person to apply for cancellation of the marketing approval if doing an act authorised by the marketing approval *"infringes a patent under the Patents Act"*.

The first instance decision held that the reference to the Patents Act meant that a claim could only be based on a past act of infringement (which had not occurred). On this basis, it was deemed impossible for claims (ii) and (iii) to succeed, and they were struck out. The first instance court concluded that the reference to the Patents Act should be interpreted in this way because otherwise a proprietor who missed the 45-day window to bring proceedings would have another opportunity after the marketing authorisation's grant, even when no infringement had occurred.

The Court of Appeal disagreed. In their decision, they opined that the TPR is not necessarily concerned with proving actual infringement of a patent.

Rather, it considers whether an act authorised by a marketing approval would infringe a patent, irrespective of whether the act has taken place or not. Whether this means that a patentee gets a second chance at using the TPR, they noted that a proprietor who does not take action when made aware of an application for marketing approval risks the market being flooded with cheap generic products: *"There is no abuse in the proprietor now wanting to have the registration cancelled if he can obtain a determination on the specified matters"*. As a result, and while not necessarily agreeing that Millennium's case would ultimately succeed at full trial, they deemed that Millennium's claims should not be struck out.

More generally, the Court of Appeal noted that a generic company cannot omit a process patent from their declaration simply because they intend to use a different process. Instead, a generic company *"has to declare the patents and then state, among several possibilities, that the patents are invalid or will not be infringed..."* It is for the Singapore authorities to decide whether notice must be served on the proprietor.

Thus, the message to generics companies is clear: declare all patents which could be considered relevant to your product (including processes), even where you are sure that you will not infringe them.

Other methods to delay generic entry to the market

Three further options are available to delay market entry of generics onto the Singapore market- though only one of these relates to the marketing approval process.

Singapore has a data-exclusivity provision in the TPR of 5 years from the date of the original marketing approval, which means that the HSA will not grant approval for a generic drug based the original test data without approval of the originator company. This protection is automatically available and guarantees at least a short monopoly period for innovator companies.

Patent Term Extensions (PTEs) and Adjustments (PTAs) are available in Singapore and are based on the equivalent provisions of US patent law. However, PTEs are typically hard to obtain in Singapore because only delays attributable to the HSA are considered when determining whether there has been an "undue delay" in granting the MA. Given that the HSA usually grants marketing approval quickly, PTE is unlikely unless the first marketing approval is obtained in Singapore. PTAs are possible due to delays in prosecution by the Singapore Patent Office or by a foreign patent office that has a similar scheme (e.g. the USPTO). The latter may be easier to obtain if one uses modified examination to obtain grant of a patent in Singapore, but it is difficult to obtain the former due to the way that the Adjustment is calculated by the Singapore Patent Office.

Conclusion

As is evident from the above, the patent-linkage scheme is generally favourable to innovator companies because the generic competitor is required to inform the innovator of any patents that might be infringed, and the innovator can bring proceedings (and hence the delay) before they are sure that there is an infringement. This highlights the importance of formulation, dosage regime and process patents in Singapore, each of which could be used to delay generic entry to the market after the expiry of an original product patent. In contrast, there is a heavy burden on generics companies to declare all patents relevant to their generic product. Failure to comply can lead to marketing authorisation being revoked and even criminal sanctions for the people responsible.

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Understanding the inventive step for pharma and bio-pharma inventions in India

Rajeev Kumar and Pankaj Musyuni of LexOrbis discuss the importance of the inventive step and the ways of establishing it.

The Indian pharmaceutical and bio-pharmaceutical industry has an important position in providing medical and alternative therapies worldwide. Both sectors have the potential to provide the most advanced and cost-effective supplies globally and to work in parallel to provide an optimum solution. Additionally, ongoing research in the pharma/bio-pharma sector for combating diseases is vital for public health and, subsequently, patent protection is equally important for the researchers.

In India, patent protection is available subject to the establishment of the pre-requisite patentability criteria of novelty, inventive step, and capability of industrial application for any invention, whether product or process. Among these criteria, establishing an inventive step is a benchmark which implies that the invention must not simply be an obvious and alternate development of what is already available. Consequently, the said criteria are much harder to comply with, and exist to establish the right balance, promoting and rewarding real inventions and avoiding undesirable patent monopolies for unworthy inventions. To ensure this, India adopted a peculiar definition for assessing inventive step under Section 2(1)(ja) of the Patents Act, whereby inventions are judged based on the establishment of the technological advancement, economic significance, or both.

Claims in pharma/bio-pharma inventions are usually directed to cover new chemical entities, compositions/formulations, technology-based inventions such as specific combinations, dosage forms, new forms of known substances such as salts, ethers and esters; polymorphs; solvates, including hydrates; clathrates; stereoisomers; enantiomers; metabolites and pro-drugs; conjugates; pure forms; particle size; complexes, isomers, and mixtures thereof. Also, claims may be drafted for kits, selection inventions, process or method, and product-by-process inventions. Since these inventions have different styles of claims to cover the nature of the invention, the obviousness issue is usually checked by evaluating the combined prior arts and checking what a skilled person would extract from the available knowledge and its interpretation. In general, the invention must be considered as a whole to check whether it is beyond the ability of a person skilled in the art to perform.

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Whilst examining these inventions, the Indian examiners usually check various factors, not limited to the hindsight approach, the reasonable expectation of success, and "obvious to try" factor apart from the technical advancement, which is generally considered in the form of identification of a problem and its solution, or unexpected results obtained by the proposed invention. The application of the hindsight approach by the examiner is common in such inventions where the invention relates to a new polymorph or a novel formulation with varying excipients, and different modes of delivery or release mechanisms such as delayed-release, sustained-release etc. are in question. It is assumed by the examiners that these inventions are obvious and can be prepared retrospectively. Contrary to the said assumption, the fact remains that developing a new product or formulation is not based on mere theory; trial and error and intensive experimentation are also required in getting a useful invention. Further, a reasonable expectation of success is usually examined in the context of the prior art not having any teaching or motivation to attempt the present invention in the absence of undue experiments. A classic example of such an invention would be the case whereby an enantiomer is obtained by purification of a racemic mixture. Similarly, the consideration for "obvious to try" approach is largely misunderstood for pharma/bio-pharma inventions despite the fact that the technology and expected outcome in product and formulation development is unpredictable. Additionally, the formulation inventions are interpreted as inherently obvious concerning choosing the variable excipients and assuming that the result for efficacy would be predictable, which again is not possible without conducting experiments.

Whilst looking for the judicial interpretation regarding the inventiveness of patent applications in India, there are only a handful of cases, and only one by the Hon'ble Supreme Court in the case of *M/s. Bishwanath Prasad Radhey Shyam v. M/s. Hindustan Metal Industries.* The Court stated that minor modification in the patented invention would make it obvious to any skilled worker based on the knowledge available at the date of the patent. About "inventive step" the Supreme Court laid down the following principles that need to be kept in mind. For the determination, several forms of the question have been suggested *"...whether the alleged discovery lies so much out of the track of what was known before as not naturally to suggest itself to a person thinking on the subject, it must not be the obvious or natural suggestion of what was previously known";* in other words, the obvious to try test has been tested to check that the patent in question lacked inventive step. A similar approach has been used by the Delhi High Court in the case of *F. Hoffmann-La Roche Ltd. v. Cipla Ltd.,* wherein the Court relied on the *Bishwanath* case (supra) case and observed that *"the same (person ordinarily skilled in the art) cannot be read to mean that there has to exist other qualities in the said person like un-imaginary nature of the person or any other kind of person having distinct qualities..."*.

Though usually adopted by the examiners, it is pertinent to understand that while applying the hindsight approach it is essential to understand that one must avoid the approach as laid down in the *Bishwanath* case (supra) *"Had the document been placed in the hands of a competent draftsman (or engineer as distinguished from a mere artisan), endowed with the common general knowledge at the 'priority date', who was faced with the problem solved by the patentee but without knowledge of the patent invention, would have arrived at the invention".* A similar interpretation was held in *F. Hoffmann-La Roche Ltd. & Anr. v. Cipla Ltd.* RFA(OS) 92/2012, wherein the High Court held that, while conducting an inquiry into obviousness, hindsight is impermissible; the legal conclusion must be reached on the basis of facts gleaned from the

Résumés

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prior art and should not include knowledge gleaned from patent disclosure. Teachings in the prior art document have to be considered as a whole. Teachings away from the patent claim are treated as non-obvious. To inquire into obviousness, two-fold inquiry is required i.e. motivation to select and motivation to modify.

In addition, the test for obviousness has been precisely dealt with in case of *Hoechst v. Unichem Laboratories and Ors,* wherein the Bombay High Court held that *"... an invention usually involves three stages, (1) the definition of the problem to be solved, or the difficulty to be overcome, (2) the choice of the general principle to be applied in solving the problem overcoming the difficulty; and (3) the choice of the particular means to be used... merit in any one of these stages, or in the whole combined, may support the invention, and it is, therefore, probably more important to consider the advance in knowledge due to the inventor rather than to examine in detail the variations from the former product".* In another important matter of *F. Hoffmann-La Roche Ltd & ANR versus Cipla* RFA (OS) Nos.92/2012 & 103/2012, the Court identified some steps to determine obviousness/lack of inventive steps to be conducted, which include:

(1) to identify an ordinary person skilled in the art;
(2) to identify the inventive concept embodied in the patent;
(3) to impute to a normal skilled but unimaginative ordinary person skilled in the art what was common general knowledge in the art at the priority date;
(4) to identify the differences, if any, between the matter cited and the alleged invention, and ascertain whether the differences are ordinary application of law or involve various different steps requiring multiple, theoretical and practical applications; and
(5) to decide whether those differences, viewed in the knowledge of alleged invention, constituted steps which would have been obvious to the ordinary person skilled in the art, and thus rule out a hindsight approach.

Among other examples in a judicial context, whilst analyzing the inventive step, another famous case for the test of obviousness was decided by the Intellectual Property Appellate Board in *Enercon vs Aloys Wobben* ORA/08/2009/PT/CH, Oder No. 123 of 2013. In particular, paragraph 43 of the decision explains that that the *"coherent thread leading from the prior art to the obviousness"* or, in other words, *"the reasonable expectation of success embedded in the prior art which motivates the skilled person to reach to the invention, is the most crucial determining factor in ascertaining inventive step".*

In India, the evaluation of the technical advancement of patent applications is somewhat clear, focusing on exhibiting technical advancement of the claimed invention and consideration of economic advantages or advancements alone or together. Although factors such as reducing the manufacturing costs, operational costs and maintenance costs involved in any product development or employed process are also essential, they are influential in the case of a proposed invention that is technically weak when comparing with prior arts. Additionally, the outcome of the invention as an unexpected result is helpful even when it might appear that it would have been obvious to choose the combination of excipients at the time of invention. Further, an invention is not obvious if it produces results that would not have been expected before the researcher started testing the invention. Such results will often be the basis for the non-obviousness of a pharma/bio-pharma invention. In general, the identification of a problem and providing a solution can be the invention wherein the inventive step resides in the identification of a previously unappreciated and unrecognized problem. While the solution to the problem might be obvious once the problem has been identified, the invention might nonetheless be nonobvious if, upon examination, it is identified that the invention would have been obvious to a person skilled in the art before the inventor identified the problem.

Though the patents are subject to the territorial regime, it is also essential to have them consistent with public health strategies and the economy. Patents are considered a fundamental incentive to innovative activities in the pharma and bio-pharma sectors; hence they need to be safeguarded. Of late, India has been witnessing an increase in patent enforcement activities and patent filings. As evident from the annual report of 2017-18 published by the Office of the Controller General of Patents, Designs, Trademarks and Geographical Indications, India, there was an increase of 5.3% in the overall filing of patent applications. That said, the report further indicated that the total number of patents granted during the year was 13,045. Out of the total granted patents, 3,318 patents were granted to applications relating to chemicals, 773 to pharmaceuticals, and 505 to the biotech domain. Further, along with various initiatives, the Indian Patent Office continually works to reduce the backlog and expediate the examination procedure.

Upon a random analysis of the decision issued by the Patent Office, it appears that analysis of the inventive step for pharma/bio-pharma inventions is primarily subjective. One major reason for different opinions would be the differing subject matter expertise of the examiners. Sometimes, the data disclosed and presented in the specification is the primary reason for biased interpretation.

While understanding that inventive step is the most common issue raised in prosecution and litigation, assessing inventive step, examining the prior arts, identifying the differential features, and defining the skilled person are the primary concerns for examiners and patent practitioners which are still open for wide and varied interpretation. Going forward, more clarity, and refined tests on the assessment of the inventive step are expected, as the number of cases filed and decided in this regard increases.

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Understanding the state of uncertainty of life sciences patents

David G. Rosenbaum, founder and chairman of Rosenbaum IP, discusses the difficulties and uncertainty facing those who wish to register patents in the life science sector.

While most of us think of patents as covering mechanical items such as combustion engines, electrical items, such as integrated circuits, or chemicals, such as polymers, they also cover a wide spectrum of inventions in the field of life sciences. Life science is a broad field encompassing, among others, biotechnology, pharmaceuticals, biomedical technologies, life systems technologies, nutraceuticals, cosmeceuticals, food processing, environmental technologies, biomedical devices, biomedical imaging biomedical engineering, cell biology, neuroscience, genetics, proteomics and tissue engineering. Patents pertaining to biotechnology inventions have been sought for over 150 years. For example, on 29 July 1873, Louis Pasteur patented his yeast-making method at the French Patent Office. On 26 June 1969, the fledgling company Badische Anilin & Soda Fabrik (BASF) filed a British patent for a synthetic process for producing the red dye alizarin, a red dye derived from the madder plant root, for use in manufacturing cotton-based textiles. Subsequently BASF obtained patents for the syntheses of methylene blue and eosin dyes, as well.

More recently, from 1992 to 2015, the United States Patent and Trademark Office issued 166,189 patents on biotechnology inventions[1], 210,992 patents on medical devices[2], and 82,238 patents on nucleotide and amino acid sequences[3]. In the biotechnology field, alone, patents granted in the United States grew at a rate of 15% per year from 1990 to 2000, which is a 300% growth rate when compared to the 5% annual growth rate in overall patent grants during the same period.

The enterprise value of patents for life sciences companies cannot be understated. Simply put, patents are the driving economic force underpinning the growth of life sciences technologies. The lifeblood of pre-revenue life sciences companies is typically investment capital. Investment capital is typically dependent upon the nature and scope of the patent portfolio created by the company. The investment capital supports the research and development, which, in turns creates new inventions that enhance the patent portfolio and enterprise value of the company. Life sciences industries typically have the highest percentage of spending on research and development of total revenue. For example, in 2016, the pharmaceutical and biotechnology industries spent approximately 15% of revenue on research and development. In 2017, pharmaceutical companies alone spent 21.4% of revenue on research and development[4].

David G. Rosenbaum

> ***The enterprise value of patents for life sciences companies cannot be understated.***

Life sciences companies are faced with a minefield of uncertainty in protecting their increasing R&D expenditures with patents. This uncertainty has largely been the result of changes in the landscape of patent-eligible subject matter in the United States. In the United States, patent subject matter eligibility of life science-related patents under 35 U.S.C. §101 has been called into question by certain decisions from the United States Supreme Court and follow-on decisions of the United States Court of Appeals for the Federal Circuit. Issues surrounding patent subject matter eligibility have primarily affected patents having composition of matter and/or method claims.

Composition of matter patent claims

Patent claims directed to compositions of matter are generally filed for drugs or vaccines, including those derived from combining different genetic material. Examples are patents pertaining to insulin, human growth hormone, erythropoietin and the like. Composition of matter patents appear at the heart of the controversy concerning patent eligible subject matter in the biotechnology and pharmaceutical fields.

In *Association for Molecular Pathology v. Myriad Genetics, Inc.* 569 U.S. 576 (2013), the U.S. Supreme Court evaluated the patentability of patent claims directed to "an isolated DNA coding for a BRCA1 polypeptide, which has the amino acid sequence set forth in SEQ ID No. 2". 569 U.S. at 584. The Court concluded that the patent claims were drawn to ineligible subject matter under 35 U.S.C. §101, finding that "the location and order of the nucleotides [comprising the BRCA1 and BRCA2 genes] existed in nature before Myriad found them. … Myriad's principal contribution was uncovering the precise location and genetic sequence of the BRCA1 and BRCA2 genes … separating that gene from its surrounding genetic material is not an act of invention". 569 U.S. at 590-91. Other claims directed to BRCA cDNA were, in contrast, were found to be patent eligible subject matter because they related to "creation of a cDNA sequence from mRNA results in an exons-only molecule that is not naturally occurring" 569 U.S. at 594-95.

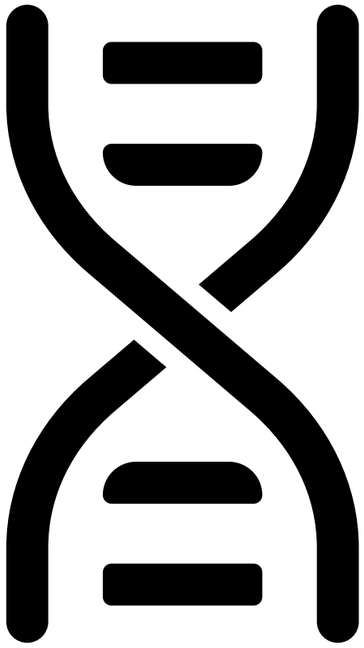
Applying the reasoning of the Myriad Court, the United States Court of Appeal for the Federal Circuit, the appellate court having exclusive jurisdiction over patent appeals in the United States, addressed claims directed to "[a] pair of single-stranded DNA primers for determination of a nucleotide sequence of a BRCA1 gene by a polymerase chain reaction … wherein the use of said primers in a polymerase chain reaction results in the synthesis of DNA having all or part of the sequence of the BRCA1 gene". The Court found that the claimed primers are "necessarily … structurally identical to the ends of DNA strands found in nature" and held the patent claims to cover patent ineligible subject matter. In re BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litig., 774 F.3d 755 (Fed. Cir. 2014).

[1] United States Patent and Trademark Office, Patent Technology Monitoring Team Report 1/1/1996 to 12/31/2015.
[2] Id.
[3] United States Patent and Trademark Office, Patent Technology Monitoring Team Report 1/1/1992 to 12/31/2013.
[4] Dunn, A., BioPharma Dive, August 13, 2018.

Résumé

David G. Rosenbaum

David has developed an extensive intellectual property law practice representing a wide spectrum of clientele from start-ups to Fortune 500 corporations in intellectual rights procurement, product development, handling transactions and strategic litigation. He counsels clients in complex intellectual property matters and supervises due diligence and positioning reviews for licensing, mergers and acquisition and strategic product development, all with the result of building and enhancing value of clients' intellectual property assets. Mr. Rosenbaum has represented clients in well over a thousand domestic and foreign patent applications and has successfully represented companies in generating over $17 Billion in value from merger, acquisition, licensing and litigation activities.



Method patent claims

Patent claims that are directed to methods or processes relate to the steps by which something is manipulated, synthesized, extracted or purified. For example, a process claim may pertain to a method by which a gene is extracted or manipulated or a process by which a drug is synthesized or administered.

In 2012, the *United States Supreme Court in Mayo Collaborative Servs. v. Prometheus Labs Inc.* 566 U.S. 66 (2012) evaluated the validity of patent claims directed to methods of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder comprising: (a) administering the drug 6-thioguanine to a subject with such disorder; and (b) determining the level of 6-thioguanine in said subject; and further recited that where the level of 6-thioguanine is less than about 230 pmol per 8×108 red blood cells, this indicates a need to increase the amount of the drug being administered and where the level is greater than about 400 pmol per 8×108 red blood cells, this indicates a need to decrease the amount being administered. In finding that the claims at issue were invalid as being directed to patent ineligible subject matter pertaining to a law of nature, the Court found that the claims "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 harm … The relation is a consequence of the ways in which thiopurine compounds are metabolized by the body – entirely natural processes". 566 U.S. at 77.

The Mayo Court extended their analysis to address the question whether the patent claims "add enough to their statements of the correlations to allow the processes they describe to qualify as patent-eligible processes that apply natural laws...." In finding that the subject claims did not describe a process that apply natural laws, the Court held that the claims were also invalid as failing to meet this standard. The Mayo Court held that the "claims inform a relevant audience about certain laws of nature; any additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community … For these reasons we believe that the steps are not sufficient to transform unpatentable natural correlations into patentable applications of those regularities" 566 U.S. at 79-80.

With respect to diagnostic method claims that only include steps for identifying a characteristic or disease in a patient, courts have found these to be almost uniformly patent ineligible. Treatment method claims, particularly those including method of pharmaceutical treatment, are at risk as well on the theory that all treatments are based upon a law of nature. Method of treatment claims, whether with or without a diagnosis step, have fared better, but some district court decisions have found such claims ineligible or, at least, "directed to" ineligible subject matter. In the process, these courts have fueled concerns of some in the pharmaceutical industry who fear nearly all pharmaceutical method of treatment claims could be at risk because, at some level, all treatments are based on natural phenomenon[5].

Recent efforts to clarify subject-matter eligibility

The United States Patent and Trademark Office has recently addressed subject-matter eligibility conundrum created by the Courts and made efforts to clarify subject matter eligibility for patent examination purposes (the "Guidance"[6]). In response to the Mayo decision, patent examiners have been directed to consider whether a claim covers patent-eligible subject matter under 35 U.S.C. §101 employing a three-step analysis:

Step 1. Is the claim directed to a process, machine, manufacture of composition of matter? If the answer is no, the claim is not deemed patent eligible and should be rejected. If the answer is yes, the analysis proceeds to step 2.

Step 2. Step two is a two-part analysis to determine whether a claim that is directed to a judicial exception recites additional elements that constitute significantly more than the judicial exception, i.e., claim significantly more than a law of nature, natural phenomenon or abstract idea. As it relates to the Life Sciences, laws of nature or natural phenomenon include naturally occurring principles, such as physical, chemical or biological principals, naturally occurring substances, or substances that do not have markedly different characteristics compared to what occurs in nature. Examples of these include, an isolated DNA, a correlation that is the consequence of how a compound is metabolized, or a chemical principle underlying the union between fatty elements and water.

Step 2A. Is the claim directed to a law of nature, natural phenomenon, or abstract idea? If no, the claim is deemed patent eligible and examination should continue for patentability based upon other statutory grounds. If yes, the Examiners are directed to proceed to Step 2B.

Step 2B. Are any element or combination of elements in the claim sufficient to ensure that the claim amounts to significantly more than the judicial exception? If no, the claim is deemed patent ineligible. If yes, the claim qualifies as eligible subject matter and patentability of the claim is determined on other statutory grounds.

As it relates to method claims, the new Guidance includes a "treatment/prophylaxis" consideration under which a patent claim may integrate a judicial exception (a law of nature, natural phenomena or abstract idea) into a practical application by applying or using it to effect a particular treatment or prophylaxis for a disease or medical consideration. By allowing patent applicants to claim a combination of a judicial exception and a practical application of it to a particular treatment or prophylaxis, the Guidance is consistent with the second consideration espoused by the Mayo Court, as discussed above.

What lies ahead?

Unfortunately, while the Guidance offers directive to patent examiner examining patent applications consistent with the current jurisprudence surrounding patent eligibility, it does nothing to reform either that jurisprudence or the statutory framework for determining patent eligibility. Concerted and largely cooperative efforts are being made by industry, the legal community, the legislature and the U.S. Patent and Trademark Office to address the uncertainty interjected by recent judicial decisions on patent subject matter eligibility. The Senate Judiciary Committee recently held hearings about "The State of Patent Eligibility in America", focusing on potential reforms to 35 U.S.C. § 101. The hearings centered on a draft bill introduced by Senators Chris Coons (D-DE) and Thom Tillis (R-NC) in May 2019, as part of a bipartisan effort to reform U.S. patent law. The draft bill, which has bipartisan support, came after months of discussions with stakeholders, industry representatives, and individual inventors who aim to clarify patent law surrounding patent subject matter eligibility.

It is clear that patent law reform on this issue is both underway and garnering a high degree of momentum. For the time being, however, those of us in the Life Sciences, must continue to account for the present state of uncertainty in evaluating what patent applications to file, how to frame claims in those patent applications, evaluate the validity of already issued patents under the current framework, and assess how the current framework of patent eligibility affects any patent enforcement strategy.

[5] See, Comments of the Pharmaceutical Research and Manufacturers of America (PhRMA), www.uspto.gov/sites/default/files/documents/comments_PHRMA_Jan182017.pdf at 5-6, citing Endo Pharmaceuticals v. Actavis, Inc., No. 14-1381, (D. Del. Nov. 17, 2015), aff'd, No. 2018-1054 (Fed. Cir. 2019).

[6] 2019 Revised Patent Subject Matter Eligibility Guidance (84 Fed. Reg. 50, 2019) and the October 2019 Update: Subject Matter Eligibility, https://www.uspto.gov/sites/default/files/documents/peg_oct_2019_update.pdf.

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Plant protection in Europe: seeds of discord?

Dr Penny Gilbert, Partner, and Dr William Hillson, Associate, Powell Gilbert LLP look at the tensions and controversies caused by the thorny issue of European plant IP rights.

Europe has long had an ambivalent relationship towards the biotechnology sector, at times seeming to give with one hand and take with the other. In a continent where many countries take pride in their agricultural traditions and there is frequently a deeply felt connection between food production and national identity, the issue of intellectual property protection for innovations in plant modification and cultivation have proven particularly contentious. In recent years the debate over the proper scope of plant patents, plant variety rights and the safety of new gene editing technologies have all found their way before European courts. While both biotechnology restrictionists and liberalizers have scored important recent victories, as we shall see, the final outcome remains far from certain.

Dr Penny Gilbert

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How a tomato divided the EU and the EPO

While the European Union (EU) and the European Patent Organization (EPO) both have their origins in a common project of European harmonization, they remain separate organizations and do not always see eye-to-eye. Rarely has this been more starkly illustrated than in the ongoing controversy over the patenting of "products of essentially biological processes", which has recently seen the President of the EPO take the extraordinary step of appealing to the EPO's highest tribunal against a decision taken by its own judicial officers. The situation is a serious one for the agricultural and biotechnology sectors – for what is ultimately at stake is a key provision of the European Patent Convention (EPC), the EPO's "constitution" and governing treaty for patents throughout much of Europe.

The controversy stems from a series of vegetable-related patentability decisions by the EPO, starting in the joined cases Broccoli/Tomato II and most recently in Syngenta (dark green peppers). These concerned the interpretation of Article 53(b) EPC, which prohibits the patenting of multicellular plant or animal varieties (though not micro-organisms) as well as "essentially biological processes", language which is mirrored in the EU's own Biotech Directive. The EU (and most commentators) had for many years assumed that this meant that the products of such processes, as well as the processes themselves, could not be patented. However, following the decision in Broccoli/Tomato II, the EPO has taken a different, more literal approach, in which the products are patentable, but the processes are not. This distinction is not mere wordplay, for if maintained it would have the effect of significantly liberalizing European patentability rules by allowing (in principle) the patenting of an organism obtained by conventional cross-breeding.

This development has not gone unchallenged, with the EPO being censured by the European Parliament and, in part due to pressure from the European Commission, changing its own interpretive rules to explicitly rule out the patenting of products of "essentially biological processes", only for their rule change itself to be held incompatible with the EPC by the EPO's own tribunals. The EPO President's latest appeal can be seen as an attempt to reverse this decision and bring the EPO into line with the EU's preferred interpretation of Article 53(b). If it fails, the only remaining recourse would be to amend the wording of the EPC itself, a challenging prospect given that it would require a Conference of the EPC's members (which include countries that are not members of the EU) and a vote by three quarters of them in favor. For these reasons, the outcome of the EPO Enlarged Board's review of the issue may be the final straw in the argument for the foreseeable future.

The CJEU's decision on gene editing – natural evolution or an aberrant mutation?

One of the biggest risks of codifying restrictions on new technologies in legal texts is that they may be rendered inadequate (or be circumvented entirely) by subsequent developments in technology, as alternative avenues are opened up by new discoveries. The CJEU (the EU's highest court) recently had to grapple with one such issue in case C-528/16. It was asked to decide whether modern gene editing techniques (such as CRISPR/Cas9) should be encompassed within the EU's stringent restrictions on Genetically Modified Organisms (GMOs), which were originally designed to regulate the older "transgenesis" techniques involving the direct transfer of genetic material from one organism to another.

A coalition of anti-GMO organizations had argued that it should be subject to stringent

Résumés

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regulation, even though the edited organisms produced were in many cases indistinguishable from mutations that could have occurred naturally. The French government argued that, instead, it should be classed under an exemption to the regulations as a form of "mutagenesis", itself a somewhat outdated provision that was originally drafted to encompass wholly random techniques of inducing mutations such as irradiating or chemically treating DNA. The CJEU was therefore put in the position of having to place a new technology within one of two legal categories, neither of which had been designed with systems like CRISPR in mind.

To the shock of many observers, the CJEU sided with the anti-GMO groups, holding that the "mutagenesis" exemption could only be used for long-established technologies with proven safety records. What is most extraordinary about this judgment is that it was not based on any assessment of the scientific evidence about the relative risk of the new, targeted gene editing methods versus older random techniques, but rather on a generalized "precautionary" approach which presumes that all new biotechnology developments are potentially harmful unless proven otherwise. As the CJEU is the EU's highest constitutional court, this represents a decisive and potentially long-term victory for GMO restrictionists, which is likely to chill investment or even force researchers to conduct their activities elsewhere (leaving aside practical concerns about whether the decision will even be enforceable, given that many gene-edited organisms cannot be distinguished from natural mutants). Of course, the Directive on GMO regulation itself could be amended, but given the many other tasks currently on the EU's plate, this seems unlikely to happen any time soon.

Forbidden fruit and plant variety rights

In the shadows of the headline-generating debates over plant patenting, it is sometimes easy to lose sight of the fact that the EU operates, unlike many areas of the world, a standalone intellectual property right to protect plant cultivars, known as a Plant Variety Right (PVR). Representing a different model of incentivizing innovation, which could potentially avoid some of the concerns raised regarding the patent system, PVRs provide something many patentees probably wish they could have - monopoly rights over a new plant variety for up to 30 years following grant, rather than following the application. However, there is a catch – unlike patents, PVRs explicitly allow the cultivation of protected varieties in order to develop new varieties – an exception which, while conceptually similar to the various types of "research exemption" in patent law, is broader in scope.

> ***The issue of intellectual property protection for innovations in plant modification and cultivation have proven particularly contentious.***

Perhaps due to this greater flexibility, there has been surprisingly little case law from the CJEU on the limits of PVRs, making its upcoming decision in C-176/18 eagerly anticipated. The case concerns the question of whether a farmer who purchased and planted clementine tree saplings that were, at the time, the subject of a PVR application subsequently infringed the granted PVR by selling the fruits from those trees. The EU Advocate General's (non-binding) recommendation to the CJEU is that such acts do not infringe the PVR. First, because the legislative history of the provisions show that the drafters did not intend the growing and harvesting of fruits to require authorization from the right-holder. Secondly, and more controversially, because the monopoly protection of the PVR only takes effect after it has been granted (with the holder being entitled only to after-the-fact compensation for acts done while the application was pending). Although the CJEU often follows the reasoning of the Advocate General, this is not always the case (a notable exception was the gene editing case discussed above), and it is to be hoped that the CJEU will provide some long-overdue clarification as to the scope of these important but often-overlooked rights.

The future – a need for root and branch reform?

As the above cases illustrate, developments in biotechnology applied to plants (especially food-bearing crops) remain an area of intense controversy in Europe, intertwining with broader concerns about food security, globalization and corporate power. It seems likely that there will be further legal challenges and, most likely, the need for modernized legislation before a durable consensus can be reached on these issues. But it is worth remembering that in such situations, there is only so much that the law can achieve. The questions of what developments in technology we should or should not allow, and the proper extent of the privileges granted to their developers, are deeply political, and ethical, ones and it is ultimately in the court of public opinion that they will find their resolution.

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Precision medicine in Taiwan

Mr. Yu-Li Tsai and Mr. Lu-Fa Tsai of Deep & Far Taiwan look at a recent memorandum of understanding between the Taiwanese National Health Research Institutes and Swiss healthcare giant Roche.

Aiming at supporting the precision medicine trend in Taiwan, the National Health Research Institutes and Roche signed a memorandum of understanding (MOU) on 14 November 2019. The two parties will cooperate to promote comprehensive genomic profiling, establish personalized medical medication mechanisms, and establish a national health and medical gene database, etc., so as to accelerate the integration of Taiwan's biotechnology and medical industry into the international market.

The MOU was signed by President Liang, Geng Yi of the National Health Research Institutes and General Manager Xu, Yan Ling of Roche Pharma Taiwan, in the witness of Minister Chen, Shi Zhong of the Ministry of Health and Welfare and Vice President Ron Park of Global Personalized Healthcare of Roche Pharma.

In the future, Roche will devote their resources to supporting specific cancer patients via comprehensive genomic profiling, and will work with the National Health Research Institutes in the following four directions:

Mr. Yu-Li Tsai

Mr. Lu-Fa Tsai

> ***The two parties will cooperate to promote comprehensive genomic profiling, establish personalized medical medication mechanisms, and establish a national health and medical gene database.***

Résumés

Mr. Yu-Li Tsai

Mr. Yu-Li Tsai received a Bachelor's degree from the Department of Electrical Engineering of the National Taiwan University (NTU) and a Master's degree from the Graduate Institute of Communication Engineering of NTU. He also received an IP Master's degree from UNH Law and the Franklin Pierce Center for Intellectual Property. Right after the graduation, he had an opportunity to work for InterDigital, Inc. in Delaware for a short period. He is concurrently majoring a law master in National Chiao Tong University. Mr. Tsai received the qualification of Taiwan Patent Attorney and China Patent Agent. He also passed US and Examination.

Mr. Lu-Fa Tsai

Mr. Lu-Fa Tsai, an attorney-at-law graduated from the Department of Law of National Taiwan University (NTU), which is the best law school in Taiwan. Out of the interest in business law, he attended the Graduate Institute of Law of NTU after he had obtained the LL.B. degree and received his LL.M. degree after three years. One year before he graduated from the graduate institute, he passed the bar examination. Mr. Tsai has also gained an LL.M. degree from the Faculty of Law of the University of Göttingen in Germany. The field of study of this degree is international economic law. After he came back from Germany, he joined the Deep & Far Attorneys-at-Law. He is working as a partner lawyer at the firm currently.

(1) to promote comprehensive genomic profiling or popularization of the related testing of the kind, including accelerating the review of laws and regulations and the study of health insurance benefits, so as to meet the demand of precision medicine in the future;
(2) to establish the personalized medical medication mechanism to help cancer patients get the chances to use the corresponding treatment for genetic mutations;
(3) to establish a national health and medical gene database in the nature of sustainable development and to integrate it with other national health databases with the informed consent of the public, and to formulate the relevant norms for subsequent data release and industrial application; and
(4) to promote the use of real-world evidence as a reference for examination and registration and payment of health insurance benefits.

The National Health Research Institutes look forward to joint efforts of both sides to improve the quality of medical care for cancer patients and jointly create Taiwan's personalized medical ecosystem.

Through this collaboration, the National Health Research Institutes have demonstrated their longstanding capacity for both basic medicine and clinical research. They can combine Roche's leading advantages in medicine, biology and information science to create a quality environment for cancer patients, clinicians and overall medical care. It is hoped that the close cooperation between both parties will not only become an important model of international industry-academia cooperation, but also jointly drive the development of Taiwan's medical testing and new drug research industry, and create new opportunities for the future of Taiwan's precision medicine and biotech industry.

> ***There is a chance that Regenerative Medicine Act will come into force next year, which will encourage foreign companies to invest in Taiwan.***

A breakthrough for the treatment of advanced liver cancer after 11 years: how research conducted by a Taiwanese team shocked the international community

The ESMO Asia 2019 Congress was held in Singapore from 22-24 November 2019. There was a research publication for the latest therapy of advanced liver cancer. There was no empty seat at the venue and the audience crowded outside of the venue, which made the speaker himself unable to enter the venue. The reason for such a great sensation was that the research results to be published by the speaker represented a breakthrough after 11 years, i.e. it was found that if two drugs are used by combination, the effect will surpass the targeted drug of the standard therapy greatly.

The chief host for the global research who was almost unable to squeeze into the venue was the dean of the National Taiwan University Cancer Center, Mr. Zheng, An-Li, was the same person who published the targeted drug of the standard therapy 11 years ago. At this historic moment, it showed that Taiwan is not only the global pioneer for liver cancer prevention and control, but also stands firmly in the key position of adapting the international treatment guidelines in the aspect of treatment of liver cancer.

The Phase clinical trial held by Mr. Zheng, An-Li received a total of 501 liver cancer patients whose lesions could not be ablated. Part of the patients' first-line solely used the targeted drug of the standard therapy (sorafenib), and part of the patients used by combination the PD-L1 inhibitor of the immunotherapy (atezolizumab) and the targeted drug of the antiangiogenesis (bevacizumab).

After a long-term tracking and comparison of the two groups, it was found that the effect of the combination treatment was obviously better. The median of the survival periods of the standard therapy is 13.2 months, and some of the patients of the combination therapy are still alive. It can be said that the median of the survival periods of the combination therapy is still undetermined. In the aspect of the side effect, the rate of having serious adverse reaction for the patients of the combination therapy is only 5%, which is 1% lower than the standard therapy. The research shows that the combination therapy can not only extend life, but also defer the influence on the quality of life caused by the disease progression.

At present, the research on anti-cancer drugs is a global activity wherein the competition is keen. Only for advanced liver cancer, six types of drug combination are on trial, the results of which will be published consecutively next year, or the year after next. Zheng, An-Li indicated that after the targeted drugs of the standard therapy emerged, only two types of targeted drugs have proven able to be solely used on the first line in the recent years. Many people have tried to challenge this, but no new drug or new therapy has successfully surpassed the traditional targeted drugs. This was the first challenge for which immunotherapy drugs were used for the first-line combination therapy of advanced liver cancer, and it has succeeded.

Zheng, An-Li indicated that compared with other combination drugs, the PD-1 inhibitor of the immunotherapy and the targeted drug of the anti-angiogenesis published this time have a price advantage. This targeted drug of the anti-angiogenesis is an old drug (20 years), whose patent protection period is about to expire, and its biosimilars are about to come to market, so it is the cheapest combination at present. The PD-1 inhibitor of the immunotherapy is awaiting the US Food and Drug Administration's approval and is expected to rewrite the international guidelines for the treatment of liver cancer.

Zheng, An-Li indicated that Taiwan has Song, Rui-Lou, Chen, Ding-Xin and other international experts in liver disease research. He is in the mood for "standing on the shoulders of giants" to make an effort to transfer the research paradigm to the research of liver cancer treatment. The price of new drugs will fall in 10 or 20 years, but in the absence of the present research, there will be fewer options in the future, so the research cannot stop. He predicted that with the progress in the treatment of liver cancer, the decrease in the carriage rate of Hepatitis B and the eradication of Hepatitis C, liver cancer would gradually cease to be the "national disease" within 30 years.

The first case where a Japanese enterprise invested in biotech in Taiwan: CellSeed and MetaTech formed a joint venture company, Ri Sheng

There is a chance that the Regenerative Medicine Act will come into force next year, which will encourage foreign companies to invest in Taiwan. A Japanese company, CellSeed Inc. (CellSeed), and a Taiwanese company, MetaTech (AP) Inc. (MetaTech), announced on 6 December 2019 that they had jointly founded a company called "Ri Sheng Cell Biotech Inc." (Ri Sheng) and retain the former deputy dean of the Academia Sinca, Wang, Hui-Jun, to be the chairman. The cell sheet technology developed in the future will be owned by Ri Sheng. The patented technology can be licensed and used for commercial operation. This is the first time that a Japanese enterprise invested in the field of cell therapy in Taiwan. It is expected that the joint venture will lead the trend with the implementation of Regenerative Medicine Act.

The paid-in capital of Ri Sheng is NT$13 million. It will focus on the research and development of clinic application of various types of cell sheets. The first task is to cooperate with the dean of the E-DA Hospital, Du, Yuan-Kun. It will use nerve cell sheets from MetaTech and combine the unique operation skill created by Mr. Du (Du's operation skill) to form a regenerative therapy for brachial plexus or spinal cord injury.

Cellseed, a listing company in Tokyo, first licensed overseas the cell sheet technology for esophageal cancer and knee cartilage to MetaTech two years ago, and joint-founded Ri Sheng this year.

The chairman of MetaTech, Hu, Li-San, indicated that with respect to the future development of nerve cell sheets of Ri Sheng, it will be concentrated on the development of the nerve cell sheets applied to the peripheral nervous system at the initial stage, whose indications include radial joint syndrome, stroke hemiplegia etc. The long-term goal will be the development of the nerve cell sheets applied to the central nervous system, which are used to treat syndromes such as spinal cord injury. As MetaTech owns the complete manufacture technology of cell sheets, it can contract with Ri Sheng for the manufacture of cell sheets.

The chairman of CellSeed, Mr. Hashimoto, indicated that CellSeed has successfully developed seven cell sheet products which obtained the marketing approval from the Japanese PMDA. With the progress of laws and regulation in Taiwan, Ri Sheng will combine the strengths of MetaTech and CellSeed and integrate the power of the academic communities in Japan and in Taiwan to jointly develop new clinic applications of cell sheet engineering to regenerative medicine. The new clinic applications will also be promoted to the regions in Asia other than Taiwan so as to satisfy more potential markets with unsatisfying medical needs.

The dean of the E-DA Hospital, Du, Yuan-Kun, indicated that he has been devoted to precise blood vessel and neural rehabilitation for the past 30 years and has achieved a dozen breakthroughs for the purposes of providing a new therapy for patients with spinal cord injury. The chances of success for brachial plexus rehabilitation were only 10% in the past. They are now raised to 85% by means of Du's operation skill, but 15% of patients are still unable to recover. Du anticipates that by cooperating with Ri Sheng, the subsequent combination of medicine and science will help bring hope to the hopeless.

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Protection of plant inventions in Mexico

Janett Lumbreras, Senior Associate, Uhthoff, Gomez Vega & Uhthoff S.C,

looks in detail at an increasingly important area of IP protection.

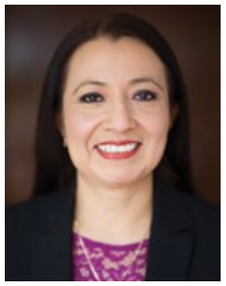
The development of biotechnology, in particular genetic engineering, has made it possible to design and subsequently create new plant varieties instead of using traditional techniques, such as crossing and selection. While it is possible that the well-known crossing or selection techniques cannot qualify for patent protection, new plant varieties created by genetic engineering can increase the likelihood that new plant varieties meet the requirements of novelty and inventive activity. Some advantages of the new plants are the following:

- improved resistance to drought or other adverse climate conditions;
- lower nutrient requirements;
- seed-resistance to certain pests, which would reduce the use of, and expenditure on pesticides, and which would also mean less environmental impact;
- increased photosynthetic performance;
- improved quality of agricultural products; and
- food with greater nutritional characteristics than those of natural species.

However, when new plants are created, some disadvantages may arise:

- loss of biodiversity;
- displacement of genes to conventional crops or related wild varieties that pollinate by wind, insects, birds, etc.;
- reduced antibiotic efficiency: by making plants resistant to pests, resistance to diseases and viruses is indirectly generated;
- increased chemical contamination, for example, with herbicide-tolerant plants, farmers might feel free to use larger amounts of herbicides to get rid of other species; and
- increased insecticidal abilities threaten the existence of species, for example that of the monarch butterfly.

These and other relevant issues, along with the moral and ethical dimensions of the protection and commercialization of biotechnological inventions, have become topics of debate in several forums. Nevertheless, this should not hinder the advancement of science, specifically the field of biotechnology.



Janett Lumbreras

It is in our hands to establish a strong and suitable legal framework that maintains an equilibrium between the benefits and side effects of new plant-related creations, while protecting at the same time the rights of innovators in this matter.

International legal framework for patenting plants in Mexico

Now then, in view of the interrelationship between plant patents and plant varieties protection, it should be clarified to the innovators which would be the appropriate way of protecting their creations. This means: which of the two would be the best option for them, which requirements must be complied with, and what is the scope of protection in each case? The table (left) can help to see the differences between both legal forms.

DIFFERENCES BETWEEN PLANT PATENTS AND PLANT VARIETIES

	PLANT PATENTS	PLANT VARIETIES
REQUIREMENTS	- novelty, - inventive step, and - industrial applicability	- novelty, - distinctiveness, - uniformity, and - stability
EXCEPTIONS	- must not be the result of an essentially biological method, - must not be a plant variety, and - for practical purposes, there must be a genetic manipulation	- there should be no genetic manipulation, - wild/natural species not improved by man are excluded from protection
VALIDITY	20 years	15 years minimum
SCOPE	claims	propagation material (seeds)
GOVERNMENT OFFICE	Mexican Institute of Industrial Property (IMPI)	National Seed Inspection and Certification Service (SNICS)
LEGISLATION	Mexican Industrial Property Law	Federal Law on Plant Varieties

The main international legal framework considered for patenting plants in Mexico includes the following:

Paris Convention

The Convention of the Paris Union for the Protection of Industrial Property of 1883 (CPU), of which Mexico is a party, is an instrument that harmonizes intellectual property rights worldwide.

The Paris Convention does not regulate the exclusions of patentable matter. However, Article 1, Section 3 states that:

*Industrial property shall be understood in the broadest sense and shall apply not only to industry and commerce proper, but likewise to agricultural and extractive industries and to **all** manufactured or **natural products**, for example, wines, **grain, tobacco leaf, fruit,** cattle, minerals, mineral waters, beer, **flowers,** and flour.*

TRIPS (Trade Related Aspects of Intellectual Property Rights)

Section 5 of Part II of the TRIPS Agreement is dedicated to Patents. This section stipulates that countries must grant patents for inventions (of products and processes) in all fields of technology, provided that the inventions are new, involve an inventive activity, and are capable of industrial application.

The TRIPS Agreement in Article 27 paragraph 3.b states that Members **may also exclude** from patentability:

- plants and animals except microorganisms, and
- essentially biological procedures for the production of plants or animals, other than non-biological or microbiological procedures.

However, Members shall provide for the protection of plant varieties either by patents, by means of an effective sui generis system or by a combination thereof.

Sui generis system

It is known that plant varieties have a specific protection system established by the International Convention for the Protection of New Varieties of Plants, signed in Paris on 2 December 1961, successively amended in 1972, in 1978 and in 1991. This Agreement creates the Paris Union on Plant Varieties (UPOV) and obliges signatory States to protect plant varieties. Thus, on the basis of the 1978 Act of this Agreement, in October 1996, the Federal Plant Variety Law in Mexico entered into force granting a breeder's right to those who obtain a plant variety, provided that it meets the novelty, distinction, homogeneity, and stability requirements.

Wild/natural species that were not improved by man are excluded from protection.

The rights are granted to varieties that are new, distinct, uniform/homogeneous, and stable.

The scope of the term **"plant"** in the context of TRIPS has been extended to include protection of plants, algae, and mushrooms; bacteria and viruses are not included within this scope, however.

USMCA (United States-Mexico-Canada Agreement)

The recent Agreement between United States, Mexico, and Canada includes in its Article 20.F.1 the considerations for patentable subject matter regarding plants. It states that:

1. Subject to paragraphs 3 and 4, each Party shall make patents available for **any invention**, whether a **product** or **process**, in all fields of technology, provided that the invention is new, involves an inventive step, and is capable of industrial application.
2. Subject to paragraphs 3 and 4 and consistent with paragraph 1, each Party confirms that patents are available for inventions claimed as at least one of the following: new uses of a known product, new methods of using a known product, or new processes of using a known product.
3. **A Party may exclude from patentability** inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect public order or morality, including to **protect human**, animal, or plant life or health or to **avoid serious prejudice to nature or the environment**, provided that such exclusion is not made merely because the exploitation is prohibited by its law. A Party may also exclude from patentability:
   (a) diagnostic, therapeutic, and surgical methods for the treatment of humans or animals;
   (b) animals other than microorganisms, and **essentially biological processes for the production of plants** or animals, **other than non-biological and microbiological processes.**
4. A Party may also exclude from patentability plants other than microorganisms. However, consistent with paragraph 1 and subject to paragraph 3, each Party confirms that patents are available at least for inventions that are derived from plants.

Mexican practice

In Mexico, plant protection could be requested via a patent

Résumé

Janett Lumbreras

Janett has a Pharmaceutical Chemistry-Biology Degree, from Universidad Nacional Autonoma de Mexico (UNAM), Mexico City, 1996, and has Diplomas in Access to Worldwide Scientific and Technological Information from Universidad Nacional Autonoma de México (UNAM), 2003; Industrial and Intellectual Property Law from Universidad Nacional Autonoma de México (UNAM), 2005; and Introduction to the UPOV System of Plant Variety Protection under the UPOV Convention from WIPO Worldwide Academy, 2007. Janett Lumbreras began her practice at Uhthoff, Gomez Vega & Uhthoff, S.C. in the Patents department in 2000. She is an active member of the Mexican Association for the Protection of Intellectual Property (AMPPI); the American Intellectual Property Law Association (AIPLA); National College of Pharmaceutical Chemists Biologists, Mexico, A.C. (CNQFBM, A.C.). Her practice Areas are in Chemistry, Pharmacy, and Biotechnology.

according to the Mexican Legislation of 1991, and via a plant variety based on the Plant Varieties Law based on UPOV 1978 which was established in 1996 for the protection of plant varieties.

Protection of plants by patent

The Mexican Industrial Property Law in Article 16 thereof states that inventions that are new, the result of an inventive activity, and susceptible of industrial application, shall be patentable, in the terms of this Law, except:

I. **essentially biological processes for obtaining, reproducing, and propagating plants and animals;**
II. biological and genetic material as found in nature;
III. animal breeds;
IV. the human body and the living parts constituting it; and
V. **plant varieties.**

For a better understanding of the exceptions of Article 16, it is necessary to define some crucial terms as **"essentially biological processes"** and **"step of a technical nature"**.

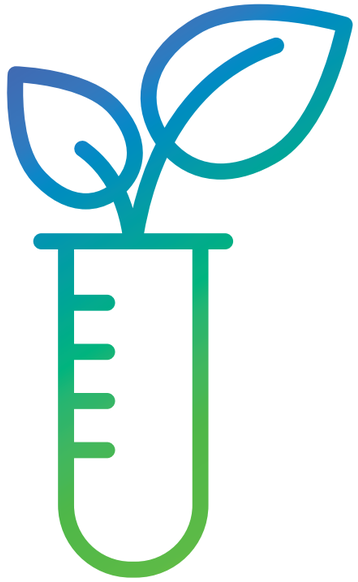
An **essentially biological process** for the production of plants encompasses a method which contains or consists of the steps of sexually crossing the whole genomes of plants and of subsequently selecting plants. Such a method would be considered an essentially biological process even if the method also contains a **step of a technical nature** which serves to enable or assist the performance of the steps of sexually crossing. However, if the method contains an additional step of a technical nature, which by itself introduces a trait into the plant genome or modifies a trait in the genome of the plant produced, so that the introduction or modification of that trait was not the result of the mixing of the genes of the plants chosen for sexual crossing, then the method would not fall under the patentability exception of Article 16.

In a **step of a technical nature** there is an indispensable human intervention, without which the final result would be different. For example, a process of production and propagation of transgenic plants is a step of a technical nature even if it includes traditional biological stages. A process for the production of plants and animals that includes at least one technical step, which cannot be carried out without the intervention of man and that has a decisive impact on the final result, will not fall within this patentability exception.

For example, if the process contains crossing and selection steps, and an additional stage of a technical nature (genetic engineering) that induces a trait of interest in the genome or modifies the trait in the obtained plant, in such a way that this introduction or modification of the feature of interest is not the result of sexual crossing, **both the method and the plant obtained through it would not be excluded and could be patentable.**

What can be protected?

1. Genetically modified plants by introduction of exogenous genetic material (transgenic plants).
2. Genetically modified plants by directed genetic modifications without introduction of exogenous genetic material.
3. Genetic engineering methods for introducing new traits into plants or animals, etc.



What is excluded?

1. Genetically modified plants by physical or chemical means, due to lack of reproducibility.
2. Breeding methods for plants or animals which contain steps of crossing and selection.
3. Marker-assisted breeding of animals or plants, etc.

Examples of patentable claims

1. A glyphosate resistant corn plant that comprises in its inserted genome the 5-enolpiruvil-3-fosfoshikimato synthase gene from SEQ. ID NO. 4.
2. A genetically modified plant comprising the mutated SHS gene of chloroplast.
3. A drought-resistant monocot plant that comprises the FIS gene (SEQ ID NO. 1) of Selaginella.
4. Method of producing a (transgenic) plant having trait X by introducing a vector comprising the sequence of SEQ ID NO: 1.
5. A plant having stably incorporated into its genome the expression cassette of claim 1, wherein said nucleotide sequence is operably linked to a heterologous nucleic acid of interest.
6. Method for the production of plants with character X comprising crossing plants A (transgenic) and B (transgenic), and selecting progeny with Marker X.
7. Use of the nucleic acid of SEQ ID NO: 1 to select a plant having trait X.

A plant variety is not patentable even if it is genetically modified. However, if it is described as a whole plant, it could be patented.

Examples of claims excluded from patentability

1. Method for the production of plants that have trait X that comprises crossing plants A and B, and selecting the progeny that has the marker X.
   Method for obtaining glyphosate resistant plants comprising:
   a) ***crossing*** *the plants that contain the characteristic FRI8017 with wild corn plants;*
   b) reproducing these plants by ***crossing and selection****;*
   c) ***propagating*** *resistant plants.*
2. Introgression of an X (transgenic) trait into a plant.
   Method for providing a Solanum lycopersicum plant with improved yield, said method comprises ***introducing*** *into the genome of said Solanum lycopersicum plant the SP3D and SP3 gene, or at least the promoter sequence thereof, of Solanum pennelli or another Solanum species selected from the group consisting of Solanum neorickii, Solanum chmielewskii, Solanum chilense, Solanum parviflorum, Solanum pimpinellifolium and Solanum peruvianum.*
3. Method for the production of plants having trait X comprising crossing plants A (transgenic) and B (wild), and selecting progeny having marker X.
4. A plant characterized by new genetic markers (without claiming the essentially biological method).
5. Methods for plant breeding comprising the step of embryo rescue.
6. Parts of the plant obtained by an essentially biological method without claiming the method.

Conclusion

Plant variety protection of (a) specific plant varieties and plant patents; and (b) plants at a more generic level, have co-existed for decades in Mexico.

Now, if a process of sexual crossing and selection includes within it an additional step of a technical nature, which by itself introduces a trait into the genome or modifies a trait in the genome of the plant produced, so that the introduction or modification of that trait is not the result of the mixing of the genes of the plants chosen for sexual crossing, then that process leaves the realm of the plant breeding and, consequently, is not excluded from patentability. This principle applies only where the additional step is performed within the steps of sexually crossing and selection, independently from the number of repetitions.

Otherwise, the exclusion of sexual crossing and selection processes from patentability could be circumvented simply by adding steps which do not properly pertain to the crossing and selection process, being either upstream steps dealing with the preparation of the plant(s) to be crossed or downstream steps dealing with the further treatment of the plant resulting from the crossing and selection process. This will be the case for genetic engineering techniques applied to plants which differ from conventional breeding techniques, as they work primarily through the deliberate insertion and/or modification of one or more genes in a plant.

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Doing justice to chemical patents

Vladimir Biriulin, Partner and Head of Legal Practice at Gorodissky & Partners, discusses the application of term extensions to patented chemical compounds

Duration of a patent has long been a concern of each individual country. Ever since Filippo Brunelleschi invented in the 15th century a barge with hoisting gear and secured an exclusive privilege for three years for the use of same, the validity term of patents varied widely, until the WTO's TRIPs in modern times sought to harmonize national laws and set the term of twenty years. Article 33 of the TRIPs Agreement provided that "The term of protection available [for patents] shall not end before the expiration of a period of twenty years counted from the filing date". This agreement streamlined the duration of patents in many countries.

Vladimir Biriulin

As time went on, it became clear, however, that inventions for pharmaceuticals, agrochemicals and pesticides were an unloved child of intellectual property. The said patented chemical products need to obtain regulatory approval before they can go to the market. This may take years, thus shortening the duration of the patent and putting at a disadvantage patents in the chemical field.

To meet this challenge, some countries introduced a "patent term extension". In Russia, this took place in 2003 and the relevant provision was retained in all subsequent versions of the patent law. The patent law became part of the Civil Code as its Part IV in 2008. In 2014, the relevant provision was complemented in that a supplementary patent should be issued covering the extension period instead of an attachment to the existing patent.

In accordance with the amended patent legislation, a patent term extension is certified by a supplementary patent granted with the claims containing the combination of the features of the patented invention characterizing the product for which the marketing authorization has been issued.

This becomes a new patent with the revised claims and with the restricted scope of rights. The claims will characterize a specific product for the use of which the first marketing authorization was obtained. The said product is an active agent or a composition/combination of ingredients of the product that has undergone clinical trials and is permitted for use in Russia.

> ***"This extension provision proved to be quite workable and hundreds of patents were extended without a hitch."***

The procedure for patent term extension is regulated by Article 1363(2) of the Civil Code. It reads: "If from the filing date of an application for the grant of a patent for an invention relating to a medicine, a pesticide, or an agrochemical, the use of which requires a statutory approval, to the date of granting the first marketing approval more than five years passed, the duration of the exclusive right to the respective invention and the patent certifying this right shall be extended upon request of the patent holder by the federal executive authority for intellectual property".

The said term shall be extended for the period from the date of filing the patent application until the date of issue of first marketing authorization minus five years but for not more than five years.

The request for the extension of term is to be made by the patent owner during the period of validity of the patent before expiration of six months from the date when the first marketing authorization was obtained or from the date of grant of the patent depending on which term expires later.

This extension provision proved to be quite workable and hundreds of patents were extended without a hitch. There have been published a number of articles on extension of patents in this country, though for the most part they make it known that extension is possible and describe the procedure of how the patent owner may obtain extension. Sometimes the procedure is not that smooth. It is worthwhile to have a look at a snag encountered by one of the patent owners.

Gilead Pharmasset LLS, a US company, obtained patent No 2651892 dated 24 April 2018.

In June 2018, Gilead Pharmasset LLS applied to the patent office with a request to extend the term of validity of the patent but was refused. The applicant filed a complaint to the patent office against that decision but was refused again.

After that the company initiated a court action at IP court against the patent office seeking to overturn the negative decision of the patent office (case No СИП-740/2018).

The company argued that the disputed decision of the patent office is in contravention of Article 1363(2) of the Civil Code (see above).

It noted that marketing authorization had been obtained for the medicine Sofosbuvir. The patent office should have determined that the scope of protection according to independent Claim 1 corresponds to that medicine. This was not done by the patent office. The company argued that Sofosbuvir completely falls within the scope of independent Claim 1 as acceptable and possible alternative of the claimed compounds because Claim 1 covers Isopropyl Ester of Propionic Acid (Sofosbuvir) or its stereoisomer. This alternative is fully supported by the specification of the patent.

The patent office refused to accept that explanation, arguing that the active ingredient shown in the marketing authorization is not identical to the compound disclosed in Claim 1. The marketing authorization indicates that the active ingredient in the medicine is Sofosbuvir, a S-stereoisomer of propionic acid. In the meantime, the claim gives the same compound or its stereoisomer without indicating specifically what stereoisomers are meant.

In this connection, the patent office concluded that Sofosbuvir represents a particular stereoisomer characterized in Claim 1 and it is not identical to the active ingredient given in the marketing authorization. Because of this, extension of term of patent No 2651892 cannot be allowed.

Résumé

Vladimir Biriulin

Mr. Biriulin advises clients on Russian and foreign IP legislation, including international IP treaties, conventions, agreements and the peculiarities of their implementation in Russia, technology transfer, licensing, copyrights and elaborating efficient strategy of company intangible assets protection. His particular interest covers enforcement and infringement of IP owners' rights, unfair competition, parallel import and litigation.

In addition to that, the patent office argued that S-stereoisomer covered by the scope of Claim 1 is not specifically disclosed in the specification; the specification does not show that the compound was really produced and that it possesses the same activity that would allow the use as intended.

The IP court examined the arguments of both sides and stated that the patent office's decision is not based on law. According to the IP court the scope of protection of the invention according to Claim 1 extends to any stereoisomer of the composition, including to Sofosbuvir which is a S-stereoisomer. In fact, the scope of protection covers S- as well as R-stereoisomers.

The company did not ask for extension of all possible alternatives in Claim 1 but only in respect of a specific S-stereoisomer of compound, i.e. in respect of Sofosbuvir. The patent office does not deny that the combination of features proposed by the company is identical to the chemical formula of Sofosbuvir. The patent office does not deny that the combination of features proposed by the company is identical to the chemical formula of Sofosbuvir.

Thus, Sofosbuvir falls within the scope of protection of the invention in Claim 1, specifically in the part of the feature termed as "or its stereoisomer" as its admissible alternative.

The law does not impose limitations on the extension of patents' validity in respect of patent claims if these claims are constructed with the use of alternative concepts. Also, requirements to the patent documents provide that one independent claim may characterize several inventions-variants if they differ only by the features expressed as alternatives.

Furthermore, Rule 46 of Patent Regulations provides that when a group of inventions is being examined patentability is checked in respect of each invention. If a claim contains a feature expressed by several alternatives each combination of features should be checked. From this it follows that one claim may contain one combination of features or several combinations.

There are other rules that echo the above citations and all of them teach that a claim may be expressed through alternatives and each alternative may represent a separate combination of features of the invention.

Those rules were not respected by the patent office.

The specification of the patent reads that there are two possible stereoisomers: S-stereoisomer as well as R-stereoisomer which is reflected in Claim 1 by the words "or its stereoisomer".

Hence, the combination of features defining the scope of protection characterizing a compound or a group of compounds described by general structural formula should be the same as the active ingredient of the pharmaceutical and it may refer to the whole claim as well as to a specific combination of features if the claim contains several combinations of features (alternatives) and only one of the combinations shown in the feature corresponds to the active ingredient.

> ***Those rules were not respected by the patent office.***

There is a similar approach demonstrated by the Presidium of IP court in case No СИП-155/2014. Different interpretation of the regulations would entail unjustified impingement of rights of the patent owners because, as was mentioned above, there are no limitations for that in the law.

Another ground of refusal put forward by the patent office was that the patent office indicated that S-stereoisomer mentioned in Claim 1 is not disclosed, i.e. the specification does not show that the compound was indeed obtained and possesses the activity allowing it to use as claimed.

The court did not agree with this statement either. Contrary to assertions of the patent office isopropyl ester of propionic acid is disclosed in the specification, there is information to the effect that such composition was obtained and possesses the claimed activity.

Obtainment of such derivatives (stereoisomers) is a standard procedure; it is evident for the person skilled in the art that they maintain their properties and activity. Hence, obtainment of such derivatives without mentioning a specific example is a necessary and sufficient condition for that group of compositions to be protected.

The IP court put forward several other arguments proving that the decision of the patent office was not based on law and regulations and obliged the patent office to reconsider its decision and extend the validity term of the invention and issue a supplementary patent.

The above case is very much demonstrative of the skills of the judges of the IP court. The rules allow the court to engage experts in complicated cases however in this case the judges showed that they themselves are competent enough to examine complex chemical cases.

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Functionally-claimed antibody patent – the *Amgen v Sanofi* case

Osamu Yamamoto, patent attorney and partner at Yuasa and Hara, examines recent Japanese drug patent litigation.

While it is the case that inventions relating to small-molecule drugs can be sufficiently protected with claims based on their chemical structure, the same does not necessarily hold true for biomedicines. Namely, it may not be possible to obtain sufficient protection for a biomedicine with claims based on a chemical structure. This issue is of great importance, and a great deal of attention has been paid to different approaches in obtaining patents due to shifts in patent dispute and litigation centered around biomedicines following market saturation for small molecular drugs.

Amgen has developed the humanized anti-PCSK9 monoclonal antibody "evolocumab" and the drug "Repatha®" containing the monoclonal antibody for treating hypercholesterolemia. Amgen's two patents, JP 5,705,288 and JP 5,906,333, each of which is directed to a "monoclonal antibody against proprotein convertase subtilisin/kexin type 9 (PCSK9)", cover these products.

Sanofi developed and produced a different humanized anti-PCSK9 monoclonal antibody "alirocumab" and the drug "Praluent®" containing the monoclonal antibody for treating hypercholesterolemia.

Sanofi filed patent invalidation trials against Amgen's two patents at the Japan Patent Office (JPO) in 2016. Amgen filed a patent infringement lawsuit at the Tokyo District Court in 2017 seeking an injunction etc. against Sanofi's activity. One of the strongly contested issues was "whether patentability requirements are met, even if the claimed monoclonal antibodies are defined only by their functional features".

In invalidation cases, the JPO and the IP High Court (IPHC) admitted validity of the two patents. Further, in the infringement case, the Tokyo District Court and the IPHC admitted validity of the two patents and infringement of the patents. These cases merit close consideration in view of the implications of obtaining and enforcing a patent right for a pioneer antibody invention that is claimed with functional features. On the other hand, it is readily apparent that the existence of a patent with merely functional features will constitute a tremendous obstacle to those who develop subsequent antibody products.

In the following a summary of the key features of the cases is elucidated.

Osamu Yamamoto

Invalidation Trials and appealed IPHC Decision

The specification of the Amgen patents includes the disclosure of two reference antibodies named 21B12 and 31H4; the claims of the first divisional patent JP 5705288 (Patent 1) recites reference antibody 21B12, and the claims of the second divisional patent JP 5906333 (Patent 2) recites reference antibody 31H4.

Sanofi filed invalidation trials at the JPO against Patent 1, Invalidation Trial No. 2016-800004, on 18 January 2016, and against Patent 2, Invalidation trial No. 2016-800066, on 31 May 2016. In both cases, the reasons for invalidation asserted by Sanofi were each based on grounds of lack of support, enablement, and inventive step.

The JPO handed down decisions maintaining the Amgen patents based on corrected (amended) claims, on 10 August 2017.

Résumé

Osamu Yamamoto

Osamu Yamamoto is the acting Chief of the Chemical Section of the Patent Division of the firm. He has 19 years of experience in intellectual property, focusing on patents, including drafting patent applications, dealing with Office Actions, providing expert opinions, defending or attacking patent rights in invalidation trials and oppositions, and infringement litigation.

Claim 1 of the maintained Patent 1 reads as follows:

Claim 1: An isolated monoclonal antibody, which can neutralize binding of PCSK9 and LDLR protein, and which is competitive for binding to PCSK9 with the antibody including a heavy chain variable region consisting of an amino acid sequence shown as SEQ ID No. 49, and a light chain variable region consisting of an amino acid sequence shown as SEQ ID No. 23.

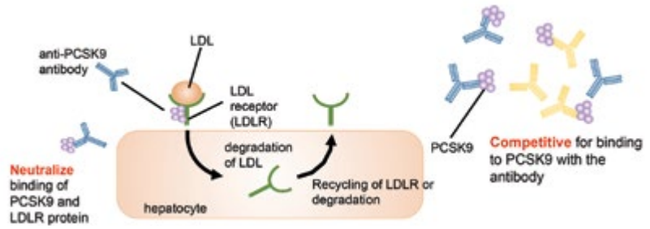
Claim 1 of the maintained Patent 2 reads as follows:

Claim 1: An isolated monoclonal antibody, which can neutralize binding of PCSK9 and LDLR protein, and which is competitive for binding to PCSK9 with the antibody including a heavy chain variable region consisting of an amino acid sequence shown as SEQ ID No. 67, and a light chain variable region consisting of an amino acid sequence shown as SEQ ID No. 12.

The corrected claims of each of the cases are essentially the same, with the exception of the recited amino acid sequences of the reference antibody. It is of note that the corrected claims are directed only to functional features; (i) whereby binding of PCSK9 and LDLR protein is neutralized; and (ii) whereby competition for binding to PCSK9 with the reference antibody is attained. This means that no structural definition is included for a claimed monoclonal antibody.

As for support and enablement requirements, in both cases Sanofi asserted that the descriptions in each corrected Claim 1 amounted to mere functional or characterizing definitions, and as a result the claimed invention encompasses an enormous number of monoclonal antibodies having a wide variety of structures; which is at odds with the detailed description in the specification in which there are disclosed only a very limited number of monoclonal antibodies. In both cases, Amgen asserted that the specification includes detailed descriptions of how to obtain the claimed monoclonal antibody having the recited functions, and of the effectiveness of the obtained monoclonal antibody for reducing LDL cholesterol level in serum, etc. The JPO dismissed Sanofi's assertion.

> ***The existence of a patent with merely functional features will constitute a tremendous obstacle to those who develop subsequent antibody products.***



Also at issue and under dispute is inventive step. Sanofi cited Lagace et al. (J. Clin. Invest., (2006), Vol.116, No.11, pp.2995-3005), which states that use of an antibody that neutralizes binding of PCSK9 to the LDLR protein may be pursued as a possible treatment for hypercholesterolemia, and discloses a purified anti-PCSK9 polyclonal antibody. Sanofi asserted that the invention of the Amgen patents could have been easily arrived at from Lagace et al. in view of common technical knowledge available in the art at the time. Again, the JPO dismissed Sanofi's assertion.

Sanofi brought the case to the IPHC in an attempt to nullify the decisions issued by the JPO. The IPHC handed down decisions in both cases on 27 December 2018 (Hei 29 Gyo-ke 10225, Hei 29 Gro-ke 10226), upholding the JPO decisions in favor of Amgen.

As for enablement and support requirements, the IPHC decisions state that the corrected claimed invention is fully enabled and supported by the disclosure in the specification, since the specification includes a detailed explanation of the process for obtaining the claimed antibody, as well as evidenced facts that a number of monoclonal antibodies having the recited functions, 15 monoclonal antibodies in Patent 1, were isolated in the example section by use of the process described in the specification.

As for inventive step, the IPHC judged that it would have been difficult for a person skilled in the art to arrive at the claimed monoclonal antibody from the disclosure of Lagace et al. The Court took into account difficulties in obtaining the reference antibodies which were isolated by Amgen with the modified and somewhat tailored method in consideration of usefulness of the reference antibodies and competitive antibodies with them, as well as the significant findings by Amgen that interactions between PCSK9 and LDLR substantially occur at the EGFa domain of the LDLR and at a specific small region in the catalytic domain of the PCSK9.

Infringement lawsuit and appealed IPHC Decision

In the first instance at the Tokyo District court, H29 (Wa) 16468, a decision admitting Amgen's request was issued on 17 January 2019. Subsequently, in the appeal case at the IPHC, H31 (Ne) 10014,

a decision rejecting Sanofi's request was issued on 30 October 2019.

It was not contested between the parties that Sanofi's products are encompassed by the literal scope of the Amgen patents.

Sanofi asserted that a scope of claims should be limited to that which is actually enabled, and as such the claimed antibody should be limited to those concretely disclosed in each of the two specifications, or to those having a substitution of one or more amino acids at specifically defined sites; and Sanofi's products do not fall within this scope.

However, both the Tokyo District Court and the IPHC dismissed Sanofi's assertion, and stating that considering the disclosure of the specifications a scope of the claims which is enabled for a person skilled in the art is not limited to those asserted by Sanofi. Consequently, the both courts judged that Sanofi's activities constitute infringement of Amgen's patents.

As for validity of patents, as in the above invalidation cases, the Tokyo District Court rejected Sanofi's assertion. The IPHC handed down a decision dismissing Sanofi's appeal stating essentially the same reasons as those stated in the decisions handed down by the IPHC in the invalidation cases.

Comments

Despite the limited procedures available for the production of monoclonal antibodies, the structure of obtainable monoclonal antibodies is diverse. This means that a sequence and structure of a monoclonal antibody that has the same function or characteristics will differ greatly even if a monoclonal antibody is produced by a similar animal immunization method.

While it is the case that functionally defined claims tend to cover a huge number of un-isolated monoclonal antibodies, it is also the case that where technical significance of an invention over prior arts is considerable and monoclonal antibodies having the recited functions can be obtained without under burden, such an approach should be admitted in pursuit of a patent. From this viewpoint, the above cases are worthy of exhaustive consideration.

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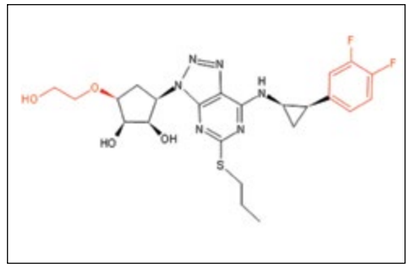
A case analysis of patent invalidation of *Ticagrelor* in China

Xiaofeng Tang, Managing Partner and Patent Attorney at Beijing Geach Intellectual Property Law Office, looks at a recent invalidation case in China concerning a blood-thinning medication.

Ticagrelor is the first triazolo [4,5-d] pyrimidine antiplatelet aggregation drug developed by AstraZeneca. Compared with clopidogrel, Ticagrelor has faster effect, stronger inhibition of platelet aggregation, and can significantly reduce the incidence of cardiovascular death, myocardial infarction and stroke.

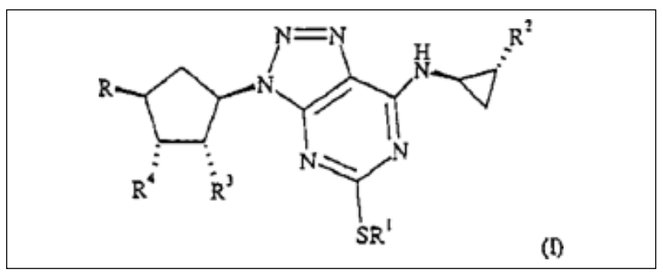
Shenzhen salubris Pharmaceuticals Co., Ltd. filed a request for invalidation of the Chinese invention patent Zl99815926.3 of AstraZeneca (Sweden) Co, Ltd, and the Patent Reexamination Board made patent invalidation examination decision No. 33591 on 10 October 2017, declaring that the patent was invalidated. After that, the administrative judgment of Beijing Intellectual Property Court upheld the invalidation decision of the Reexamination Board. On 24 December 2018, the Beijing Higher People's Court issued the second trial decision (2018) No. 6345, which revoked the invalidation decision and the first trial decision. The case has had an extensive influence on the issue of compound patent inventiveness in China, but there is also a huge controversy.

Xiaofeng Tang



I. Basic case

During the invalidation procedure, granted claim 1 is limited to a specific compound from the compounds of the following general formula (I):



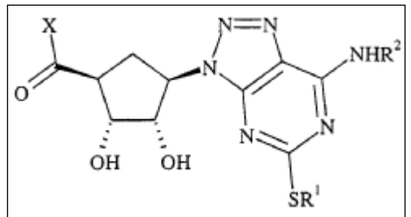
(I)

Wherein:

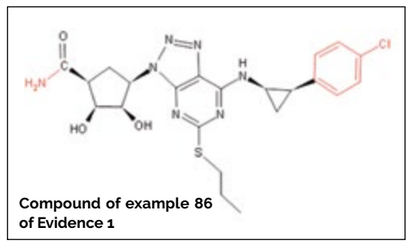
R^2 is a phenyl group, optionally substituted by one or more fluorine atoms;

R is XOH, where X is CH, OCH_2CH_2 or a bond;

Evidence 1 (WO98 / 28300 A1) disclosed the compounds of formula (I) below and the compound of example 86 on July 2, 1998



Compounds of formula (I) of Evidence 1



Compound of example 86 of Evidence 1

Wherein, X is OH or NHR^3; R^2 is C_{1-8}-alkyl optionally substituted by aryl, or C_{3-8} cycloalkyl optionally substituted by one or more phenyl, and optional phenyl is further optionally substituted by one or more halogen atoms (Preferably R^2 is C_{1-6}-alkyl or C_{3-8} cycloalkyl group optionally substituted by phenyl; Most preferably R^2 is butyl or 2-phenylcyclopropyl, recited in description); R^3 is C_{1-6} alkyl which is substituted by one or more hydroxyl groups.

Distinguishing technical features found by the invalidation examination decision and by written judgement of First instance are as follows:

The compound of amended claim 1 differ from the compound of example 86 in: (1) the substituent on phenyl; 3,4-difluoro in the present patent instead of 4-chloro in example 86; (2) the R substituent on cyclopentane; OCH_2CH_2OH in claim1 instead of $C(O)NH_2$ in example 86.

II. Opinions of Patent Reexamination Board and the Courts

The Reexamination Board holds that the technical problem actually solved by claim 1 is to provide triazolo [4,5-d] pyrimidine compound with different substituent.

For the above distinguishing technical feature (1), both fluoro- and chloro- are halogen substituent, and evidence 1 also discloses that the phenyl contained in R^2 on formula (I) structure can be optionally replaced by one or more halogen atoms, and the substitution of the halogen atoms on the phenyl belongs to the conventional group substitution by those skilled in the art; for the above distinguishing technical feature (2), no matter for the substituent OCH_2CH_2OH, or for substituent C(O)NH2,in the design of pharmaceutical compounds, they are widely used by those skilled in the art to modify the structure of a parent compound. This kind of group replacement belongs to the conventional technical means of those skilled in the art. The evidences 3, 4, 5 or 7 submitted by the petitioner also prove this and said group replacement has not achieved any unexpected technical effect. Therefore, it is obvious for those skilled in the art to obtain the technical solution of claim 1 on the basis of evidence 1 in combination with common general knowledge in the art, so claim 1 possesses no inventiveness.

According to the court of second instance, with regard to the distinguishing feature (1), fluorinated or chlorinated compounds are common forms of halogen substitution in the art, and mono- or multi- substitution of halogen is easy to choose when halogenated. Moreover, evidence 1 has disclosed in claim 1 and the description that the phenyl of the compound can be optionally substituted by one or more halogen atoms.

> ***"There is no doubt that the invalidation decision and the first trial decision are wrong."***

Therefore, it is a conventional choice for those skilled in the art to replace 4-chloro- on the 4-chlorophenyl of example 86 compound of evidence 1 with 3,4-difluoro-. With respect to the distinguishing feature (2), the compound of example 86 disclosed in evidence 1 shall be understood in the overall technical solution of evidence 1. Claim 1 in evidence 1 is a *Markush* claim. As we all know, the *Markush* claim includes an unalterable skeleton part and a changeable Markush element. In the overall technical solution of evidence 1, the carbonyl group connected with the cyclopentane at the upper left corner belongs to the unalterable skeleton, rather than the changeable variable group. The Reexamination Board has incorporated the carbonyl which belongs to the unalterable skeleton part into the variable group, which is contrary to the general cognition of those skilled in the art and belongs to the fact-finding error, and the court has corrected it.

According to the overall teaching of evidence 1, those skilled in the art will think that the skeleton part of evidence 1, including carbonyl, is a chemical structure unit that produces pharmacological activity. Once any part of the skeleton has been changed, whether it is a large part such as the ring structure or a small part such as the carbonyl group, it is impossible to predict whether the same drug activity can be retained, so it is impossible to predict whether the technical effect of evidence 1 can be achieved. In this case, those skilled in the art have no technical motivation at all to remove the carbonyl group in example 86 of evidence 1 and replace it with other groups. It is wrong that the invalidation decision find that replacing the corresponding R substituent of compound 86 of evidence 1 from C(O)NH2 to OCH2CH2OH is a conventional technical means of a skilled person, and it is also improper to maintain the original judgment, and the court correct it.

In view of the error in the First judgment and the sued decision on the determination of the distinguishing technical features between claim 1 and the reference document, which directly affects the determination on whether claim 1

Résumé

Xiaofeng Tang

Xiaofeng Tang is a founding partner of Beijing GEACH IP Law Office and before then worked at China's largest Intellectual Property Office. As a seasoned patent attorney with more than twenty years of experience in life sciences, he concentrates his practice on patent prosecution, litigation and validation, covering various technical fields such as pharmaceuticals, biotechnology, chemistry, medical devices, among others. He also provides legal advice relating to patent infringement, validation and strategy.

possesses inventiveness, the Patent Reexamination Board shall, on the basis of the modified determination of the distinguishing technical features, make a new decision on the examination of the request for invalidation.

III. Comments on inventiveness

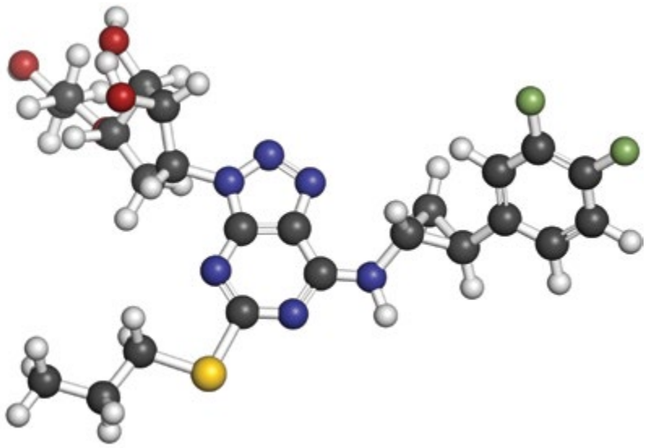
There is no doubt that the invalidation decision and the first trial decision are wrong. Although the conclusion of the second trial decision is correct, the way of judgment and argumentation is also questionable, because the concept of unalterable skeleton introduced by the second trial court is not related to the general assessment of compound inventiveness. Assuming that both evidence 1 and the present invention are specific compounds without general formula structure, this method is not applicable.

The examination of this patent shall be governed by the Patent Law 1992 and the Patent Examination Guideline 1993.

At that time, there was not a three-step process in the guideline for assessing inventiveness, but a non-obvious concept. There is special provision for the assessment of compound inventiveness, which mainly depends on whether the structure of compound is close to that of known compound. A novel compound that is not close to the known compound in structure and has certain use or effect can be considered to be inventive without requiring it to have unexpected use or effect; compounds close to the known compounds in structure must have unexpected use or effect.

Under these circumstances, in theory, both TSM method in US and three-step process in EPO can be used to determine whether the invention is obvious or not. The invalidation decision applied three-step process in combination with the special provision but made mistake in determination on whether the invention is obvious or not.

> ***"It is author's opinion that there is a substantive defect in the patent."***



The invalidation decision takes the compound 86 of evidence 1 as the starting point, which violates the whole teaching of evidence 1; the decision ignores the technical effect of the invention when reformulating the technical problem actually solved by claim 1 relative to evidence 1 and thus violates three-step process and the logic of inventiveness assessment; and the decision does not demonstrate that there is technical motivation in prior art for a skilled person to replace substituent $C(O)NH_2$ with the substituent OCH_2CH_2OH.

In addition, in terms of structure, the compound of claim 1 in the patent has the above two distinguishing features compared with the compound 86 in evidence 1. A person skilled in the field of pharmaceutical chemistry can directly recognize that the corresponding R-substituent $C(O)NH_2$ of compound 86 in evidence 1 and OCH_2CH_2OH in the patent belong to different kinds of groups with different properties in pharmaceutical chemistry. The fact that the substituent OCH_2CH_2OH in this patent and the substituent $C(O)NH_2$ in evidence 1 can be replaced equally in evidence 3, 4, 5 or 7 does not necessarily mean that they can also be replaced equally in this case. Moreover, there exist two differences at the same time between the both. That the Court of second instance regard it as a conventional choice for those skilled in the art to replace 4-chloro- on the 4-chlorophenyl of the compound 86 in evidence 1 with 3,4-difluoro violates the preferable teaching of evidence 1 and lacks the factual basis. Apparently, the compound of claim 1 is not close to the compound of evidence 1 in structure and has novelty and has certain therapeutic use. Therefore, inventiveness of claim 1 should be recognized, and it is not necessary to require that the present patent has unexpected effect. On the other hand, there is no clear and objective criterion to judge whether the structure of two compounds is close to each other or not. Even if according to illustration of the Guideline, "for compounds with similar structure, they must have the same basic core part or basic ring", logically speaking, prerequisite "have the same basic core part or basic ring" is only a necessary condition for identifying "compounds with similar structure", rather than a sufficient condition. Therefore, compounds with "the same basic core part or basic ring" may not be similar in structure. Moreover, term "basic core part or basic ring" is a controversial concept of scope ambiguity in a specific case.

Therefore, the Invalidation Decision and the Court Decisions are not convincing, and the invention is completely non-obvious over evidence 1 in combination with common general knowledge in the art. In fact, assuming that the scope of claim 1 had not been limited during invalidity proceeding, claim 1 is also inventive, although the limitation of the claim 1 to the specific compound has no adverse effect on the patent protection of Ticagrelor- the specific drug finally marketed.

IV. Analysis on the defects in patent

It is the author's opinion that there is a potential insubstantive dislosure issue in the patent, and it is very possible for the patent to be invalidated in China as the result of following reasons. Certainly, the Patent Reexamination Committee and the Courts shall not raise and hear the facts and reasons that have not been put forward by the invalidation petitioner.

It is clearly recorded on page 2 of the specification of the patent that the compounds of the patent have unexpected high metabolic stability and high bioavailability compared with the triazolo [4,5-d] pyrimidine compounds with P_{2T} antagonist activity of WO9905143. It can be seen that the technical problem to be solved in this patent is to provide compounds with high metabolic stability and high bioavailability, rather than P_{2T} antagonist activity in WO9905143. However, the description does not provide any pharmacological experiments to prove the technical effect, let alone experimental data. Therefore, the description is not sufficiently disclosed and does not conform to the provision of paragraph 3, Article 26 of Chinese patent law. Moreover, based on the prior art, those skilled in the art cannot expect that the compound in the patent has high metabolic stability, so the patentee will not be allowed to prove the technical effect of the metabolic stability not confirmed in the original description by now submitting the experimental method and data.

V. Conclusion

In summary, in order to maintain a patent right or to invalidate a patent, the parties need to skillfully manipulate the complexities of patent laws and regulations and the practical intricacies of technologies in combination with the experience on patent prosecution and patent litigation so as to safeguard their respective legitimate rights and interests to the maximum extent.

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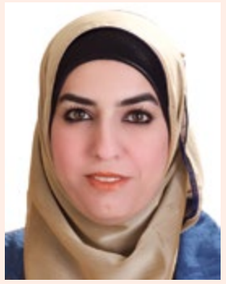
Announcing the birth of "Baianat Intellectual Property" – the new sister company of SMAS Intellectual Property

Shadya Ahmed Awad details some recent developments at SMAS Intellectual Property, and highlights the challenges posed by an ever-challenging IP landscape.

Baianat Intellectual Property have recently launched as a new sister entity with close affiliations to our SMAS Intellectual Property Group which is one of the largest and leading Intellectual Property Firms in the Middle East and North Africa operating in the IP field for more than 50 years with a solid IP team and solid practice and experience of having managed the Intellectual Property Rights of a huge volume of prominent local and International clients through evaluating, protecting and litigating such rights and with the competent Intellectual Property departments which are one of our firm figures of growth started in Kingdom of Saudi Arabia then expanded through the Middle East and North Africa region (Bahrain, Egypt, Jordan, Iraq, Kurdistan, Kuwait, Lebanon, Libya, Morocco, Oman, Palestine, (West Bank, Gaza Strip), Qatar, Saudi Arabia (Riyadh, Jeddah, Dammam), Sudan, Syria, Tunisia, UAE (Dubai, Abu-Dhabi), Yemen, and Turkey); in addition to the increasing network of offices and local representatives worldwide and has a large network of associates and agents in multiple jurisdictions that add to its scope of work to best serve its clients' interests all around the world.



Shadya Ahmed Awad

> ***"Baianat Intellectual Property will follow the fast path of the e-services in the region."***

Today; on behalf of Mr. Nedal Al Kharouf, the CEO of **Baianat Intellectual Property**, who has been the General Manager of SMAS-IP for over 25 years.

Mr. Nedal Al Kharouf, CEO of Baianat IP

We are delighted to share such important news regarding the birth of our new entity **"Baianat Intellectual Property"** as of October 2019 and how such news will serve our valued clients better.

Our businesses have undergone a significant transformation and we have been working since then on developing our services and engaging new human and artificial resources.

The decision to open such a new entity is a response to our clients' and partners' demands and requirements in the region. While SMAS-IP is taking in charge enforcement and litigation. **Baianat Intellectual Property** will deliver more comprehensive and new IP services.

Baianat Intellectual Property provides an extensive range of top-notch services that include, but not limited to,

Competition Analysis, IP Auditing, IP Researches, Online Watch for social medias and E-commerce besides the trainings for several Government agencies we have signed MOU with in addition to the Legal Advice; Registration and Maintenance of IP rights; Brand Watch services; Drafting of Licensing and Franchising agreements; Certified Patent & legal translation services; Market Search; all types of litigation and legal proceedings in respect of trademarks, patents, copyrights, industrial designs and domain names; Raid Action and Seizure Measures; Border Measures; IP Auditing and Counseling; Anti-Counterfeiting Measures; Competition Analysis; Trademark Portfolio Management; Patent Drafting ; Patent Due Diligence & FTO; Customs Recordals; and Patent & Legal Translation.

Baianat Intellectual Property is proud to have more experts, qualified staffing, IP experts, patent counsels, and legal assistants or paralegals who are well organized for each assigned tasks according to the complexity of the legal matter in a cost-effective manner in order to develop our services and offer different solutions to our clients with our collective objective to provide superior, cost-effective legal services to our valued clients consistent with the highest standards of integrity and professionalism.

In **Baianat Intellectual Property** various excellent services in the field of intellectual property, based on the outstanding legal expertise through the in-house legal advisors will be provided. before the competitive courts and relevant government authorities.

This challenging move has been adopted to satisfy the existing expectations, whilst moving forward to embrace technology, making, as always, the interest of our clients the cornerstone of our change.

Baianat Intellectual Property will offer new methods of work and services to the client to follow the fast path of the e-services in the region exploiting the richness of the data we own and engaging new human and artificial resources to offer innovative solutions to our clients.

In **Baianat Intellectual Property**:

- *Our responsibility is to protect the intangible of Intellectual assets*
- *Our pledge is to uphold the highest standards of the legal profession*
- *Our motto is finding new possibilities of an existing service in order to deliver a better experience*
- *Online or on field, our team will grant the right protection and consultation*

In **Baianat Intellectual Property** the major change is **"digitalizing all the process of work"**.

Innovation and IP Consulting are one of our emerging services and are key to achieving our business goals by focusing on maximizing our clients' financial results.

Moreover, in Baianat Intellectual Property we are focusing on Management & IP Consulting including the combination of:

- **Intelligence Services:**
  Conducting the appropriate search and analysis, matching

Résumé

Shadya Ahmed Awad

Shadya Awad has the bachelor's degree in chemical engineering from Jordan University of Science and Technology. Shadya is a patent expert with more than 20 years of experience in the IP field. She manages Patent and Design Prosecution & Registration for the Middle East and North Africa countries, is in charge of Patent Foreign Filings on the International Level and is a specialist in patent & legal translation process. Shadya participated in the establishment of the Patent & Legal Translation Departments referring to the wide expertise in the Technical & legal translation; and manages proposals and surveys and concluding agreements with clients in the field of IP, especially Patents worldwide. Shadya is highly professional in preparing responses to the office actions in relation to patents, providing technical and legal opinion in the field of patents, conducting preliminary patent search for patent applications, professional in drafting patent specification and claims according to the local and international requirements. Shadya is a member in several organizations such as AIPPI, PTMG and GRUR.

the business issues with the direction of the competitive landscape and then the intellectual property strategy to support the business goals

- **Strategy Services:** Assessment of the company vision and mission against the intelligence obtained suiting the IP tactics in order to develop a data-driven IP strategy. Thereafter the implementation plan of portfolio projects, which may include a balance of IP creation, IP monetization, and intelligence investments.
- **Management Services:** Developing methods and capabilities to align the IP strategy and business strategy, working with clients to establish IP processes and management criteria creating new IP and methods for IP monetization.
- **Creation Services:** creation of a strategic IP portfolio using best invention creation processes. Strengthen, invent, and document IP business.

The Future of Intellectual Property
• Data-driven IP

The development of **Artificial Intelligence (AI), Digitalization and Automation**, namely the advanced data-driven digital technology will obviously positively affect the IP practices in the future, and it will be the propellent force of the digital economy.

By adopting the advanced digital technologies including AI, new fruitful services will be developed through the manipulation of data by assessing the value of the intellectual property rights with the aid of algorithms minimizing the costs for IPR owners.

Concurrently, the implementation of AI necessitates the access of greater quantities of data in the presence of many complex policies of making the data available in the digital economy, let alone that the systems will became more complicated and creative in view of placing machine-created inventions in IP.

However, the strong business will support this digital transformation by focusing on cost and innovation. In addition, the quick and proper selection of cloud provider with the adoption of the IT tools to shift data to the cloud, and the early digital transformation management developing new capabilities, all will have the positive effect of AI, Digitalization and Automation.

In conclusion, IP-interested parties must ensure that the people working in the field are able to realize the benefits and improvements of such digitalization and automation under the new working style with the best preparation and implementation in order to face the AI and automation. Now is the time to pause thinking which skills, competencies, capabilities, and tools are needed for the future. Only when reaching the positive disposition and way of thinking among all interested parties involved, a successful new digital way of working can be achieved.

Can machine-created Inventions in IP acquire a property right?

Intellectual Property Protection is critical to aiding the development of innovation and it is essential for economic advancement. Without protection of ideas, businesses and individuals would not reap the full benefits of their inventions and would focus less on research and development, and this may disincentivize people from manufacturing the products and providing the services that the market relies on. Human progress would ultimately suffer.

Intellectual Property rights are valuable assets for your business and IP rights is very important because they can:

- keep your business away from competitors
- be invested or licensed, providing important revenues
- present something new and different; and
- constitute an essential part of your marketing or branding

Humans are able to build towering and durable buildings that can withstand stronger weather and meet the high safety standards. Humans possess the excellence for the production of AI systems, then they use machine-algorithms and cloud-computing to sort through many options, yielding solutions that human alone could not have designed.

Humans believe that what intelligent machines are doing is just the execution of a program or algorithm which is produced by a human itself. As such, the Human should be given any intellectual property rights that flow.

AI-based machines will become more human-like – more capable of learning, more complicated and more intelligent in finding complex solutions. Such machines will become better at making decisions that have very important to our business. **Therefore, if we want to protect the value of intelligence, we must recognize AI as being capable of owning intellectual property.**

That doesn't mean that Machine-Created Inventions in IP will render Humans obsolete. On the contrary, when the problems are getting bigger and more difficult, humans have to be increasingly augmented to solve them.

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