COMMENTARY

DRUG DEVELOPMENT

Pharmaceutical biotechnology emerges in Mexico

Octavio T. Ramirez and Rodolfo Quintero

In the early 1980s, when modern biotechnology emerged in the US, Mexico had a very closed economy heavily dependent upon its oil reserves and other natural resources. The result was an extremely protected industry relying on traditional technology, with only mild competition arriving from abroad. Biotechnology—such as it was—consisted of processes for the production of antibiotics, food and feedstock, enzymes, and alcoholic beverages.

Nonetheless, the hot start of modern biotechnology in the US ignited the "new biotechnology" wick in Mexico. The first response came from the academic community, where the number of researchers (less than 30 in 1980) working in biotechnology increased by 1997 to more than 300 working in at least 37 institutions and graduating about 15 PhDs and 40 MScs every year from 20 separate programs. The political scenario also changed drastically. In a very few years, Mexico transformed from one of the most protected economies in the world to one of the most open.

The initial response of the government was to solicit studies through various agencies under its auspices to diagnose the situation of biotechnology in the country and to identify priority projects for investment. However, in lieu of a national policy, most of its actions were limited to a continuous, though modest, support to biotechnology-related academic projects through the National Science and Technology Council (CONACyT). Probably the government actions with the largest effects on biotechnology, some of them negative, were regulatory changes.

In 1987 the patent law was modified to allow the possibility of patenting biotechnology products and processes in Mexico, but only after 1997. Such a 10-year moratorium provided Mexican industry with an opportunity to catch up with international counterparts. However, new modifications to the patent law in 1991 and 1994 truncated the process by canceling the moratorium. These policy swings resulted in resentment on the part of the national industrial sector, which canceled some of their projects. On the other hand, abolishment of the moratorium resulted in a flood of patent applications (792 in 1994), mostly from abroad, reflecting a new interest by the international sector in developing biotechnology in Mexico.

With the approaching prospect of patent expirations for most of the first-generation recombinant therapeutics, and within this new environment, the first Mexican pharmaceutical company to develop and produce recombinant therapeutic proteins has now appeared. Probiomed is the result of an R&D strategy put together at the end of the 1980s by Proquifin, its parent company. At that time, Proquifin (Mexico City) founded nearly 30 years ago, was a typical mid-sized Mexican pharmaceutical company, producing bulk chemicals and drugs, such as heparin, amikacin, and vitamin B_{12}. However, a shrinking profit margin caused by the influx of lower priced pharmaceutical commodities, mostly from China and other South East Asia countries, forced Proquifin to turn its sights to new alternatives, and, given the now more favorable environment, it turned to biotechnology.

As explained by Jaime Uribe, president and CEO of Probiomed (Azcapotzalco, Mexico), the first efforts were undertaken in 1987 to produce human leukocyte interferon, mostly with the aim of introducing it to the Mexican market within the legal framework of the time. The project soon came to a halt, however, as a result of bureaucratic inefficiencies and regulatory obstacles associated with the blood supply in Mexico. It was thus clear that bacterial recombinant interferon would be the only effective way to proceed, and research on this front led eight years later to the development of interferon-α2a. The project's success was based on in-house developments supported by solution of specific problems by universities and contract companies from Mexico and abroad. Nonetheless, the patent law changes of 1991 and 1994 prevented its commercialization, and it will be 2001 before this particular product will finally enter the market. Accordingly, Probiomed switched to other products and processes that had been simultaneously developed, and last year launched its first two recombinant proteins: Urifron (rHu interferon-α2b) and Gramal (rHu GM-CSF). And this year, its third protein, Bioyetin (rHu erythropoietin), entered the marketplace.

Combined, these three proteins have a value in Mexico of around $20 million per year, with rHu erythropoietin accounting for about two-thirds. By the end of 1998, and after an overall investment of around $40 million, Probiomed had sold $3 million worth and can reasonably expect to double that this year. "The goal," says Uribe, "is to penetrate the Mexican public and private drug markets during the following years, and then step into the worldwide arena within the next decade." With this in mind, Probiomed built a multipurpose plant in Mexico City, integrating in the same facility all the production processes, from the generation of bulk active principle to the elaboration of finished drug.

The Probiomed work force (at present about 70 employees) is composed of young professionals with masters and doctoral degrees (almost all earned in Mexican universities), who interact in a nonhierarchical and interdisciplinary atmosphere with an active scientific advisory board composed of respected Mexican and international scientists. Such a structure resembles the early start-up biotechnology companies in the US and constitutes a paradigm for industries in developing countries like Mexico. Probiomed intends to develop all analytical tests in-house and to perform its own clinical trials. This is also a paradigm for a pharmaceutical company in Mexico, as traditionally clinical trials and analytical tests for imported recombinant pharmaceuticals were accepted from abroad without hesitation. The performance of these tests and trials in Mexico constitutes the emergence of an important adjunct activity that did not exist there before.

Circumstances in Mexico are still far from those that existed during the early days of biotechnology in the US, and many difficulties remain before Mexican pharmaceutical biotechnology can develop to its full potential, including legislative voids, patent law pitfalls, and unsuitable financing. Nonetheless, the lessons learned from Mexico's entrance into pharmaceutical biotechnology are clear. New players will increasingly appear as patents of the first recombinant proteins expire, and many will arrive from developing countries, as genetic engineering, and fermentation and bioprocessing techniques in general, have been mastered worldwide. Such a scenario should drive the multinational pharmaceutical companies to improved second- and third-generation therapeutics as protections for the original ones expire, and simultaneously bring the benefits of biotechnology to the people of developing countries by offering them lower priced, improved and more diverse products. ///

Octavio Ramirez is an investigator at the Institute of Biotechnology, UNAM, Cuernavaca, Mexico (tonatiuh@ibt.unam.mx). Rodolfo Quintero is an investigator in the Institute of Engineering, UNAM, Mexico City, Mexico (quintero@ibt.unam.mx).