nature biotechnology

Drugs in crops—the unpalatable truth

In the United States, genetically modified (GM) wheat (containing predictably a gene for resistance to a proprietary herbicide) is on the verge of approval. In Europe, having come unscathed through the UK farm-scale trials, GM maize has received the go-ahead from both ACRE, the UK government advisory group on GM crops, and from English Nature, the UK government's advisor on the environment. And yet, despite the progress with these crops, biotech companies seem determined to embark on another suicidal tussle with the anti-biotech lobby, in the process exposing their businesses not only to accusations of high-handedness and negligence but to unnecessary commercial risks. It seems that an industry in which the PhD is the intellectual norm is either incapable of learning a simple lesson from the past or cannot bring itself to act appropriately, despite what it has learned previously.

This time around, the tussle concerns the production of pharmaceuticals in GM food crops. Many companies, among them Diversa, Dow, Epicyte, Samyang Genex, Meristem Therapeutics, Maxygen and ProdiGene are exploring the expression of biopharmaceuticals in corn (maize)—130 acres of which were grown in the United States in 2002 (of a total transgenic acreage of 31.1 million). Other organizations are looking at other major crops: rice, potatoes, alfalfa. One might expect—and some in the industry obviously do—that drug production in plants could be good for the image of GM crops. After all, new/cheaper medicines are the sort of thing that consumers want.

The problem is—as anti-GM lobbyists have argued already—that the production of drugs or drug intermediates in food or feed crop species bears the potential danger that pharmaceutical substances could find their way into the food chain through grain admixture, or pollen-borne gene flow (in maize, at least) or some other accidental mix-up because of the excusably human inability to distinguish between crops for food and crops for drugs. The 'contamination' of soybeans and non-GM corn in 2002 with a corn engineered by Prodigene to produce an experimental pig vaccine shows just how plausible this is (*Nat. Biotechnol.* **21**, 3, 2003). This position is not anti-GM (something industry should appreciate)—we *should* be concerned about the presence of a potentially toxic substance in food plants. After all, is this really so different from a conventional pharmaceutical or biopharmaceutical manufacturer packaging its pills in candy wrappers or flour bags or storing its compounds or production batches untended outside the perimeter fence?

The difficulty is that, when it comes to pharming, the biotech industry and some of its supporters seem to be taking a stand that is principled and libertarian, rather than sensible. They argue there is an unalienable right for every corporate entity to develop whichever technology it wants and to undertake that development wherever it wants (as long as it is safe to do so, of course). The specific right in question is the right to grow drug-containing corn crops in the US Corn Belt. After a shift in position at the beginning of 2003, the US Biotechnology Industry Organization (BIO) is now firmly in this libertarian camp.

But if an industry association has a role—and BIO certainly does—then it should be to represent the longer-term interests of its broad membership. It should be trying to ensure that in the not-too-distant future, the commercial prospects for pharma plants are unhindered by predictable and avoidable political and social concerns. BIO's role ought to be to steer its membership past the obstacles, rather than plotting a course for a head-on collision.

The predictable obstacles are: that regulatory oversight will become more stringent and exhaustive because of the juxtaposition of drug crop and food crop; that protest lobbies will obstruct the drugs-in-food-crops companies directly through the legal system; that they will also obstruct them indirectly by applying pressure on corn producers generally; that producers and farmers' interest groups will run away very quickly from the fight as soon as any of their markets are threatened; that European corn producers will decry the potential commingling of food-corn and drug-corn; that a consignment of drug-corn will find its way into bird-feed mix and, by an amazing coincidence, be picked up by random tests conducted by Friends of the Earth; that 'Pigeon Fanciers [Twitchers] Against GM' will mobilize celebrity ornithologists against drug-corn; that politicians in technologically lagging nations will introduce trade barriers, such as traceability, that have little technical merit but much populist appeal. In short, the whole farce of GM food could play out again, only this time with much greater justification.

It is possible to preempt such a mess. The key is to put in place some form of foolproof segregation between food crops and drug crops. And that does not mean increased fallow zones, special cleaning routines for farm machinery, increased frequency of inspections or any other of the measures introduced last year by the US Department of Agriculture.

Instead, there are two rather obvious and nontechnical levels at which that segregation could work effectively. The first is geographical. If drugs must be produced in food crops, then those crops should be grown away from non-drug food crops. Drug crops are not commodities; it shouldn't be necessary to use the highest yielding strains of corn under the climatic conditions for which that strain has been designed (a back-of-the-envelope calculation suggests that even with present low yields, only 0.19% of total US corn production would be required to supply every insulin-dependent diabetic on the planet). So don't grow your drug-corn in the Corn Belt—grow it in California or New England. Better still, if you want to segregate geographically, grow the crop on an island where that crop is not grown for food or feed. There is already a company, for instance, that is planning to develop pharmaceutical barley and grow it in Iceland, a country that can grow the crop, but doesn't.

The second and possibly more effective form of segregation would be culture. Simply don't use food plants for producing drugs. Why not? Precisely because they are food plants. This is not a biological distinction, it is a cultural one, but it is the source of most of the anxiety that the public is likely to feel and which the lobby groups are likely to mobilize. In essence, the only reasons that the major food crops are attractive as pharming hosts are we know how to grow/harvest them efficiently and we know how to manipulate these species genetically. Let's grow pharma plants, but let those plants be *Arabidopsis*, or flax, or duckweed.

Erratum: Drugs in crops—the unpalatable truth

Editorial
Nat. Biotechnol. **22,** 133 (2004)

On line 16 of the editorial, both Samyang Genex (Daejeon, Korea) and Maxygen (Redwood City, CA, USA) were wrongly indicated to be exploring the expression of biopharmaceuticals in corn. This erroneous information was obtained from a report *A Strategic Evaluation of Transgenic Plant and Animal Biomanufacturing Systems* (Revelogic, Ft. Collins, CO, USA, 2003). In fact, Samyang Genex has a corn processing plant and uses plant cell culture to produce paclitaxel, whereas Maxygen has no program focus on expressing biopharmaceuticals in corn.

Erratum: Make or break for costimulatory blockers

Ken Garber
Nat. Biotechnol. **22,** 145–147 (2004)

In Box 1 on p. 147, column 1, line 13, the sentence "Antigen-presenting cell (APC) B7 signaling induces T cells to express the enzyme indoleamine 2,3 dioxygenase (IDO), which catabolizes the amino acid tryptophan, presumably starving T cells and causing proliferation arrest" should have read, "B7 signaling in antigen-presenting cells (APCs) leads them to express the enzyme indoleamine 2,3 dioxygenase (IDO), which catabolizes the amino acid tryptophan, presumably starving T cells and causing proliferation arrest."

Corrigendum: Visualization of tumors and metastases in live animals with bacteria and vaccinia virus encoding light-emitting proteins

Yong A Yu, Shahrokh Shabahang, Tatyana M Timiryasova, Qian Zhang, Richard Beltz, Ivaylo Gentschev, Werner Goebel & Aladar A Szalay
Nat. Biotechnol. **22,** 313–320 (2003)

On page 319, column 1, line 9 from bottom, the phrase "subcutaneous colon fibrosarcoma" should have read "subcutaneous fibrosarcoma."

Corrigendum: Phenotypic alteration of eukaryotic cells using randomized libraries of artificial transcription factors

Kyung-Soon Park[1,2], Dong-ki Lee[1,2], Horim Lee[1], Yangsoon Lee[1], Young-Soon Jang[1], Yong Ha Kim[1], Hyo-Young Yang[1], Sung-Il Lee[1], Wongi Seol[1] & Jin-Soo Kim[1]
Nat. Biotechnol. **21,** 1208–1214 (2003)

In the author list, the name of author Seong-il Lee was misspelled as Sung-Il Lee.