Academia given a helping hand in drug development

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At a time when R&D productivity is under intense scrutiny, any measures that could help push more drug candidates safely and efficiently through to clinical trials would be warmly received by industry and patients alike. Recognizing this, the FDA seems to have loosened its regulatory restrictions with the release of new guidelines designed to make it easier to get drugs into early-stage human trials.

The announcement was, perhaps predictably, taken as evidence by critics that the agency favours industry over consumers. But the agency contends that the measures have been designed to help other players enter the drug development arena**.** The initiatives address "the huge concern that many discoveries at the academic level were not translating into treatments available to patients," says Janet Woodcock, FDA's Deputy Commissioner for Operations. "We were not seeing the payoff."

Under the new guidances, researchers will now be able to manufacture and test smaller amounts of drug candidates in humans. One set of guidelines, known as Phase I Current Good Manufacturing Practice (cGMP), reduces the amounts of experimental drug that must be made for clinical trials. "It takes off some pressure without compromising patient safety," says Hans-Jürgen Federsel, Head of Project Management at Process R&D at AstraZeneca.

Before this, anyone testing drugs in humans was required to make large amounts of compound, even if they were uncertain about the drug's future. This was particularly burdensome for academics and small biotechs, who have much smaller budgets than big pharmas.

"We have been at the mercy of large biotechs and pharmas who have the resources to take these products to large numbers of patients," said the National Cancer Institute's Steven Rosenberg, during a press conference to announce the guidelines. Rosenberg described his own frustration, and that of colleagues, who labour for years on what seem to be promising targets or compounds, but which industry ignores.

Now those scientists can do human trials, but on a much smaller scale than previously required. The second new guidance, called Exploratory Investigational New Drug Studies, describes how to do very early or 'Phase 0' trials, which will allow researchers to analyse 'microdoses' of experimental drugs in a small group of people before Phase I clinical trials begin, and before preclinical tests are completed. These Phase 0 studies mainly provide information about pharmacokinetics, and can help to identify candidates that are more likely to fail in humans before investing in costly clinical trials.

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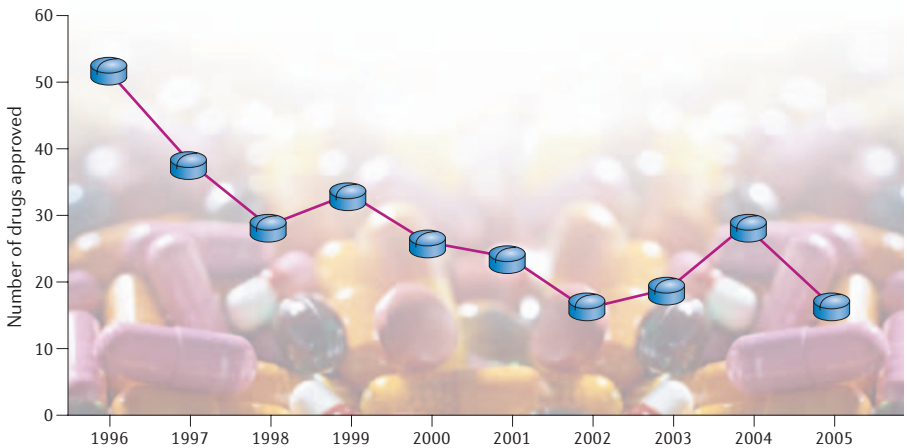
Such microdosing trials have been tried in Europe in the past few years, and were already permitted to a certain extent in the United States. "We are just trying to make it clear how to do these," says Woodcock. One of the agency's big hopes is that academics could use such trials to further validate targets, or do proof of concept for particular approaches.

A similar approach is working in Australia, says Jaye Chin-Dusting, Head, Vascular Pharmacology at the Baker Heart Research Institute, Melbourne. Australia's Clinical Trial Notification scheme is widely used to get drugs much more quickly, but safely, into humans, and "boosts academic participation hugely," says Chin-Dusting. Currently, the vast majority of trials in Australia go through the CTN scheme, and some scientists say this accounts for the country's capacity to do trials more cheaply and quickly.

A key question is whether these small, early trials will lead to more successful products reaching patients? "I'm worried we'll just get a big mass of more uninterpretable data," says clinical researcher Cy Stein of New York's Albert Einstein College of Medicine. "This will either be fabulously successful, and you'll see lots of new products, or the academics will use it to generate lots of papers. Then, they'll still think it's a smash hit," says John Mirsalis, toxicology director at PharmaStart, a consortium of research organizations that offers translational drug development services to help California-based laboratories.

Experts also question whether Phase 0 data will be sufficient to entice financial backing for a project. Before buying something in, "We'd probably want to do most of this type of work in-house," says Federsel. Still, biotechs in particular might turn to such studies to help drive partnerships if they can't afford more extensive trials.

Major companies such as AstraZeneca, meanwhile, see the guidances as a perfect fit. Now they can get a lot more information about early-stage compounds before investing heavily. So why did it take so long to get such simple steps? "The trend is to demand more and more from companies, until suddenly everyone realizes it is not sustainable," says Federsel. "At least that realization seems to have finally matured."



The FDA hopes its new initiatives will help buck the recent downturn in innovative drugs approved.

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