genetic tests that measure the absence or presence of an analyte such as a gene or gene product—e.g., where microarrays are commonly used in research laboratories today.

When ASR regulations were first introduced in 1997, the agency considered making genetic-based ASR's exempt from class 1 status. They decided against it, choosing instead to wait for the science to mature before revisiting the question, and AmpliChip may be just the sort of challenge they were waiting for. Martel says that the AmpliChip is a good first test for the regulation of microarray diagnostics, because the knowledge of the biology behind CYP450 is better understood than the science behind most of the first generation gene chips.

Most within the industry expect that microarray diagnostics will require PMAs because they are industrially made products. "I think it [PMA] will be a good thing, because gene chips deliver so much information [and] interpretation of that information can be very complicated. You do want to provide physicians with a tool that's going to help them treat their patients, so I think that needs to be very well validated," says Martel.

The stringency of the validation could vary with a microarray's intended use, similar to what the FDA has done with immunohistochemical assays and other tests, according to Thane Kreiner, senior vice president of corporate affairs for Affymetrix (Santa Clara, CA, USA), which in January licensed to Roche the technology that underlies AmpliChip. A microarray such as AmpliChip that helps a doctor select a drug treatment after the diagnosis is confirmed might face softer tests than a chip that diagnoses the disease in the first place. Such a product would pose a higher risk to a patient because of potential misdiagnoses.

Jim Kling, Washington

Brussels takes EU states to court over biopatent law

On July 10, the European Commission (EC; Brussels, Belgium) referred eight member states to the European Court of Justice (ECJ; Luxemburg, Luxemburg) for their failure to transpose into national law EU directive 98/44/EC, which aims to clarify the principles of patent law applied to biotechnological inventions. The industry expects the court decision to end a period of uncertainty in which investors feared that biotech patents would not be protected if they were challenged in one of the eight noncompliant countries.

EU member states agreed on the directive in 1998, following a decade of negotiations at the European Parliament and in the Council of Europe. Member states had until July 30, 2000, to transpose the directive into national law. However, Austria, Belgium, France, Germany, Italy, Luxemburg, the Netherlands and Sweden still have not done so. Failure to implement the directive triggered the EC to take court action against the noncomplying member states, after three conciliatory meetings between the EC and noncompliant states held between January 1999 and 2003 and a formal warning sent to these states by the EC in November 2002.

The directive is an attempt to clarify the conditions of the existing patent law in Europe—known as the European Patent Convention (EPC)—for biotech patents. But the industry is concerned that by not implementing 98/44/EC, member states create a climate of uncertainty that will harm the biotech industry. "Everybody is in a waiting position, and that is negative for the industry," says Bo Hammer Jensen, chairman of the intellectual property working group at the European bioindustry association, EuropaBio (Brussels, Belgium).

> The industry expects the court decision to end a period of uncertainty in which investors feared that biotech patents would not be protected if they were challenged in one of the eight noncompliant countries.

Should a patent invalidity or infringement case be brought in one of the noncomplying countries, their national courts should, in theory, base their decision on the wording of the EC directive because European law supersedes national law. However, according to Jensen, many people, including investors, are not familiar with this twist in European law and are reluctant to invest in the biotech field. "This could have serious negative implications, especially for small new companies or medium-size companies," says Jensen.

Unlike previous noncompliance cases, an ethical concern is behind a lot of the member states' reluctance to implement the directive. In particular, several countries question article 5 of the 98/44 directive, which allows the patenting of "an element isolated from the human body or otherwise produced by means of a technical process." Article 5 goes on to say, "the sequence or partial sequence of a gene may constitute a patentable invention, even if the structure of that element is identical to that of a natural element."

France and Germany, in particular, oppose the ability to patent human genes on the grounds that it could 'instrumentalize' human beings and goes against their national law. French law, for example, forbids commercialization of the human body. However, the ECJ, in its ruling of October 9, 2001, concluded that the directive gives precise provisions safeguarding the integrity of human beings by requiring disclosure of utility for patents on genes (*Nat. Biotechnol.* 19, 1095–1097, 2001).

Alternatively, Sweden and the Netherlands fear that the directive undermines the aims of the Rio Convention on biodiversity, since it does not require the disclosure of the geographical origin of biomaterial used in a patent application. And the most extreme concerns stem from the Dutch, who are reluctant to allow the patentability of plants or animals at all.

The commission disagrees with France and the Netherlands, which have drafted their laws in a way that objects to patents on human beings and, respectively, on plants and animals (*Nat. Biotechnol.* 21, 349–351, 2003). "The implementation as decided by [the Dutch] Parliament is not in line with the European directive," says Janssen. "For us as industry, this [inadequate implementation] is not acceptable."

The eight member states risk a fine if the ECJ deems them guilty. But countries have previously avoided paying fines by implementing the directive during the court proceeding that could take up to two years, according to an EC insider. "I would expect in this case, too, that while the case is going on, most member states will have felt enough pressure to actually legislate," says the insider. "That is very often the benefit of the court case."

Martina Habeck, London