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The Great Shift to Specialty Drugs

By Scott Gottlieb

Economics and regulatory policy are driving pharmaceutical manufacturers away from the market for treating ordinary medical conditions toward a greater focus on drugs for major health problems.

When drug maker GlaxoSmithKline held a showcase day for investors late last year, the company bragged about its burgeoning pipeline of new medicines, but also a fruitful restructuring it undertook a few years ago. Glaxo broke its sprawling research shop into smaller units focused on a dozen or so disease areas. In was an emphasis on major health problems, such as cancer, heart disease, and brain disorders like Alzheimer's disease. Gone were the same concerted efforts to focus the majority of its research on more routine medical problems such as sniffles, sore muscles, and nicotine addiction. Like a lot of other drug makers, Glaxo is moving its research upstream into weighty maladies that have remained unsolved by modern medicine and away from primary-care problems.

The triple threat of regulatory pickiness, legal madness, and reimbursement prickliness is making the chase for drugs that treat ordinary conditions extraordinarily risky for drug companies. It no longer pays as much to be in the business of developing primary-care drugs—the sorts of medicines that treat subtle, chronic conditions patients do not readily recognize or the minor nuisances of daily living.

But even small improvements offered by slightly better medicines like new generations of drugs for pain or blood pressure can yield big benefits when aggregated over large populations. If chasing these public health achievements is no longer the bread and butter of the big drug makers, a lot of this work will remain undone, and patients will lose the chance to gain relief from more of life's daily medical problems.

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Risk Factors

The increasing stringency of regulatory hurdles for these kinds of primary-care drugs is one reason drug makers are exiting. Today the average new drug application requires, among other things, a study involving more than 4,300 patients, compared to 1,300 typically required during the mid-1980s. Clinical trials are even larger for primary-care drugs. The smaller the perceived medical benefit that a new drug offers, the more safety assurances that drug regulators require.

Satisfying the FDA's concerns is achieved through a crude numbers game: regulators want companies to expose more patients to a drug before it is approved to try to unearth any rare side effects. Many advanced trials for drugs that treat high blood pressure can reach 10,000 patients or more. One recent trial for a new blood thinner enrolled 30,000 patients.

The bigger trials are not more likely to assuage regulatory concerns, but rather to raise subtle questions that require further study. The FDA evaluates drugs in what it refers to as a review cycle, which can range from six to ten months, depending on how important a breakthrough the FDA thinks a

new drug could make, and how quickly it commits to reviewing it. Often, a drug will undergo multiple review cycles, in which FDA reviewers spend those ten months reviewing a new drug application, only to find that they have new questions and need more information to reach a definitive answer about the drug's safety and benefits.

This is especially true for primary care drugs, where the perceived benefit is often lower, and so the hurdles are higher. The division inside the Food and Drug Administration that reviews heart drugs (including pills for ordinary high blood pressure) did not, in more than four years, approve a single one on its first pass through the agency, ranking the division dead last among the FDA's different drug review groups.

Liability risks also are higher for primary-care drugs as big populations are exposed to more medicines, revealing rare side effects. This is especially true when those pills are aimed at seemingly less serious conditions. It is one thing when a cancer drug causes some uncommon but devastating side effect, quite another when a common cold pill is at question, or a routine pain medicine like Merck's drug Vioxx, approved for arthritis pain among other conditions, but recently withdrawn after it was linked to rare but worrisome heart problems.

The safety of Vioxx, as well as the entire class of painkillers known as Cox II inhibitors, was the subject of FDA hearings in late 2004 because these drugs selectively block a chemical that causes pain without interfering with a sister substance that protects the stomach lining. It has become customary for the audience at these hearings to be replete with trial lawyers looking for legal openings. These hearings were no exception. By some estimates, Merck faces more than $30 billion in liability. The public—and, by extension, juries—are only willing to tolerate side effects when it comes to potent pills that treat the most serious conditions.

Finally, more competition at the low end of the drug market as a result of the Medicare prescription drug benefit, as well as a fundamental change in healthcare that exposes patients to more of the cost of their decisions to take expensive but routine drugs, means the cost of developing better medicines for ordinary conditions may be rising, but the potential profits are declining.

The entire research and development enterprise that created these drugs, not to mention the task of selling them through big armies of "detail" salespeople visiting doctors' officers, was expensive, too expensive in fact to be underwritten by these declining profits. As drug makers now quit these markets and move research upstream into the refuge of more serious medical conditions like cancer—where reimbursement is still comparatively generous, regulations still reasonable, and lawyers morally challenged to wage aggressive war—you can already hear pharmaceutical critics cheer. The big drug makers, they argue, should not have been developing these "lifestyle" drugs anyway and then charging high prices for them. In fact, it is fair to debate the real value of a drug that is a little better at controlling blood pressure, but that debate could never be aired under our old insurance model, in which patients made all of the demands but bore none of the cost since insurers footed the entire bill.

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What Now?

But this does not resolve the question of who will develop better generations of medicines for ordinary conditions, or whether we still need them. Some economists believe that the task of making primary-care pills could fall increasingly to companies like Procter & Gamble that make their trade in consumer staples and specialize in building brands that can be marketed more cheaply by selling directly to consumers rather than through physicians.

This is the direction in which a few of the big drug makers may even choose to go, especially if they face more failures in the lab—moving downstream to the mass market. But economics, politics, and regulation mean most will move the other way, and the companies left to pick over the primary-care market may not be able to make the investments needed to make new drugs.

Most primary-care medicines will then be the accidental molecular by-products of research into weightier medical maladies. The problem is that the cost of developing a new molecule is relatively fixed—it is not cheaper to make a new blood pressure pill than it is to make a new cancer drug. In fact, owing to the bigger trials for the primary-care drugs, the opposite is true.

Unless selling costs for primary-care drugs can be driven very low—for example, by taking more drugs over the counter, which the FDA resists—then the kind of downstream, mass-market business model that Procter & Gamble can undertake may generate the outsized profits that support expensive research and marketing programs.

Pharmaceutical research and drug delivery is a costly enterprise, a fact evidenced by the $29 billion that the National Institutes of Health go through every year with disproportionately fewer practical benefits than industry. This simple math holds equally well both for new cancer cures and for a better pain reliever. When it comes to money, science does not discriminate along the same business lines as our health plans and our political leadership.

The answer to the second question, whether it will matter that people in 2020 are still taking the same cold pills and Cox inhibitors, is partly revealed in the actions of a few employers like Pitney Bowes, who drive patients to the best new primary-care drugs, despite the higher costs. They recognize that the real value of these medicines was never realized on the health care equation but the social one, through increased productivity and fewer missed workdays.

But as the drug market continues its bifurcation between innovation on the high end, and value at the low one, we may all be making do very soon with a lot less. The days of expensive research into ordinary problems is ending, and with it the population-wide public health gains that we may have taken for granted.

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