Off-target:
Tuberculosis reduction goals seen as under-ambitious

Last resort:
Researchers call for clarity on FDA's animal rule

Adhesives adapt:
Nature inspires next generation of medical adhesives

Near-record number of approvals signals drug development shift

As most people prepared to ring in the New Year this past December, regulators at the US Food and Drug Administration (FDA) were still busy at work. On the final day of 2012, the agency managed to squeeze in one last drug approval for a pill called Fulyzaq (crofelemer) that mitigates diarrhea in patients with HIV who are undergoing antiretroviral therapy. This, the eighth new drug approval in December alone, brought the total number of new molecular and biological entities for the calendar year to 39, a number not seen in a decade and a half.

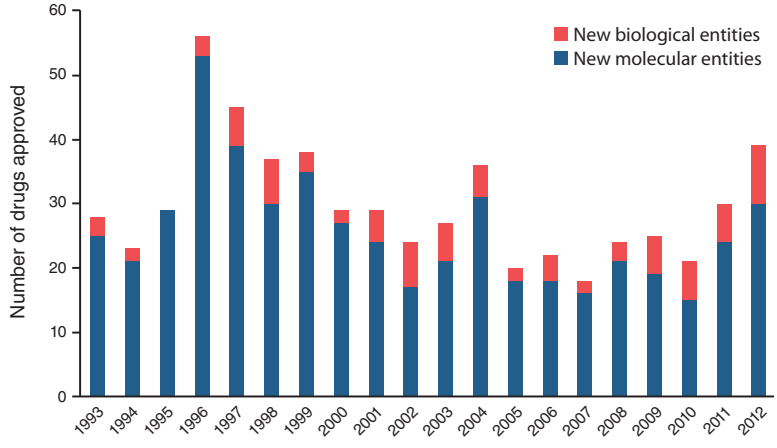
In the short term at least, this trend is expected to continue. Analysts at McKinsey & Company, a management consulting firm headquartered in New York, have predicted that new drug approvals will average around 35 per year for the next five years, with comparable forecasts coming from many experts who track the drug industry. Throughout most of the past decade, the number per year generally fell in the low 20s.

"No longer is the FDA seen as a hurdle for drug approval, but as an ally," says Reni Benjamin, managing director of research at Burrill & Company, a San Francisco–based financial services firm focused on the life sciences industry. Just as importantly, "companies are developing better designed clinical trials. That's helping the FDA's ability to review the quality of the data," he says.

Yet, notably absent from this year's crop of newly minted drugs was a clear number of blockbuster candidates, such as the bestselling cardiovascular and psychiatric medications that have traditionally earned drugmakers billions of dollars each year in revenue. The enormous expense, time requirement and failure rate of clinical trials for agents designed to treat common medical problems have led to a shift in focus, for both the FDA and the drug industry, toward niche diseases. Out of the 39 total approvals in 2012, almost half received orphan-drug designation, meaning they target diseases or indications affecting fewer than 200,000 people in the US each year.

Orphan drugs are an attractive target for pharmaceutical companies, says Eric Schmidt, an analyst with Cowen & Company in New York, as "they require less cost to develop and tend to get the benefit of the doubt at the FDA." However, there's a tradeoff for companies: even though drugs for rare diseases typically come with a hefty price tag, the number of buyers usually remains low. For example, Juxtapid (lomitapide) was approved on 24 December for the treatment of homozygous familial hypercholesterolemia, a rare genetic disorder involving the breakdown of natural mechanisms for removing bad cholesterol from the body. The drug's manufacturer, Aegerion Pharmaceuticals of Cambridge, Massachusetts, plans to sell Juxtapid for between $235,000 and $295,000 per year. Yet, with a target population of just 3,000 patients in the US, the drug could never achieve blockbuster status, even in best-case scenarios.

The math is echoed by internal research from Boston Consulting Group (BCG). According to Ulrik Schulze, global leader for biopharma research and development at the management consulting firm, BCG has pegged the average peak sales value of the 2012 cohort of drugs at about $800 million apiece, a figure that has trended downward over the past few years. The median peak sales amount for the newly approved medicines is even lower, at about $400 million. Given that a drug typically has to generate at least $600 million to offset development costs, "the industry is barely getting a return on investment," Schulze says.



On the upswing: FDA drug approvals over the past 20 years.

Ándale, FDA!

Much of the FDA's recent flurry of approvals can additionally be traced to streamlined review processes. Around half of the new approvals in 2012 went through with either 'fast track', 'accelerated approval' or 'priority review' designations, and three-quarters managed to get through on their first cycle of review. For example, in January 2012 the FDA approved Erivedge (vismodegib) for late-stage basal cell carcinoma, the most common form of skin cancer, in less than five months. Efficacy was evaluated through a single clinical trial with results from 96 patients that looked for complete or partial shrinkage of cancerous lesions after treatment. In total, around a dozen drugs that target specific cases of cancer were approved, most with expedited reviews.

Ultimately, it remains to be seen whether the FDA's increased efficiency will be of benefit beyond the realm of oncology and niche products, particularly for diseases with higher barriers to review. In cardiovascular disorders, obesity and diabetes, for example, the FDA's requirements for clinical trials are increasing even as the number of submissions decreases, and there are no signs that the streamlined review processes that facilitate orphan-drug approvals will translate over. "From an industry standpoint [the number of approvals] is good news," says Dirk Calcoen, a partner and managing director at BCG in San Francisco. "But from a public health standpoint, there's still going to significant regulatory hurdles in diseases with huge unmet needs."

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