Efficient drug approval and monitoring must rely on sound regulatory science

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The path to drug approval is long, hard and often perplexing. In recent months, the US Food and Drug Administration (FDA) has promised to bolster ‘regulatory science’, which aims to transform its decision-making process to be more efficient, transparent and accountable. However, diverse stakeholders, including patients, drug developers and the US Congress, will have to rise to the challenge of coordinating their priorities if this endeavor is to succeed.

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It seems that a month can't go by these days without the FDA announcing a new measure aimed at improving the methods it uses to evaluate therapeutics, food, cosmetics and medical devices. In August, the agency released a strategic plan calling for sweeping updates to how products are monitored and approved; a month earlier, the FDA's drug arm outlined its own regulatory policy priorities, and the agency's device unit has followed suit. It's clear that the FDA is serious about modernizing its decision-making processes.

This push by the regulator toward grounding decisions in science is commendable. An evidence-based update of regulatory processes should engender credibility with patients, researchers and drug companies, as well as promote the FDA's stature in the world. Although basing arguments on science is no defense against political attack, it is surely preferable to basing them on ideology; for most of the public, facts still do matter. Indeed, a focus on regulatory science might ultimately help the agency rearrange the incentives in drug development better to reward innovation and focus more attention on quality rather than speed. They could do this by reducing the benefits of rushing to be ‘first in class’ and by emphasizing early exploration of the full spectrum of drug action in humans rather than waiting for unpleasant surprises to emerge more expensively in large-scale trials or even after drug approval.

For now, the goals set out by the FDA to improve the regulatory process include modernizing toxicology tests, refining the prediction and detection of adverse effects, developing regulatory approaches to personalized medicine and improving product manufacturing and quality. But these steps represent only the tip of the iceberg. At meetings of the New York Academy of Sciences and the US Institute of Medicine that we attended, those present agreed that the field needs ‘it’—and although there was disagreement as to what precisely ‘it’ is, they recognized ‘it’ would be a challenge. This calls to mind the comment of the filmmaker Samuel Goldwyn: “It's absolutely impossible, but it has possibilities.”

Regulatory science has a remarkably diverse set of stakeholders, ranging from industry to academia and from funders of biomedical research to the public and their representatives. Although there is considerable overlap between the objectives and expectations of the various players, what they emphasize as important often differs. Thus, industry might favor simplified drug approval guidelines, a relaxation of requirements for comparative effectiveness and approaches to prioritize and reward true innovation. The public, meanwhile, might prefer a focus on prediction and monitoring of food and product safety and the accelerated development of effective therapies. Finally, lawmakers might place particular weight on the delivery of measures to protect health and security.

The biomedical community should adopt a variety of tools—from crowdsourcing to soliciting information by public and private funders—

to define collectively the big questions for regulatory science. Such approaches can link the priorities in drug development to their intended consumers. We do too many trials to gain drug approval rather than to address unmet medical needs; these needs are more usefully defined by patients and their advocates than by pharma. In contrast, academia, together with industry, is best positioned to highlight the opportunities and challenges posed by emerging technologies such as metabolomics and next-generation sequencing.

Once the community agrees on a set of key issues, next comes the challenge of how those should be addressed by the FDA. The agency's staff cannot, should not and do not profess to be at the cutting edge of biomedical science, yet they need to be aware of it, judge it and integrate it into their regulatory decisions. In 2007, the FDA's Science Board suggested that academia should be harnessed as a repository of such expertise in areas such as innovative clinical trial design, informatics, translational medicine and therapeutics. However, to date, the agency has not deployed sufficient resources to make this happen. An example of the agency's limited approach is its decision in October to allocate just \$2 million to establish the first two Centers of Excellence in Regulatory Science and Innovation, with the quaint requirement that they both be located within 50 miles of the FDA campus. (The University of Maryland and Georgetown University will house the new centers.)

Regulatory science involves updating processes to make better decisions regarding drugs and other products, and, given that people are the engines of decision-making, the need to develop and sustain human capital is crucial. A newly launched FDA partnership with the US National Institutes of Health (NIH) will be incorporated into the NIH's pending National Center for Advancing Translational Sciences (NCATS). A politically uncontroversial role for NCATS would be to prioritize training in regulatory science and the complementary discipline of translational medicine and therapeutics, which integrates basic and human pharmacology in a translational endeavor at the heart of medicine.

The demands placed on regulatory agencies are complex, and the stakeholders in their decisions are diverse. Yet it is crucial that their decisions be grounded in science. Diverse stakeholders have widely differing perceptions of what is meant by regulatory science and expectations of what it might deliver. Coming together to prioritize the objectives of this discipline will not only render regulatory science possible but help realize its possibilities.

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