UK bans reproductive cloning

The UK Human Reproductive Cloning Act 2001 was hurriedly signed into law in early December, making it a criminal offense to implant in a woman an embryo that hasn't been created by fertilization. In January 2001, the 1990 Human Fertilization and Embryology Act was expanded to allow therapeutic cloning, giving the Human Fertility and Embryology Authority (London) oversight of use of nuclear transfer technology to create embryos for stem cell research (*Nat. Biotechnol.* **19**, 97, 2001). While the law forbids reproductive cloning, the anti-abortion group Pro-Life Alliance, which opposes all cloning, sought to overturn the decision in the UK High Court. The group argued that the 1990 legislation did not cover cloning because embryos created by cell nuclear replacement are not generated by "fertilization" and thus do not satisfy the definition of "embryo" in the act. In November, the Court agreed, effectively leaving cloning unregulated. While the new law bans reproductive cloning, and therapeutic cloning is effectively on hold, research on stem cells from embryos created by fertilization is not affected. Meanwhile, a United Nations committee has been formed to draft a global convention to prohibit human cloning. The committee will meet initially next month, but it could be years before a final treaty is ratified. *ED*

OGT retains Southern patent

On November 23, the European Patent Office (EPO; Munich) upheld the validity of an Oxford Gene Technology (OGT; Oxford, UK) patent that broadly covers most oligonucleotide microarrays on the market. Since it was granted in 1994 to OGT co-founder Ed Southern, the patent has been under opposition from companies including Nanogen (San Diego, CA) and Roche (Basel, Switzerland). Affymetrix (Santa Clara, CA) had also opposed the patent, but settled with OGT for a license in March 2001 (*Nat. Biotechnol.* **19**, 399, 2001). In light of the EPO's ruling, OGT can expect many microarray firms to license the technology, according to OGT's outside counsel from Manches (Oxford, UK) Chris Shelley. Southern's technology is covered by two unopposed patents in the United States (*Nat. Biotechnol.* **19**, 13, 2001). *AB*

Business and Regulatory News Briefs written by Aaron Bouchie, Emma Dorey, Liz Fletcher, Jeffrey L. Fox, and Haim Watzman.

Court upholds broad plant patenting rights

In a December ruling, the US Supreme Court upheld Pioneer Hi-Bred International (Des Moines, IA) in a patent infringement suit brought against JEM Ag Supply (Belmond, IA) and three other seed companies (*Nat. Biotechol.* **19**, 981, 2001). More to the point, the decision reaffirms a broad interpretation of plant patenting rights, agreeing that researchers may make utility claims for improved plants—including GM plants and seeds. JEM and its co-defendants had argued that farmers should be allowed to retain and plant harvested seed and that current statutes and recent patent rulings are not meant to prohibit them from doing so. Attorneys representing Pioneer Hi-Bred counter-argued that the 1980 Supreme Court decision *Diamond v. Chakrabarty*, though explicitly focused on microorganisms, also applies more broadly to, and supports the patentability of, other organisms, including plants. They also argue that the 1970 Plant Variety Protection Act and the 1930 Plant Patent Act offer further proof that Congress intends to protect intellectual property rights as they apply to agriculturally useful plants. In a 6-to-2 ruling, the Justices said these other laws are alternatives, not substitutes, for more general patent protections granted under the Constitution. *JF*

NIAID boosts bioterror efforts

US National Institute of Allergy and Infectious Diseases (NIAID; Bethesda, MD) announced early in December that it is boosting several bioterrorism defense-related research programs, including several involving collaboration with industry. For instance, the Small Business Program on Bioterrorism-Related Research is seeking proposals for research on agents of bioterrorism; it promises "streamlined" administrative and review processes. Another program, the "Partnerships for Novel Therapeutic, Diagnostic, and Vector Control Strategies in Infectious Diseases", will support research into drug development and faster, more accurate diagnostics for diseases caused by bioterrorism. It is seeking "to foster partnerships among government, academia, and the biotechnology and pharmaceutical industries," and builds on a program supporting research on infectious diseases that are "not a high priority for industry." Yet another program focused on anthrax vaccine development will be run for NIAID under the Science Applications International Corporation (SAIC; San Diego, CA). In particular, NIAID wants to support work on one of the most promising types of vaccines, called a recombinant protective antigen vaccine. *JF*

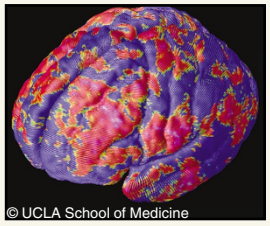
WTO TRIPS statement

On November 14, the World Trade Organization (WTO; Geneva) issued a statement recognizing the importance of patents for developing new medicines, but also emphasizing the right of WTO members to protect public health by allowing them to ignore patents (so as to access cheaper generics) in a "national emergency". This declaration refers to the Trade-Related Aspects of Intellectual Property (TRIPS), a global agreement to protect intellectual property, and has extended the TRIPS deadline for when WTO members must respect patents from 2006 to 2016. Activist groups have hailed this as a victory that prioritizes health above trade. But industry representatives say the declaration doesn't change the status quo in any meaningful way, as such activities—determining what constitutes a public health crisis, for instance—are still subject to the terms of TRIPS itself and review by the WTO. Industry continues to argue that it is not patents that prevent access to medicines in developing countries, but a lack of health care infrastructure. Indeed, a recent study of the patent status of anti-retroviral drugs in Africa in 2001 concluded that patents do not really impede access to drugs (*JAMA*, **286**, 1886, 2001). *ED*

Publishing bias exposed

Negative biomedical research results are considerably less likely to be published if the research has been funded by drug companies, a study has found (*Family Practice* **18**, 565–568, 2001). The authors looked at 314 articles that appeared between 1994 and 1995 in five leading medical journals: the *New England Journal of Medicine*, *Lancet*, the *Journal of the American Medical Association*, the *British Medical Journal*, and *Annals of Internal Medicine*. Only 13% of articles resulting from commercially funded research reported negative results, compared with 35% of those stemming from government sources. While the authors suggest industry may support trials on drugs at a later stage of development or be quicker to terminate projects yielding negative results, they conclude that their results, taken together with those of similar studies, suggest publication bias. One of the authors, John Yaphe, told *Nature Biotechnology* that because family physicians make decisions about which drugs to prescribe by considering the balance of results reported in professional journals, such a bias can directly affect both the care received by patients and the profits of drug companies. Yaphe said the article was first submitted to four of the five journals examined in the study, but that all rejected it. *HW*

Human brain proteome project underway



On November 20, nine academic groups and three biotech companies from Germany (located in Berlin, Bochum, Braunschweig, and Kiel) participated in the first meeting of the Human Brain Proteome Project, which aims to help understand the mechanisms of complex brain diseases like Huntington's and Alzheimer's. Over the next three years, the German Federal Research Ministry (Bonn) and the three firms will provide a total of DM 20.5 (US $9.4) million and DM 7.5 million, respectively, to develop proteomics platforms that can correlate gene expression with protein-profiling data from human brain samples. In addition, microarray provider Scienon (Berlin) will contribute its technology for both gene expression and protein–protein interaction studies; proteomics firm Protagen (Bochum) will develop protein analysis tools using mass spectrometry and 2-D electrophoresis gels; and informatics company MicroDiscovery (Berlin) will manage data integration and mining. All data produced by the academic groups will be published, and the biotech firms retain rights to commercialize any resulting technologies. Another proteomics project, focused on cancer, is currently in the works in Munich. *AB*

Drug development costs rising

The cost of developing a new drug is now $802 million, according to an unpublished report from The Tufts Center for the Study of Drug Development (CSDD; Boston, MA). This figure is 250% higher than the $318 million calculated for 2000, a figure that was extrapolated from a 1991 study (*Nat. Biotechnol.* **19**, 803, 2001). Joe DiMasi, principal investigator of both studies, says the increase reflects the rising clinical costs resulting from an increased focus on developing treatments for chronic and degenerative diseases, which require larger, lengthy comparative trials rather than those based on placebo. However, DiMasi says costs may drop in the future, as industry improves at recognizing failures earlier in the development stage. The results of the study, which were released on November 30, surveyed 10 drug companies and 68 randomly chosen drugs from their internal drug R&D programs, 7 of which were biologics. *AB*

New product approvals

Product	Companies	Details
BrachySeed Pd-103 (palladium radioactive brachytherapy implant)	Draxis Health (Mississauga, ON, Canada), Cytogen (Princeton, NJ)	This treatment for prostate cancer was approved by the US Nuclear Regulatory Commission on November 12. Brachytherapy involves implanting small radioactive "seeds" directly into a tumor, and palladium-based implants now account for ~$125 million in the brachytherapy market. Draxis will market the product in Canada, and Cytogen in the United States.
Kineret (anakinra)	Amgen (Thousand Oaks, CA)	Approved by the US FDA on November 14 for rheumatoid arthritis (RA), which affects ~2.1 million Americans. Kineret is a recombinant interleukin-1 receptor antagonist and therefore inhibits inflammation in RA patients. Kineret will compete with Immunex's (Seattle, WA) Enbrel and Johnson & Johnson's (New Brunswick, NJ) Remicade, and analysts project US annual sales to reach $350 million by 2005. EU approval of Kineret is expected in the first quarter of 2002.
Focalin (*d*-dexmethyl-phenidate HCl)	Celgene (Warren, NJ), Novartis AG (Basel, Switzerland)	The single active isomer of Novartis's Ritalin for attention deficit/hyperactivity disorder (ADHD), purified by Celgene using its biocatalytic chiral chemistry. Although only one-third of the 3.5 million American children with ADHD are being treated, total annual sales of Ritalin and its generic equivalents are ~$400 million. Novartis maintains worldwide development and marketing rights outside Canada for Focalin, which was approved by the US FDA on November 15.
Tracleer (bosentan)	Actelion (Allschwil, Switzerland), Genentech (S. San Francisco, CA)	An oral endothelin antagonist for pulmonary arterial hypertension (PAH), Tracleer was approved by the US FDA on November 20 and in Canada on December 3; it remains under review in the EU, Switzerland, and Australia. Approximately 100,000 people are afflicted with PAH in the United States and Europe, where Tracleer was given orphan status. Genentech may co-promote Tracleer in the United States for both PAH and congestive heart failure (CHF) once ongoing phase 3 trials for CHF are completed; Actelion retains all marketing rights outside of the United States.
Xigris (recombinant activated drotrecogin alfa)	Eli Lilly (Indianapolis, IN)	Formerly named Zovant, Xigris was approved by the US FDA on November 21 for adult patients with severe sepsis and a high risk of death. Xigris is the first therapeutic ever approved for severe sepsis (*Nat. Biotechnol.* **19**, 1095; 2001).

AB

Lion, IBM informatics deal

On November 28, 2001, bioinformatics firm Lion Biosciences (Heidelberg, Germany) and International Business Machines (IBM; Armonk, NY) agreed to combine their respective data search (SRS) and integration tools (DiscoveryLink) to allow researchers to use "the widest range of data sources" to accelerate drug development for genetically linked diseases. Michael Clulow, research analyst for UBS Warburg (New York), says the deal validates Lion's SRS integration platform as the best search engine for finding biological data; Lion currently has access to more than 450 public and private databases. IBM's DiscoveryLink will allow researchers using SRS to then organize and manipulate data on their own computer. Clulow says the deal with IT powerhouse IBM should lay to rest concerns about Lion's high cash-burn rate (more than € 190 ($169) million in the year ending September 30, 2001), and prompt more drug-discovery deals similar in scale to that struck with Bayer in June 1999 (*Nat. Biotechnol.* **17**, 742). Lion's share price closed up 4% at $18.24, one week after the news was announced. *AB*

Millennium acquires COR

On December 6, Millennium Pharmaceuticals (Cambridge, MA) agreed to acquire cardiovascular drug developer COR Therapeutics (S. San Francisco, CA) for around $2 billion in shares. The acquisition provides Millennium a sales and marketing team and entry into the cardiovascular area, broadening out from its previous focus on oncology, metabolic disease, and inflammation. Although Millennium has long touted genomics-based medicines, it still has just one drug, Campath, on the market, and it recently returned rights to the drug to its developer, Ilex Oncology. COR's Integrilin, an intravenous anti-platelet agent, will generate about $225 million in sales in 2001, and sales are predicted to grow at 30% in the coming years. The new enlarged company will have nine products in clinical trials, $2 billion in cash, and an estimated $400 million in combined revenue. Millennium paid a 77% premium on COR's share price, in a deal that gives each COR shareholder 0.9873 shares of Millennium stock. COR's share price rose 43% to $28.20 by close of trading after the announcement, whereas Millennium's share price slid 17%. *LF*

MedImmune buys Aviron

On December 3, biopharmaceutical firm MedImmune (Gaithersburg, MD) announced the purchase of vaccine company Aviron (Mountain View, CA) in an all-stock deal worth ~$1.5 billion. The driving factor behind the deal is Aviron's FluMist, an inhalable influenza vaccine that MedImmune hopes will reach annual sales of $1 billion five years after an expected launch in 2002. FluMist's only competitor, Berna's (Bern, Switzerland) Nasalflu, was approved in Switzerland in October 2000 but is currently not on the market because of concerns about side effects. MedImmune's existing lead product, Synagis, a monoclonal antibody for the prevention of lower respiratory tract infection caused by respiratory syncytial virus, generates US annual sales of nearly $500 million. Bill Tanner, research analyst for SG Cowen (Boston, MA), says the deal will expand MedImmune's core franchise of infectious diseases and vaccines, although he notes that the rest of Aviron's pipeline is too early-stage to properly value. One week after the deal, MedImmune's share price was up 2% at $44.79, and Aviron's had jumped 28% to $47.43. *AB*

Selected research collaborations

Company 1	Company 2	$(Millions)	Details
Genzyme Molecular Oncology (Framingham, MA)	Kirin Brewery (Tokyo, Japan)	2	A two-year deal to develop and commercialize fully human monoclonal antibodies as therapies for angiogenesis and cancer. Genzyme will receive $2 million upfront in addition to milestone payments to validate its tumor endothelial markers as targets, against which Kirin will generate antibodies. For any resulting antibody products, development costs and worldwide profits will be split evenly.
Paradigm Genetics (Research Triangle Park, NC)	StemCo Biomedical (Research Triangle Park, NC)	*	A collaboration to elucidate biochemical profiles of adult stem cells for the identification of new markers that will allow for easier identification of different stem cell lines. Paradigm will identify every small molecule present in the cells, and will retain all rights to the compounds for potential use in drug discovery. StemCo will provide the stem cells, and retain all rights related to the stem cells for diagnostic or therapeutic purposes.
Myriad Genetics (Salt Lake City, UT)	Biosearch Italia (Gerenzano, Italy)	*	A venture to discover novel therapeutic compounds from microbial extracts. Myriad will screen its internal targets against Biosearch Italia's collection of ~100,000 microbial samples and its library of ~50,000 identified molecules. The two firms will share development rights to any resulting compounds.
Epimmune (San Diego, CA)	Bavarian Nordic A/S (Copenhagen, Denmark)	*	A non-exclusive collaboration to develop vaccines for the prevention or treatment of HIV. Epimmune will contribute its T-cell epitope identification expertise and vaccine design technology. Bavarian Nordic will contribute its vaccine delivery technology, as well as its HIV vaccine manufacturing expertise. While commercial rights to resulting products were not disclosed, Bavarian Nordic retains manufacturing rights.
AxCell Biosciences (Newtown, PA)	Mount Sinai School of Medicine (New York, NY)	*	A collaboration to research the binding of ligands to certain proteins that contain a WW domain, which are believed to play a role in the development of muscular dystrophy and neurodegenerative diseases such as Alzheimer's. Mount Sinai researchers will use AxCell's map of the WW protein domain family to design inhibitory peptides of the proteins for the identification of potential drug therapies.
MultiCell (Escondido, CA)	Pfizer (New York, NY)	*	A non-exclusive deal to predict the toxicological and therapeutic properties of drug candidates. MultiCell's immortalized liver cells will be used to screen Pfizer's compounds. Financial details were not disclosed.

*Financial details not disclosed *AB*