THE PERSONAL TOUCH:
GENOME SERVICES

Therapeutic use
“Effective” treatment

Medtronic
Burden of proof

SPCs
Clearer waters

Section 3d
Glivec in India

FEATURING 2014 PATENT EXPIRY RUNDOWN
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Hello, and welcome to the second edition of the *Life Sciences IP Review* quarterly. In this issue, we take a look at the year ahead, and specifically, changes in the patent position of some of the largest blockbuster drugs on the market. Three of the world's top 10 largest-selling drugs lose exclusivity this year, including Teva's Copaxone and AstraZeneca's Nexium. We consider how the losses affect the various patentees concerned, whether there is anything they can do to preserve their position in the market, and what generic alternatives are in the offing.

Two of the key areas for development in the life sciences industry over the next few years are embodied in personal genome services: personalised medicine and genetics. This new and potentially thrilling field has already seen companies offering customers the ability to have their genome looked at, merely by providing a saliva sample, in order to establish whether they are predisposed to develop certain conditions.

However, from a regulatory perspective, it's a tricky area, especially since there is no medical professional acting as an intermediary to interpret the results—while this provides patients with a degree of freedom, it clearly raises issues, and that's perhaps why the US Food and Drug Administration has stepped in. In this issue, we look at how that regulation is taking place, the various safety and privacy issues at stake, and also whether these services are likely to change the way in which people access medical knowledge.

Staying in the US, we have an extensive analysis of the Supreme Court's recent decision in *Medtronic*, and discuss what its implications are for patentees and licensees. On the other side of the Atlantic, recent decisions at the Court of Justice of the European Union covering supplementary protection certificates have partially cleared and partially muddied the waters. As so often, in answering questions, the court has raised some new ones.

As ever, we also have the news highlights of the past quarter, and longer features from across the globe. We hope you find it interesting, and look forward to a productive 2014.

Peter Scott, Managing editor
With thanks to the members of the Life Sciences IP Review editorial board.

Contact the editor for more information.
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The rise of so-called personalised medicine presents new challenges and opportunities for drugs companies, says Robert Andrews.
South African drug companies have been accused by advocacy organisations of planning a "deceptive" campaign to delay new laws which could see the introduction of more generic medicines.

The campaign, revealed in leaked documents, was planned to cost more than $400,000 ($6 million) and was set up in protest at proposed changes which the government is currently discussing.

The new laws, outlined by the Department for Trade and Industry (DTI), which was set up in protest at proposed changes which the government is currently discussing.

The campaign is an email sent by South Africa’s representative for pharmaceutical companies, Innovating Pharmaceutical Association South Africa (IPASA). The email, dated January 10, was sent to a majority of the country’s leading pharmaceutical groups and, according to The Guardian newspaper, talks of “identifying a high-calibre consultancy group to work with us”. Washington, DC-based Public Affairs Engagement (PAE).

Another leaked document, seen by LSIPR, is a plan of action by PAE involving placing editorials in newspapers and distracting campaigners in favour of the proposals.

It adds that it will mobilise voices “inside and outside” South Africa to send the message that the proposed policy threatens investment.

The document, called Campaign to Prevent Damage to Innovation from the Proposed Draft National IP Policy in South Africa, also names MSF as one of the companies which had “pressured the government” into “producing the draft policy in the first place”.

“Without a vigorous campaign, opponents of strong IP will prevail—not just in South Africa but eventually in much of the rest of the developing world,” the document says.

PAE did not respond to requests for comment when contacted by LSIPR.

In a statement, IPASA’s chief operating officer, Val Beaumont, said it had not engaged PAE to lobby on IP “or any other matter” in South Africa.

“PAE submitted a proposal for a campaign, which was reviewed and subsequently rejected by IPASA members, and no payment or pledge has been made in any respect,” Beaumont said.

Beaumont added: “The draft IP policy is a matter of vital importance to the future of the healthcare sector in our country … IPASA has participated in the DTI’s public consultation process and has made a written submission to the DTI with respect to the draft national IP policy published last year.

“IPASA has raised questions in the submission on how such existing legislation will be integrated under the proposed policy framework. Innovative medicines from our sector have contributed significantly in improving healthcare and we are committed to working with government into the future.”

Julia Hill of MSF said spending money to “dissuade” the government from pushing legislation that “promotes access to more affordable medicines” was “outrageous”.

Hill applauded South African health minister Aaron Motsoaledi who criticised the campaign and added that it was right to “take a stand against pharmaceutical companies that seek to protect their profit margins at the expense of ordinary South Africans”.

However, according to Danie Dohmen, partner at Adams & Adams in Pretoria, the advocacy groups who are “essentially calling for a weakening of the patent system” are themselves “well-funded and have a well-developed strategy”.

“The irony is that it is their advocacy campaign which resulted in the innovator organisations having to consider similar strategies to have their perspectives on the matter heard,” Dohmen told LSIPR.

“One of the concerns with the draft policy is that some of the proposed policies will result in a weakening of the patent system which is likely to have a negative effect to the long-term access to new medicines in South Africa.

“If patent rights are eroded the incentive for manufacturers to seek improved drugs and to bring them to market in South Africa will also be eroded and future South African generations will probably not have access to the required new and improved products”

Dohmen added: “There is a lot of misinformation on the current South African patent law and its effect on access to medicines. Any campaign which would result in an honest, open, informed and rational discussion on these aspects should be encouraged.

“There is still a long road to go before any of the draft policies find their way into legislation and it is thus important that all interest groups are allowed the opportunity to voice their concerns and for the issues to be properly debated and considered.”
FDA approval adds new life to Copaxone

On January 28, Teva announced that the US Food and Drug Administration (FDA) had approved its supplemental new drug application for a new formulation of its biggest selling drug Copaxone (glatiramer acetate).

Copaxone 40mg/mL has been formulated for use by patients three times a week with relapsing forms of multiple sclerosis (MS). Tevá’s patent covering its 20mg/mL daily dose of Copaxone is due to expire in May this year when generic companies Sandoz, Momenta, Mylan and Natco are expected to launch their own versions.

In a statement on its website, Teva said the new formulation of Copaxone will allow for less frequent administration of the drug, reducing the number of injections needed by 60 percent.

Larry Downey, president of North America Specialty Medicines at Teva, said: “We have progressively invested in the innovation of Copaxone in an effort to understand the needs and to ease the burden of patients who live with relapsing forms of MS every day. Today we are proud to continue to deliver on that investment by offering the freedom to dose three times a week with Copaxone 40 mg/mL.”

Federal Circuit rules against USPTO on PTA case

The US Court of Appeals for the Federal Circuit has upheld a ruling which found that the US Patent and Trademark Office (USPTO) had been incorrectly calculating Patent Term Adjustment (PTA) lengths.

The US District Court for the Eastern District of Texas first ruled against the USPTO on the issue in 2012, finding in favour of pharmaceutical company Exelixis.

In a subsequent decision, the US District Court for the District of Columbia ruled in favour of Swiss pharmaceutical company Novartis AG on the same issue.

The USPTO appealed against the judgments, culminating in the Federal Circuit’s decision on both cases, which was published on January 15.

A PTA is a period of adjustment of a patent’s term which is caused by a delay in examination proceedings on applications.

The USPTO is obliged to meet time requirements during examination, including a guarantee of taking no more than three years on an application’s issuance.

If the requirements are not met, the patentee is given PTA and, under Section 154(b)(1)(B) of the Patent Act, there is a guarantee of a one-day term extension for every day it takes the patent to issue following on from the three-year cut-off date. That period is referred to as a ‘B period’.

However, during the trial, the USPTO said that if a Request for Continued Examination (RCE) had been filed, as it had in these cases, an applicant should have its B period delay reduced, depending on how long it took for the patent to be given issuance.

An RCE is a mechanism for submitting claim amendments on patents. It is used to conclude prosecution when it is indicated that additional examination is necessary to determine whether the amended claims are allowable.

The USPTO said that, even if the patent had been allowed, any time up to the patent’s issue should be excluded from the PTA awarded to the patentee if there has been continued examination.

However, Novartis argued that the “time consumed by RCE examination” should be limited to the time before allowance, as long as no later examination actually occurs while waiting for its issuance.

The Federal Circuit agreed, saying: “We reject the USPTO’s view that the time after allowance, until issuance, is ‘time consumed by continued examination’ and so is excluded from adjustments given to the patentee.

“Such time from allowance to issuance would indisputably count toward the USPTO’s three-year allotment in a case not involving a continued examination. There is no basis for distinguishing a continued examination case.”

In a statement, Honigman Miller Schwartz and Cohn LLP (Honigman), which represented Exelixis, said the case would have a “significant impact” on the calculation of PTA in cases where the applicant filed an RCE.

“It will benefit clients with patents in which the value of the invention remains, or is even amplified, towards the end of the patent term,” it said.

“The outcome of this case has ultimately determined how PTA is interpreted for all patentees. In particular, companies in the pharmaceutical and biotechnology industries are likely to benefit, as the regulatory approval process often results in the product being introduced into the market late in the term of the patent,” Honigman added.

The patents in question were US numbers 8,067,436 and 7,989,622 for Exelixis, and numbers 7,807,155, 7,968,518, and 7,973,031 for Novartis.
Appeals court ruling blocks Lyrica competition until 2018

The US Court of Appeals for the Federal Circuit has upheld a patent covering Pfizer’s pain drug Lyrica, closing the market to any generic challengers until 2018.

On February 6 it confirmed a district court’s decision that a group of generic makers, including Teva, Actavis, Sun and Mylan, had infringed a patent covering Lyrica’s active ingredient pregabalin by seeking to market a generic version of the drug.

The court also said that a challenged claim of the patent was valid, despite the generics’ arguments that there is lack of enablement, insufficient written description or obviousness.

Lyrica is used in the treatment of fibromyalgia, nerve pain and pain after shingles. It is Pfizer’s biggest selling drug, making the company nearly $4.6 billion in revenues in 2013.

Pfizer sued the generic makers at the US District Court for the District of Delaware in 2009 after they sent Abbreviated New Drug Applications (ANDAs) to the FDA seeking approval to market a generic version of Lyrica.

In its complaint, Pfizer initially asserted four patents, although the appeals court found that the case rested entirely on a single claim of the composition of matter patent covering pregabalin, US patent number 6,197,819.

“We hold that the district court did not err in its conclusion that claim 2 of patent ‘819 has been infringed, and that appellants failed to prove that the claim is not enabled, insufficiently described, or obvious,” Judge Prost wrote in the judgment. He added that the generics’ arguments about the validity of the other disputed patents were moot.

The generic companies may now request a rehearing by the appeals court or a review by the Supreme Court.

US Supreme Court reverses Medtronic ruling

The US Supreme Court has ruled that when licensees seek a declaratory judgment of non-infringement, the patentee bears the burden of proof of showing infringement [see p28 for analysis]. An earlier Federal Circuit ruling held that a licensee seeking such a declaration must prove non-infringement.

Medical device company Medtronic, the licensee in this case, was accused by Mirowski Family Ventures of using its patents, which cover implantable defibrillators, without paying royalties. The companies had already been in a licensing agreement, but Mirowski said Medtronic was developing new technology that required it to pay more licensing fees.

In 2007 Medtronic asked a US district court to rule that it was not infringing Mirowski’s patents. The US District Court for the District of Delaware said that Mirowski should prove infringement, adding that Medtronic did not infringe the patents.

Mirowski appealed to the US Court of Appeals for the Federal Circuit, which switched the burden of proof from the patentee to the licensee.

The appeals court said that while the patentee normally bears the burden of proof, because the party seeking declaratory judgment—Medtronic, in this case—is the only party “seeking the aid of the court,” that party must prove non-infringement.

But in a unanimous ruling on January 22, the Supreme Court reversed that position. “When a licensee seeks a declaratory judgment against a patentee that its products do not infringe the licensed patent, the patentee bears the burden of persuasion on the issue of infringement,” wrote Justice Breyer on behalf of the court.

“This conclusion is strongly supported by three settled legal propositions,” he stated. The first, he said, citing case law, is that a patentee ordinarily bears the burden of proving infringement.

He added: “Practical considerations lead to the same conclusion. Shifting the burden based on the form of the action could create post-litigation uncertainty about a patent’s scope. It may also create unnecessary complexity by compelling a licensee to prove a negative.”

Finally, he continued, burden-shifting is difficult to reconcile with the declaratory judgment act’s purpose of ‘ameliorating the ’dilemma’ posed by ‘putting’ one challenging a patent’s scope ‘to the choice between abandoning his rights or risking’ suit’.

Bill Baton, partner at Saul Ewing LLP, said the decision turned the state of the law back to the previous status quo.

“The Supreme Court disagreed with the Federal Circuit, holding that suits like this one are an exception to the ‘ordinary default rule’, whereby declaratory judgment plaintiffs bear the burden of proving their claims.

“They are not, however, an exception to the longstanding rule that a patentee bears the burden of proving infringement. In short, even though Medtronic was the declaratory judgment plaintiff, defendant Mirowski, the patentee, bore the burden of proving to the court that Medtronic, its licensee, infringed Mirowski’s patents.

“The Supreme Court suggested that, to do otherwise, would have subjected Medtronic to prove a negative—ie, that it was not an infringer,” he said.

The case now goes back to the Federal Circuit, which will reassess it in light of the Supreme Court’s findings.
KRKA to receive damages in Nexium case

The UK High Court has decided to award Slovenian generic pharmaceutical company KRKA damages after a preliminary injunction enforced against the company by AstraZeneca was discharged. In a decision handed down on January 24, Justice Sales found that AstraZeneca’s injunction deprived KRKA and its marketing partner Consilient of an element of ‘first mover’ advantage.

AstraZeneca holds a European patent covering heartburn drug Nexium’s active ingredient, esomeprazole, which is due to expire in May 2014. According to drugs.com, Nexium made $1.5 billion in sales during the third quarter of 2013.

From its launch in 2000 to 2011, Nexium was the only product of its kind on the market. In 2010 AstraZeneca successfully obtained a preliminary injunction to keep KRKA from marketing a generic version of Nexium, Emozul, in the UK.

After a successful challenge to the patent by Ranbaxy, which also sought to launch its own Nexium, the preliminary injunction was discharged.

However, by the time KRKA was allowed to launch Emozul, the UK market had been “completely transformed” by the entry of Ranbaxy, Mylan and Teva’s generic versions of Nexium.

In fact, days after the Nexium patent was revoked in July 2011, AstraZeneca had launched a generic version in partnership with generic company Arrow.

In the judgment, Sales said that there is a wide divergence between the parties regarding the extent of the ‘first mover’ advantage and its value.

“AstraZeneca says the damages to be awarded should be of the order of £6 million. The defendants say they should be of the order of £32 million,” he wrote.

Paul England, a senior associate at Taylor Wessing LLP in London, said Nexium is an important drug for AstraZeneca and a loss of market to a further competitor is “always going to be a commercial blow”. However, he added: “In this case, several other companies have already reached the market with rival proton pump inhibitor drugs similar to Nexium, including AstraZeneca’s own product sold under the Arrow brand. AstraZeneca will therefore have had time to plan for this latest development.”

The decision is interesting because of Sales’ approach. “The judge, who is not normally associated with patent matters, assesses damages based on the prescription recommendations made by medicine managers in Primary Care Trusts, rather than the expert evidence of accountants,” England continued.

“It may provide a model for assessing damages in similar cases and, indeed, could be raised as a reason why injunctive relief should not be awarded in the first place.”

Aaron Wood, an associate at Swindell & Pearson Ltd, said that after losing the case AstraZeneca is now in a better commercial position than if it had not pursued it to begin with.

“Although they’ll have to pay some damages to KRKA, the amount they’ve probably made will be greater than the amount they’ll have to pay out,” he said.

AstraZeneca told LSIPR: “AstraZeneca is disappointed with aspects of the court’s decision. We are reviewing the decision and evaluating our legal options.”

KRKA said it had no comment about the decision.
US Supreme Court rejects Monsanto seed case

The US Supreme Court has refused to hear the Organic Seed Growers and Trade Association (OSGATA)’s case against Monsanto, along with two other patent cases as revealed in a document released on January 13.

OSGATA, an association formed of 73 American organic and conventional family farmers, seed businesses and public advocacy groups, sued Monsanto in March 2011 to challenge the agriculture company’s patents on genetically engineered seed.

It also sought assurance that Monsanto may not sue the association’s members for patent infringement if their crops are accidentally contaminated by the seed.

OSGATA urged the court to hear the case in a brief filed in December 2013.

Battistelli buoyant on Unitary Patent

European Patent Office (EPO) president Benoît Battistelli has praised the “steady” progress that the Unitary Patent and its associated court have made in the past 12 months.

In a blog post dated December 16, Battistelli said the outlook for ratifying the Unified Patent Court (UPC) was positive, meaning that the first patent could be issued in 2015.

“This will also ensure that time remains available in the coming year to fine-tune the preparatory work for a system which will be sound and will deliver the highest quality,” Battistelli claimed.

The European (EU) parliament and council approved the regulations governing the Unitary Patent deal in December 2012, while EU ministers signed an agreement in February this year that establishes the UPC.

Since then, Battistelli noted, the select committee overseeing the patent deal has become operational (in March 2013) and the participant member states have met seven times.

“Important decisions on the committee’s rules of procedure have been adopted. Significant advances have been made in the drafting of the legal texts for the implementation of the Unitary Patent, which would make a final decision possible in the first half of 2014,” Battistelli said.

“The practical implementation of the compensation scheme for translation costs and the procedure for setting fee levels has also been discussed,” he added.

Battistelli praised the preparatory committee, a group responsible for setting up the UPC, where Unitary Patents will be litigated. In a number of cases, he noted, the same member state representatives are participating in both the select and preparatory committees.

“Given the close connections between the two parts of the Unitary Patent package,” he said, “this is important for the success of the venture as a whole.”

The Brussels I Regulation, which will bind UPC judgments in law, was passed by the EU council in December, and represents another “decisive step”, said Battistelli, adding that he expects the EU parliament to approve the regulation in the first half of 2014.

While Battistelli’s report is upbeat, said Jonathan Radcliffe, partner at Charles Russell LLP, “like most Christmas lists it contains its fair share of ‘optimistic’ gifts that no-one is realistically going to give”.

“There is still much to be done before the new patent and UPC system go live, ranging from structural issues such as finalising the details of the various sets of rules and procedures, through to agreeing budgetary contributions from member states and the commissioning of a new UPC IT system,” Radcliffe said.

“Implementation in 2015 was always going to be a stretch, no matter how much it is wished for,” Radcliffe explained.

Battistelli’s claim that the first patent could be “issued” in 2015 is confusing, said Avi Freeman, partner at law firm Beck Greener, as this term could refer to a patent application or a granted patent.

“If he means ‘granted’ then it’s entirely unrealistic, so I can only think he is referring to ‘filed’, which is certainly possible.”

Even if the first patent is filed in 2015, said Freeman, it would not be published for another 18 months and not granted for another 12 months thereafter “at the very quickest”, taking the grant date to about 2016 or 2017.

“While we are closer than we have ever been, the timescales look optimistic, however you understand it (file and grant),” Freeman said.

To date, Austria is the only UPC signatory to ratify the court package. The remaining signatories are: Belgium; Bulgaria; Croatia; Cyprus; Czech Republic; Denmark; Estonia; Finland; France; Germany; Greece; Hungary; Ireland; Italy; Latvia; Lithuania; Luxembourg; Malta; the Netherlands; Poland; Portugal; Romania; Slovakia; Slovenia; Spain; Sweden; and the UK.
Pfizer allows Teva’s generic Viagra

Viagra maker Pfizer Ltd and Teva Pharmaceutical Industries have agreed to settle patent litigation related to Teva’s generic version of Viagra (sildenafil citrate) tablets.

Under terms of the agreement Teva may launch a generic version of the erectile dysfunction drug in the US on December 11, 2017, more than two years before the Viagra patent is due to expire in 2020.

The US FDA has granted tentative approval for Teva’s generic Viagra tablets in 25mg, 50mg and 100mg strengths.

Teva will pay Pfizer a royalty for a licence to produce its Viagra generic.

In June, Teva and Actavis launched generic versions of Viagra immediately after Pfizer’s patent covering the drug expired in several European countries.

According to drugs.com, Viagra is the 42nd biggest selling drug in the world. In 2012, it made $313 million in US sales for Pfizer.

“It appears that Teva will be the first generic on the Viagra market,” said William Baton, a partner at Saul Ewing LLP in Newark.

The agreement appears to be a business decision on Pfizer’s part. “All litigation bears risk—Pfizer might have chosen to accept a royalty rather than continue litigating,” said Ewing.

“If Pfizer lost the lawsuit against Teva, then presumably any generic that receives approval could go on the market at some point. Perhaps Pfizer thinks it better to settle and have its opponent become someone that pays a royalty to them, as opposed to risking a decision of non-infringement or invalidity—in which case, they would have no way to negotiate anything further and would lose any share of exclusivity.”

The agreement makes Teva a “partner” on some level, which helps Pfizer “control the risk”, he added.

Neither Pfizer nor Teva responded to LSIPR’s requests for comment.
The High Court in Australia has said for the first time that a method of medical treatment for the human body can be a patentable invention.

The ruling stems from the Apotex Pty Ltd v Sanofi-Aventis Australia Pty Ltd case covering a method for the treatment of the skin disease psoriasis.

Pharmaceutical company Sanofi and generics company Apotex had been in a dispute since 2008 over the claims of a patent that describes a method for treating the disease.

Sanofi is the registered owner of Australian Patent 670,491, called "pharmaceutical for the treatment of skin disorders". Its claims centre on a method for treating the disease using a compound called leflunomide.

However, in 2008 Apotex registered a version of the compound with the intention of selling it to treat rheumatoid arthritis and psoriatic arthritis.

Sanofi said the generic product would infringe its patent, before Apotex responded with a challenge to the patent's validity, arguing that it is not patentable as a method of manufacture.

The case was the first time Australia had considered whether claims of a medical treatment could be deemed a manner of new manufacture within the scope of the Patents Act 1990.

On December 4, the High Court was split 4–1, but the majority ruling stated that assuming all other requirements for patentability are met, a method for medical treatment of the human body is deemed a manner of manufacturing and is therefore patentable.

"While this question had been considered by various tribunals and courts in a number of major jurisdictions, it was the first time that the High Court of Australia had the opportunity to decide the question in the context of the law in Australia," said Virginia Beniac-Brooks, partner at Marks & Clerk LLP in Melbourne, Australia.

"While this decision … merely confirms the judicially-sanctioned orthodoxy that an invention directed to a method of medical treatment is proper subject matter for letters patent, it is nevertheless significant as it now provides patentees in the life sciences industry with greater certainty as to what is patentable subject matter."

The court wrote: "The exclusion from patentability of methods of medical treatment represents an anomaly for which no clear and consistent foundation has been enunciated."

It added: "Whatever views may have held in the past, methods of medical treatment, particularly the use of pharmaceutical drugs, cannot today be conceived as 'essentially non-economic'."

According to a blog post by Simone Mitchell and Nicholas Tyacke, partners at DLA Piper LLP, the Australian Patent Office has been granting patents for methods of medical treatment, particularly in relation to pharmaceutical products, for many years.

However, they added: "This decision now provides the Australian life sciences sector with certainty that patents are available for inventions that are methods of medical treatment, provided that the invention is otherwise patentable (that is, it meets the requirements of novelty, utility, inventive step and no prior use)."

The court also concluded that Apotex's generic product had not infringed that of Sanofi-Aventis because the product information expressly excluded using the generic product for the patented purpose.

The court found that because the product was indicated for the treatment of active rheumatoid arthritis and active psoriatic arthritis, and not for the treatment of psoriasis, it did not infringe the patent.

India considering new patent filing rules

India is considering altering its requirements for filing drug patents in a bid to create more transparency in the pharmaceutical market, it has been claimed.

The Indian Patent Office (IPO) is thought to be considering a proposal which would make it mandatory for drug firms to disclose the International Non-Proprietary Name (INN) of a drug when applying for a patent.

If the proposal is accepted, India would become the first country in the world to implement the procedure.

An INN, which is granted by the World Health Organization, is a generic name given to a pharmaceutical substance and is designed to be unique and distinct to avoid confusion.

However, they have been concealed from patent applications in the past in a bid to discourage oppositions and challenges to patent validity.

It is thought the changes will make it easier for patent examiners, generic drug makers and public health groups to block frivolous patents from being granted.

It will also make it difficult for innovator drug firms to get patents for incremental innovations, which do not show any enhancement in efficacy of an existing method.

An anonymous "official" at the IPO has been quoted in The Economic Times of India saying it is "currently consulting key stakeholders on the feasibility of mandating disclosure of WHO-assigned INNs in pharmaceutical patent applications, wherever applicable."

The official adds that a final decision has not yet been taken on the matter.

According to Ashwani Balayan, partner at ALG India Law Offices in New Delhi, India, the provisions would "go beyond" an applicant's obligations and would clearly set up an "additional burden".

"Identification of the corresponding INN only helps out the examiner in its job of determining the novelty and inventiveness," Balayan said.

"By doing this it appears that the IPO, instead of upgrading its workforce and infrastructure, is attempting to pass some of its searching responsibilities directly on to the applicants."

Balayan added: "I am of the view that the lack of applicant's knowledge of the corresponding INNs and/or failure to disclose all the requisite INNs in respect of some or all of the involved substances … therein cannot and should not be prejudicial … to the applicant's rights in the invention in any manner. That being so, such a requirement should not be made mandatory."

The news comes at a time when the Indian patent regime is under the spotlight and has faced criticism from the US and Europe for some of its recent decisions.

In March 2012, it granted its first compulsory licence, allowing local manufacturer Natco to legally make and sell a low-cost version of Nexavar, a drug made by German pharmaceutical company Bayer used to treat kidney and liver cancer.

Earlier this year, the Supreme Court ruled that Novartis' cancer drug Glivec was not significantly more effective than alternatives and that its active ingredient was already known, denying it a patent.

In September, LSIPR reported that The Alliance for a Fair Trade with India, a specially formed coalition, had written to US President Barack Obama urging him to address India's drug policy with the country's Prime Minister Manmohan Singh.

The IPO was unavailable for comment at the time of writing.
RPG domain name challenge backfires in WIPO ruling

Mumbai-based pharmaceutical company RPG Life Sciences Ltd has been found guilty of reverse domain name hijacking in a dispute fought at the World Intellectual Property Organization (WIPO)’s Arbitration and Mediation Center.

Reverse domain name hijacking is the practice of misusing the rules of the Uniform Domain Name Dispute Resolution policy to deprive a registered domain name holder of a domain name.

The disputed domain name rpglife.com was registered in October 2005. Wisconsin resident James Mathe has been using the domain name as a social media platform for people who play role-playing games. Examples of role-playing games include Dungeons and Dragons and World of Warcraft.

In December 2013, RPG filed a complaint with the WIPO Arbitration and Mediation Center, claiming the domain name is “confusingly similar” to its Indian trademarks ‘RPG’ and ‘RPG LIFE’, which cover pharmaceutical, veterinary and sanitary preparations for medical purposes.

It said that Mathe “has no rights or legitimate interests” to use the domain, as he has not registered any trademarks covering RPG or RPGLIFE, and argued the domain name was registered in bad faith.

Mathe said consumers are not likely to be confused as the domain name comprises the word ‘RPG’, a widely used abbreviation for the term ‘role-playing game’ said to have been coined in 1974. RPG’s marks do not grant it exclusive rights to the word, he added.

He argued that he has a legitimate interest in the domain because he has used it since 2008 “for bona fide offerings of goods or services”, and added that the domain name’s use as a retail site is “entirely unrelated” to the trade channels RPG uses as a pharmaceutical and biotech business.

Writing in the decision, panellist Nicholas Weston said: “The complainant’s professional representative should have appreciated, even on a rudimentary examination of the policy and its application in this area, that the complaint could not succeed where the respondent’s disputed domain name is a widely recognised acronym and is being used to promote goods and services available for purchase in that field.”

The panel granted Mathe’s request for a finding of reverse domain name hijacking, and denied RPG’s complaint, finding it to be made in bad faith.

According to reverse domain name hijacking case database rdnh.com, 26 complainants were found guilty of the practice in 2013, up from 14 in 2012.
FDA orders 23andMe to cease PGS sales

The US FDA has told genetics company 23andMe to stop selling its Personal Genome Service (PGS) product immediately.

FDA director Alberto Gutierrez wrote to the company on November 22 to say that the product, which the agency defines as a medical device, is being marketed without approval.

In a statement on its website, 23andMe said it had received the letter and recognised that “we have not met the FDA’s expectations regarding timeline and communication regarding our submission” and that “we are committed to fully engaging with them [the FDA] to address their concerns”.

Gutierrez, addressing 23andMe’s chief executive Ann Wojcicki, said the PGS meets the “medical device” criteria under the Food, Drug and Cosmetic Act, as it is intended to help diagnose or treat diseases. Conditions listed on the company’s website include diabetes and breast cancer.

But most of the intended uses have not been classified, Gutierrez claimed, and therefore require approval, while some of the uses are “particularly concerning”. These include the assessments for breast cancer gene BRCA-related genetic risk and drug responses, which could cause worrying health consequences if not administered correctly.

“For instance, if the BRCA-related risk assessment for breast or ovarian cancer reports a false positive, it could lead a patient to undergo prophylactic surgery, chemoprevention, intensive screening, or other morbidity-inducing actions,” Gutierrez said.

The FDA has told 23andMe on “numerous occasions” about the need to approve the PGS, including after the company submitted two pre-marketing notifications—510(k)—in June and September 2012.

“Since July of 2009, we have been diligently working to help you comply with regulatory requirements regarding safety and effectiveness and obtain marketing authorisation for your PGS device,” he said.

But after “many” interactions with 23andMe, the FDA still does not have “any assurance” that the firm has analytically or clinically validated the PGS for its intended uses, which have expanded from the uses identified in the firm’s submissions, Gutierrez explained.

“Instead,” he added, “we have become aware that you have initiated new marketing campaigns, including television commercials that … show that you plan to expand the PGS’s uses and consumer base without obtaining marketing authorisation from FDA.”

If the company fails to adequately address the FDA’s concerns, Gutierrez noted, the agency can take action including seizures, injunctions and fines.

The agency’s concerns raise interesting questions about the future of genetic testing, said Kevin Noonan, partner at McDonnell, Boehnen, Hulbert & Berghoff LLP, particularly under circumstances where the Supreme Court has raised significant barriers to obtaining patent protection for these types of testing.

“In such an environment there may be a much lower impetus for disclosing the ‘natural law’ correlations between disease propensity and genetic variability, because once that disclosure is made it cannot be retracted. If patent exclusivity is not possible, there could easily arise a ‘tragedy of the commons’, where no company is motivated to undertake the type of efforts demanded by the agency of 23andMe, just to have those efforts co-opted by its competitors.”

“Even if the agency were willing to permit nondisclosure for a time, Noonan said, it is unlikely to agree to less than a reasonable term, for example 20 years from the date the application was submitted for approval.

“Thus it could be that in such a roundabout way agency action could achieve what the patent system has always provided, but perhaps in a form less amenable to meddling from the court.”

GE life sciences expansion costs $1.06 billion

General Electric (GE) has bought three life sciences divisions from US company Thermo Fisher Scientific in a deal worth about $1.06 billion.

The businesses—cell culture (sera and media), gene modulation and magnetic beads—will be transferred to GE Healthcare, a unit of GE. Combined, the businesses’ 2013 revenue is estimated to be $250 million.

GE said the acquisition will allow it to expand its offering of technologies for the discovery and manufacturing of new medicines, vaccines and diagnostics.

Subject to regulatory approval, the deal was expected to close in the first part of 2014, GE said in a statement.

Life sciences is one of GE’s strongest and fastest-growing business areas, driven by the world’s demand for improved diagnostics and new, safer medicines, noted John Dineen, president of GE Healthcare.

“Combining GE’s engineering expertise with our capabilities in life sciences is already bringing great benefits to industry, research and patients,” he said. “This deal makes a good business even better and will help us realise our vision of bringing better healthcare to more people at lower cost.”

Kieran Murphy, president of GE Healthcare’s life sciences division, added: “We look forward to the HyClone cell culture and other businesses joining the GE family. They are a great fit with our key areas of focus, and bring exciting new technologies, enhanced manufacturing capabilities as well as a great group of talented people to help grow our business.”

The deal is expected to make way for Thermo Fisher’s acquisition of Life Technologies, according to a Thermo statement.
FDA approves first generic versions of Lilly’s $5bn Cymbalta

The FDA has approved the first generic versions of antidepressant drug Cymbalta (duloxetine hydrochloride), after Eli Lilly’s primary patent covering the product expired on December 11.

Generic makers including Aurobindo Pharma, Dr. Reddy’s Laboratories and Teva Pharmaceuticals have all received approval to make and sell duloxetine hydrochloride in various strengths.

Cymbalta is Lilly’s biggest earning drug, generating $4.994 billion in revenue worldwide in 2012. In the same year, Lilly secured six months of paediatric exclusivity for the product in the US.

Lilly has three patents, two of which remain in force, related to Cymbalta listed in the Orange Book, the FDA-published list of approved drugs. The patents cover delayed release duloxetine tablets in 20mg, 30mg and 60mg strengths.

Kathleen Uhl, acting director of the Office of Generic Drugs in the FDA’s Center for Drug Evaluation and Research, said healthcare professionals and consumers can be assured that the new FDA-approved generic drugs have met “our rigorous standards”. She added: “Generic drugs offer greater access to healthcare for many people.”

In October 2013, Lilly’s chief financial officer Derica Rice said that in the medium term, the loss of the Cymbalta patent will stabilise revenue in the company’s Bio-Medicines division, although the company is hopeful that later in the decade, the division “could provide significant revenue growth through a combination of new molecules currently in Phase 3 development, including solanezumab, evacetrapib, baricitinib, ixekizumab, tabalumab and edivoxetine”. ■
EXPIRING SOON: PRODUCTS UP FOR GRABS

Several of the world’s 10 top-selling drugs lose exclusivity this year. LSIPR takes a look at the products, their major competitors, and their manufacturers’ strategies for keeping a grasp of market share.
PATENT EXCLUSIVITY

Copaxone (glatiramer acetate)

By far Teva’s biggest selling drug, Copaxone has received challenges from generic makers Sandoz, Momenta, Mylan and Natco all vying to launch their own versions of the multiple sclerosis drug.

In an effort to extend the life of the drug, which is worth $4.3 billion a year, Teva formulated a new formulation for the drug, which was approved by the US Food and Drug Administration (FDA) in January.

It will now be working to convert as many patients as possible to the three-times-weekly injection before the patent expires in May.

“2013 was an important year for Teva and its shareholders,” said Eyal Desheh, Teva’s former acting president and chief executive.

“Many seeds were planted to ensure our long-term success and prosperity. 2014 will be a pivotal year in terms of execution and further enhancement of our strategic direction.”

A spokesperson for Teva told LSIPR: “We do not know whether a generic form of Copaxone will be approved and we do not believe a generic glatiramer acetate should be approved without appropriate clinical trial testing.

“Copaxone is a very complex synthetic mixture of an enormous number of polypeptide sequences with a higher order structure and unidentified active sequences. As such, it is our position that untested versions of Copaxone should not be prescribed without demonstrating efficacy and safety in patients with relapsing forms of multiple sclerosis.”

Among those aiming to launch a Copaxone generic on May 24 is India-based Natco Pharma, which plans to release the drug through its marketing partner Mylan.

Nexium (esomeprazole magnesium)

Due to lose patent exclusivity in November this year, heartburn drug Nexium is the second biggest selling drug in the world, making AstraZeneca $3.8 billion in 2013.

However, the effect of Nexium’s impending expiry has already been felt, as this figure was down from more than $3.9 billion in 2012.

AstraZeneca’s chief executive Pascal Soriot said that in the short term, the impact from the loss of “key brands” would be challenging, although he expects 2017’s revenues to be “broadly in line” with those of 2013.

In a statement, he said that the company’s pipeline has 11 new molecular entities in Phase II or registration—almost double last year’s total.

AstraZeneca recently acquired Bristol-Myers Squibb’s diabetes portfolio and will be working to maximise its potential.

“I’m pleased with the momentum we have built in 2013,” he said. “We continue to focus our organisation on the areas that will drive growth, redeploying our resources to fund the promising late-stage pipeline.”

In 2011, Ranbaxy, Mylan and Teva launched generic versions of Nexium in the UK, and after the patent expires on May 27, they are likely to enter the US market.

Cymbalta (duloxetine hydrochloride)

Indiana-based Eli Lilly has been preparing for a double-hit with two of its blockbuster drugs facing the so-called patent cliff. Last spring it started laying off hundreds of sales staff, and posted disappointing financial results at the end of the year.

Still Lilly’s biggest selling drug, antidepressant Cymbalta brought in more than $880 million in the last quarter of 2013, though this was down by 38 percent compared with the same period in 2012.

Immediately after the drug lost exclusivity last December, six generic makers including Teva, Lupin and Sun Pharma rushed into the market. Another one of Lilly’s Cymbalta patents, covering the formulation of duloxetine in pellets, will expire in July this year.

“Lilly’s fourth-quarter 2013 results reflect the initial impact from the US patent expiration for Cymbalta,” said Lilly’s chairman, president and chief executive John Lechleiter.

“The loss of the Cymbalta patent, along with the expiration of the US patent for Evista in March of this year will result in a substantial decline in revenue and earnings in 2014.

“Yet, far from seeing 2014 as a tough year for Lilly, we see it as a moment of tremendous opportunity. We expect to launch several new medicines this year and returning our company to growth in 2015 and beyond,” he added.

Lilly says it expects revenue declines following patent expiries to be partially offset by “growth from a portfolio of other products including [diabetes treatment] Humalog”.

Evista (raloxifene hydrochloride)

An osteoporosis drug that has also been approved to reduce the risk of breast cancer, at the end of 2013 Lilly’s Evista was still going strong, with global...
sales reaching $1 billion in 2013—an increase of 4 percent on the previous year.

Due to lose exclusivity in March, its main competitor will likely be Teva’s generic offering.

In 2010, the US Court of Appeals for the Federal Circuit dismissed Teva’s appeal against a district court’s permanent injunction preventing any manufacture of distribution of a generic version of Evista.

Lilly’s strategy for weathering its big patent losses is developing new medicines. It has entered into an agreement with Pfizer to develop and commercialise tanezumab, a monoclonal antibody under consideration for the treatment of moderate-to-severe chronic osteoarthritis pain, chronic low back pain, and cancer-related bone pain.

It has also announced that a new drug application for long-acting insulin filed with alliance partner Boehringer Ingelheim has been accepted by the FDA.

Micardis (telmisartan)
The hypertension drug worth $274 million annually to Boehringer Ingelheim slipped off the patent cliff in January, with Actavis receiving FDA approval for its generic version immediately after.

As the first filer of an Abbreviated New Drug Application (ANDA) with the FDA, Actavis has been granted 180 days of generic exclusivity on the market.

However, Boehringer has a backup with its MicardisPlus formulation, a combination of active ingredient telmisartan and diuretic hydrochlorothiazide. A supplementary protection certificate (SPC) covering the product will extend its life to 2017, although this has been challenged by Actavis in a case that was referred by the UK Patents Court to the Court of Justice of the European Union (CJEU) late last year.

Boehringer is waiting for the CJEU to decide whether it may keep its SPC on the combination product; decisions on three cases handed down in December could provide a window as to which way the court will go.

Restasis (cyclosporine)
Allergan’s Restasis eye drop solution for chronic dry eye will lose exclusivity in May, although in January the US Patent and Trademark Office issued three new patents covering the formulation and method of using the drug.

Hoping to secure first-filer status to enter the generic market is Actavis, which in January confirmed that its subsidiary Watson Laboratories had submitted an ANDA to the FDA. After issuing guidelines related to the approval of generic versions of Restasis products, the FDA informed Actavis that its application had been refused.

Actavis then notified Allergan that it had amended its application to include a Paragraph IV certification to the newly issued patent. Actavis is currently discussing the filing status of its application with the FDA.

Restasis made $940 million in worldwide sales in 2013. Allergan expects this to reach $1 billion by end of 2014.

Nasonex (mometasone furoate monohydrate)
Nasonex has proven something of a cash cow for Merck, which acquired the product when it bought company Schering-Plough in 2009. By the end of 2013, worldwide sales of the hayfever nasal spray were still climbing, from $1.268 billion in 2012 to $1.335 billion.

Two of the patents covering use of mometasone furoate expired at the end of January, and Merck has six months to hone its strategy before paediatric exclusivity runs out in July.

Nasonex has already experienced some competition—in 2012, a US district court decided that Canadian pharmaceutical company Apotex did not infringe Merck’s patent covering the active ingredient, which expires in 2017.

Even though the court found the composition of matter patent to be valid, Merck appealed against the ruling of non-infringement to the ruling to the US Court of Appeals for the Federal Circuit, which dismissed the case.

PATENT EXPIRATIONS AT A GLANCE

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A BIG MOMENT: REGULATING PERSONAL GENOME SERVICES

An individual gene profile provides a window into a person’s medical future, by examining DNA samples, but what are the best ways of regulating this developing technology? LSIPR looks at the challenges and possible solutions.

The technology of genetic screening has come on leaps and bounds since the Human Genome Project finished sequencing the entire human genome, after 13 years’ work, in 2003.

Now direct-to-consumer genetic testing companies can look at sections of your genome to determine risks of developing certain diseases, and deliver the results in a matter of weeks.

California-based 23andMe offers such a service. Describing itself as the largest DNA ancestry service in the world, 23andMe’s personal genome service (PGS) will analyse the DNA it receives from the saliva kit it sends and provide a detailed report about a person’s risks of developing certain diseases.

The service, available online at a price of $99, offers reports on more than 250 diseases and conditions.

Intervention

No doubt part of its appeal is the autonomy 23andMe’s service allows its customers, who can decide whether to take preventive measures after receiving their results.
However, the US Food and Drug Administration (FDA) saw this freedom in a medical context as a red flag. In November last year it ordered 23andMe to stop offering the service immediately, as it was being marketed without the administration's authorisation.

The FDA defines the service as a medical device, because it is “intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or is intended to affect the structure or function of the body.”

The FDA’s director of in vitro diagnostics and radiological health Alberto Gutierrez wrote in an open letter to the company: “Some of the uses for which PGS is intended are particularly concerning,” because of how customers may manage their results, which could present a false positive or negative.

Gutierrez said that a false positive could lead a patient to undergo preventive procedures that could be “morbidity-inducing”, while a false negative “could result in a failure to recognise an actual risk that may exist”.

In December 23andMe said it would immediately comply with the FDA’s requests, although a spokesperson for 23andMe told LSIPR that the company was not commenting on matters related to its conversations with the FDA. “We are actively engaged in the regulatory review process,” she said.

“Our goal is to work with the FDA in a manner that demonstrates the value of testing for individuals and the validity of the science that underlies our service.”

**Self-management**

Kevin Noonan, partner at McDonnell Boehnen Hulbert & Berghoff LLP in Chicago, says that while the FDA’s definition of the PGS as a medical device was “creative”, it was not “beyond the pale”.

“It’s just that the FDA is trying to get a handle on the services that are different from the way it handles most laboratory services in the US,” he says.

“The FDA’s saying that this falls within the provisions of a medical device part of what the FDA can regulate is an interesting extension of what they can do and inconsistent with what they’ve done in other instances,” he continues.

Most lab services are compliant with the clinical laboratory improvement amendments (CLIA), he explains. These are guidelines laid out by the US government for businesses offering clinical lab services to the public.

23andMe said it made the decision to comply with the CLIA guidelines to be consistent with other types of laboratory testing, although Noonan says it is a lot less regulated than the FDA with regards to drugs and medical devices.

He says that the real point in this case is the absence of a medical provider to interpret the test results for the customer.

“Even assuming the test results are right, there’s no doctor there to help you interpret what they mean,” he says. “For example, cancer diagnostics company Myriad has genetic counsellors.”

The easiest thing for 23andMe to do at this point is show that its sequencing methods are robust and reliable, Noonan adds.

The FDA said that companies offering devices intended to interpret genetic data for health purposes would generally need clearance or approval by the FDA, and that the type of regulation required would depend on the specific activities.

“The agency has extensive guidance that is applicable to the regulation of this type of test that can help manufacturers understand the regulatory options and data requirements,” a spokesperson for the FDA told LSIPR.

“The FDA is also working on draft guidance specifically outlining policies for direct-to-consumer genetic tests,” she adds.

Many companies are offering a similar service to 23andMe’s, though some critics have suggested the companies use different methods to arrive at their results, raising issues of accuracy.

New York Times reporter Kira Peikoff sent her DNA to three PGS companies, including 23andMe, each of which gave different results. In some cases the results couldn’t be more opposed: 23andMe named Peikoff’s most elevated risks as psoriasis and rheumatoid arthritis, which Genetic Testing Laboratories pegged as her lowest risks.

**(Very) personal information**

While the accuracy of these tests is a worry, there is also the challenge of preserving the privacy of individual donors.

Jeff Matsuura, of counsel at Alliance Law Group, said that critics of PGSs are concerned that the information provided by the services is not presented in the context of information, research and education. Rather, they claim that the information can be used “directly by consumers for health and medical services”.

He continues that supporters of open access argue that these services are presented as information services, not health recommendations.

Matsuura says that in the US, the primary rights of individuals, with regards to their genetic data, are privacy and protection against discrimination.

“Although US privacy laws are, in general, not very strong, one area that is increasingly provided federal law protection is personal health and medical information,” he says.

“A substantial amount of an individual’s genetic data is protected from disclosure by federal rules such as those imposed by the Health Information Portability and Accountability Act,” he says, which protects people against having their personal genetic information used against them.
“It is also possible that state regulators in charge of licensing providers of medical services may become involved to the extent that the PGS offerings are viewed as medical services.”

A moving target

With the technology for these services evolving so rapidly, nailing down a definitive set of guidelines going to be a challenge.

Matsuura says he is certain there will be future regulatory issues. “As the dispute between the FDA and 23andMe illustrates, regulators are currently trying to understand at what point provision of genetic information becomes delivery of some type of medical service.”

There’s also the issue of permissible uses of genetic information by employers, insurers and other outside parties, as well as the rights of ownership, access, and control by an individual over his or her personal genetic data, he adds.

“One important theme that will have a dramatic impact on regulation of PGS is the fact that those services are, in effect, becoming mass market consumer services instead of highly sophisticated medical services,” he says.

“As PGS moves into the mass consumer marketplace, the regulators—such as the FTC and regional consumer protection authorities—will become involved and the legal, regulatory and policy issues will start to look more and more like traditional consumer protection issues.”

Noonan says it is in everyone’s interest to arrive at a solution “as soon as possible”. However, he says that while we have some understanding about a person’s genetic properties and how they’re relevant to a diagnosis, we’re still “a long way away” from having enough knowledge about how the components interact, and why they are significant.

“The biggest global problem that these companies have, and they all acknowledge it, is that there’s a lot more information that we need to understand,” he says.

It’s definitely early days, but progress in drawing up regulations in the area of personal genomic services will certainly blaze a trail, as access to personal genetic data becomes the norm in an era of personalised medicine. ■
Supplementary protection certificates (SPCs) are national rights in Europe that extend patent protection for medicinal and plant protection products. Their aim is to compensate patentees for the years of patent term lost during lengthy regulatory approval processes that are necessary to get such products to market. Given that up to five-and-a-half years of additional protection can be gained beyond patent expiry, SPCs are often hard fought over before patent offices and the courts.

In the aftermath of the Court of Justice of the EU (CJEU)’s ruling of 2011 in Medeva (C-322/10), two issues concerning the allowability of SPCs have arisen. One is the extent to which an active ingredient (or a combination of active ingredients) should be defined in the claims of the patent in order to be deemed ‘protected’ under Article 3(a) of the SPC Regulation (EC 469/2009).

Another is whether multiple SPCs can be granted, based on the same basic patent, under Article 3(c) of that regulation. These have been considered by the CJEU in C-484/12 (Georgetown University v Octrooicentrum Nederland), C-443/12 (Actavis v Sanofi), and C-493/12 (Lilly v HGS).

**Background**
The Lilly and Actavis cases both considered the meaning of ‘protected’ by the basic patent under Article 3(a). The English High Court found it difficult to apply the “specified in the...
wording of the claim” test set out in the CJEU’s Medeva judgment, and sought further clarity on how the matter should be addressed. In Lilly, the issue arose in relation to antibodies defined functionally by way of their binding to a particular target antigen.

In Actavis, the dispute was whether claims to the anti-hypertensive agent, irbesartan, in combination with a diuretic, could be said to protect the combination of irbesartan and the particular diuretic, HCTZ, even though the patent contained no mention of HCTZ.

The Georgetown University and Actavis judgments concern Article 3(c), and particularly whether obiter comments made in the CJEU’s ruling in Biogen C-181/95 meant that only one SPC could be granted for each basic patent (regardless of how many products were protected by that patent). Prior to obiter comments made in Medeva, national patent offices had been interpreting the comments in Biogen as allowing one SPC per product per patent.

In line with this previous thinking, Georgetown University had filed several SPC applications related to a cervical cancer vaccine (Gardasil®). The vaccine comprised multiple antigens, each of which was described for the first time in the basic patent, and SPCs were filed to either individual antigens or combinations thereof, based on the same marketing authorisation (MA) and the
same basic patent. Each SPC based on Gardasil* will expire on the same day.

Sanofi’s SPCs related to (i) irbesartan (Aprovel®) and (ii) a combination of irbesartan and HCTZ (CoAprovel®), both SPCs being based on the same basic patent but on different MAs. The authorisation for the combination was granted later than that for irbesartan alone, such that the combination SPC expired 14 months later than that for irbesartan alone.

CJEU’S judgments

The CJEU decided the following:

Article 3(a)

1. Where a basic patent protects more than one active ingredient, then more than one SPC may be granted for that patent, under most circumstances, including those of the Georgetown University case.

2. However, where a basic patent protects only one active ingredient and the combination of that active ingredient with another, and an SPC has been granted for the first active ingredient on the basis of a relevant MA, an SPC for the combination cannot be granted under the same basic patent on the basis of a subsequent MA. Thus, Sanofi’s combination SPC is invalid.

Article 3(c)

The CJEU has finally clarified the statements made in the earlier Biogen and Medeva decisions regarding the number of SPCs that may be granted per patent: under most circumstances, it is clear that more than one SPC may be granted for a basic patent where that patent protects more than one product. The CJEU did, however, outline an exception to this general principle, which applies to the circumstances surrounding Sanofi’s SPCs.

The court expressed that a second MA cannot be used as the basis for an SPC for a combination product where one component of that combination was already the subject of an SPC based on the same basic patent, but the remaining product(s) are not protected as such by that patent.

It is noteworthy that this exception has been crafted such that it cannot easily be circumvented by way of a divisional application filing strategy. In what appears to be an effort to address concerns regarding evergreening, the CJEU states that each separate patent can confer entitlement to a new SPC only insofar as the combination represents “a totally separate innovation”.

In principle, this could mean that the claims of parent and divisional patents would need to be examined by the national patent offices to determine whether the relevant products are “totally separate innovations” for SPC purposes, similar to the assessment of double patenting that is made for continuation and divisional applications at the US Patent and Trademark Office.

Without further guidance on the criteria for making such an assessment, it is likely that different national patent offices will adopt divergent approaches when determining the validity of such SPCs.

Conclusions

The decision to allow multiple SPCs based on a single patent will surely be welcomed by many innovators and patent holders. However, the “fix” that has been introduced to address Sanofi’s situation may bring about additional complexity for patentees seeking SPCs for combination products, along with an examination burden for national patent offices that is unlike anything previously experienced on SPC applications.
It is also difficult to see how the new Article 3(a) test can be applied to the cases at issue here with any greater success than the previous tests put forward. If the CJEU continues to refuse to provide further guidance on this question, then more calls for a substantive review of the SPC legislation can be expected.

All in all, the decisions do provide some clarity, but as we have come to expect with decisions on SPCs, they also raise many questions that leave lingering uncertainty.

This is the second successful case before the CJEU in which Potter Clarkson has acted for Georgetown University, the first being Georgetown University and Others (C-422/10).

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David Carling received his undergraduate master’s degree in chemistry and doctorate in bioinorganic chemistry from the University of Nottingham. Following further research and a period working in regulatory affairs, he joined Potter Clarkson in 2008. Carling is now an associate at Potter Clarkson specialising in the fields of chemistry and pharmaceuticals.

Michael Pears is a senior associate at Potter Clarkson who advises clients on a wide range of biotechnological patent matters. Over recent years he has developed experience in niche area of SPCs. As well as authoring various articles on the topic, he has been involved in coordinating the prosecution of several high profile SPC portfolios throughout Europe, and in taking a case to the CJEU (namely Georgetown University et al, C-422/10).
BURDEN OF PROOF: US SUPREME COURT BACKS LICENSEES

The US Supreme Court has again reversed a Federal Circuit decision, this time over burden of proof, says Matthew Nielsen.

What would you say to (i) limiting your liability for patent infringement by obtaining a licence that establishes a royalty rate and prevents the owner from obtaining an injunction, and then (ii) asserting in court that the patent is invalid and not infringed so you might ultimately pay the patent owner nothing?

Potentially, it’s not a bad approach.

The Supreme Court gave further incentive to aggressive strategies such as this in January in Medtronic, Inc v Mirowski Family Ventures, LLC. Relying on well-settled law and the public
“MIROWSKI, AS THE PARTY ASSERTING INFRINGEMENT, BORE THE BURDEN OF PROVING INFRINGEMENT, AND MIROWSKI FAILED TO PROVE INFRINGEMENT EITHER LITERALLY OR UNDER THE DOCTRINE OF EQUIVALENTS.”

interest in limiting patents to their proper scope, the court held that patent owners bear the burden of persuasion when a licensee raises the issue of non-infringement in a declaratory judgment action. This underscores the need for patent owners in licence negotiations to consider the potential for later declaratory judgment actions, and how shrewd licensees will consider bringing such actions in appropriate circumstances.

Procedural history

Medtronic licensed several patents covering implantable heart stimulators from Mirowski Family Ventures. Under the licence, Mirowski could notify Medtronic of new Medtronic products that Mirowski believed infringed the licensed patents, whereupon Medtronic had the option to: (i) pay royalties; (ii) seek a declaratory judgment of non-infringement, but simultaneously pay royalties such that it would avoid a breach of the licence (the parties later agreed Medtronic could deposit royalties in an escrow account); or (iii) pay nothing, at which point Mirowski could terminate the licence and sue Medtronic for infringement.

Years later, Medtronic developed new products that Mirowski said infringed its patents. Medtronic disagreed, and responded by depositing royalties in an escrow account and suing Mirowski in federal district court for a declaratory judgment of non-infringement and invalidity.

Facts such as these, where the licensee continues paying royalties but contends a licensed patent is not infringed or is invalid, create a dispute sufficient for federal courts to have declaratory judgment jurisdiction under the Supreme Court’s decision in *MedImmune, Inc v Genentech, Inc* (2007).

After a bench trial, the district court ruled that Mirowski, as the party asserting infringement, bore the burden of proving infringement, and that Mirowski failed to prove infringement either literally or under the doctrine of equivalents.

On appeal, the US Court of Appeals for the Federal Circuit vacated the district court’s non-infringement judgment, holding that Medtronic, as the declaratory judgment plaintiff, bore the burden of proving non-infringement. The court acknowledged that the patent owner typically bears the burden, but in a declaratory judgment action where the “continued existence of the licence precludes the very infringement counterclaim that would normally impose the burden of proving infringement on the patentee,” the licensee bears the burden.

The Supreme Court’s decision

In a unanimous (9–0) decision, the Supreme Court reversed, holding that “when a licensee seeks a declaratory judgment against a patentee to establish that there is no infringement, the burden of proving infringement remains with the patentee”.

“Simple legal logic,” the court said, “resting upon settled case law, strongly supports our conclusion.” The court boiled that down to three legal propositions: (i) the burden of proving infringement generally rests upon the patent owner; (ii) declaratory judgment jurisdiction is procedural, leaving substantive rights unchanged; and (iii) the burden of proof is a substantive aspect of a claim.

The court then discussed how “practical considerations” lead to the same conclusion, focusing on the negative impact (that the court perceived) a burden shift would have on licensees asserting non-infringement. A burden shift could lead to situations where each side, in separate actions, failed to satisfy the burden of proof, “creating uncertainty among the parties and others who seek to know just what products and processes they are free to use.”

“It could also at least on occasion, create unnecessary complexity by making it difficult for the licensee to understand upon just what theory the patentee’s infringement claim rests.” In addition, a burden shift “makes the declaratory judgment procedure—compared to, say, just refusing to pay royalties—disadvantageous.”

The court rejected the argument that placing the burden on patent owners would permit a licensee “at its sole discretion—to force the patentee into full-blown patent infringement litigation.” There must still be a genuine dispute, the court said, and, more important than any burden on the patent
owner, the public has a “paramount interest in seeing that patent monopolies . . . are kept within their legitimate scope,” and “licensees may often be the only individuals with enough economic incentive to litigate questions of a patent’s scope,” which weigh against a burden shift.

Where does this leave patent owners and licensees?

Medtronic has an impact on a relatively narrow category of lawsuits—suits brought by non-breaching licensees under MedImmune. And many people already thought patent owners always bear the burden of proving infringement, even when raised in a declaratory judgment action. But Medtronic may provide licensees with a little more incentive, particularly where the benefits substantially outweigh the costs, to seek declaratory judgments of non-infringement.

Under MedImmune, a licensee could already do this without first breaching the licence, which would otherwise expose it to potential liability (if the licensee lost in court) for increased damages for willful infringement, the patent owner’s attorney’s fees and costs, and additional payments if licensees seek to maintain their licenses.

However, such provisions must withstand judicial scrutiny, and the courts have struck down provisions that bar or penalise challenging a patent’s validity. This practice goes back to Lear, Inc v Adkins (1969), which the court cited in Medtronic, where the court held licensees are not estopped from later challenging the validity of licensed patents (and struck down as unenforceable a provision requiring ongoing royalty payments even if the licensed patent was held invalid).

A recent instance of this was in Rates Technology Inc v Speakeasy Inc (2012), where the Second Circuit applied Lear in holding that a no-challenge provision in a pre-litigation “settlement” agreement was unenforceable (as opposed to a post-litigation agreement in combination with a court judgment given res judicata effect).

The direction of the Supreme Court

Does Medtronic tell us anything about how the Supreme Court will rule in future patent cases? It’s interesting that the court, in ruling on which party bears the burden of persuasion on infringement, emphasised the importance of limiting patents to their legitimate scope (drawing on its reasoning in Lear) and potential public uncertainty about the scope of patents.

Somewhat along those lines, the court has weakened patents in cases such as Ass’n for Molecular Technology v Myriad Genetics, Inc (2013) (genomic DNA not patent-eligible), Mayo Collaborative Services v Prometheus Labs, Inc (2012) (method involving administration of a prior-art drug and measuring a metabolite not patent-eligible), KSR Int’l Co v Teleflex Inc (2007) (common sense may be evidence of obviousness), and eBay Inc v MercExchange, LLC (no automatic injunctions in patent cases).

But not all of the court’s recent decisions have weakened patents. In Kappos v Hyatt, (2012), the court held that the only limits on a patent applicant’s introduction of new evidence in a 35USC §145 district court action (to review an adverse decision of the Patent Office in ex parte patent prosecution) are the limits imposed by the Federal Rules of Evidence and Civil Procedure. And in Microsoft Corp v i4i Limited Partnership (2011), despite much speculation that the outcome would be otherwise, the court upheld the longstanding rule that clear and convincing evidence is required for proving invalidity (as opposed to a lower preponderance-of-the-evidence standard), even regarding prior art not considered by the Patent Office.

Decisions like these suggest the Supreme Court is attempting—borrowing the words of Chief Justice Roberts—to “limit itself to calling balls and strikes”, with Medtronic being just the latest example.

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TACKLING THE BACKLOG IN BRAZIL

It’s been a long time coming, but perhaps the Brazilian patent office is finally going to deal with the logjam of patent applications, says Gabriel di Blasi.

The Brazilian Patent Office (INPI) has been facing a huge backlog of patent applications, which has led to an average waiting time for examination of about 10 years, an extremely long period compared with other countries. The delays apply for both patent and utility model (UM) applications, with the examination of UM applications being slightly less, around eight years. According to the INPI, the number of patent applications pending examination, mainly in the biotech, pharmaceutical, electronic and telecommunication industries, has been increasing every year, and is estimated to reach nearly 200,000 by 2015.
The initial cause for the backlog was a change from the Brazilian Industrial Code (CPI) to the Brazilian Industrial Property Law (LPI), finally recognising patent rights for pharma, agriculture and biotech. This allowance caused an overwhelming surge in patent applications in Brazil. For example, in 1995 the number of patent applications filed was about 16,000 per year. In 2013, this number reached approximately 34,000 patent applications.

Several other factors have contributed to the backlog. The INPI did not have sufficient infrastructure, especially examiners, to support such an increased demand, and its workers were frequently on strike with demands for wage increases, better working conditions, and the hiring of new examiners.

Additional delay for the examination of applications in biotech and pharma is caused by the double patent examination performed by the Brazilian Health Surveillance Agency (ANVISA). In 2001, in order to promote and develop generic drugs in Brazil, the Brazilian government established a special provision for patent examination in these technical areas. Originally, the government provision regarding ANVISA’s review of pharma patent applications applied only to ‘pipeline’ cases, which allowed for applications by owners of existing patent applications in these areas between May 15, 1996 and May 15, 1997.

It was later expanded to include all new, regular pharma applications as well as biotech applications. This causes several problems for granting patent rights in both sectors and creates legal uncertainty for overseas pharmaceutical companies.

The effects caused by the backlog have been tremendous. Aside from the legal uncertainty, because there is no guarantee as to when the patent rights will be granted, such delays in protection can have a spiralling effect on manufacturing costs, as the owners do not have the patent rights to prevent third parties from using their technologies, incurring a higher cost for bringing their products to market. These effects weaken the Brazilian IP system as a whole.

The INPI has also implemented an electronic filing system for patent applications, known as the E-Patent system. This system started in the spring of 2013 and will provide access to all information regarding patent issues, including the technical opinions of patents and their respective charters, all procedures of patent applications and patent lawsuits among others. The INPI expects this system to be fully functional by 2015.

In addition, the INPI has reorganised the channels for application examination, creating examination lines for each type of application, and entered into cooperation with the National Council of Technological and Scientific Development to increase the number of examined patent applications.

However, these actions and measures are not enough to reduce the patent examination time, nor are they enough to substantially reduce the backlog in Brazil. The INPI needs to move forward with hiring and training new examiners, especially in pharmaceutical and biotech areas, and review the guidelines for examination in order to simplify the procedures of the examiners for examination.

According to the INPI, decisions related to rejections and allowances of patent applications and granted patents decreased between 2009 and 2012. However, if the INPI hires and trains new examiners for 2014 the prediction will be to reach 49,000 and 35,000, respectively, by 2015. Based on this scenario, the INPI expects to reduce the time frame for examination to as little as four years.
The INPI needs to move swiftly to enact the changes it has set to address the massive backlog and reduce the examination time for patent applications in Brazil. These measures have the potential to bring the Brazilian patent system more in line with the rest of the developed world and will provide more legal security for foreign investments. In the meantime, being aware of measures to expedite applications can help both foreign and domestic patent seekers better protect their interests.

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THE GLIVEC CASE: GETTING BEYOND EFFICACY

The Indian Supreme Court has failed to provide the clarity which is craved by practitioners in its latest pronouncement on the controversial Section 3(d), says Jitesh Kumar.

The judgment of the Indian Supreme Court concerning Novartis’ anti-cancer drug Glivec has dominated all recent discussions on Section 3(d) of the Indian Patents Act. Despite being a landmark reference for issues pertaining to Section 3(d), it is often forgotten that there is much more to Section 3(d) beyond the “enhanced efficacy” requirement, which the judgment did not address.

While cogent in many aspects, the ruling has evaluated issues primarily in the context of specific facts and circumstances of the case, leaving us with dicta rather than binding precedence.
The scope of Section 3(d)

To begin with, the Supreme Court has not thrown much light on the scope of Section 3(d). Careful analysis will show that the court’s position is that Section 3(d) sets up a second tier of qualifying standards for chemical substances and/or pharmaceutical products in order to check any attempt at repetitive patenting or extension of the patent term (i.e., evergreening), but at the same time leaves the door open for true and genuine inventions.

A seemingly clear assertion which is in agreement with the legislative intent behind its enactment, it should imply that Section 3(d) may not be applicable to genuine inventions which do not entail any attempt at evergreening or repetitive patenting. However, the assertion may not be of any practical significance because the court has not laid down any guidelines/parameters in this regard. The Indian Patent Office continues to raise objections under Section 3(d) against the majority of pharmaceutical applications, at times even in the case of applications for new chemical entities and new synergistic compositions of two or more known active substances.

Efficacy as “therapeutic efficacy”

Another inadequate explanation in the judgment is with regard to the interpretation of efficacy as “therapeutic efficacy”. Will this interpretation stand the test of time? Many stakeholders have already shuddered at the court’s interpretation, which is narrow and unscientifically limiting. Many, like me, believe that the jurisprudence will evolve to a better explanation, if only because science and technology develop and stabilise along several different pathways, which prohibits the possibility of a general rule, especially for a term as important as “efficacy”.

In fact, a deliberate reading of the judgment shows that the Supreme Court has left open the question of how to interpret “therapeutic efficacy” and has only affirmed that physicochemical properties must be excluded from its domain. The exclusion itself may have to be reconsidered in future, as in certain circumstances it may become necessary to take physicochemical properties into consideration. As a simple case in point, take for instance a situation where the already known compound is toxic, so that generating *in vivo* therapeutic data may not be practically possible on account of moral and ethical issues.

What is a “new form”?* GLIVEC

Another important aspect left out in the *Glivec* case is with regard to the scope of the term “new form” and the extent of its application in real situations. The “new form” claimed in the *Glivec* case was a new crystalline polymorph and the Supreme Court did not have the opportunity to analyse aspects related to other forms mentioned in the explanation part of Section 3(d) such as esters, ethers, complexes and combinations. The only dictum made by the apex court with regard to these forms is the generalisation that each of the different forms mentioned in the explanation part has some properties inherent to that form.

The court generalised it as: “While dealing with the explanation it must also be kept in mind that each of the different forms mentioned in the explanation have some properties inherent to that form. The generalisation, which may be difficult to apply to forms such as complexes and

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*GLIVEC*
GLIVEC

many applications pending before the Indian Patent Office.

Conclusion

Apart from the above, there are other aspects related to Section 3(d) which need resolution and the observations/affirmations of the Supreme Court are inadequate to provide any insights as to the paths which may be taken for their resolution. It is apparent that the judgment of the Supreme Court will act as a limited precedent because, instead of the legal clarifications that almost everyone was hoping for, the court followed a very facts-specific approach which arguably does not give this case the legal teeth it deserves.

So, as the debate on Section 3(d) saunters on and many more patent cases enter into contentious battles for a resolution of these issues, I am reminded of words of Robert Frost: "But I have promises to keep, And miles to go before I sleep, And miles to go before I sleep."

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Several significant patent cases were heard by the UK courts over the course of the last year and common themes are emerging which impact on the life sciences industry, in particular in the context of second medical use claims and dosage regimes. One such theme, which runs throughout the judgments in *Hospira v Novartis* [2013] EWHC 516(Pat) and *Eli Lilly v Janssen Alzheimer Immunotherapy* [2013] EWHC 1737(Pat), is the question of what amounts to a disclosure of ‘effective’ treatment and the consequences which follow when assessing entitlement to priority and sufficiency.

While the standard itself may be familiar to many in this industry, the criterion to be applied in the context of patentability was hotly contested by the parties and explored in detail by Arnold J, who heard both cases at first instance.

**Background**

Novartis is the proprietor of two dosage regime patents claiming the use of zoledronic acid for the treatment of osteoporosis by intravenous administration, at a range of dosages and with dosing intervals of at least six months. Hospira and Generics t/a Mylan sought to revoke these patents to ‘clear the way’ for launch of their own generic products. *Lilly* was another ‘clearing the way’ case concerning Janssen’s second medical use patent, which claimed a class of antibodies which bind to the amyloid-β peptide, for use in preventing or treating Alzheimer’s (and related) disease.

**Claim construction**

It was common ground in both cases that the term “for” in the claims should be construed as
meaning 'suitable for' (or, in the Hospira case, required the dosage regimes to be 'effective').
Arnold J held this to mean that the product does in fact achieve the claimed therapeutic efficacy. While acknowledging the importance of context, he concluded that the primary criterion for determining efficacy in Janssen’s patent was success in a Phase II trial. Further, he agreed with Lilly that Phase III trials (if available) are the “best guide” since the skilled team recognises them as “the gold standard for determining efficacy”.

Entitlement to priority
This was not contested in Lilly but considered in detail in Hospira. Arnold J found that Novartis’ patents lacked priority for two reasons, the first being failure to disclose the particular combination of features ultimately claimed in the patents. For example, there was nothing in the general disclosure of the relevant priority document to link the claims which covered a defined dose and dosing interval of zoledronic acid with the other integers, ie, treatment of osteoporosis and intravenous administration.

Second, even though the priority document included Phase II studies, Arnold J decided there was no actual disclosure that zoledronic acid will be effective in reducing fractures in osteoporosis patients—the skilled team would appreciate that a Phase III trial was required.

Lack of priority was determinative of the outcome at first instance (it was common ground that the patents lacked novelty if priority was lost), a finding that was upheld by the Court of Appeal in Hospira v Novartis [2013] EWCA Civ 1663.

Sufficiency
In Hospira, Arnold J found that Novartis’ claims which were open-ended should not be interpreted as extending to any dose and any dosage interval but only to those which work. Nonetheless, since their potential scope was “quite broad” and placed an “undue burden on the skilled team to find out what doses and dosage intervals work”, he held the claims invalid for insufficiency as they were not enabled across their breadth.

Insufficiency issues were key in the Lilly case (since novelty and obviousness objections failed) and Arnold J set out a more detailed and structured approach. Citing the Court of Appeal decision in Regeneron v Genentech [2013] EWCA Civ 93 (which in turn applies well-established principles of European patent law) he confirmed that the patentee must demonstrate that the claimed therapeutic effect is “plausible”, adopting the following two-stage enquiry:

1. Determine whether the patent disclosure, in the light of the skilled team’s common general knowledge, makes it “plausible” that the invention will work across the scope of the claim; and
2. If satisfied, consider whether later evidence establishes that in fact the invention cannot be performed:
   (a) Without undue burden at all (‘classical insufficiency’); and
   (b) Across the scope of the claim without undue burden (‘excessive claim breadth/Biogen insufficiency’).

Arnold J concluded that the plausibility threshold in stage one was satisfied on the basis of in vivo data, but only in respect of antibodies which bind to the N-terminal portion of amyloid-β rather than any antibody, as claimed. So the patent was insufficient for excessive claim breadth, as in Hospira.

Arnold J then considered post-published evidence in stage two, concluding that Janssen’s patent was also classically insufficient given the failure of Janssen’s Phase III trials of its own antibody to amyloid-β. In doing so he acknowledged again that Phase III trials are a “better guide” to efficacy than Phase II.

Conclusion
While patentees may tend to favour early filing strategies, it is important to ensure that priority documents disclose the actual combination of features ultimately claimed in the patent. Interestingly, had this been disclosed in Novartis’ priority document, the Court of Appeal indicated (obiter) that “I think one would conclude that the patentee was teaching that the regimen would be effective”. This suggestion that no more data was required may be of some comfort to patent applicants, who now face a potential dilemma between current moves towards greater transparency of clinical trials and the risk of destroying novelty in their own inventions.

Broadly drafted patent claims continue to cause difficulties for patentees in the wake of excessive claim breadth objections, particularly in the medical use field. Therapeutic use patents invariably require disclosure of appropriate experiments to survive allegations of insufficiency. Exactly how much and what type of data is required will be a question of degree based on the nature of the invention and the state of the art in any given case, and expert evidence will no doubt be key.

“WHILE PATENTEES MAY TEND TO FAVOUR EARLY FILING STRATEGIES, IT IS IMPORTANT TO ENSURE THAT PRIORITY DOCUMENTS DISCLOSE THE ACTUAL COMBINATION OF FEATURES ULTIMATELY CLAIMED IN THE PATENT.”

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Nonetheless, while finding in Janssen’s favour on plausibility in the Lilly case, Arnold J’s suggestions that Phase II (ideally Phase III) clinical trials are required to establish efficacy seem concerning for patentees. This can be contrasted with the earlier appellate guidance in Regeneron that it is not always necessary for a patentee to provide clinical trial data or animal testing, and that patents are not insufficient merely because they do not demonstrate therapeutic efficacy if, nevertheless, there is enough information upon which to found a reasonable prediction.

Although granted permission to appeal Arnold J’s decision, it seems that Janssen’s appeal is not proceeding, so we will have to wait for further guidance from the Court of Appeal on the threshold for patentability of therapeutic use claims.

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MORE BANG FOR YOUR BUCK:
SECOND MEDICAL USE AND THE EPC 2000

Second and further medical use claims provide companies and patent lawyers with interesting opportunities, as Caroline Pallard explains.

Under Article 54(5) of the European Patent Convention (EPC) 2000, known substances or compositions are deemed novel provided they are for any specific use in a medical method provided that such use is not comprised in the state of the art (ie, second or further medical use) (this is derived from Article 54(4) EPC 1973).

In 1983, the Enlarged Board of Appeal (G5/83) defined the way to formulate a second or further medical use of a substance or composition for the manufacture of a medicament for any “specified new and inventive therapeutic application”, based on Article 54 EPC 1973. Since then, case law decisions have primarily dealt with new diseases or conditions defining such second or further medical use.

In 2010, the Enlarged Board of Appeal (G02/08), redefined the way to formulate a second or further medical use of a substance or composition from Article 54(5) EPC 2000 and emphasised that “any specific use in a therapeutic method” as stated in Article 54(5) EPC 2000 could potentially be considered as a second or further medical use of a substance or composition, provided that such use was not comprised in the state of the art, thereby opening up the possibility to protect “any such specific use in a therapeutic method” as long as it meets all other EPC requirements.

Novelty based on patient groups
In 1987, the Board of Appeal held that a distinct group of patients could provide evidence for a second or further medical use provided the group is not arbitrarily chosen: the new group of patients must be distinguished from the former by its physiological or pathological status. An example of this situation was illustrated in T19/86, which held that the therapeutic
application of a vaccine against Aujeszky’s disease, known for treatment of a particular class of animal (seronegative pigs), to a new and different class of the same animal (seropositive pigs), is a further medical use.

Later, in T108/09, the use of fulvestrant as a third line of treatment for breast cancer patients who had first been treated with tamoxifen and subsequently with an aromatase inhibitor, was considered as a further medical use of fulvestrant. Fulvestrant was already known to be used for treating breast cancer patients. The board held that the tumours of patients first treated with tamoxifen and subsequently with an aromatase inhibitor acquired resistance to first tamoxifen and subsequently to the aromatase inhibitor and that as a result had changed from a biological point of view, defining a new subgroup of disease which could also be seen as a new subgroup of patients.

Novelty based on administration

In 2004 the board, in T1020/03, anticipated G02/08 and held that a distinct administration regimen of a known substance or composition for the treatment of the same disease for the same group of patients could be considered a second or further medical use. In T1020/03, insulin-like growth factor was used for treating chronic renal failure in mammals. A second or further medical use was solely constituted by the specific discontinuous administration pattern of insulin-like growth factor.

A new mode of administration of a known substance for treating a known disease could also considered as a second or further medical use as illustrated in T 51/93, wherein subcutaneous administration of human chorionic gonadotropin (HCG) was the only distinguishing feature compared to the use of HCG administered intramuscularly as known in the prior art.

Novelty based on a different technical effect

In T290/86 applying G05/83, it was held that a therapeutic use of a known therapeutic compound (the element lanthanum) for a similar therapeutic purpose (preventing tooth decay) was found novel if a new (and inventive) technical effect is taught in the patent. In T290/86, the prior art disclosed as technical effect of lanthanum the reduction of solubility of tooth enamel such as those developed in saliva and in the patent the technical effect was the removal of dental plaque.

In order to be novel, the effect must lead to a new use and not only constitute a mere explanation of the known use. In T254/93, the known composition was retinoic acid combined with corticosteroids used against dermatosis. The alleged new use of this composition was to prevent skin atrophy. The board held that the final effect obtained in this use was known in the prior art when using the known composition for treating dermatosis. The mere explanation of this final effect (preventing skin atrophy) when using a compound (retinoic acid) in a known composition (retinoic acid and corticosteroid) can not confer novelty to a use if the skilled person was already aware of the occurrence of the desired effect.

Such effect may be somehow ‘linked’ to the effect known in the art. In T1955/09, a substance (peptide) was used for killing bacteria. The prior art used the same substance for neutralising the toxins secreted by the same bacteria. The board held that such antibiotic effect could not be seen as a mere explanation of the final effect as found in T254/93, and held that the prior art teaches a direct effect of the substance on the toxins produced, whereas the patent teaches an indirect effect of the substance on the production of the toxins via their antibiotic action.

The foregoing illustrates that “any specific use in a medical method” as defined in Article 54(5) EPC 2000 seems to offer broad possibilities for defining a further medical use of a known substance. However, it should be borne in mind that such new further medical use must also be considered inventive in view of the prior art in order to constitute a patentable invention.

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Caroline Pallard joined NLO in 2006 after working at DSM/Gist-brocades in Delft and as a postdoctoral fellow at the Dutch Cancer Institute, where she specialised in immunology and biochemistry. She practises in biotechnology and in particular molecular biology, genomics, biochemistry, haematology and microbiology. Pallard has extensive experience of drafting and prosecuting complex patent applications and supporting licence negotiations and IP due diligences, and she frequently advises biotech start-ups on their IP strategies.
The BIO IP Counsels Committee Spring Conference will be held April 23-25, 2014 at the Omni Rancho Las Palmas Resort & Spa in Palm Springs, CA. The conference is a must-attend event for in-house IP counsel of biotech or pharma companies. Relevant, timely educational sessions give practical tips for real challenges. Hear USPTO representatives and industry experts discuss patent reform, claim construction, divided infringement, and federal circuit cases to watch. Join us for informal networking events designed to promote discussion and foster relationships among industry colleagues. To read attendee testimonials, review the program agenda and register, visit www.bio.org/ipcc. Register early and save!
In the not-so-distant past, obtaining patent protection for a new therapeutic drug (or new use of a known drug) was simpler than it is today. The therapeutic landscape was comparatively unexplored, and our knowledge of disease pathology was uninformed by the battery of molecular techniques available today. This lack of detailed information meant the factors to consider when assessing a new therapeutic application were relatively few and, consequently, the required analysis was relatively straightforward.

Fast-forward to today, and the number and sophistication of the analytical techniques available mean that it is not uncommon for researchers to make discoveries beyond simply which disease(s) a compound has the potential to treat. For example, the research may characterise the subset of patients in which a drug works best (or not at all). Illustrations of this type of ‘personalised’ medicine abound in the scientific literature, and patients can be defined by, for example, genotype, single-nucleotide polymorphisms (SNPs), or protein markers.

This allows targeted treatment of the patients who respond best, and the avoidance of non-responders or those likely to suffer adverse effects. In some cases, defining the patient group means the difference between clinical trial success and failure, enabling rational design of smaller trials with high success rates in defined patient sub-groups.

The progression toward a personalised approach to therapeutics poses a challenge for the patent system: can it protect this type of contribution, which has such clear benefits for patients and practitioners? And, if IP rights protection is available, how should the patent office decide which ‘personalised medicine’ inventions meet the requirements for patentability?

In Europe, at least, the law has developed in a way that is favourable to patent applicants in the field of personalised medicine. The European Patent Office (EPO) has long recognised that a newly-discovered medical use of a known agent is patentable over the earlier use of the same agent. Through successive decisions of the Boards of Appeal, this principle has developed to the point where identifying a new class of patient treatable using a known drug or a new clinical situation constituted patentable subject matter.
Significantly, the board in T1020/03 explicitly acknowledged that the investment in clinical trials needed the reward of patent protection to justify it on economic grounds.

**Legal platform**

Following on from the T1020/03 decision, the revised version of the European Patent Convention (EPC), which came into force on December 13, 2007, brought with it, for the first time, an explicit legal basis in the EPC for medical use inventions by way of a new “composition for use in a method for treatment” claim format. This new claim format defines a method of treating patients, rather than obliquely referring to manufacturing drugs such as the earlier ‘Swiss claim’ format, and can be easily adapted to ‘test and treat’ claims in which results from analyses identify patients as being eligible for treatment.

The combined results of these changes mean that, by defining markers or other clinical criteria by which patients can be selected for treatment, applicants can define a subset of patients who would not have been treated without the insight obtained through the analytical step. This definition can provide the basis for acknowledgement of novelty and inventive step.

The situation gets more complex in situations where the identified target patient group overlaps with the group of patients that the drug was already known or intended to treat. For example, a drug may already have received regulatory approval for treating a certain disease and may have been administered to a diverse population of patients with the disease. Naturally, inventors wish to obtain patents that include claims directed to the drug for use in treating the disease in the well-responding patient subgroup.

However, the EPO has struggled with the question of whether treatment of the same disease in a newly-defined patient subgroup represents a genuinely new medical use of the drug, or whether such claims are merely the old medical use described in a different way (and therefore not novel).

To the advantage of applicants, the EPO has decided that it is possible to obtain personalised medicine patents under these circumstances. For example, if the former use was described only in theory, with no patients actually treated (or there was a poor or unknown response to the limited clinical use), then use of the drug for treating patients who have a biomarker indicative of good drug response may be considered novel when the biomarker is specified in the claim.

The EPO has also indicated that reciting an active step of determining a patient’s biomarker status (eg, genotype) will be considered to render a claim novel, since the step of testing the patient to determine the presence of the biomarker is new, even if the drug was previously used successfully for treating the same disease in the same type of patients.

While specifying a particular genotype is a common way of defining a patient group, the new European patent medical use claim format lends itself just as easily to defining sub-groups by responders, assays or patterns of administration. This was approach was backed by the EPO’s Enlarged Board of Appeal in G2/08, where the board explicitly confirmed the potential patentability of medical use claims in which the pattern of administration was the only novel feature.

This means that, by performing follow-up patient studies, companies have the possibility of identifying patient sub-groups and obtaining personalised medicine patents. Such patents would effectively lengthen protection for treatment of key patient groups and so provide additional revenue to the companies. Moreover, patients and healthcare providers would reap the benefits of better targeted treatment, in terms of fewer unnecessary or ineffective treatments.

Applicants seeking European protection for inventions in the personalised medicine field are currently well placed, as is reflected by the increasing numbers of applications that define patient subgroups. The European patent system is managing to keep pace with the fast-moving therapeutic field—to the advantage of innovator companies, healthcare providers and patients alike.

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Robert Andrews is qualified as a chartered patent attorney and European patent attorney. He joined Mewburn Ellis in 2006. He holds a degree in biochemistry from the University of Oxford, and a PhD in developmental and cellular biology from the University of Cambridge. He specialises in patent work in biotechnology, particular protein engineering, enzymology, cellulosic processing and immunology, and deals mainly with patent drafting, prosecution, and opposition & appeal before the EPO. His clients include US and international biotech companies, US and UK universities, and biotechnology companies in Europe, Korea and the US.
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