Approving new drugs

As the Trump administration takes shape, there is much speculation as to what major changes will be made. A dominant theme of the Trump campaign was to cut through bureaucracy in Washington, D.C., thereby enhancing innovation and bringing new technology to Americans more quickly. Nowhere could such a philosophical change have more impact than on Food and Drug Administration (FDA) approval of new drugs.

Decades ago, it was not unusual for the FDA to approve a drug simply on the basis of its effect on disease biomarkers. For example, approval of the first statins, including Merck's Mevacor and Zocor, was based on their ability to lower low-density lipoprotein (LDL) cholesterol, known to be associated with the buildup of deadly atherosclerotic plaque. It wasn't until many years later that long-term clinical trials involving thousands of patients actually proved that these drugs reduced heart attacks and strokes.

However, there are far more examples of drugs that failed to provide the desired health outcome despite having favorable effects on disease biomarkers. One example comes from another class of lipid modulators, the cholesteryl ester transfer protein inhibitors (CETPis). When discovered, these drugs looked promising in that they raised high-density lipoprotein (HDL) cholesterol, long associated with cardioprotection, as well as lowered LDL cholesterol, thereby completely remodeling the lipoprotein profile of patients with heart disease. Despite their promise, the FDA would not approve a CETPi without evidence that it did in fact reduce adverse cardiovascular outcomes. To date, clinical trials for these drugs have shown that they do not reduce heart attacks and, in one case, actually increased deaths.

Such occurrences are not exclusive to the cardiovascular field. For Alzheimer's disease (AD), several companies have discovered experimental drugs that reduce the level of amyloid proteins, which are believed to be an initiating factor in AD. However, despite successfully lowering amyloid levels in AD patients, long-term studies showed that these drugs do not improve cognition in this population. These examples are not unique. There are cases where drugs that lower plasma glucose do not prevent the adverse health consequences of diabetes, and where drugs that shrink tumors do not reduce cancer deaths.

Favorably affecting disease biomarkers is an important step in drug research and development (R&D) because it indicates that the experimental drug could potentially prevent the long-term consequences of disease. However, only long-term clinical trials, although time-consuming and expensive, can prove the value of a new medicine. President Trump and Tom Price, the newly sworn-in Secretary of Health and Human Services (which oversees the FDA) want to streamline the FDA's approval process for drugs. But changing the current drug approval paradigm would hurt everyone. What if the FDA simply rules that early-stage drugs are safe solely on the basis of biomarker effects? Suppose doctors and patients decide on whether to take such a drug with unproven long-term effects? This would certainly get experimental drugs to patients faster and enable companies to recoup their R&D investment more quickly. However, based on historical precedent, many of the drugs approved in this way would be ineffective. At best, they would be glorified placebos. At worst, they could prove harmful.

As a result, patients would not have benefited by taking such a drug, physicians would be called into question for prescribing such a drug, payers would have wasted millions (even billions) of dollars reimbursing the costs of such a drug, and companies would face the inevitable lawsuits that arise in these situations. Everyone loses. Over the years, the FDA has learned that, for many diseases, it is important that the drug maker prove the benefits of the drug before unleashing it on the public. Does this slow the process and greatly add to the R&D costs? Absolutely. But it is good medical practice.

—John L. LaMattina

John L. LaMattina is a senior partner at PureTech Health and the former president of Pfizer Global Research and Development. john.lamattina@comcast.net
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