BIO/TECHNOLOGY

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THE FIRST WORD/

THE LIMITING CASE

How much effect could biotechnology *really* have on the pharmaceutical industry? We polished up the crystal ball the other night and, Faust-like, called up the Erdgeist under the sign of the Makrokosmus.

Anyway, the Erdgeist responded with a series of utterances that would be Delphic if they were clearer. We've pondered them hard and long, and offer here the dicta and our glosses.

The pharmaceutical business is the movie business. Well, this one isn't so hard. We've noted before that similar market dynamics have molded both industries: Skyrocketing production and development costs dictate that executives in both businesses must pursue blockbuster successes. Each must follow massive up-front expenses with even more massive marketing outlays. The result is a declining crop of new product with more and more of the company's future riding on each.

Proteins can do so much and then no more. All of the top 25 or so drug sellers are oral formulations. Therapeutic peptides have a shot at the pharmaceutical big time only if researchers succeed in developing safe, convenient delivery alternatives to injection. If not, then the pressure to develop peptidomimetics will increase in direct proportion to the drug's market potential. If mimesis is indeed possible, then at some sales level the drive to convert a peptide drug into a conventional drug will become irresistible as drug makers try to a) lower unit production costs, and b) greatly enlarge the market.

All drugs are biotechnology drugs. Market forecasts for biotechnology are notoriously unreliable. At last year's PaineWebber-*Bio/Technology* meeting, a number of speakers estimated that protein therapeutics (and perhaps some oligonucleotides) could account for 5-10 percent of total pharmaceutical revenues in the year 2000. But that tells only part of the story. Four out of four major company pharmaceutical CEOs we talked to last year agreed: The tools of molecular biology will soon become—if they are not already—the *sine qua non* of drug discovery, design, and development. Biotechnology should be expected to point the way towards likely drug candidates, accelerate screening, speed bioassays, illuminate pharmacophore structure, explain drug action, speed production, predict side-effects, and generally grease the rails of pharmaceutical development. The drug-makers are only beginning to feel the impacts.

Of quest and trial, only the trial must remain. Product development costs will decline, but how much? Depending on whom one talks to, "average" development costs range from $110 million to $350 million, including the costs of discovery, development, scale-up, clinical trials, and amortizing the costs of development projects that have dead-ended. Right now, even the biggest companies can afford to have only two or three serious products in development at any one time. Biotechnology could conceivably—conceivably, you understand, in the limiting case—drive R&D expenses almost down to the $10-million level, or about the cost of regulatory paperwork and clinical trials alone.

Indications will divide and multiply. Molecular biology continues to show that many "indications" are actually families of closely related but molecularly distinct entities. Therapeutics efficacious on one sub-indication may be useless for another. Regulatory authorities and good medical practice will require drug-makers and physicians to discriminate at the molecular level if that precision will improve clinical outcome. Already, pharmaceutical houses find they must couple drug development to diagnostic development (for both initial diagnosis and later therapeutic drug monitoring). Thus, markets for blockbuster drugs may fission, diminishing their unit potential even as inventories of diagnostics and therapeutics expand.

The stream will rise and the dam will shudder. So, more companies will be pushing more products—perhaps ten times more—into the regulatory stream. The current pace of approvals is taxing both the fabric of the regulatory agencies on the one hand, and the patience of industry on the other. Something will have to give.

As the souk grows, it grows more modest. If the regulatory edifice does not collapse into the product stream and choke it, more products should reach the market. With more products to sell to smaller markets drug-marketing campaigns will be scaled down. Niche markets will again become economically viable.

Biotechnology is cable television. A few years after cable television became widespread in the U.S., the broadcast networks found their markets slipping; the movie production companies found themselves depending on these narrowcast sales to turn a profit; and consumers found their information options suddenly expanded. Where they had once had a choice of ABC, NBC, or CBS, they now confronted as many as a hundred new viewing options, each of them less expensive than a movie, less elaborately produced, but much better tailored to individual needs and tastes.

—Douglas McCormick