IN brief

EU impasse over GM deepens

Austria and Hungary have asserted their right to ban cultivation of a genetically modified (GM) corn, known as MON810. On March 2, an overwhelming majority of environment ministers rejected the European Commission's initiative to order these member states to adhere to European Union legislation and lift their national bans on planting the GM maize. MON810 is an insect-resistant corn engineered by Monsanto and the only GM product approved for growing in Europe. It is cultivated in Spain, Czech Republic, Romania, Portugal, Germany, Poland and Slovakia. But after the recent vote, it now seems likely that when the council of ministers next meets in June, it will uphold similar bans currently in place in France and Greece, intensifying the disarray. "By failing to defend the EU approval system European governments undermine public trust. Why make tough laws on GM crops and then break them?" asks Nathalie Moll, spokesperson for the association of bioindustries EuropaBio. Things will deteriorate further if Germany confirms statements released by its ministers of environment and agriculture Sigmar Gabriel and Ilse Aigner that Berlin is considering a cultivation ban. In February, an EU regulatory committee deadlocked over whether to allow planting of two other insect-resistant maize lines, BT-11 and 1507. Final approval will now depend on the council of ministers and, in case of stalemate, on the Commission. A more propitious wind blows in Asia, where Monsanto has started field trials of GM corn in India and is eyeing Indonesia next. *Anna Meldolesi*

Cellulosic ethanol stimulus

Young companies are likely to benefit from the $1.3 billion earmarked for cellulosic fuel projects in the US stimulus package. The bill, passed in February, gives the US Department of Energy (DOE) up to $500 million to spend on loan guarantees for experimental biofuel facilities and $800 million for research projects spanning "the whole range of biomass development," says Christina Kielich, a DOE spokesperson. The agency says it will put scientists to work finding new ways to break down cellulosic feedstocks—like switchgrass and woodchips—into chemical compounds, convert the compounds into fuels and address feedstock sustainability. The funding may help more startups get off the ground but isn't nearly enough to transform the fuel industry, say biofuel experts. "The government will need to come up with an energy bill that funds innovation more comprehensively," says David Aldous, CEO of Range Fuels, a cellulosic biofuel company in Broomfield, Colorado. Aldous points to Brazil's ethanol program in the 1970s, which financed the development of ethanol-only cars, guaranteed ethanol purchases and loans, fixed prices and mandated ethanol blending with gasoline. "It's that kind of commitment that transforms a country," he says. Indeed, US regulators may soon increase the blend rate for ethanol in gasoline to 13% from 10%, according to the Governors' Biofuels Coalition. *Emily Waltz*

proteins. The original ATryn-producing goats were developed by microinjection, but animals currently used for production have been bred by nuclear transfer. The cloning technique allows production to be ramped up as all animals carried to term will be transgenic, says Newberry.

Transgenic animals could prove useful for producing proteins that are difficult to manufacture using traditional recombinant systems, such as plasma proteins. GTC hopes to apply its goat transgenic technology to produce clotting factors VIIa, IX and VIII, the missing protein in type A hemophilia. Other commercial targets include monoclonal antibodies (mAbs) and biogenerics. In February, for example, GTC announced that it had entered into collaboration with Ruakura, New Zealand–based AgResearch to develop transgenic founder animals for the production of two follow-on biologic mAbs.

The transgenic system lends itself to proteins that need to be produced in large volumes, such as mAbs, because it can reduce manufacturing costs by an order of magnitude, according to Newberry. This could be critical for the production of biogenerics, which will likely be required to undergo expensive clinical trials to show therapeutic equivalence to the innovator product. A transgenic animal production system could lower manufacturing costs enough to reduce the final cost substantially.

Others hope to replicate GTC's early success. PharmAthene of Annapolis, Maryland, is also working on transgenic goat milk, whereas Pharming, a company in Leiden, The Netherlands, is developing rabbit milk as a protein production system. Technical barriers have been largely overcome. "Nowadays there is a whole variety of ways to generate transgenic animals, and the behavior of transgenes is pretty well known. You can't always predict what's going to happen [to an introduced gene], but given enough founder animals, you can almost always get what you want at the end of the day," says Bob Wall, research physiologist at the US Department of Agriculture's Agricultural Research Service, in Beltsville, Maryland.

One issue for protein production has been surface glycosylation, which can affect a protein's therapeutic potential and immunogenicity. Glycosylation in goats (and in cows and sheep) typically involves *N*-glycolylneuraminic acid, a monomer virtually absent in native human proteins, whereas rabbits and chickens contain oligosaccharides (containing *N*-acetylneuraminic acid) that resemble those in humans. But ATryn's approval in Europe and now in the US is a sign that these differences will not pose insurmountable regulatory hurdles. "Early on in the development of bioreactor animals [different glycosylation and post-translational modification profiles] had sort of surprised and concerned the sponsors of these projects, but given that we now have a product on the market in the states in Europe, I guess that's not an issue," Wall says.

Most are confident that these developments herald a new era for transgenic animal development in the US. "I think there hasn't been as much activity in the US as in Europe, in part because industry hasn't gotten a clear sign from FDA as to how these products will be regulated. I think that's one of the pressures that FDA felt in realizing they needed to put out a guidance," says Sheldon Bradshaw, a former chief counsel of the FDA and now a partner at Hunton & Williams LLP in Richmond, Virginia.

FDA's guidance has been years in the making and many believe that the uncertainty took a toll on the US animal biotech industry. The delay may have been natural, given the novelty of the technology. It took FDA some time to decide exactly how to regulate the products from a transgenic animal and the agency ultimately decided to classify the transgene product as a drug and to regulate it as such. "It has been a long evolution with respect to determining that, and then achieving coordination between its centers and bringing forward [the guidelines] on paper," says Glenn.

But recent developments have made Glenn more upbeat. The lack of guidance "had the potential to (affect) the industry's viability in the US. It didn't come as soon as we wanted it, but we're on a positive path right now."

Jim Kling *Bellingham, Washington*

IN their words

"This is cosmetic medicine. Others are frightened by the criticism but we have no problems with it."

Jeff Steinberg, director of the clinic Fertility Institutes, on the advertisements on their website offering to screen embryos for gender, eye color, hair color and complexion. (*Wall Street Journal*, February 12, 2009)

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