It’s time to reassess what drives the discovery of new drugs. In its advertisements, one pharmaceutical company links innovation directly to its revenues: “Today’s medicines finance tomorrow’s miracles.” If that formula really worked, we would have long since entered the golden age of therapeutics. After all, the pharmaceutical industry has been one of the most profitable businesses in America for years. Yet the number of new drugs emerging from most major pharmaceutical companies has been disappointing. What’s wrong and how could things go better?

From one narrow perspective, nothing is wrong. These companies are investor-owned, publicly traded entities whose main responsibility is to provide shareholders with an optimal return on their investment. For most of the past 15 years, they have done a very good job at this, responding to signals sent from the marketplace. However, those signals often lead industry priorities in a direction that is lucrative but not well aligned with the health needs of the public. For example, the patent laws usually allow a company bringing a final product to market to keep all the marbles, often shutting out the upstream basic research on which those products are based. Those same laws also guarantee a brand-new patent to a manufacturer that makes a trivial change in an existing molecule, even if the “new” drug has the same clinical effect.

The U.S. Food and Drug Administration (FDA), for its part, sends forth only a weak signal. Approval is frequently granted if a new drug is merely better than a placebo at improving a surrogate measure in brief, modest-sized clinical trials. The agency rarely comments on the therapeutic importance of a new drug and never on its cost-effectiveness. Clinical trials comparing a new drug with existing treatments are typically required only when placebo controls are ethically unacceptable. Other agencies disdain funding such studies or lack the resources to do so. Large payors inside and outside the government hardly ever mount the comparative trials whose results could be so valuable to them. Physicians also bear responsibility for these degraded marketplace signals by relying too heavily on promotional information and company-sponsored education to drive prescribing decisions. Direct-to-consumer advertising now enlists patients as well in this triumph of marketing over science.

The ultimate market signal—dollars—comes from the country’s health care payors. With the notable exception of the U.S. Department of Veterans Affairs and a few large health maintenance organizations, most payors in both the public and private sectors willingly, if complainingly, pay for whatever doctors prescribe and companies charge, however unremarkable a drug’s therapeutic value or cost-effectiveness. This particular signal is likely to become even more problematic in January 2006, when Medicare begins paying for outpatient drugs, because the new benefit prohibits the government from considering these issues.

How can we change these noise-laden signals into a message that could foster more useful pharmaceutical innovation? We can start by using patent laws to increase rewards for the basic science that undergirds so much of what the industry does. Those laws could also take a more conservative view of whether a company’s one-atom changes or isomerization of an existing molecule warrant monopoly protection. The FDA could require more useful and demanding pre-marketing studies and ask its advisory committees to comment on whether a newly approved drug is an important therapeutic contribution or an unremarkable addition to an already-full class. Prescribing physicians could focus more on actual clinical trial data and refuse to help sell a drug just because it has a zippy marketing campaign. And patients could learn that advertisements are not the best measure of a medicine’s therapeutic value. Payors inside and outside government could make purchasing decisions based solely on critical reviews of the clinical and economic evidence.

Marketplace solutions are by no means a panacea. They will never be adequate to foster the development of drugs for which the market is too poor or too small to generate a profit. But for the major common diseases of the developed world, these changes could help reform and rescue an industry trapped by its own clever marketing successes. Major change will have to come from inside the large pharmaceutical manufacturers as well. Presenting them with more intelligent incentives would help move them along the right path. Those companies are adept at responding to signals; we need to send them the right ones.

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Editor's Summary

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