

to independent growers in eastern North Carolina. Ventria is testing two industrial proteins already in use as dietary supplements, lysozyme and lactoferrin. After several unsuccessful attempts in other states⁵, Ventria secured US Department of Agriculture (USDA)-Animal and Plant Health Inspection Service permits for North Carolina for the years 2005 and 2006, and contracted with independent growers in coastal North Carolina. Last year's planting was 335 acres of rice (*Oryza sativa*) transgenic for lactoferrin or lysozyme.

Scaling up such PMIP crops presents these growers with several challenges. First is the problem of containment in this hurricane-prone riparian ecosystem. In the Ventria case, this is a minor objection because rice is a self-fertilizing plant, which minimizes the possibility of pollen escape. Still, concerns have been voiced about long-distance dispersal of PMIP rice pollen via hurricane-speed winds and about consumption of PMIP rice by birds and other wildlife.

Second, compliance guidelines for PMP and PMIP crops require a steep investment in new equipment and infrastructure. It is not clear whether North Carolina growers other than those with a large land base and deep pockets will be able to make the necessary capital outlay to produce these products. US regulators now require each grower to set aside special farmland, farm equipment and separate areas for cleaning and processing PMIP crops. Costly employee training is also required as part of compliance with new US Food and Drug Administration and USDA regulatory statutes for molecular pharming⁶. At this early-stage PMIP market, Ventria covers all costs for the North Carolina contract growers. In the future, however, independent growers will be expected to provide a seed-to-harvest package deal for the firm's recombinant protein product. Only the larger, wealthy growers in North Carolina will profit.

The third issue, liability, is the most critical. Who is liable in the event of a food or feed mixup with PMP or PMIP crops? The unanswered question of liability blocks entry even more than capital outlay. And liability risk will be highest where GM food plants are grown side by side with PMP and PMIP crops.

With these caveats in mind, field-grown PMP crops by independent growers in North Carolina (or other agrarian-based US states) is not a practical solution for drug firms either. These firms place a premium on uniformity and purity of recombinant proteins. Field-grown PMP crops require

more complex processing, produce uneven protein quality and yields and are more likely to include residues from herbicides, pesticides and fungicides. Non-food crops grown in containment systems provide a better solution for PMP production.

Such systems have been built around higher plants, such as duckweed (*Lemna* spp.)⁷ and tobacco (*Nicotiana* spp.)^{8,9}, or algae (*Chlamydomonas reinhardtii*) or moss (*Physcomitrella patens*). In the case of duckweed, the containment system allows unlimited scale-up, efficient product purification/processing and no residues from pesticides. Proteins exuded via roots of genetically modified plants are harvested from the container's aqueous media also offer some advantages over processing green tissues. Indeed, North Carolina already has a competitive edge in producing PMPs through the use of duckweed, tobacco and other non-food plants safely cultivated in containment systems^{7,10,11}.

Perhaps Ventria's field-grown PMIP tests in North Carolina are a stray outlier and not indicative of a larger trend towards non-local molecular pharming field operations positioned to contract with independent North Carolina growers. True, growers in North Carolina badly need new markets but molecular pharming based on food crops in open fields is not the answer.

We should strongly consider legislative support for biotech firms developing containment systems. This would be especially important for PMIP products, as well as PMP products, because the former are less valuable and more sensitive to cost-of-goods arguments, with the impetus on field-grown systems rather than containment. Such support would attract private sector investment while protecting small growers and consumers. By doing so, legislators will have found the fit between PMP production and local food suppliers.

For densely populated states like North Carolina, politicians, scientists and growers alike must live, work—and eat—within the same narrow geographic coordinates. The citizens in these states may rely on a globalized food transport system, but grocery prices will favor local food production as prices soar with rising fuel costs. And rising fuel costs—not just catastrophic weather events—will favor local food production and organic farming. Those pursuing field-grown molecular pharming will likely find themselves up against an increasingly vocal group of opponents—not only activists, but also independent growers and consumers—with the following mantra: “not in my backyard.”

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COMPETING INTERESTS STATEMENT

The author declares that she has no competing financial interests.

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Nature Biotechnology responds:

Although industry organizations, such as the Biotechnology Industry Organization (BIO), continue to support food crops for PMP and PMIP expression systems, we hold to our original view that they pose too many problems and nonfood crops are a better alternative (*Nat. Biotechnol.* **22**, 133, 2004). In relation to Williams' concern over litigation, in our view, neighboring certified (e.g., GM free) organic growers in particular represent a litigation risk for farmers who elect to grow PMP/PMIP food crops in close proximity. Even if certified organic growers are comparatively scarce—only 73 organic growers are certified in North Carolina—their livelihood and certification status are under threat from PMP/PMIP crop admixture/introgression/hybridization events and thus they are likely to be especially vigilant for such events, more willing to file suit to protect their business interests and serve as rallying points for opposition.