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Biotechnology: Promise and Potential in Animal Healthcare

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First, biotechnology, like any other rapidly developing technical area, requires a strong academic base for both training and research purposes. The current system of funding by NIH and NSF based on peer review of research proposals, has worked well at the national level in research universities and should be continued. However, problems remain in areas such as the academic preparation of high school students in basic disciplines such as math, science, reading and communications skills, problems which are the province of state and local administration.

Second, it must be recognized that while the United States leads in many areas of high technology, including the principal components of biotechnology, our ability to successfully commercialize that technology is under tremendous competitive pressure from Europe and Japan. Much has recently been written about the death of the competitive spirit in America. This debate misses the point. Whatever the state of the American competitive spitit, that spirit is very much alive and well in the rest of the world. This is particularly true in biotechnology, a technology that easily crosses borders in the form of scientific publications and international technical meetings. Students from other countries, trained in U.S. research institutions, return home to work in industrial and academic facilities with colleagues that equal, in most respects, those in the United States. A sense of complacency in matters relating to biotechnology would certainly have the same predictable result for the United States economy that is currently being seen in the automotive and electronics industries.

Third, we need a better informed public. In many areas of high technology, the United States is becoming a two-tiered society: the minority who know about and understand the technology and its implications and the rest, who don't. This has several undesirable consequences including the abdication of decisionmaking power to the knowledgeable minority leading inevitably to mistrust, overregulation, and lost opportunities. It also diminishes the attractiveness of a technical career, reducing the number of U.S. students pursuing advanced technical education, and forcing U.S. academic institutions to go abroad in search of adequately prepared students. Obviously, this accelerates the development of strong foreign competition in high-technology fields, including biotechnology.

Biotechnology: Promise and Potential in Animal Healthcare

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I would like to present my views on the promise and potential of biotechnology as it relates to the animal healthcare industry. Using various examples, some of which are based on experiences at Molecular Genetics, I will attempt to discuss current and future barriers to commercializing biotechnology in this area, review what progress has been made to date in the animal healthcare field, and briefly touch on some policy issues relating to the above.

Recombinant DNA-derived bovine somatotropin (rDNA-bGH) or growth hormone is clearly one of the most visible animal healthcare products to undergo commercialization. The promise of biotechnology for this hormone is the potential to produce huge quantities of this protein at a very economical cost. Current estimates claim that rDNA-bGH will cost about five cents a dose, and that thousands of kilograms will be produced annually for the dairy and beef cattle markets. Treatment of cattle with this synthetic form of a naturally occurring hormone may result in a 15% increase in milk production and a 10 to 15% increase in feed conversion efficiency. These figures mean that farmers will be able to produce significantly more milk and meat per animal while using the same, or perhaps, less feed costs resulting in cheaper costs of production.

Unlike many other extravagant promises you hear from biotechnology advocates, the benefits of rDNA-bGH are real and attainable in the near term. Only a few technical barriers prevent rDNA-bGH from reaching the marketplace; few other rDNA-derived proteins or substances can make that claim. With rDNA-bGH, the barriers to commercialization are either in marketing or regulatory approval. The market issues concern the impact increased milk production will have on the price support structure within the dairy industry. There is a very real danger in producing 15% more milk per year without reducing the number of producing animals. With introduction of rDNA-bGH, dairy farmers will have to consider reducing the size of their herds so that the real benefit from using this hormone can be realized (i.e., reduced labor and feed costs). The public should not fear rDNA-bGH because of the science or technology involved or because milk may contain the hormone (native bGH has probably been in the milk you have

been drinking since birth). What the public ought to be concerned with is the economic impact this hormone will have on the food industry in this country.

The animal vaccine industry is my second example of the promise and pitfalls of biotechnology. Molecular Genetics was founded on the premise that biotechnology, more specifically recombinant DNA technology, could make safer, more efficacious viral and bacterial vaccines. We believed that all that was necessary was to clone and express the viral genes coding for those viral coat proteins known to induce immunity in bacteria. The promise of the technology was the availability of cheap, efficacious, and safe vaccines. Unfortunately, biotechnology has not borne the bountiful "fruit" everyone had expected. In human medicine, there have been some stunning successes. Chiron Corp., in conjunction with Merck, Sharpe, and Dohme, has produced an effective hepatitis B vaccine manufactured in yeast. The virtues of an rDNA-derived hepatitis B vaccine are many, the principal of which is that it is free of any contaminating infectious agents. In animal healthcare, however, there are no equivalent success stories. Although a few rDNA-derived vaccines have been developed for certain animal pathogens, similar vaccines for viral and bacterial diseases of economic importance in livestock have not been introduced. Many biotechnology companies, including Molecular Genetics, spent considerable time and money in developing rDNA-derived vaccines for a $100 to 110 million annual market (U.S.), and have very little to show for their efforts.

However, some technology that evolved out of ill-fated rDNA vaccine projects has given companies like Molecular Genetics a second opportunity to develop relatively inexpensive, effective vaccines. I like to call this technology "middle-tech" versus the "high tech" of rDNA technology. I believe that middle-tech holds as much promise as rDNA technology for revolutionizing vaccine development in both humans and animals for several reasons. Middle-tech represents a conglomeration of techniques embodied under the term biotechnology, none of which are associated with recombinant DNA technology per se. Middle-tech encompasses such methods as liquid chromatography, hybridoma/monoclonal antibody technology, analytical and preparative electrophoresis, and other techniques. These techniques can be used in various combinations to isolate and purify components of viruses and bacteria, which can then be used to prepare vaccines.

The advantages of middle-tech are many. First, the aforementioned techniques can be used with naturally occurring viruses and bacteria. Native proteins of most pathogens are generally antigenic and can adequately stimulate a protective response from an animal's immune system, which has not always been the case with rDNA-derived proteins. Second, the regulatory issues surrounding middle-tech do not appear to be as formidable as those associated with rDNA technology. Third, less sophisticated labor is involved in manufacture and quality control, which can reduce the costs of production.

There are already some examples of successful products developed through middle-tech. Molecular Genetic's Genecol (R) 99 monoclonal antibody against coliform scours or diarrhea in calves has proven to be very successful in the market. I believe it remains the only proven monoclonal therapeutic product on the market.

Another Molecular Genetics product that has entered regulatory testing is a therapeutic monoclonal antibody against a swine herpes virus called pseudorabies virus (PRV). PRV is an economically devastating disease of swine. It is a regulated disease, meaning that infected animals are quarantined and severe restrictions are imposed on movement of the animals. Accurate diagnosis of the disease is complicated because a reliable diagnostic is not available to differentiate vaccinated animals from naturally infected ones. Moreover, conventional PRV vaccines have been relatively ineffective in preventing this disease. However, animals receiving a subunit vaccine that contained one or two principal antigens (viral coat proteins) could be differentiated from naturally infected ones using a compatible diagnostic. Molecular Genetics has used middle-tech to develop a commercially acceptable vaccine and compatible diagnostic for PRV. In this case, a monoclonal antibody to certain PRV coat proteins is used to isolate and purify these subunit proteins for formulation into a vaccine. The protein(s) that remain(s) are subsequently used in the diagnostic test. This vaccine/diagnostic combination product means that the swine producer can protect the pigs while preventing them from being quarantined.

As my examples have shown, the technology exists today to produce a new generation of vaccines and therapeutics that do not necessarily rely on recombinant DNA technology. I am somewhat disappointed that more progress has not been made in recent years. Perhaps progress has been hindered because of the biotechnology industry's insistence on viewing projects and, to a lesser degree, company missions as dependent on singular, high visibility techniques such as recombinant DNA. Millions of dollars have been spent by the U.S. government, the biotechnology and pharmaceutical industries, and academia attempting to develop better subunit vaccines, via recombinant DNA technology, for foot and mouth disease, a major viral disease of cattle outside the continental United States. To date, none of these efforts has proven successful in producing a safer, more efficacious vaccine than that currently available on the market. Perhaps if those same monies had been used to develop middle-tech approaches, a new generation foot and mouth disease vaccine would be undergoing regulatory testing at this time.

In essence, I am here today to argue that you carefully study the latest technology that is being espoused as the next great leap forward. A company that is based on a single technical approach is risking failure because it lacks the alternative resource or resources to ensure success. A successful approach to a biological problem should encompass a number of backup techniques that will yield the process or product desired. Biotechnology, as a field, certainly provides a rich repertoire of techniques and the future looks very bright for the development of more powerful and sophisticated approaches. Commercial success in the biotechnology industry will ultimately depend on careful selection of the right complement of technologies.