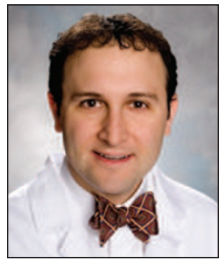
The NIH translational research center might trade public risk for private reward

Jerry Avorn & Aaron S Kesselheim



Jerry Avorn/Aaron Kesselheim

The new National Center for Advancing Translational Sciences planned for the US National Institutes of Health intends to help transform biological findings into new therapeutic products. But if taxpayer funding of risky biomedical research translates into lucrative new medicines, the public should share in the economic benefits as well.

As the US National Institutes of Health faces a $300 million budget reduction, it is creating a unit to facilitate the development of new drugs. The National Center for Advancing Translational Sciences (NCATS) envisioned by NIH Director Francis Collins would redeploy resources from the agency's existing programs to identify discoveries that could be transformed into therapeutic products.

The road that brings treatments from bench to bedside is notoriously bumpy, and recent years have seen a scarcity of transformative medications and novel drug designs. Of the 47 new products approved in 2009–2010, by our count approximately two-thirds were members of an existing therapeutic class or managed their indicated condition about as well as available treatments. We clearly need more and better innovation.

The assumption underlying NCATS is that many potential drug targets or compounds have been identified but are not being adequately exploited, so the new NIH unit would pursue leads that drug companies or investors have overlooked or have chosen not to invest in. NCATS will also facilitate the exchange of ideas about common therapeutic approaches across different conditions by bringing together similarly oriented mechanism-based researchers currently separated in the NIH's disease-specific institutes.

These plans raise important questions. Are there really many clinically promising compounds or targets that have been discovered but are languishing, neglected, in some laboratory—or that remain unexploited even though their properties are known? This may be true for some antibiotics, since the need for their restrained use makes them potentially unprofitable products for industry to develop. In such cases, the NCATS model could fill an important niche. But for treatments for conditions such as common cancers or Alzheimer's disease, how likely is it that a new NIH center will be able to develop candidate therapies that armies of smart investigators, drug companies and venture capitalists have all somehow overlooked? It also isn't clear that a governmental agency will generate more creative decision-making than the time-tested approach of investigator-initiated research.

Pulling together mechanism-focused research teams has some appeal, as differing conditions may share common etiological pathways. Yet the merits of a centralized drug-development program must be weighed against the dislocations caused by separating this work from disease-oriented institutes. Moreover, the disease-focused NIH model, whatever its conceptual limits, has been a key means of generating congressional support for funding—a fact not to be taken lightly.

The greatest concern is what will happen when NCATS uses public funds to absorb the costs of the chanciest early phases of drug development to spare companies that expense. According to Collins, the institute's approach "will be to 'de-risk' projects that might otherwise be seen as economically unattractive. As soon as the risks are reduced sufficiently to attract commercial attention, we plan to hand over projects to companies to carry out the next step. There is absolutely no intention of turning the NIH and its grantees into competitors with the private sector."[1]. Thus, NCATS could require the public to absorb even more of the costs of risky basic biomedical research and then hand off the fruits of such investigation to manufacturers that have traditionally not been generous in sharing the profits from medications based on such discoveries. Key initial steps in development of paclitaxel (Taxol), zidovudine (AZT), imatinib (Gleevec) and erythropoietin alfa (Epoetin), among others[2], were all made possible by NIH funding, but the resulting profits were lucratively retained by their manufacturers. This places a double burden on taxpayers, who pay once for drug development and again for heavily marked-up products.

Part of the challenge here stems from our patent system, which makes it easy to own rights to a compound (such as one that blocks COX-2 or tumor angiogenesis), but much harder to benefit financially from the key discoveries that make such treatments possible (the existence of a distinct COX-2 mechanism or the phenomenon of tumor angiogenesis itself). For their part, universities and other nonprofit research institutions have tried to patent more and more of their NIH-funded basic-research findings. This response can also be problematic if the resulting thicket of patents hampers the drug discovery process. Collins has stated that NCATS intends to adhere to principles of "open access" in drug development, which would help address the restrictive movement toward patenting basic-science tools and products[3]. This is encouraging but not yet well defined.

When a pharmaceutical manufacturer invests substantial sums in discovery, evaluation and development of a drug, it is entitled to a fair return on that investment, and companies justify high medication prices by citing the expensive and chancy developmental research they undertake. The public deserves the same benefit. If development of a future drug is subsidized by NCATS, it would be reasonable to expect some payback mechanism to make that product more affordable—or some other means of returning a share of its revenues to the public infrastructure, perhaps by being plowed back into more NIH-funded research. Collins has suggested the NIH could somehow share in the royalties that flow from successful NCATS projects; but as *Nature Medicine* went to press details were still lacking about how such an arrangement would be implemented. This is particularly pressing at a time of constrained support for basic research, including the reality of a shrinking NIH budget.

In the nineteenth century, a congressman voiced a similar fear about the government's underwriting of bonds for the rail industry: "If there be profit, the corporations may take it; if there be loss, the government must bear it." More recently, the finance and energy sectors demonstrated what can happen when the private sector benefits from the gains of risky activities while the public covers their downside. If the new NIH center asks the citizenry to become pharmaceutical venture capital funders, more discussion will be needed of how they can be fairly compensated.

Jerry Avorn is a professor of medicine and Aaron S. Kesselheim is an assistant professor of medicine at Harvard Medical School and Brigham and Women's Hospital, Boston, Massachusetts, USA.

1. Collins F. *Nat. Rev. Drug Discov.* **10**, 14 (2011).
2. Stevens A.J., *et al. N. Engl. J. Med.* **364**, 535–541 (2011).
3. Collins, F. 27 Apr 2011. The NIH National Center for Advancing Translational Sciences: How Will It Work? <https://www.dtmi.duke.edu/website-administration/files/Collins%20NCATS%20slides.pdf> (2011; last accessed 16 Sept 2011).