IN brief

Irish bioethics council axed

Stem cell research in Ireland has been thrown into a state of confusion, after a recent government decision to cut all funding for the Irish Council for bioethics at the end of the year. Paradoxically, the move coincides with a recent Supreme Court decision that removes some of the legal uncertainties surrounding human embryonic stem cell research in the country. The judges denied a woman the right to proceed with *in vitro* fertilization without the consent of her estranged husband. In doing so, the court ruled that embryos outside the womb are not protected by the country's constitutional protection of the unborn. Although this ruling affects human embryonic stem cell (hESC) research by providing clarification on the status of pre-implanted embryos, scientists remain wary of proceeding until a supporting framework is in place. "I'm going to behave responsibly. It's going to be done by the book," says Barry Moore at University College Cork (UCC), who has already received clearance to carry out hESC research from UCC's research ethics committee. Ireland has no laws governing human stem cell research and scientists have been operating in a legal limbo. "The lack of an independent bioethics board will have serious repercussions for how Ireland is seen as a hub for medical research, and that will have to be addressed as a matter of urgency," says scientific director Stephen Sullivan of the newly formed Irish Stem Cell Foundation, which is calling on the government to reinstate the council. *Cormac Sheridan*

Amgen trumps Roche

A 5-year patent dispute between Roche and Amgen over the anti-anemia drug Mircera (methoxy polyethylene glycolepoetin beta) has ended. Roche of Basel acknowledged in court that Mircera, its pegylated-erythropoietin, infringed on Amgen's erythropoietin patent and would drop its challenges. The ruling ensures that Mircera sales are barred and Roche is kept out of the US market until mid-2014, when Amgen's patents expire. Amgen currently dominates the US market with erythropoiesis-stimulating agents (ESAs)—Epogen (epoetin alfa) and Aranesp (darbepoetin alfa)—which together generated $5.6 billion in sales last year. However, Thousand Oaks, California–based Amgen may now have to contend with US Food and Drug Administration (FDA) regulations, as a panel of outside experts expected to meet in 2010 will re-examine safety concerns over ESAs (*Nat. Biotechnol.* **25**, 607–608, 2007). Writing in January in the *New England Journal of Medicine* (doi:10.1056/NEJMp0912328), FDA officials are urging proper dosing of ESAs in individuals with chronic kidney disease, as certain regimens appear to increase the risk of cardiovascular events and death. The panel may impose regulations on the ESA market or decide that additional clinical trials are needed. The outcome of this meeting, says Eric Schmidt, a biotech analyst at Cowen and Company in New York, is that it may bring down sales, as drug companies may no longer be allowed to push high-dose regimens. *Nazlie Latefi*

Report blames GM crops for herbicide spike, downplays pesticide reductions

A recent report published by the Organic Center, an organic farming advocacy organization headquartered in Foster, Rhode Island, claims that the use of herbicides in weed control has risen sharply since transgenic crops' commercial introduction in 1996. Increasing cultivation of glyphosate (*N*-phosphonomethyl glycine)-tolerant transgenic crops, particularly soybean, has led to an aggregate increase in herbicide use of 383 million pounds over the past 13 years, on top of what the Organic Center's chief scientist Charles Benbrook models suggest would have been applied had the technology never been deployed (http://www.organic-center.org/science.pest.php?action=view&report_id=159). The report also downplayed that transgenic corn and cotton have delivered reductions in insecticide use totaling 64.2 million pounds over the same time period.

The report's findings on herbicides are in stark contrast to the standard agrochemical industry line that transgenic crops have reduced the chemical load on the environment. Several critics have questioned the assumptions underlying the analysis and any significance that can be drawn from it, particularly as the report comes from an advocacy group seeking to "communicate the verifiable benefits of organic farming and products to society."

Rising glyphosate resistance is a plausible explanation for the increasing use of herbicides, however. Among plant scientists, there is little disagreement on the problem of glyphosate-resistant weeds. "It certainly is fair to point out the failure in glyphosate stewardship, that the threat of resistance wasn't appreciated, that more diverse management wasn't used to try to prevent or delay resistance emerging," says Chris Boerboom, extension weed scientist at the University of Wisconsin in Madison.

The issue of herbicide resistance has already become acute in some US states. Report author Benbrook claims that the cotton and soy industries in the Southeast are on "the brink of collapse" because of the cost of dealing with glyphosate-resistant weeds. Benbrook goes on to argue that increasing reliance on herbicides paired with more expensive, engineered tolerance traits will erode farmers' profitability, while compounding environmental and public health risks (through increased chemical exposure).

The report's other main finding—that insect-resistant transgenic crops have helped cut pesticide use—was downplayed by Benbrook, who claims the increase in the volume of herbicides applied "swamps" the

Crop spraying on the up. Glyphosate-resistant weeds may be driving an increased reliance on herbicide use.

benefits of decreased insecticide use attributable to corn and cotton expressing genes that encode one or more *Bacillus thuringiensis* (*Bt*) insect toxins. *Bt* crops could have a brighter future than herbicide-resistant transgenic varieties, the report states, "but if, and only if, [insect] resistance is prevented."

The report is based on extrapolations of pesticide use survey data compiled by the US Department of Agriculture's (USDA) National Agricultural Statistics Service (NASS). Benbrook relies on annual trait acreage data compiled by St. Louis–based Monsanto to disaggregate transgenic crops from the total crop acreage. However, no NASS data on corn or soy are available for 2007 or 2008, years for which Benbrook posits unusually large pesticide increases of 20% and 27%, respectively. The main uncertainties stem from gaps in NASS data, which, since 2001, have only been gathered intermittently, and from that data's failure to distinguish between pesticide use on transgenic crop varieties and on their conventional counterparts.

Benbrook postulates the emergence of glyphosate resistance has fueled a sharp upswing in the use of other herbicides on glyphosate-tolerant crops, whereas levels of herbicide used on conventional crops have fallen because of ongoing improvements in potency. But Janet Carpenter, formerly of the Washington, DC–based US National Center for Food and Agricultural Policy and now an independent agricultural biotech consultant, disagrees. "That's all extrapolation," she says. "The bottom line is we don't know what has happened to pesticide use in the last couple of years."

Benbrook says that additional data from future surveys can be factored into his model when it becomes available. "The valid criticism—or valid question—is these are all average numbers," he says. "I would place a fair amount of confidence in these averages as a reflection of what's going on out there."

In a published critique of the report, Dorchester, UK–based consultancy PG Economics argues that Benbrook overestimates herbicide application rates for biotech crops and underestimates them for conventional crops (http://www.pgeconomics.co.uk/pdf/OCreportcritiqueNov2009.pdf). It cites a new study from the US Geological Survey, which found that concentrations of several major pesticides either declined or remained constant in US corn belt rivers and streams during 1996–2006 (http://pubs.usgs.gov/sir/2009/5132/). However, the study period does not include the two most recent years, during which Benbrook claims the greatest increase in herbicide use has occurred. PG Economics, which also published a lengthy study on the global socioeconomic and environmental impacts of transgenic crops in May last year, has drawn on two sources: pesticide use data from a commercial source, DMR Kynetec, of St. Louis, which Benbrook says is in general agreement with his own findings; and what he describes as 'faulty' simulation data generated by the Washington DC–based National Center for Food and Agricultural Policy, based on exercises run with university extension weed scientists. "It's impossible to reconcile their estimates with the NASS data," Benbrook says.

In the meantime, several scientists have voiced support for the general thrust of the study. "There's nothing surprising there," says Matt Liebman, who holds the H.A. Wallace chair for Sustainable Agriculture at Iowa State University in Ames. Dealing with glyphosate-resistant weeds will require alterations in cropping systems that rely solely on the marriage of the herbicide-tolerance trait and the associated herbicide to control weeds. Widespread convergence on a narrow range of options, such as the rotation of glyphosate-resistant corn and glyphosate-resistant soybean, has been a significant factor, says Liebman. "You have good conditions for rapid selection of herbicide resistance."

Monsanto and its competitors are responding to the problem by offering farmers subsidies to include third-party herbicides in their weed control systems. They are also stacking additional tolerance traits that can be paired with other herbicides, such as dicamba (3,6-dichloro-2-methoxybenzoic acid), glufosinate (phosphinothricin) and 2,4-D (dichlorophenoxyacetic acid). External factors have hampered progress, however. "The biggest contributor to weed resistance has been the European Union's slow approval process for new biotech-enhanced seeds. After many years of delays, the EU finally granted approval of Liberty Link [phosphinothricin-acetyltransferase] soybeans, which are resistant to a different active ingredient [L-phosphinothricin]," says Bob Callanan, communications director of the American Soybean Association, located in St. Louis.

Critics argue that more diversified approaches will be needed, such as alternative crop rotations, novel herbicides—it's 20 years since a new mechanism of action was commercialized, notes Boerboom—and alternative weed control methods. "If you want to keep this tool available and effective there has to be some way, short of fallowing a field, of delaying the development of resistant weeds," says Robert Kremer, of the USDA's Agricultural Research Service at Columbia, Missouri. The market dominance of transgenic crop varieties limits some of the options, however. "It's very difficult to go and find nontransgenic soybean," he says. "Conventional corn rotated with Roundup Ready [glyphosate-resistant] soybeans would be very logical," says Boerboom. "We have an excellent selection of conventional herbicides we can use in corn."

That Monsanto's Roundup Ready cropping system has been a major hit with farmers is not in dispute. "The simplicity, the high efficacy and the perceived low cost have been very attractive," says Liebman. In this respect, even Benbrook agrees: "The weed management systems that Roundup Ready [crops] replaced were unforgiving and required a high level of skill and management to get the benefits out of them," he says. What's more, glyphosate, which inhibits 5-enolpyruvylshikimic acid-3-phosphate synthase, a plant enzyme involved in amino acid biosynthesis (the engineered trait comprises a bacterial form of the enzyme, which is unaffected), has a relatively benign environmental profile in comparison with many other herbicides. Moreover, it has allowed many crop growers to shift to no-till agriculture, which reduces fossil fuel inputs.

The problems farmers are encountering now are not new. "The selection for glyphosate resistance is not unique. We've selected for a whole lot of other herbicide families as well," says Aaron Hager, weed science extension specialist at the University of Illinois at Urbana-Champaign, Illinois. "There's a plant somewhere in the world that's resistant to an herbicide that hasn't even been discovered yet. That's how selection occurs."

As glyphosate has played a central role in US crop production over the past decade, it can be argued the technology has become a victim of its own success. For many farmers, weed control will, however, soon become more complex. Some of the alternatives offer less favorable environmental profiles. Dicamba, a synthetic auxin or plant hormone, can drift off-site and interfere with flowering plants, for example. "There will be objections raised to it by the environmental community because of nontarget effects," says Liebman.

Nevertheless, US agriculture is not facing a doomsday scenario, according to Boerboom. "I don't think it's like we're going into some dark age of chemical use on the landscape," he says. But a new phase in the molecular arms race between biotech and nature is getting underway.

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