Debate re-ignites on contribution of public research to drug development

Nearly 10% of the 1,541 drugs approved by the US Food and Drug Administration (FDA) since 1990 have their roots in public sector research according to a paper published earlier this year in the *New England Journal of Medicine* (**364**, 535–541, 2011). The study injects new data into a perennial question: just how much does publicly funded research contribute to drug development? Polarized views have in the past veered from virtually nothing to most of the important discoveries that the pharmaceutical industry relies on for products and profits. As the US National Institutes of Health (NIH) in Bethesda, Maryland, plans the launch a new translational medicine center, the study has re-ignited the debate concerning the role of public institutions in the drug discovery and development process.

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Remicade (infliximab), a Johnson & Johnson antibody used to treat rheumatoid arthritis, Crohn's disease and psoriasis was developed by Junming Le and Jan Vilceck at the New York University School of Medicine.

According to Joel Kirschbaum, director of technology management at the University of California, San Francisco, the new findings supply convincing evidence that public sector science is directly responsible for some of the drugs on the market today. "Publicly funded scientists might not have created the final products, but they did move these compounds along to the extent that they were picked up by biotech and pharmaceutical companies," he says.

To create a data set linking approved drugs to published research in the public sector, lead author Ashley Stevens, special assistant to the vice president for research at Boston University School of Management in Massachusetts and former president of the Association of University Technology Managers in Deerfield, Illinois, and his collaborators at the NIH combed through patent records, technology-licensing agreements, personal stories from university technology managers, legal records, newspaper articles and other data sources. The research tallied approvals since 1970 by therapeutic category and since 1990 by chemical type.

Approvals climbed dramatically, according to Stevens, after 1980, the year Congress passed the Bayh-Dole Act, which allowed federally funded scientists to patent and license their discoveries. Those approvals peaked in the mid-1990s and then dropped off, he says, reflecting long cycles in the path from discovery to commercialization. "We don't view this as the low-hanging fruit being plucked," Stevens says. "Drugs discovered in the past 15 years are still going through the development process." In what Stevens says is a completely new finding, the data also show that nearly 20% of the 348 drugs given priority review by the FDA emerged from public research. The agency assigns priority review status to drugs that offer major advances in treatment or satisfy unmet clinical needs. This suggests that NIH scientists are particularly likely to discover compounds with novel applications, says Stevens. And that's not surprising, he adds, given that university scientists, who derive much of their funding from the NIH, are given incentives to publish groundbreaking discoveries, whereas industry scientists are oriented to work in areas where their companies see a potential for increased profits.

But others are unconvinced that the public sector's contributions stretch much beyond basic science. Benjamin Zycher, a senior fellow at the Pacific Research Institute, a conservative economic think-tank in San Francisco, says industry contributions dominate throughout applied phases of drug development (that is, beyond target discovery identified in basic research). Moreover, industry is responsible for most of the potency enhancements and other clinical improvements required to get a drug to market, he says. Zycher's conclusions are drawn from his own investigation of 35 drugs and drug classes published last year (*Am. J. Ther.* **17**, 101–120, 2010).

Observers remain divided on whose conclusions are right. Stevens' co-author, Mark

IN brief

Supreme setback for pharma

In a fraud case closely watched by biotech and pharma companies, the US Supreme Court sided with investors suing a drug maker for not disclosing adverse events to them. In *Matrixx Initiatives, Inc. et al. v. James Siracusano et al.* investors claimed that Matrixx's failure to disclose adverse events (anosmia, or loss of smell) concerning its blockbuster cold remedy nasal spray Zicam led to investment losses. On March 22, a unanimous Supreme Court declined to adopt a bright-line rule that would protect Matrixx from liability. The company argued it had no duty to disclose because such events were not statistically significant (*Nat. Biotechnol.* **28**, 1142, 2010). However the Court's opinion, written by Justice Sonia Sotomayor, said the absence of statistical data "does not mean that medical experts have no reliable basis for inferring a causal link between a drug and adverse events." She continued, "This is not a case about a handful of anecdotal reports, as Matrixx suggests. Matrixx received information that plausibly indicated a reliable causal link between Zicam and anosmia. This included information about more than ten patients who had lost their sense of smell after using Zicam. Sotomayor added that the court's ruling did not mean that drug makers must disclose all reports: "[S]omething more is needed, but that something more is not limited to statistical significance and can come from the source, content, and context of the reports." *Michael Francisco*

Blue skies ready for investors

Scientists can now apply to a €10 ($14.3) million fund aimed at helping academic researchers package their 'blue sky research' into ideas that appeal to investors. The European Research Council (ERC)—the first pan-European science funding agency—is offering proof of concept (POC) grants of up to €150,000 ($215,200) to allow existing grant holders to demonstrate the commercial potential of their work. The aim, according to the ERC, is to speed the outcomes of research into the marketplace. Investigators awarded POC grants will have 12 months to package their research to make it attractive to venture capitalists or companies looking to in-license technologies. The money can be spent on setting up a company, clarifying intellectual property rights, carrying out market research or validating a technology. However, POC grants are for preparatory work only—not to commercialize an idea or develop a novel technology—leaving it up to grant holders to decide if they want to be involved in the commercialization of their research. ERC President Helga Nowotny points out that they are "looking at ways to make the ERC more attractive to industry." Nowotny envisages that as the scientific and technological outcomes of ERC research projects, including those supported by POC funding, gain visibility "startup companies will take up results produced by ERC grantees and develop them further towards innovation." The deadline for POC applications is June 15. *Nuala Moran*

Rohrbaugh, director of technology transfer at the NIH, says that of all the studies investigating the public sector's role in drug development, theirs is the most complete. "What allowed us to do this was our own involvement in the university technology transfer sector," he says. "We've got insights […] acquired from working in the field," says Rohrbaugh.

But according to Joseph DiMasi, director of economic analysis at the Tufts Center for the Study of Drug Development, in Boston, the roles of the public sector and industry in drug development cannot and should not be strictly delineated. "It's a complex picture," he says. "But in reality, the roles are highly complementary; it's fair to say that the public sector leans heavily towards basic science while industry leans heavily towards the clinical development aspects."

Andrew Toole, a research economist at the US Department of Agriculture (USDA) has been modeling public funding for basic research and product development in different industries. He estimates that NIH investments in biomedical science generate a 43% return, as measured by average sales revenue from 'new molecular entities' in perpetuity. Toole agrees with DiMasi that the roles of the public and private sectors in drug development are synergistic. He also points out that, though comprehensive, the Stevens group's analysis misses other interactions between public and industry scientists that don't leave a paper trail. "Our research shows that much of what industry learns about public research comes from consultations, meetings and other types informal, bidirectional communication," he says. "These interactions aren't easily quantified, however."

According to Toole, the public's role in drug development has sparked renewed interest in light of a planned translational research center at the NIH (*Nat. Biotechnol.* **29**, 91–92, 2011). Slated to open its doors in October (pending Congressional approval), the National Center for Advancing Translational Sciences (NCATS) aims to help publicly funded researchers bring their discoveries closer to market. Kathy Hudson, deputy director for science outreach at the NIH, says a priority for the new center will be to find bottlenecks that block promising compounds and other biomedical inventions from reaching consumers. "And then we'll see which of those bottlenecks are amenable to study and re-engineering science by NIH investment," she says. Kirschbaum adds that too many promising inventions paid for with public money are simply collecting dust in technology transfer offices because those offices lack sufficient resources or university researchers lack either the funding to 'de-risk' their inventions for industry or the incentive to engage in development efforts beyond publishing in peer-reviewed journals.

Kirschbaum says the NCATS will ideally boost the public sector's contribution to drug development, but not everyone thinks that's a good idea. Zycher, for instance, predicts the center will flop because the NIH isn't set up for applied research. Moreover, he worries that by enhancing public sector contributions, the center could invite congressional meddling in pricing, fast-track approval decisions and other business-related concerns.

For the biotech industry in particular, USDA's Toole pictures two outcomes arising from the establishment of NCATS. On the one hand, companies could benefit from being relieved of some of the upfront R&D groundwork. On the other hand, it's also possible that publicly funded scientists could seek more patent protection for their work, continue to overestimate the commercial value of their intellectual property and slow down tech transfer from academia to industry, turning them into competitors as much as collaborators, he says.

Yet Hudson counters that the NIH has no interest in creating a small drug-development company. "Our critics rightly point out that it would be silly for us to do that," she says. According to Hudson, the NIH budget is already split evenly between basic and applied research, the fruits of which are evident in Stevens' paper. But she adds that public sector scientists can do more to address the dwindling pharmaceutical pipeline; for instance, by humanizing mouse antibodies or developing new methods for high-throughput screening or new models for detecting liver toxicity. "In the early days of biotech, the venture capital folks would invest in interesting ideas," Hudson says. "Now they only look for really compelling ideas. We want to help NIH-funded scientists move from point A to point B more effectively so we can get this pipeline moving."

Christopher Milne, associate director at the Tufts Center for the Study of Drug Development, admits he has little patience for the more polarized sides in the debate over public and industry contributions. "It's divisive and inaccurate to say that one side does more than another," he says. "And it's also very difficult to quantify the relative contributions from each because for every molecule that that ends up being successful there are many more that aren't."

Charles Schmidt, ***Portland, Maine***