Globalization of European Biotechnology: Commercialization of Agbiotech Products Despite Political and Legal Restrictions

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Agricultural biotechnology has its roots in Europe. The basic technology–*Agrobacterium tumefaciens*-mediated gene transfer into plants—was discovered and developed by Jeff Schell and Marc van Montagu in Cologne, Germany, and Ghent, Belgium. Despite these successful research activities and patenting of the technology, efforts to put these inventions into practice and launch profitable products on the European market were unsuccessful due to fierce and continued protests from non-governmental organizations (NGOs) prejudicing the general public and political leaders against genetically modified (GM) plants.

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The first commercial cultivation of GM plants took place in 1995 in the United States. Since then, the industry has seen double-digit growth every year, but only outside of Europe. The EU moratorium on approval of GM plants in 1998 was a particularly serious blow. Most biotechnology companies, especially those financed by venture capital, went out of business, lacking strategies for surviving a 6-year-period without launching products. Even large multinationals fell victim, and had to merge or were sold to competitors to increase shareholders' values. Small and medium-sized companies survived only if they had products other than GM plants in their portfolios and with global markets.

Successful Business Strategy

Phytowelt GreenTechnologies offered services and contract research in addition to developing products for industry and consumers. Our main technologies—the proprietary genetic marker system ISTR, patented genes to improve plants and tissue-culture technologies such as somatic hybridization—led to projects with ornamental, food and fodder plants. Furthermore, we improved procedures for the production of phytopharmaceuticals and platform chemicals for our clients in the chemical and pharmaceutical industries.

The success and steady development of the company are based on an international orientation and embracement of globalization since the beginning. Clients in Japan, New Zealand, Canada, United States and Europe are proof of this strategy. Another critical factor was the self-sustained financing by private shareholders, assignments and contracts. Grants from public institutions were used to implement new technologies.

Political Obstacles

Nowadays, the European biotech landscape shows an uneven distribution of companies, with concentrations along the Rhine and the River Thames as well as uneven application. Medical and pharmaceutical biotech companies outnumber, by a factor of five, those with an agricultural orientation.

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Besides the lack of consumer acceptance, absence of consistent and reliable legislation prevent commercialization of GM products in Europe. The discussion revolves around thresholds, labelling, traceability, monitoring, coexistence, admixture, liability and biopatents without reaching firm conclusions to provide a legislative framework. Instead, more research has been demanded to prove the safety of GM crops, serving to postpone their introduction. Interest on the part of the industry to conduct appropriate research has declined in recent years. The number of field trials (Figure 1) reached its peak in 1997/1998, and since then has decreased significantly. A small increase in 2006 may indicate a turning point, but it is too early to be certain.

Spain leads the current EU member states with 53,000 ha planted to GM crops in 2005, and with an increase in 2006. Romania, which will become an EU member in 2007, has an even greater area, of GM soybean. However, because the cultivar is not approved within the EU, its cultivation will be forbidden once Romania enters EU-25. Three other European states, Germany, France and the Czech Republic, together had around 1,000 ha of GM crops in 2005. This probably hit the 10,000-ha threshold in 2006, largely because of ten-fold increases in France and the Czech Republic; Germany planned only a doubling to around 900 ha.

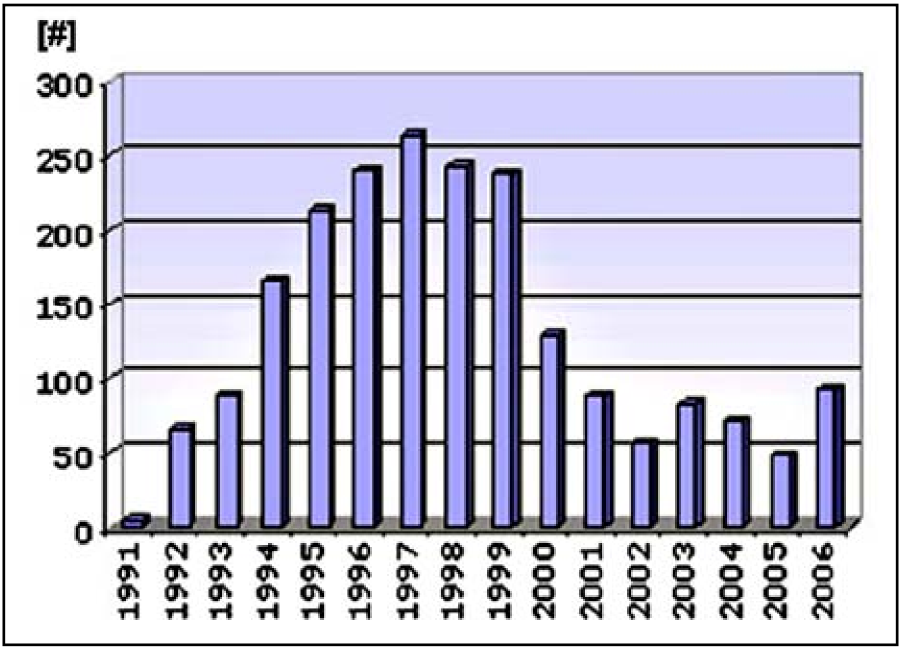

Figure 1. The number of field trials of GM plants increased steadily until 1997. The European Commission's 1998 moratorium, preventing commercialization of GM plants, adversely affected R&D.

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End of the Moratorium

A turning point occurred in 2004 when the EU ended its moratorium and approved importation of GM corn. In 2005, Germany turned its attention to GM after the Green party failed to win re-election in their last two strongholds, the NRW state government and the federal government of Germany; three varieties of GM corn were approved for cultivation within the first 100 days of the new federal government. Coincidentally, Phytowelt sold the first license of its proprietary parthenocarpy technology to a US seed company. But the general situation in Europe is unchanged: to stay in business, produce either non-GM products (Figure 2) or non-food value-added products like monoterpenes (Figure 3). This is also the strategic line of the European Commission. In their *Plants for the Future* program, the emphasis is on bioenergy and biobased chemicals to promote development of a biobased economy. Their decade-long timeframe indicates that even in the Commission no one expects short-term implementation of the technology in Europe. And to avoid the term “genetic engineering” “precision breeding of renewable resources” has become the fashionable, politically correct term.

Figure 2. Non-genetically engineered, non-food products currently have the best chances of success on the European market. Despite the end of the moratorium, GM plants are still underrepresented.

Industrial Plant Biotechnology

A fairly new trend, but not a new industry, is so-called “white” or “industrial” biotechnology in Europe. Because of the success of some European companies (*e.g.* DSM, Novozymes, BRAIN), this field is considered as more promising than biotechnology of plants for food and feed. In the beginning, companies tried to avoid being connected with genetic engineering of plants. But it is becoming accepted that industrial biotechnology needs to be combined with plant biotechnology to fully exploit its potential.

Instead of using agriculture only as a source of feedstock for fermenters in the form of sugar and other low-value commodities, it was realized that plants can deliver a whole range of complex chemical entities. Precursors for steroid hormones and cancer medication (*e.g.* taxol) for the pharmaceutical industry and polymers like caoutchouc, a polyterpene, for the rubber industry are already being delivered by plants. Mint plants can produce a

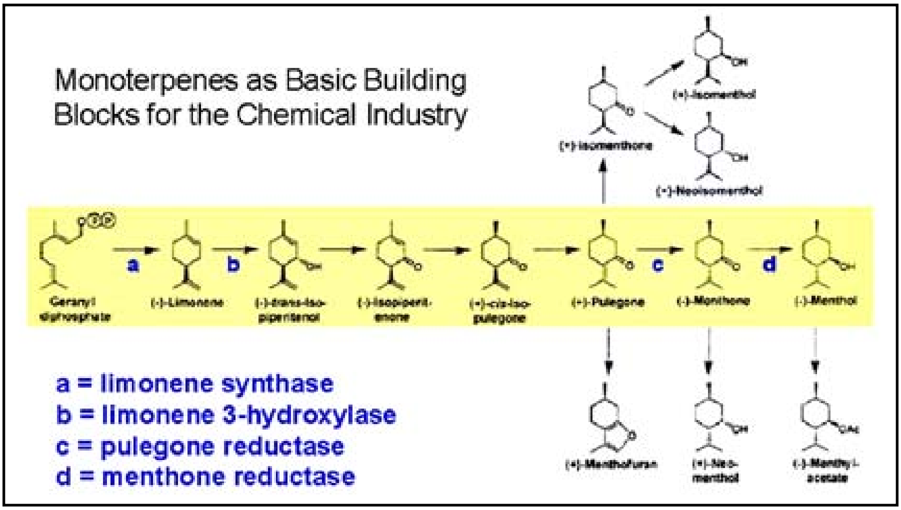

Figure 3. The biosynthesis of menthol as an example of the production of platform chemicals in mint plants exploiting their biodiversity for the sustained production of chemicals; a, b, c and d are known enzymes of the biosynthetic pathway that can be genetically modified to direct the production of a particular monoterpene.

whole range of monoterpenes depending on the variety, thus biodiversity may be exploited to increase the use of renewable resources for sustained production of chemicals (Figure 3). With genetic engineering, plant biotechnology can combine the primary production of agriculture and the conversion technology in fermenters to shorten the process and reduce costs. By providing higher concentrations of basic precursors, such plants will improve fermentation processes. Due to removal of contaminating by-products by inhibiting their synthesis *in planta*, the higher purity of products from GM plants will secure their usefulness to the chemical industry.

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Financial Aspects

Encouraging signals from the technological side are supported by recent news of mergers and acquisitions. Plant biotechnology companies are again the target for multinational corporations to improve their pipelines, *e.g.* BAYER incorporated Icon Genetics, BASF bought CropDesign in Belgium, and Biolex (USA) acquired Lemnagene (France). The formation of Phytowelt GreenTechnologies was a merger of equal partners, Phytowelt and GreenTec, the latter a spin-off of the Max-Planck-Institute for Plant Breeding Research in Cologne. The increased interest in plant biotechnology from the financial community is also shown in a new round of financing for Novoplant, Germany: they raised 3 million euros. And new companies are being founded, such as Solucel, a combined effort involving Finnish and Belgian governmental institutions.

Conclusion

These examples show that biotechnology is on the rise again in Europe. Instead of being paralyzed by the scaremongering of anti-GMO-activists, we should spread the good news. There are enough examples to show the benefits of applying genetic engineering of plants and thereby convince the general public. We have only to inform people correctly and constantly about the progress and the benefits of this new technology. Millions of farmers worldwide cannot be wrong!

Labelling should be mandatory for products improved by genetic engineering (Figure 4) to show that we are proud of the technology and convinced of its benefits. Conferences like NABC's and ABIC's are important and supporting them helps to improve acceptance and distribution of this beneficial technology. NABC 19 will convene in Brookings, South Dakota, May 22–24, 2007, and ABIC2007 in Calgary, September 23–26, 2007.

Figure 4. GO indicating modern, innovative genetic engineering to improve a product labelled according to quality standards defined by the academic and industrial communities.

AFTER STUDYING chemistry, biochemistry and food chemistry in Germany, Peter Welters spent 4 years at the Max-Planck-Institute for Plant Breeding Research, there obtaining his Diploma and PhD. He worked in Jeff Schell's group on promoter control in the legume/rhizobia nitrogen-fixing symbiosis. After 3 years at the University of California, San Diego, in the laboratories of Maarten Chrispeels and Scott Emr, researching protein-transport regulation in plants and yeasts, he was chosen as head of the *Production of Pharmaceutical Proteins in Plants* project in Rouen, France.

Dr. Welters's innovative ideas led to the foundation of Biotechnology and Molecular Biology, which became Phytowelt GmbH in 1998. Four years later, he became CEO of GreenTec GmbH, a spin-off company of the Max-Planck-Institute, founded by Schell, Klaus Hahlbrock, Frederico Salamini, and Heinz Saedler.

Since January 2006, Welters has been CEO of Phytowelt GreenTechnologies GmbH, a fusion of GreenTec and Phytowelt, located in Nettetal (head office) and Cologne (R&D). The company offers laboratory and know-how services in agricultural biotechnology, *e.g.* somatic hybridization, tissue culture, marker technologies, contract studies and project coordination. He is also a board member of the ABIC Foundation, Canada, and BioCologne eV, Germany.