THE LAST WORD

DRUG DEVELOPMENT: WHO FOOTS THE BILL?

by Robert K. Oldham

Who pays for new drugs? The patient does. Today, when patients buy approved drugs they pay for research done on other patients. Pharmaceutical companies sell Food and Drug Administration (FDA)-approved drugs with huge margins—both to recover R&D costs and to provide a generous profit. In fact, drug companies' profits are among the most liberal in the entire healthcare delivery system (a characteristic that appeals to investors).

Traditionally, drug development has been controlled by a regulated monopoly of government, major pharmaceutical houses, and the FDA. The National Institutes of Health (NIH), and for anti-cancer drugs, the National Cancer Institute (NCI), fund and conduct a great proportion of the research in developmental therapeutics. Much of this work is done in conjunction with major pharmaceutical companies in a process regulated by FDA. For anti-cancer drugs, this system has allowed several hundred thousand compounds to be tested over the last three decades, bringing approximately 40 new drugs to market—each at a cost of $60–100 million, each requiring 6–10 years of development.

Who pays? In effect, the taxpayer, the patient, and the insurance company pay for the clinical costs required to bring new drugs to market. In Phase I trials (which assess the toxicities of a new drug), the taxpayer and pharmaceutical company have largely paid the cost. Increasingly, however, insurance companies are picking up the tab for hospital components of Phase I clinical trials conducted by universities and government agencies. In Phase II trials (designed to test new drugs for therapeutic efficacy), the patient assumes some costs by paying for hospitalization directly or through his insurance company. Anti-cancer drug trials have been sponsored largely by NCI and the pharmaceutical company: Taxpayer dollars carry part of the cost, and the patient supports the rest. Pharmaceutical company dollars recovered from patients are part of the research and development cost recovery paradigm. In Phase III trials (designed to demonstrate definitively the role of a new therapeutic approach and compare it with existing approaches), patients pay most of the cost. Many of these trials are indistinguishable from the practice of medicine; they are often conducted in the hospital without disclosure to the insurance company that they represent experimental trials. These trials are often approved by NCI and carried out by NCI clinical trials groups; insurance companies are billed for the full clinical costs without disclosure.

Costs for these experimental clinical trials are often supplemented by pharmaceutical companies and government on a "per head basis"; this amounts to a stipend on each patient tested. The potential for conflicts of interest in such a system is obvious.

The new era in molecular and cellular biology has spawned at least 100 biotechnology firms that aspire to develop new biological substances for treating cancer. There is ample evidence that biological substances are less toxic and more selective than the chemicals previously developed as anti-cancer drugs. With the possible exceptions of Genentech, Cetus, Hybritech, and Genetic Systems, however, none of these companies have sufficient resources to fully develop drugs under the classic paradigm. Biotechnology could—and should—beget a new paradigm for drug development.

Cancer patients have known for more than a decade that they need greater access to research-based technology. Only now, due to the current AIDS epidemic, has the public's (and FDA's) attention focused on the issues of speed and cost in drug development. For the first time in two decades FDA is considering a major revision of its drug development guidelines to allow some cost recovery and perhaps even a limited profit in the very early development of new drugs for seriously ill patients. This liberalization of regulatory policy could be revolutionary. It would allow small companies to participate in drug development; it would deregulate the current research-regulatory alliance between major pharmaceutical houses, government, and universities; and it would allow patients with serious illnesses broader and more efficient access to promising new treatments.

The proposed diversification in developmental therapeutics would also support and expand experimental medicine in the United States: Biotechnology firms, working in concert with clinicians in the private sector, could develop an open and diversified system to responsibly and safely test experimental therapeutics.

This revolution will stimulate controversy and criticism from those special interest groups in the current research-regulatory alliance. The Pharmaceutical Manufacturers Association, major university clinical research programs, and FDA staff will argue that diversification will increase patient risks. Questions of ethics and the spector of a new thalidomide (a drug that was prescribed before its devastating effects on fetal development were discovered) will also arise. If those with the power to effect these changes will listen to the man in the street instead of the man in the ivory tower, if they will listen to the patient with cancer or AIDS rather than staff at FDA, if they will consider the opportunity of diversification and the strength of the private sector rather than blindly following the status quo of the current alliance, the whole system, and most particularly the patients, will benefit.

Robert K. Oldham, M.D., is the Chairman and Scientific Director of Biotherapeutics, Inc., Riverside Drive, Franklin, TN 37064. These opinions are the author's own and are not necessarily those of *Bio/Technology*.