WORLDWIDE OPPORTUNITIES IN GENETICALLY ENGINEERED VACCINES

Vaccines occupy an important, if sometimes uncomfortable, place in the overall healthcare business. A successful product can achieve an enormous market—especially if competition is light and vaccination is mandated by public policy. Despite this, manufacturers have been leery of vaccines: lawsuits and huge awards have made the business unattractive.

Now, new technologies are changing the picture, with the dual promise of safer, more effective replacements for existing vaccines, as well as vaccines for diseases previously beyond science's reach.

The same technologies are having similar impact on veterinary medicine, and on the whole business of animal healthcare. Vaccines now in development will prevent conditions that annually cause billions of dollars in agricultural losses. There are, moreover, major markets for new pet and specialty-animal vaccines.

History and Prospects

Conventional methods of vaccine development have had tremendous results. Products reduced and even eliminated the threats of smallpox, tuberculosis, and, in developed countries, many of the common diseases of childhood. After the first spurt of success, however, progress slowed markedly; few major advances occurred in the 20 years before biotechnology was brought to bear on the problem. Innovations—particularly subunit and anti-idiotypic vaccines, but also including recombinant glycoproteins and polypeptides—opened up new markets.

by **Manny Ratafia**, president of Technology Management Group, 25 Science Park, New Haven, CT 06511. This article is adapted from *Genetically Engineered Vaccines—A Worldwide Study on Market Opportunities for New Vaccines in Healthcare and Veterinary Medicine* published last June by Technology Management Group.

1. Human Diseases for which Vaccines may be Developed

Disease	Developed Countries	Important in: Developing Countries
AIDS	x	x
Chicken Pox	x	
Cholera		x
Coccidioidomycosis (valley fever)	x	
Cytomegalovirus	x	
Dengue		x
E. coli enterotoxins		x
Filariasis		x
Gonorrhea	x	
Hemophilus influenza Type B	x	x
Hepatitis A	x	x
Hepatitis B	x	x
Herpes Simplex 1 and 2	x	
Influenza viruses A and B	x	
Japanese Encephalitis virus		x
Leishmaniasis		x
Leprosy		x
Malaria		x
Meningitis		x
Parainfluenza	x	x
Pertussis	x	
Rabies		x
Respiratory Syncytial virus	x	x
Rotavirus	x	x
Schistosomiasis		x
Shigella (dysentery)		x
Streptococcus Group A		x
Streptococcus Group B	x	
Streptococcus pneumoniae		x
Tetanus		x
Trypanosomiasis		x
Tuberculosis		x
Typhoid Fever		x
Yellow Fever		x

Source: "Genetically Engineered Vaccines—A Worldwide Study on Market Opportunities for New Vaccines in Healthcare and Veterinary Medicine," Technology Management Group, June 1987

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2. Companies and Organizations Involved in 20 Selected Human Vaccines

Disease/Condition	Companies	Other Orgs.	Total
Hepatitis B	33	53	86
Malaria	11	27	38
Influenza	9	25	34
Herpes	9	9	18
Diphtheria/Pertussis/Tetanus	8	16	24
Polio	7	14	21
Hepatitis non A, non B	6	2	8
Caries	5	7	12
Hepatitis A	5	2	7
Typhoid	4	10	14
Schistosomiasis	4	8	12
Cholera	4	4	8
Leprosy	2	10	12
Rabies	2	10	12
Gonorrhea	2	6	8
Cytomegalovirus	2	4	6
Tuberculosis	1	8	9
Toxic Shock Syndrome	1	—	1
Epstein-Barr Virus	—	8	8
Yellow Fever	—	3	3

Source: "Genetically Engineered Vaccines—A Worldwide Study on Market Opportunities for New Vaccines in Healthcare and Veterinary Medicine," Technology Management Group, June 1987

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Table 1 lists human diseases for which vaccines may be developed, and it specifies where these new products will be most important. The number of organizations pursuing some 20 human and 13 veterinary vaccines, surveyed in Tables 2 and 3, reflects the intensity of the quest. And the geographic distribution of vaccine-hunting organizations (Table 4) shows how resources are being allocated.

When will these vaccines become available? By 1990, vaccines for 45

percent of the 31 human diseases studied will have been developed; vaccines for another 13 percent should be available by 1996; and preventives for the remainder should be out by 2000 (Table 5).

The Role of Public Policy

Public policy plays an especially large role in vaccine development and distribution because these products, like many other drugs, have certain undesirable side effects. And since vaccines are, after all, adminis-

tered to *healthy* individuals, balancing risk and benefit is particularly tricky. Group benefit of a vaccination program must be carefully weighed against the statistical inevitability of harm to a small percentage of those inoculated. This problem has been particularly vexing to makers of diphtheria-pertussis-tetanus vaccine, one of the most frequently administered in the western world.

Thus, the testing of human vaccines is fraught with particular problems. There is, of course, the tradi-

3. Veterinary Vaccines by Type

Condition	No. of Companies Involved Worldwide
Bovine viral diarrhea	11
Infectious Bovine Rhinotracheitis	4
Mastitis	4
Foot & Mouth Disease	14
Scours in Cattle	10
Pseudorabies	10
Scours in Pigs	17
Equine Influenza	8
Poultry Vaccines	12
Coccidiosis	7
Feline Leukemia	9
Rabies	14
Vaccines for Sheep and Goats	3
Total	over 145

Source: "The Impact of Biotechnology in Animal Care—An Assessment of Worldwide Market Opportunities in Diagnostics, Vaccines, Drugs, Growth Enhancers, and Other Products," Technology Management Group, December 1986
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4. Companies and Organizations Involved in Vaccines by Country

Country	Co.'s	Other Orgs.	Total
United States	132	154	286
United Kingdom	16	36	52
Japan	16	13	29
France	11	20	31
Australia	11	9	20
Switzerland	8	4	12
Netherlands	7	12	19
Canada	7	11	18
W. Germany	4	9	13
Israel	4	4	8
Belgium	3	2	5
Portugal	3	—	3
Sweden	2	7	9
India	2	5	7
Italy	2	2	4
Austria	2	—	2
Spain	2	—	2
Brazil	1	5	6
China (PRC)	1	2	3
Mexico	1	1	2
Cuba	1	—	1
Holland	1	—	1
Iran	1	—	1
Singapore	1	—	1
South Korea	1	—	1
Africa	—	3	3
Yugoslavia	—	3	3
Columbia	—	2	2
E. Germany	—	2	2
Taiwan	—	2	2
Thailand	—	2	2
U.S.S.R.	—	2	2
Denmark	—	1	1
Finland	—	1	1
Haiti	—	1	1
Norway	—	1	1
Total	240	316	556

Source: "Genetically Engineered Vaccines—A Worldwide Study on Market Opportunities for New Vaccines in Healthcare and Veterinary Medicine," Technology Management Group, June 1987
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5. Projected Development Dates for 31 Selected Vaccines

Disease	by 1990	1991–1996	1996–2000
Chicken Pox		x	
Cholera		x	
Coccidioidomycosis (valley fever)		x	
Cytomegalovirus	x		
Dengue			x
E. coli enterotoxins			x
Filaria			x
Gonorrhea			x
Hemophilus influenza Type B	x		
Hepatitis A	x		
Hepatitis B	*		
Herpes Simplex 1 and 2	x		
Influenza viruses A and B	*		
Japanese Encephalitis virus		x	
Leishmaniasis			x
Leprosy		x	
Malaria	x		
Meningitis	x		
Parainfluenza	x		
Pertussis	x		
Rabies	*		
Respiratory Syncytial virus		x	
Rotavirus	x		
Schistosomiasis			x
Shigella (dysentery)			x
Streptococcus Group A		x	
Streptococcus Group B		x	
Streptococcus pneumoniae		x	
Trypanosomiasis			x
Typhoid Fever	x		
Yellow Fever	*		

*Vaccine already exists or has recently been developed; remaining issues regarding its usage pertain to distribution and acceptance.

Note—the dates shown in this table are estimates of the time at which a vaccine will be developed and trials under way in preparation for licensing. Licensing and distribution of the vaccine will occur at different times in different countries.

Source: "Genetically Engineered Vaccines—A Worldwide Study on Market Opportunities for New Vaccines in Healthcare and Veterinary Medicine," Technology Management Group, June 1987

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6. Annual Costs of Selected Animal Diseases (\$ millions)

Condition	U.S.	World
Cattle:		
Mastitis	\$5,400	\$35,000
Shipping fever	500	3,000
Bovine scours	250	1,700
Parasites	300	2,000
Foot and mouth*	n.m.	50,000
Swine:		
Scours	\$ 250	\$ 1,800
Pseudorabies	60	650
Parvovirus	225	1,250
Poultry:		
Coccidiosis	\$ 300	\$ 1,800
Fowl cholera	30	200
Pets:		
Feline leukemia	\$ 75	\$ 350

*Includes goats and sheep as well as cattle.

Source: Abstracted from tables in "The Impact of Biotechnology in Animal Care—An Assessment of Worldwide Market Opportunities in Diagnostics, Vaccines, Drugs, Growth Enhancers, and Other Products," Technology Management Group, December 1986

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tional issue of common good versus individual risk—especially with conventional vaccines, which may, albeit very infrequently, cause the very disease they are meant to prevent.

The scientific necessity of a control group further complicates the ethical issues. To obtain meaningful data, a substantial number of people have to remain uninoculated; if the vaccine is successful, the controls are thus constrained to suffer much higher risks than their vaccinated counterparts. Researchers face similar problems when they must compare the effects of a candidate vaccine against those of a vaccine of established effectiveness and known risks. Trials of new vaccines for pertussis, rabies, and yellow fever will face just this kind of problem.

The issue of deleterious side effects is especially important in the United States, where the trend since the 1970s has been to sue the manufacturer if a vaccine produces any serious side effects—even if the vaccine itself is properly manufactured and properly used.

In developing countries, especially in the tropics, certain chronic diseases afflict as many as 200 million people—almost as many as live in the entire United States.

In order to achieve a large market by 1992, any vaccine should be completely or nearly developed right now. Testing delays make it unlikely that any Johnny-come-lately will make it onto the market before then, no matter how big the scientific breakthrough. (An AIDS vaccine is an important exception.)

In addition to the annual markets—generally consisting of people who reach the optimum age for inoculation—new vaccines should enjoy large, early, one-time sales as the general population enters into a “catch-up” inoculation program. A malaria vaccination program, for example, might require a billion doses within a few years after it is begun, with the precise rate dictated by the availability of funds, political acquiescence to the program, and distribution logistics.

Veterinary vaccines offer similarly attractive market potentials, largely because of the economic incentive each farmer sees in the lost value of animals weakened or killed by disease. (Table 6.) And development, testing, and administration of animal vaccines are less constrained by ethical issues than is the development of human vaccines. ■

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