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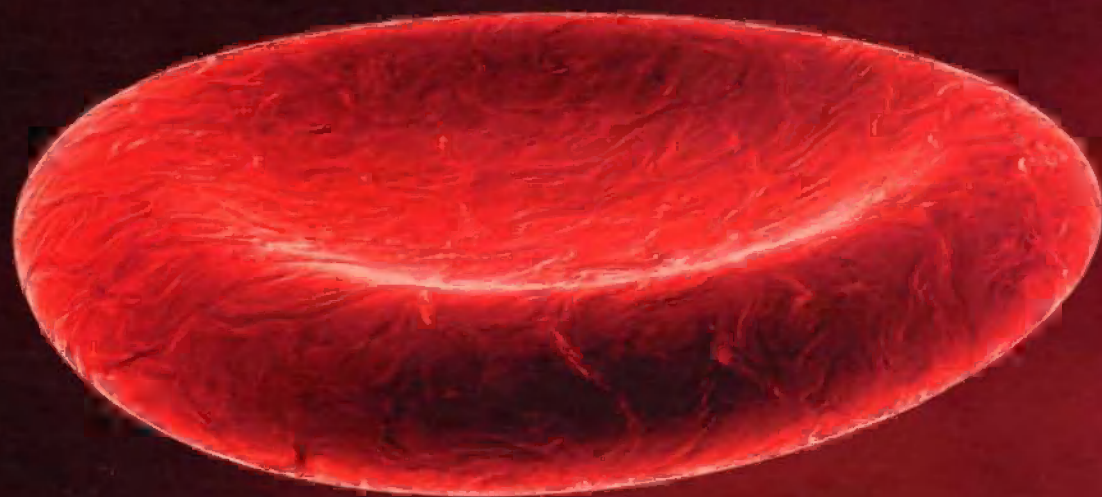
BIOTECH CASES THAT WILL SHAPE THE INDUSTRY

CUT YOUR UK
LITIGATION
COSTS

A PATENT
TROLL
BATTLE PLAN

LICENSING IN
EUROPE AFTER
MEDIMMUNE

AN OPEN
LETTER
TO EBAY



Five cases that will shape your strategy

With the growth of the biotech industry and the maturing of the first breakthrough inventions, litigation over patents is becoming more frequent and spreading around the world. MIP has selected five important cases from the US, Australia, France and Germany that highlight some of the issues that have arisen in the past year. Emma Barraclough, James Nurton and Peter Ollier look at how the cases developed, and why they are significant for the industry

The other EPO battle

It was one of the first great biotech inventions, and led to a product that has proved a lifesaver for thousands of anaemia sufferers (and, in some cases, an illicit boost to Tour de France cyclists) – and which earns the company that created it \$2.5 billion annually. But, more than 30 years after Epogen was invented, lawyers are still arguing over whether it really was an invention.

Since litigation over the key patents protecting the hormone erythropoietin (known as EPO) started in 1997, the biotechnology industry has been through several business cycles and two of the parties in the case have changed hands, one of them twice: TKT has been taken over by Shire Pharmaceuticals,

while HMR became Aventis Pharmaceuticals, now part of Sanofi-Aventis. As the Chief Judge of the US Court of Appeals for the Federal Circuit, Paul Michel, said in a dissenting opinion in the latest ruling in the US arm of the dispute last August: “This litigation has dragged on for almost ten years, yet the end is nowhere in sight.”

That was the Federal Circuit’s second judgment in the case, following two decisions from the District Court for the District of Massachusetts (totalling 360 pages). A remand back to the district court will lead to a third trial, the outcome of which will almost certainly also be appealed, and so on. As Michel said: “When will it end? Ironically, the patents in dispute may expire before this litigation concludes.” There has also been parallel litigation in Canada, Europe and Australia: in the UK, the House of Lords – the country’s highest court – revoked the UK arm of Amgen’s European patent in a rare IP ruling in October 2004.

While the Federal Circuit’s August 2006 decision sent the case back to the district court, in a separate ruling the Court’s



13 judges decided nine-four not to hear the case *en banc* – after considering whether to revisit the precedent that says that the Federal Circuit must construct claims afresh, without deferring to the judgment of the district court. That question has now been put before the Supreme Court, which will decide whether to take the case later this spring.

The infringement question

The technology at the heart of this dispute is groundbreaking and the details complex; but the fundamental argument between the parties is simple. Amgen identified an exogenous means of artificially producing EPO in the 1970s using recombinant DNA technology; its product is called Epogen. In the 1990s, rival Transkaryotic Therapies developed an alternative method of making EPO, which is endogenous; its product is called Dynepo. The question the parties are fighting over is: does TKT's method infringe Amgen's patents?

That simple question becomes complicated when you learn

that Amgen's case is based on 17 claims in five separate patents filed in the mid-1980s covering recombinant DNA technology relating to the production of human EPO. Since April 1997, when Amgen first sued TKT and its licensee Hoechst, courts have grappled with each of these claims, asking whether they are valid and infringed. And they have not always come to the same conclusions.

In the latest twist, the Federal Circuit held that the district court wrongly construed the fundamental term "therapeutically effective amount" in claim 1 of Amgen's patent number 5,995,422, and remanded the case to the district court to determine the validity of that claim. It also reversed the district court's finding that TKT infringed three claims of another Amgen patent, but affirmed the other two findings of the court.

In his dissenting opinion, Chief Judge Michel voiced his "strong disagreement" with the ruling that claim 1 of the '422 patent could be invalid in what he admitted was an "extraordinarily complicated, highly-technical, and very difficult case". He also said that, whatever the result of that particular legal wrangle, an injunction would probably end up being issued, because of the other findings of infringement.

So what is a "therapeutically effective amount"? The district court said the phrase means "a quantity that produces a result that in and of itself helps to heal or cure". But the Federal Circuit said instead that it merely means an amount that "elicits any one or all of the effects often associated with *in vivo* biological activity of natural EPO".

Unless the Supreme Court steps in and changes the law, it will now be for Judge William G Young of the District of Massachusetts to revisit the construction of that claim using the Federal Circuit's new definition and to rule, once again, whether the patent is valid and infringed. But, in this highest of high-stakes cases, don't hold your breath for a final resolution.

The case

Amgen v Hoechst Marion Roussel and Transkaryotic Therapies

Court of Appeals for the Federal Circuit

For Amgen: Lloyd R Day of Day Casebeer Madrid & Batchelder (Cupertino, California) leads a team of 19 lawyers and of counsel from Amgen and four law firms.

For Hoechst: Carter G Phillips of Sidley Austin Brown & Wood (Washington DC).

The ethical angle

Like all scientists, researchers in the life science sector push the limits of human knowledge. But, more so than in any other scientific field, they also push the boundaries of ethics. Their questions – when does life begin and who owns it – are fundamental ones that go to the core of who we are. And how societies choose to answer those questions can put them on a collision course with the ambitions of their scientists.

Now the German courts have helped to clarify the boundaries that researchers in the country must work within.

On December 5 last year the German Federal Patent Court was asked by campaigning organization Greenpeace to consider the ethical dimensions of deriving cells from human embryonic stem (ES) cells. The case related to patent issued in April 1999 to Oliver Brüstle, a cell biologist at the University of Bonn.

Brüstle was granted a German patent for a method of converting ES cells into nerve cells that could potentially be used to treat neurological trauma and disease. The German patent – DE 1975864 C1 – contained claims directed to neural precursor cells derived from embryonic stem (ES) cells and methods for producing the neural precursor cells. However, the claims did not mention the use of embryos for producing the ES cells.

In its decision the Court upheld in amended form a patent containing claims directed to neural precursor cells derived from ES cells, but – crucially – excluded cells which are derived from ES cells prepared from human embryos on the grounds of morality.

“German scientists are now more or less excluded from collaborative stem cell research in Europe”

The decision means that only cells derived from human ES cells which are prepared from other sources such as human oocytes or human embryonic germ cells are now patentable in Germany.

Similar cases are being dealt with elsewhere. The EPO Enlarged Board, for example, is now considering a case (T 1374/04) that deals with comparable ethical issues relating to the use of stem cells. The applicant in that case applied for a patent relating to cell culture that comprises primate embryonic stem cells. Examiners refused the application on the grounds that the use of human embryos as starting material to create the claimed culture amounted to a use for industrial purposes. This is banned under Rule 23d(c) and Article 53(a) of the European Patent Convention. The Enlarged Board is now considering whether the claims are excluded from patentability.

Although many researchers will wait for that decision before they make big changes to their patenting strategies (given that the majority of patents are filed with the EPO rather than the through the German Patent and Trade Mark Office), the German Court’s decision could, nevertheless, have far-reaching implications for science in the country.

“Even if the EPO agrees to grant patents for these kinds of applications, the German courts will be the ones dealing with any litigation relating to them,” says Thomas Friede, a lawyer with Bardehle Pagenberg Dost Altenburg Geissler. As such, the latest decision sends out a clear message about the Federal Patent Court’s position.

Friede says that the ruling means that patent advisers now need to take far more care when drafting patent applications by listing as many alternatives for preparing human embryonic stem cells as possible, other than from human embryos. And he says that this latest decision, along with the 2002 Act on Stem Cells, which tightened restrictions on stem cell research, has made it harder for scientists in the field to work in Germany, and to take part in cross-border research.

“German scientists are now more or less excluded from collaborative stem cell research in Europe,” he says.

Appeal

Brüstle is unsurprisingly unhappy with the ruling, despite his partial victory. In a statement, he said he was disappointed and declared that the Court’s approach would have an impact on Germany’s attractiveness to biotech investors. Martin Grund, the scientist’s lawyer, says that Brüstle will appeal. The case will be heard by the Supreme Court, which accepts appeals on

nullity proceedings from the Federal Patent Court, and a decision is expected between 2009 and 2011.

But Christophe Then, a patent specialist at Greenpeace which led efforts to nullify the patent in Germany, is happy with the ruling, despite failing to convince the Court to extend its ban to human ES cells prepared from human oocytes or human embryonic germ cells.

“The ethical limits of patentability are now very well defined,” he says. “We thought we should try and find out where the German courts would draw the line.”

Greenpeace has other patents in its sights relating to plants, animals and genes (almost all granted by the EPO). “Stem cells are just one issue that we think is problematic,” says Then. “Our reasons are not always the same. We think that patents on genes can block research, and we believe that patenting seeds creates a food security issue. With stem cells it is a moral issue – we say that you shouldn’t grant patents for the industrial use of human embryos.”

“Our main message is that there should be no patents on living beings.”

Expect similar battles to be played out in courts around the world.

The case

3 Ni 42/04 – *Greenpeace v Oliver Brüstle*

For Greenpeace: Robert Schnekenbühl of DTS law firm.

For Oliver Brüstle: Martin Grund of Grund Intellectual Property Group.

France opens the floodgates

Unlike jurisdictions such as the US and the UK, French courts have seen little biotech action. But a decision handed down earlier this year could change that.

On February 7 the Tribunal de Grande Instance in Paris dismissed a patent suit launched by French research organization Institut Pasteur against Chiron (now Novartis Vaccines and Diagnostics). The ruling is significant because it is the first French decision ever issued relating to the infringement of a molecular biology patent.

“There is a process in biotechnology research,” says Thomas Bouvet, a partner of Véron & Associés who advised the defendants in the case. “Companies that start searching for breakthroughs require a lot of investment. Then they begin to apply for patents – and then they start to file litigation. The fact that this is the first decision in this area shows that the industry in France has matured.”

The dispute began when Institut Pasteur, a non-profit private research body, accused Chiron of infringing its European patent 178,978. The HIV-related patent dealt with “cloned DNA sequences, hybridizable with genomic RNA of the LAV”, which the French research organization said had been infringed when Chiron marketed kits for the detection of the HIV. It asked the Court to award it €8 million in interim damages.

But in its decision the Court held that Institut Pasteur’s patent could not be given the broad scope claimed by the plaintiff in view of the prosecution history and the patent description. It also argued that if the patent were to be given such a broad scope, it would be invalid in view of the prior art.

It went on to rule that Institut Pasteur did not provide suf-

ficient evidence that Chiron's HIV detection kits would reproduce the claimed characteristics nor that the defendant would supply means relating to an essential element of the invention. As a result, the Court decided that Chiron's products did not fall within the scope of the patent and that the sale of the kits was not an act of contributory infringement.

The dispute between Chiron and Institut Pasteur is one of a number of lawsuits filed by the French institute against companies manufacturing HIV blood test kits in France. A trial in another of the cases is expected to be heard within one year.

Véron & Associés' Bouvet says that the Court's ruling in the Chiron case should give IP owners confidence. "The biotech industry wants to ensure that the French courts are able to handle this kind of litigation. The Court was able to deal with the case using the same principles of infringement used in other patent cases. In my opinion the quality of the decision was reassuring for the industry."

And Bouvet says that the decision could lead to many more cases being filed in France. "It signalled that the first cases are arriving, and there are already other cases pending."

The case

Institut Pasteur v SAS Chiron Blood Testing and Chiron Healthcare Ireland Limited

Tribunal de Grande Instance, Paris, February 7 2007

For Institut Pasteur: Marina Couste, Howrey.

For SAS Chiron Blood Testing and Chiron Healthcare Ireland Limited: Pierre Véron and Thomas Bouvet, Véron & Associés.

End of the line for extensions

Generic drugs companies in Australia waiting impatiently for patents to expire received a boost in March when the High Court refused to hear an appeal against a decision by the Commissioner of Patents to shorten the extension granted to four patents belonging to pharmaceutical company Pfizer.

The Commissioner reduced the extensions on September 23 2005 on the grounds that Pfizer had used the wrong date as the starting point for its claim to an extension.

In Australia the standard term of a patent is 20 years, which is calculated from the date of filing the specification. But the patent can be extended if the goods disclosed in the patent are included in the Australian Register of Therapeutic Goods (ARTG) and if there is a five-year gap between regulatory approval, usually indicated by inclusion on the register, and the date the patent was filed. The maximum extension that can be granted is five years.

The disagreement lies in how to define the relevant date of regulatory approval. The Australian register contains a section relating to listed goods, where products are assessed for quality, safety and manufacture, and one for registered goods, which also assesses efficacy.

Pfizer made a claim for extension arguing that the first regulatory approval date was the date on which it entered that the part of ARTG relating to registered goods. The patents had, however, already been listed for export on the register 10 months earlier.

After the discrepancy was brought to his attention, the

Commissioner of Patents changed the extension so that it began from the date of listing in ARTG. Pfizer appealed, claiming that the terms of the Patent Act relating to extensions should only apply to the date when the goods are approved for marketing in Australia.

Pfizer appealed to the Federal Court in March 2006, at which point Spirit Pharmaceuticals joined the case, claiming that if Pfizer won and one of the patents (patent 540769) was reextended by 10 months, it would lose A\$5.5million (\$4.6 million). Patent 540769 is for the medicine known as Amlodipine in Australia, Norvasc in North America and Istin in the UK. It is used to treat high blood pressure and chest pain and is one of Pfizer's bestsellers, with global sales last year of \$4.87 billion.

Three judges of the Full Federal Court dismissed the appeal in December 2006. Special leave to appeal to the High Court was refused in March 2007.

The Commissioner reduced the extension of each of the four patents by between 10 and 13 months. Although this seems a minor alteration, given that pharmaceutical companies can make tens of millions of dollars each month on a blockbuster drug fighting over patent extensions is a big money issue. The crucial question now, according to Robert Cooper, a partner with Mallesons Stephen Jaques, is: "How many other patents are out there on extensions that aren't totally valid?"

Generic pharmaceutical companies will certainly be examining the decision and looking to see whether other patents may be vulnerable. Fighting over extension terms seems to be a quicker and cheaper way of getting rival products onto the market than fighting a revocation action.

The case

Pfizer Corp v Commissioner of Patents [2006] FCAFC 190 (December 20 2006)

For Pfizer: Spruson & Ferguson

For Spirit Pharmaceuticals: Blake Dawson Waldron

The legal issues revolved around Section 70 of the Australian Patent Act 1990. This says:

Applications for extension of patent

- 1) The patentee of a standard patent may apply to the Commissioner for an extension of the term of the patent if the requirements set out in subsections (2), (3) and (4) are satisfied.
- 2) Either or both of the following conditions must be satisfied:
 - a) one or more pharmaceutical substances *per se* must in substance be disclosed in the complete specification of the patent and in substance fall within the scope of the claim or claims of that specification;
 - b) one or more pharmaceutical substances when produced by a process that involves the use of recombinant DNA technology, must in substance be disclosed in the complete specification of the patent and in substance fall within the scope of the claim or claims of that specification.
- 3) Both of the following conditions must be satisfied in relation to at least one of those pharmaceutical substances:
 - a) goods containing, or consisting of, the substance must be included in the Australian Register of Therapeutic Goods;
 - b) the period beginning on the date of the patent and ending on the first regulatory approval date for the substance must be at least 5 years
- 4) The term of the patent must not have been previously extended under this Part.

Full speed in reverse

Political analysts predicted that a Democrat-controlled Congress would lead to a less favourable climate for big pharma in the US – and they were right. In one of the new Senate's first actions, on February 15, four Democrat Senators and one Republican on the Senate Judiciary Committee introduced a bill to ban so-called reverse payment deals, in which brand name drugs companies pay rivals to delay the launch of their generic versions.

The Senators claimed that these deals are anti-competitive and prevent affordable versions of drugs being brought to market. The deals are increasing: in 2006, according to the Federal Trade Commission (FTC), 14 out of 28 final deals submitted involved reverse payments, compared to three out of 11 in 2005 and none out of 14 in 2004. And the stakes are high: Bristol-Myers Squibb fired chief executive Peter Dolan and general counsel Richard Willard in September last year over a botched attempt to do a deal with generic maker Apotex over the blockbuster drug Plavix.

Congress, however, moves slowly. It may be overtaken by the US Supreme Court, which is now considering whether to take a case on reverse payments for the second time in less than a year. The case now before it involves the patent for the drug tamoxifen – which expired five years ago and was held to be invalid in the litigation that initially prompted the case.

The tamoxifen patent was filed by AstraZeneca (then ICI) in the US in 1985. Marketed as Nolvadex, it became the world's most successful breast cancer drug. When, four months later, generic maker Barr Laboratories filed an abbreviated new drug application (ANDA) with the FDA, AstraZeneca retaliated with a patent infringement suit against both Barr and its supplier Heumann Pharma. But, in April 1992, a district court judge found the patent invalid on the grounds that the applicant had withheld information from the USPTO.

Predictably, in the high-stakes world of US pharmaceutical patents, AstraZeneca appealed the decision to the Federal Circuit. Unpredictably, it then settled the dispute: AstraZeneca agreed to pay Barr \$21 million and Heumann up to \$45.4 million and granted Barr a licence to sell AstraZeneca-made tamoxifen under Barr's label. In return, Barr agreed to change its ANDA application so that it would not market its own generic version until at least 2002, when the patent expired. But it also reserved the right to invoke its 180-day exclusivity period for a genuine generic version of the drug should another generic company attempt to market a version. At the parties' request, the Federal Circuit vacated the district court's patent invalidity judgment.

Between 1994 and 1996 three other generic companies sought approval for generic versions of tamoxifen. In each case, the courts upheld the validity of AstraZeneca's patent. In addition, further litigation took place between the various generic companies right up until August 2002, when the patent expired and generic versions of tamoxifen were launched.

Antitrust concerns

While the generic companies were busy fighting each other over the patent and marketing rights, a group of consumers and consumer groups sued AstraZeneca and Barr alleging that their 1993 agreement breached the antitrust Sherman Act. They claimed it resuscitated an invalid patent, continued a

monopoly, kept the price of tamoxifen artificially high and prevented competition. In 2001, some 30 lawsuits were consolidated into a class action in the Eastern District of New York.

But in 2003 the district court dismissed the motion, saying the plaintiffs had not sufficiently alleged a bad-faith settlement, and in any case had not suffered any antitrust injury from the settlement. On appeal, the Second Circuit affirmed the decision and declined to transfer the case to the Federal Circuit (which hears appeals in patent cases) in a two-to-one split.

But the unions, insurers and patients who made up the class action have not given up. In February this year they called on the Supreme Court to address whether the Sherman Act prohibits so-called reverse payment settlements of drug patent litigation. AstraZeneca and Barr oppose the application, but the Supreme Court has asked the US Solicitor General for his views on whether it should answer the question.

In the last case on reverse payments presented to the Court, in which the Federal Trade Commission sued Schering-Plough, the Solicitor General last year advised against hearing, and the Court declined to take the case. That decision brought to the fore an apparent split between two federal agencies: the Department of Justice backed the Solicitor General's view, revealing a more tolerant approach to reverse payment deals than the FTC, which argues that they are de facto anti-competitive – a split that has prompted analysts to pick over the minutiae of recent statements from both DoJ and FTC.

The Schering-Plough case arose from the Eleventh Circuit. Some observers have pointed to a split between the Second and Eleventh Circuits, which have found that reverse payment agreements are not illegal, and the Sixth Circuit, which ruled in *In re Cardizem* in 2003 that a reverse payment deal was illegal. Others claim the facts of each case are significantly different.

Ken Cafferty of Cafferty Faucher, a class action specialist, is representing the plaintiffs and petitioned the Supreme Court to take the case. In the Schering-Plough case, he says, there were some exceptional facts, including a debate over whether there was even a reverse payment. By contrast, he says: "In *Tamoxifen*, there was a reverse payment and then some. We lost on the big picture rather than the little details." He believes this gives the *Tamoxifen* case a good chance of winning a hearing at the Supreme Court. We should all know the answer by the end of this year.

Even if the Supreme Court does not review this case, reverse payments will remain in the spotlight. The economic and political importance of the drugs industry, the demand for health-care reform and the canniness of US litigators will ensure a steady stream of similar cases. For example, some 38 class actions have been filed against a \$400 million Bayer-Barr deal over the Cipro antibiotic. One of them has reached the Second Circuit, which has stayed the case while it considers a transfer to the Federal Circuit. This article will surely not be the last one you read on reverse payments in the US.

The case

In re: Tamoxifen citrate antitrust litigation (aka Joblove et al v Barr Labs and AstraZeneca Pharmaceuticals)

Court of Appeals for the Second Circuit

For Joblove et al: J Douglas Richards of Milberg Weiss & Bershad LLP (New York) and Patrick E Cafferty of Cafferty Faucher LLP (Ann Arbor, Michigan).

For Barr and AstraZeneca: Joel M Cohen of Davis Polk & Wardwell (New York, New York) and George C Lombard of Winston & Strawn (Chicago).