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Revisiting the National Institutes of Health Fair Pricing Condition: Promoting the Affordability of Drugs Developed With Government Support

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The federal government's substantial contribution to the development of many products has fueled controversy over the high cost of prescription drugs in the United States. A quarter of new drugs developed during the past decade had key, late-stage contributions from publicly funded research (1)—most commonly by the National Institutes of Health (NIH)—prompting concerns that Americans are "paying twice" for these expensive medications.

Senators and other policymakers have proposed that the NIH should more actively work to ensure fair pricing of drugs developed with its support (2). In response, critics have noted that such an intervention was attempted. In 1989, the U.S. Public Health Service—the parent organization of the NIH—incorporated a fair pricing condition into its model cooperative research and development agreement (CRADA), which allows private institutions to work with government agencies and negotiate exclusive licenses for inventions stemming from such work. However, the NIH removed this condition 5 years later, with the then–NIH director claiming it chilled government–industry collaboration.

We reviewed this episode to better understand the rationale for the fair pricing condition and the effect of its removal. On the basis of our findings, we offer recommendations on how the NIH can incorporate a reasonable pricing condition for drugs developed with taxpayer money that preserves necessary incentives for bringing these drugs to market.

History of the NIH Fair Pricing Condition

The CRADA process existed for 3 years before the NIH integrated a fair pricing condition in 1989. The original impetus for the condition was public backlash over the high cost of zidovudine (Retrovir, GlaxoSmithKline) which was first synthesized in 1964 by an NIH-funded scientist and recognized 2 decades later by the National Cancer Institute and Burroughs Wellcome (now GlaxoSmithKline) to be an effective treatment of HIV infection (3). Burroughs Wellcome's launch price of zidovudine in 1987 was $10 000 per patient per year, making the drug among the most expensive in the world at the time (4).

In 1989, the U.S. Public Health Service adopted a new fair pricing condition to its model CRADA to ensure that future inventions made with government support were more equitably marketed. The condition expressed "concern that there be a reasonable relationship between pricing of a licensed product, the public investment in that product, and the health and safety needs of the public" and stated that exclusive licenses to inventions stemming from collaborative work "may require that this relationship be supported by reasonable evidence" (5).

Although popular with some patient and public interest groups, this fair pricing condition faced immediate resistance from industry. Several large manufacturers announced their refusal to work with the NIH. Some NIH scientists later claimed the condition impeded their negotiations with the private sector.

But evidence at the time was not consistent with this perception. First, the average annual number of CRADAs after the condition was implemented (n = 32) was similar to that in the 2 years prior (n = 31) (**Figure**). Second, in practice, the fair pricing condition was replaced or omitted from many executed CRADAs. From 1990 to 1992, the National Cancer Institute, National Institute of Allergy and Infectious Diseases, and National Institute of Diabetes and Digestive and Kidney Diseases used modified CRADAs that replaced the condition with language more favorable to the manufacturer in 21% (13 of 61) of cases (6). The most egregious example involved paclitaxel (Taxol, Bristol-Myers Squibb). Although the NIH spent $85 million conducting 5 of the 6 clinical trials Bristol-Myers Squibb submitted to secure U.S. Food and Drug Administration approval, a course of treatment was priced at $20 000 for patients with breast cancer, helping generate more than $9 billion in revenue from 1993 to 2002 (7). Widespread knowledge that the condition could thus be weakened or removed undercuts claims of its outsized effect.

Nonetheless, to address stakeholder concerns, the NIH held a panel in September 1994. The panel concluded that a perception existed that the fair pricing condition impeded technology transfers but that there was "no decline in the number of NIH CRADAs or technology licenses" (5). Reviewing this feedback, the NIH removed the condition in April 1995. In 1996, the number of executed CRADAs increased from 32 to 87; in 1997, this number almost doubled to 153.

The often-cited statistic of the increase in CRADAs after the withdrawal of the policy, however, belies a more complicated story. In fact, in 1996, the NIH created a new materials CRADA (mCRADA) pathway (8), fashioned to accelerate negotiations about NIH's receipt of propriety research materials. From 1996 to 1998, an average of 90 mCRADAs and 40 standard CRADAs were executed annually. The number of standard CRADAs executed in the post–reasonable pricing condition period was therefore similar to the average

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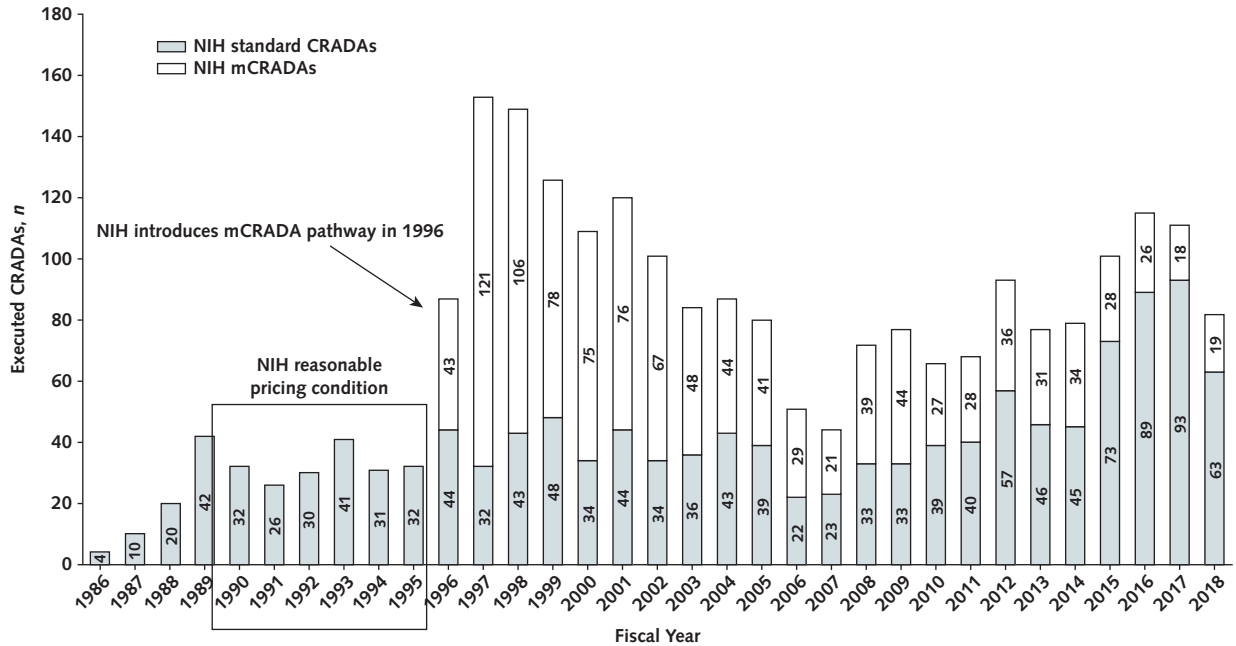
Figure. The NIH executed CRADAs.



Executed CRADAs refer to the number of standard CRADAs or mCRADAs–introduced in 1996–signed per fiscal year by the NIH with a private or public sector institution. CRADA = cooperative research and development agreement; mCRADA = materials cooperative research and development agreement; NIH = National Institutes of Health. (The authors' data from fiscal years 1986 to 2018 are from Schacht [6] [1986–1994] and the NIH Office of Technology Transfer Activities' Office of Technology Transfer [1995–2018]).

number when the condition was in effect (n = 32). Although some pre-1996 CRADAs may have qualified for the mCRADA pathway, it clearly spurred agreements that otherwise would not have been executed, accounting for the dramatic rise in total CRADAs.

Lessons From the NIH Fair Pricing Condition

Thus, the fair pricing condition did not suppress the number of CRADAs to the extent commonly perceived but was plagued by vague wording and inconsistent application. Should legislators choose to resurrect this policy, its terms must better clarify manufacturer responsibilities. For example, requiring that applicable drugs be priced no higher than those in similar countries would provide more certainty than requiring a "reasonable relationship" between price and public investment. Alternatively, a rule requiring that drugs be priced in line with the value they provide would richly reward manufacturers for bringing transformative drugs to market.

Second, the condition should be applied consistently to the licensing of all drugs benefiting from key, late-stage, NIH-supported contributions–not just CRADAs, which account for only a small proportion of NIH-supported translational research. The recently introduced We Protect American Investment in Drugs Act would apply a reasonable pricing condition to all drugs with patents disclosing federal support (2). To ensure compliance, details of the condition should be publicly reported.

Perhaps the most important question is: If an NIH fair pricing condition is introduced in the modern era, will manufacturers respond negatively by seeking to avoid commercialization relationships with government-funded entities? This is unlikely given that private industry reliance on government-sponsored research has increased as more large manufacturers have reduced investment in their own laboratories (9, 10). A new fair pricing condition that is well designed and well enforced could better ensure that Americans can affordably access drugs created with NIH support.

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