

NEWS ANALYSIS

By Lisa Miller

Biotech's Babies: Doing Well by Doing Good **Biotech's Babies: Doing Well by Doing Good** **As Big Pharma pulls out of the low-margin vaccine** **business, upstart outfits are exploiting new** **technologies to tap niche markets**

Thanks to the unfortunate pairing of an abundance of flu and a dearth of flu shots this season, the humble vaccine industry is now suffering the kind of public scrutiny normally reserved for its sexier cousin, Big Pharma. For decades, vaccine makers could count on reaping steady, if unspectacular, profits as each new year promised a fresh batch of kids needing immunizations. But incentive-stifling price controls, liability fears, and greener pastures elsewhere finally prompted a massive flight of big drug companies out of vaccines. The figures tell the story: In 1967 there were 26. By 1996, that number had shrunk to eight. Today, only four big players survive.

While the industry may appear stagnant to outsiders, major changes are already under way -- thanks in part to a slew of small and midsize biotechs that see the big companies' exit as an opportunity for the little guy.

EYE OF THE BEHOLDER. One reason for this optimism is the simple fact that one outfit's spare change is another's windfall. "The revenues from a vaccine division are like a rounding error to a Merck ([MRK](#))," says Sharon Seiler, vice-president and senior biotechnology analyst with Punk, Ziegel & Co. "But," she adds, "it's very profitable for a small company."

According to Seiler's data, over the first three quarters of 2003, Merck made about \$800 million on vaccines -- a meager 6.2% of total revenues over that period. Similarly, for GlaxoSmithKline ([GSK](#)), Wyeth ([WYE](#)), and Aventis-Pasteur-MSD ([AVE](#)), vaccines accounted for between 5% and 10% of total revenues -- mere pocket change in comparison with Big Pharma's earnings from other drugs.

Biotechs like Chiron ([CHIR](#)) have greeted the larger players' disinterest with glee. The California-based biotech garners more than 33% of total revenues from vaccines, pulling in about \$400 million over the first three quarters of 2003. A leap to Merck's totals would reflect a growth spurt of 100% --

definitely not something that Chiron or its smaller peers would dismiss as a "rounding error."

Biotechs won't be content to simply pick up the profits Big Pharma left behind, however. They want more, and signs suggest they might get it. The vaccine industry as a whole is growing, pushed by a combination of expanded immunization recommendations from governments, emerging niches in rich countries' consumer markets, immunization programs in the developing world, and concerns about bioterror attacks.

TARGET: TB. Since the early 1990s, the global vaccine market has expanded by about 10% per year on average -- from \$2.9 billion in 1992 to \$6 billion in 2002 -- according to a report by Mercer Management Consultants. That rate is expected to continue or even accelerate, as companies craft new vaccines to tackle diseases never previously addressed.

A report released by the Institutes of Medicine last year lists 23 prophylactic vaccines the industry expects to develop by 2010. These include vaccines for Epstein-Barr, multiple sclerosis, and sexually transmitted diseases such as chlamydia and human papilloma virus, the latter a risk factor for cervical cancer.

Such high-value vaccines are the key to future revenue growth, because the pricier products are increasingly coveted by the developed world, which has the money to pay for them. Mercer estimates that rich-country demand already accounts for over 80% of revenues, but only 12% of volume. Meanwhile, the developing world also is looking more interesting, because private foundations are pouring money into vaccine initiatives there.

PUSH AND PULL. Tuberculosis is one of the hot targets, with millions of dollars moving from organizations such as the Bill & Melinda Gates Foundation to groups like the Aeras Global TB Vaccine Foundation -- run by a former Merck clinical director, Jerald Sadoff -- which is developing new TB vaccines for use in poor countries (see BW Online, 12/4/03, "[TB: Battling an Old Foe's Resurgence](#)").

Also important are efforts to make sure suppliers can afford to sell to these traditionally low-profit markets. This attempt by foundations to address not only the "push" of R&D but also the "pull" of adequate profits is paying off. In some instances, suppliers are lowering prices while increasing production volumes. In other cases, foundations are willing to pay more for newer vaccines, thus giving suppliers incentives to stay in the game.

Public health is not the only area where small and midsize biotechs can find

new opportunities. Governments' military needs are also opening doors. For example, Bavarian Nordic, a Denmark-based biotech, is targeting the biodefense market with its work on smallpox vaccines. The 100-employee company has contracts with the German, British, U.S., and Greek governments, and is expanding its manufacturing facilities to make sure it can meet current demand and to reassure future clients that will have the capacity to continue doing so.

"Governments aren't going to give orders to a company with good products if it can't manufacture," notes Peter Wulff, Bavarian Nordic's president and CEO. "Governments are looking for certainty of delivery."

TINY FOES. Governments are also looking for vaccines unrelated to the threat of biological warfare. Soldiers are routinely exposed to naturally occurring diseases when serving in faraway places, and military planners want to stockpile arsenals of vaccines capable of foiling those unseen enemies. A report by the National Academy of Sciences in 2000 urged the military to work closely with the biotech industry to develop fast, small-scale production methods for vaccine development. Other wish-list items included edible vaccines, and vaccines tailored to genotypes, so each soldier can get the formulation most effective for him or her.

If all this new money -- from governments, foundations, and individual consumers -- is the grease for the machine, technology is the power that actually makes things go. "The technology has changed, so we're talking about a different cat than we used to be," says Dan Adams, CEO of Protein Sciences, a Connecticut-based biotech that's developing vaccines for SARS and influenza, among other projects.

Adams is well-placed to know what kind of "cat" he's talking about. Whereas current flu vaccines rely on growing the virus in chick embryos, a process that uses up millions of specially bred chicken eggs each year, biotechs like Protein Sciences use genetic engineering to culture the cells they need in the lab. Since this method is much faster and more flexible than the old production model, shortages are far less likely, and new strains of flu can be addressed rapidly.

HARD TO COPY. Just how rapidly? In 1997, Protein Sciences got a call from the National Institutes of Health during a scare about a nasty flu virus that was spreading from chickens to humans in Hong Kong. Asked to come up with a vaccine, the company obliged by cranking one out in just eight weeks. Compare that period with the six-or-more months it takes to brew up the current, egg-based influenza vaccines, and it's clear biotechnology outfits are onto something.

This swanky new technology also helps keep imitators at bay. Since each vaccine has a unique production procedure, that process functions as a sort of built-in protection against copycats. Conversely, old-style vaccines are easy to knock off and sell cheaply in countries where patents aren't recognized. "When you stick a virus in an egg, what's proprietary about that?" Adams says. "But today, the product in biologics is the process.... That's patentable, that's proprietary -- so people can't use that product to make a competing vaccine."

Thus, when Protein Sciences finishes shepherding its influenza vaccine through the Food & Drug Administration's daunting regulatory process, it will have a patented product that fits neatly into one of those rich-country niche markets that are proving so lucrative.

In 2000, three proprietary vaccines accounted for 30% -- \$1.7 billion -- of the total market, yet they represented only 1% of total market volume, according to Mercer. One of these products is Prevnar, a pneumococcal vaccine released by Wyeth in February, 2000. It racked up over a half-billion in sales that year, and now brings in about \$1 billion annually. Its success has so inspired suppliers that many talk about "blockbuster" vaccines the way Big Pharma talks about blockbuster drugs.

HIGH HURDLE. Niche vaccines may be hot, but they're also often voluntary. Consumers can choose whether or not to get a flu shot, for example, in contrast to the vaccinations that children must have before than can enter school, or for adults traveling to other countries. This makes it crucial to reach the consumer directly. For instance, MedImmune's (MEDI) FluMist, which it produces with Wyeth, routinely shows up in television commercials. This is a "very different approach" for a vaccine, according to Andy Pasternak, director of Mercer Management Consulting in Chicago. But it's one that will become increasingly necessary as suppliers try to exploit these markets.

That presents a high hurdle for smaller outfits, which lack the huge sales teams and marketing departments necessary to both educate consumers and then distribute the product to them. "You obviously need a distribution strategy," says Pasternak. "You're not, as a biotech company, going to distribute [vaccines] yourself, so you're going to do it through one of the big four."

Such alliances between biotechs and the big pharmaceuticals are now fairly common in vaccines, a trend that will likely continue. Big Pharma is increasingly willing to look outside its own R&D departments for new vaccine

products and technology, but that hasn't always been the case.

FICKLE BUSINESS. "Historically, the major companies have, for the most part, controlled everything in the value chain -- so, they've made the drug and distributed the drug [in vaccines]. That's changing," Pasternak says. With the move to partnerships, "the biotech company develops the drug and the pharma company distributes it. That's a classic model that has been used in [non-vaccine] pharmaceuticals for the last 10 to 15 years."

Besides marketing and sales, other big worries for smaller outfits include meeting regulatory requirements -- which, in the U.S., means building the factory before the FDA will approve production -- and staying alive financially during the many years it can take to get a vaccine from laboratory to market.

The sometimes fickle nature of the industry presents yet another challenge, especially since opportunities can dry up as quickly as they appear. Governments now so attentive to biodefense might lose their focus in a few years, with a corresponding decline in appropriations for vaccine projects. Foundation money for poor-country vaccines may not keep pace with the demand for the drugs, causing the carefully crafted economic incentives to unravel.

MISSED POTENTIAL. Similarly, a promising deal with a major pharma outfit could fall apart -- no big deal for the larger partner, but a disaster for a biotech outfit with a thin pipeline. "It's a little tough, doing these deals with these big companies," says Protein Sciences' Adams. "They think differently than we do. It's not life-threatening to them if something doesn't work out. Your product isn't life or death for them."

That metaphor is particularly apt, when a product can not only make or break a company but also save millions of lives around the world. Even the flu kills about 36,000 people on average each year in the U.S. Profit potential and sexy technologies aside, many involved in vaccines are drawn to the industry because they want to make a difference in people's lives. Adams gets good and angry when he considers the gap between the biotech industry's potential and where it is now. "It's not doing a fraction of what it could be doing," he says. "People are dying who shouldn't die."

Hopefully, with so many new outfits getting involved in vaccines, biotech is poised to take a giant leap forward, saving more and more lives along the way.