BIOTECHNOLOGY PATENT DISPUTES

Market machinations

Washington

THE race to market a genetically engineered monoclonal antibody (mAb) for the treatment of Gram-negative bacterial infections took an unexpected turn last week when Xoma Corporation filed for infringement of its newly issued patent by its rival biotechnology company, Centocor Corporation.

At the same time as the US Patent and Trademark Office issued a patent, Xoma, based in California, filed a declaratory judgement against Centocor of Philadelphia, asking a San Francisco court to declare that the marketing of Centocor's mAb, Centoxin, would infringe Xoma's patent.

This latest action by Xoma could spark off the kind of protracted legal battles already seen over conflicting patent rights to the blood-clot dissolving agent tissue plasminogen activator, and erythropoietin, used to treat anaemia in patients with kidney failure. The broad patent issued to Xoma covers a "method for treating humans with Gram-negative sepsis and/or septic shock using anti-endotoxin mAbs from any mammalian source, including mouse or human", says Carol deGuzman of Xoma.

In the United States, about 250,000 patients are affected by Gram-negative sepsis each year, 80,000–100,000 of whom die from septic shock. Hospitalized patients recovering from surgery are at greatest risk.

This is regarded as the first major therapeutic use of mAbs, and both Xoma and Centocor are awaiting approval of their respective products by the US Food and Drug Administration (FDA). Xoma's product, Xomen-E5, and Centocor's Centoxin represent an important short-term earnings potential for both companies. At stake is an annual US market projected at $350–400 million.

Responding to last week's court action by Xoma, Charles Cabot, of Centocor says it is without merit and that it "will not hold us [Centocor] off the market, or delay our product coming to market by a single day".

Although Xoma filed for FDA approval of Xomen-E5 in March 1989, seven months ahead of Centocor's Centoxin, stock analyst Peter Drake believes "the FDA will address both applications roughly concurrently", with Xoma having no more than "a few months lead time with the commercialization of its product — if at all".

Both Xoma and Centocor will receive a series of patents, and ultimately the two companies will reach some form of cross-licensing agreement as they commercialize their respective products, says Drake.

Until now, much of the controversy between the two companies had focused upon clinical trial data. Xomen-E5, which Xoma is marketing in conjunction with Pfizer Pharmaceuticals, is a mouse-derived mAb, whereas Centoxin is a human mAb. Cabot points out that in phase III trials, no human antibody response was elicited against the drug Centoxin, and there were no side effects. This represents a "strong safety profile for any pharmaceutical product".

Although safety and efficacy are important criteria for market acceptance of a product, Centocor may be unduly handicapped by its lack of marketing muscle. The question remains as to whether Centocor, which says it will retain marketing rights to Centoxin, can build up a hospital-based sales effort that will allow it to compete effectively with Pfizer.

Centocor has 20 days in which to respond to the court action. **Diane Gershon**

Amgen plays for time

Washington

THE convoluted saga over US rights to erythropoietin (EPO) twisted in Amgen's favour last week when a Washington federal appeals court upheld a request by Amgen to stay the injunction that would have been imposed had Amgen failed to tender a temporary cross-licensing agreement with its rival, Genetics Institute. In short, the court's decision has removed Amgen's incentive to comply with an earlier district court order issued by Judge Young in Boston on 14 March, which would have compelled both Amgen and Genetics Institute to cross-license their respective EPO products, until the patent dispute surrounding the original patent ruling of 11 December 1989 is resolved (see *Nature* **344**, 278; 22 March 1990).

Stock analyst Peter Drake sees this as "a very smart and clever strategy", and hails it as "an important and meaningful victory for Amgen in this ongoing battle". As Melinda Lindquist of Genetics Institute points out, "it removes the 'stick' that Judge Young had to compel the parties to comply. Genetics Institute had already complied with his request, so the stick was to be used against Amgen".

For the first time in this patent dispute, Genetics Institute would seem to have been outmanoeuvred by Amgen. "Amgen has further delayed the approval of Marogen through this particular court action", says Drake, which allows Amgen's EPO product, Epogen, to become more entrenched in the US marketplace. In his view, the reason that Amgen wants to delay is that the "US Food and Drug Administration (FDA) will not approve Marogen [Genetics Institute's EPO product] until the two companies have come to a resolution of this particular patent problem".

Once again, Genetics Institute has been thwarted in its attempt to find a legal loophole around the 'orphan-drug' status awarded to Epogen, which provides Amgen with seven years of marketing exclusivity in the United States. FDA could still approve Marogen without the court's backing if, as Genetics Institute claims, Marogen is found to be a different product due to differences in glycosylation. Or the FDA could remove Epogen's orphan-drug status, because by manufacturing and selling Epogen in the United States, Amgen is in infringement of Genetics Institute's patent.

In addition, Genetics Institute argues that the number of kidney dialysis patients who could be treated with EPO is above the 200,000 level for orphan-drug status eligibility.

In order to speed the resolution of this seemingly never-ending patent dispute, the appeals court has agreed to expedite reviews of the December court ruling, which upheld the central claims of both companies' US EPO patents, while considering both patents partially invalid and mutally infringing (see *Nature* **342**, 846; 1989). Although the courtroom confrontation is set to continue, no dates have been set for the appeals.

Diane Gershon

UK RESEARCH COUNCILS

Advisory board in place at last

London

THE independent membership of the reconstituted Advisory Board for the Research Councils (ABRC) was announced last week, nearly three weeks after its planned start-up date of 1 April (see *Nature* 344, 12 April 581, 1990).

Sir Eric Ash (rector of Imperial College, London), Sir Charles Reece (a member of the Universities Funding Council) and John Flemming (executive director of the Bank of England) survive from the last incarnation of the ABRC. The three newcomers are Professor Richard Gardner (director of the Imperial Cancer Research Fund's Developmental Biology Unit in Oxford), Professor Michael Hart (from the Physics Department at the University of Manchester) and Professor Ian Shanks (chief scientist with Thorn EMI and visiting professor at the University of Glasgow).

Peter Aldhous