

## Pharma positions to survive the impending patent cliff

Over the next few years, patent protection ends for so many top-selling drugs that analysts have dubbed the upcoming landscape as a ‘patent cliff’. In 2008, the world’s top 50 pharmaceutical companies sold \$533 billion worth of prescription pharmaceuticals, according to the research firm Datamonitor. In 2014, lost sales from expiring patents will cost these pharmaceutical companies \$115 billion, but the October 2009 issue of Datamonitor’s *PharmaVita Explorer* still predicts that annual sales for the top 50 pharmas will grow to \$578 billion.

“The \$115 billion sales decline is huge, but sales growth from new launches and existing products is bigger than the decline,” says Chris Phelps, Datamonitor’s director of company and strategic analysis. In 2014, according to his firm’s estimates, drug companies’ new products will bring in \$87 billion, and sales from existing products should grow by \$73 billion. That \$160 billion increase in sales more than offsets the \$115 billion lost to expiring patents.

However, Japanese pharmaceutical companies, which make up about 15% of the top 50, face a treacherous patent cliff. By June 2012, for example, Osaka-based Takeda Pharmaceutical will lose US patent protection—held by its US subsidiary, Takeda Pharmaceuticals North America—on its drugs Actos, Bropress and Prevacid, which treat diabetes, hypertension and heartburn, respectively. These three medications alone generated an estimated \$6 billion in US sales in 2008, according to Fumiyo Sakai, a pharmaceutical analyst at Credit Suisse in Tokyo.

“This is this first wave of patent erosion that Japanese companies face,” explains Sakai. Nonetheless, Japanese pharmaceutical companies have already been working to offset upcoming losses. In April 2008, for instance, Takeda acquired Millennium Pharmaceuticals, which specializes in oncology drugs. But Sakai expresses doubt that such mergers will completely make up for the upcoming loss of patents.

Large US pharmaceutical companies are also trying to limit their losses by merging, either to cut managerial costs or to acquire new drugs. For example, according to Bloomberg.com, Merck’s Singulair for asthma and allergy generated \$4.3 billion in sales in 2008, and its patent is currently set to expire in August 2012. Long before that expiration, though, Merck should merge with Schering-Plough. In fact, this business deal is expected close this year.

Still, Merck sees even more ways to handle

expiring patents. “There is no doubt that innovation in pharmaceutical discovery and development is the way forward to deal with patent expiries,” Merck’s chief strategy officer Mervyn Turner told *Nature Medicine* via email. He added that “a keen focus on life cycle management—especially in emerging markets that may not have had access to some of our medicines—is critical.”

Pharmaceutical companies that stand out in oncology, immunology, monoclonal antibodies or vaccines will sidestep much of the upcoming cliff, Phelps predicts. Consequently, he says, Swiss giants Roche and Novartis will “enjoy good growth.”

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Ups and downs: Drug profits vary

### Prometheus v. Mayo case in the spotlight

A woman with Crohn’s disease, which causes severe intestinal problems, takes immunosuppressant drugs to manage her condition. Her doctor would like to measure her metabolite levels to see how she’s reacting to it. The situation seems straightforward, except that her physician is not allowed to run the check himself—the testing method legally belongs to someone else.

A legal battle surrounding this scenario has pitted Prometheus Laboratories, which patented the test, against the Mayo Clinic, which believes the test is simply an observation of natural processes, and thus nonpatentable.

Notably, the test equipment that measures the metabolite levels isn’t patented. What’s patented is a range of numbers: 250 pmol to 400 pmol per 100,000,000 red blood cells. If a patient’s metabolite levels fall within this range, the drugs—in this case, thiopurine immunosuppressants—are working.

As a patented invention, the test using these numbers costs \$270 per test, a price tag that makes it unavailable to some. “As a clinician, I can live without the tests,” says Richard Gearry, a gastroenterologist at Christchurch Hospital in New Zealand, “but life is much easier with them.” The same goes for the patients.

However, doctors have been giving these drugs and measuring their corresponding metabolite levels in patients since the 1970s, says Joe

Calaiano, legal counsel at the Mayo Clinic. “Prometheus did not invent the test,” he says. “They just assigned reference numbers to it... according to them, you’re not allowed to think about these numbers [without their permission].”

Yet Prometheus was the one to combine the steps of administering the drug, running the test and running their calibration—a process that improves upon previous methods.

“Under traditional methods, to determine whether you are dosing a patient correctly could take months,” says Rick Bress, who represents Prometheus in the case. “Prometheus patent... allows you to determine the correct dosage right from the get-go.”

In 2004, the Mayo Clinic decided to do the testing in house rather than sending samples off to Prometheus—they already had all of the necessary equipment to do so and went about it using a wider efficacy range.

Prometheus sued for patent infringement, and this past September, more than five years later, the US Federal Circuit Court ruled in their favor, stating that the Prometheus test met the requirements of patentability (see ‘Machine or transformation test’ put to the test itself, on page 1241). The Mayo Clinic isn’t giving up—they are appealing their loss to the Supreme Court, and have filed amicus briefs with the American Medical Association.

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