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The NIH Experience with the Reasonable Pricing Clause in CRADAs FY1990-1995*

A large increase in the number of NIH Cooperative Research and Development Agreements (CRADAs) followed the removal of the "reasonable pricing clause" late in FY1995. To better understand why this occurred, we compared CRADA activity during five years with the pricing clause (FY1991-1995) to five years after its removal (FY1996-2000). We concluded that the primary stimulus for the increase in CRADAs most likely was the removal of the reasonable pricing clause rather than the introduction of the Materials-CRADA model agreement at about the same time or other factors external to the NIH.

Q: What is a CRADA?
A CRADA is a collaborative agreement between a federal laboratory and an outside party to conduct specified research or development. (see 15 USC §3710a) It is not an external (extramural) research funding agreement like a grant or contract. CRADAs are authorized with collaborators who will make intellectual contributions to a research project including essential research materials or technical resources not otherwise reasonably available to NIH. CRADAs cannot attempt to direct or restrict research in an NIH laboratory, and thus NIH does not conduct fee-for-service research on behalf of a company.

Under a CRADA, the NIH laboratory can provide to the collaborator personnel, services, facilities, equipment, or other resources (but not funds), and the collaborator can provide to NIH funds, personnel, services, facilities, equipment, or other material and/or technical resources. The CRADA mechanism is unique in allowing NIH to grant a collaborator an option to negotiate an exclusive or non-exclusive license to inventions government scientists might make within the scope of the CRADA. Under other collaboration mechanisms, opportunities to license new inventions are open to applicants.

Q: How does NIH use CRADAs?
A: CRADAs allow NIH scientists to collaborate, most often with companies, to conduct basic research or advance the commercialization of technologies originating with either the NIH or the collaborator. CRADAs may involve joint basic through clinical research or NIH studies using the collaborator's proprietary research materials such as drug candidates. While few CRADAs (<10%) result in new inventions, CRADAs advance scientific research, which directly or indirectly leads to improvements in health treatment options.

Q: Why allow companies the right to negotiate an exclusive license?
A: Companies invest heavily in their own technology and protect it with patents and trade secrets. Often, they will not share their technology and resources with research institutions when there is a chance that those institutions might license their scientist's invention to the company's competitors. The invention could even be a new use for the company's technology. CRADAs guarantee that NIH will instead give the collaborator the first right to negotiate a license to any new CRADA inventions made at NIH within the scope of the CRADA research plan.

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* based on an analysis of NIH CRADAs by Mark L Rohrbaugh, PhD, JD, and Jennifer Wong, PhD, Office of Science Policy, National Institutes of Health

Q: What was the "reasonable pricing clause" in NIH CRADAs?
A: From Fiscal Year (FY) 1990 to 1995, NIH attempted to address concerns about high drug prices by adding a "reasonable pricing clause" to its CRADAs. Under the clause, a company taking an exclusive license to bring an NIH invention to market could be compelled by the NIH to submit documentation showing a "reasonable relationship between the pricing of the product, the public investment in that product, and the health and safety needs of the public." "Reasonable relationship" was never defined.

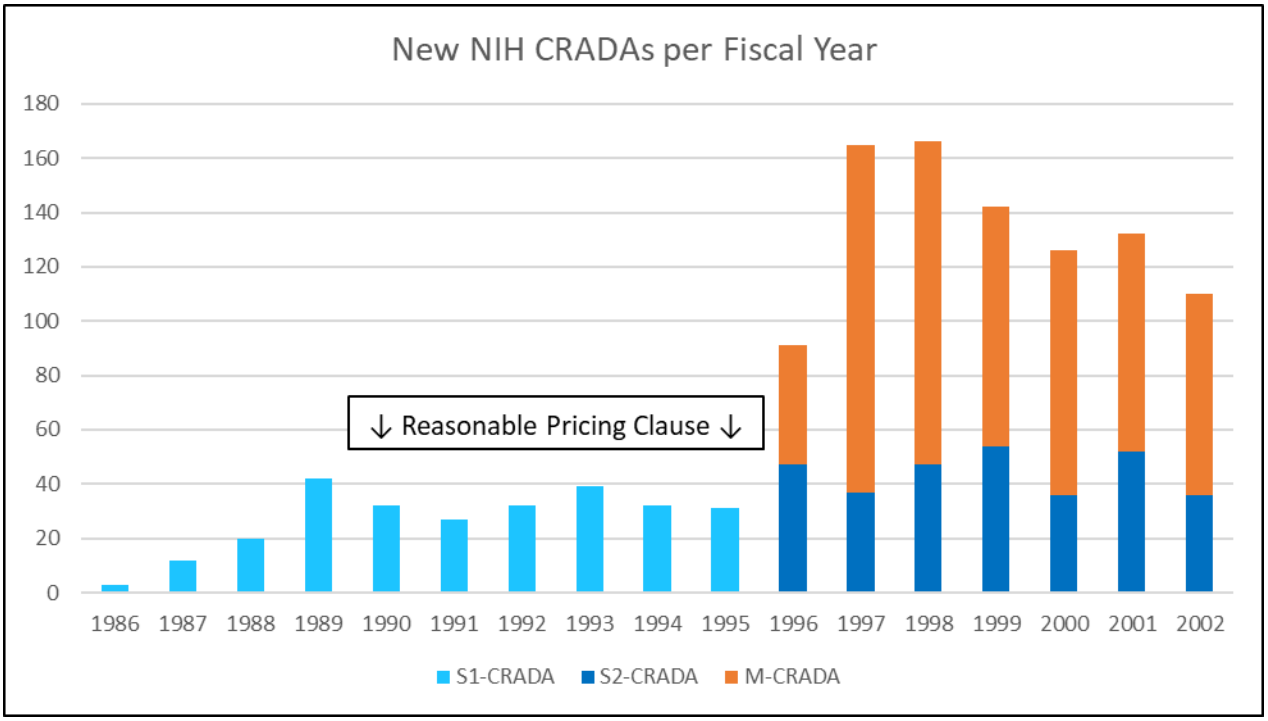
Q: Why did NIH decide in 1995 to remove the reasonable pricing clause from CRADAs?
A: In the early 1990s, NIH leadership began to receive reports from companies and researchers about the negative impact of the reasonable pricing clause. NIH held two public meetings in 1994 with companies, patient advocates, and researchers, which came to a consensus that companies were avoiding collaborations with the NIH because of the pricing clause. As a result, the NIH Director announced in 1995 the removal of the clause from CRADAs and exclusive licenses.

Q: What leads NIH to conclude that removal of the reasonable pricing clause was likely the primary stimulus for the large increase in CRADAs?
A: Several observations lead NIH to this conclusion:

1. Serious concerns about the pricing clause from companies, NIH scientists, and technology transfer staff were documented in 1994. There is no reason to doubt the negative impact from the use of the clause.
2. After a thorough study, the NIH Director stated in 1995, "the pricing clause has driven industry away from potentially beneficial scientific collaborations with [NIH] scientists without providing an offsetting benefit to the public…Eliminating the clause will promote research that can enhance the health of the American people." See the full report here.
3. Companies that stated in 1994 they would avoid CRADAs with the reasonable pricing clause kept their word and re-engaged only after its removal.
4. NIH began developing the Materials (M)-CRADA model agreement after the decision was made to remove the reasonable pricing clause in anticipation of a large increase in CRADAs for proprietary materials that companies had previously denied because of the reasonable pricing clause. To facilitate negotiations, NIH developed the M-CRADA by removing terms from the model Standard- (S-)CRADA that were not relevant to the receipt of companies' materials with no joint research plan. The timing was no coincidence.
5. In the five years after NIH removed the pricing clause, there was a four-fold increase over the previous five years with the clause in the numbers of CRADAs overall and more than a doubling of individual collaborating companies. (see below) The large increase is difficult to explain by any slimming down of the CRADA format to shorten negotiation of the final agreement. Companies had engaged in only a few CRADAs for the transfer of materials using S-CRADAs with the pricing clause in place. Their primary reluctance was potential government involvement in the pricing of their products rather than any irrelevant terms in the S-CRADA model agreement.
6. The number of new CRADAs per year when the reasonable pricing clause was in use (FY1990-1995) was lower than the year before it was added and the year after it was removed.

Q: What is the difference between S1-, S2- and M-CRADAs?
A: Before FY1996, all CRADA research collaborations were negotiated based on one CRADA template, here designated as Standard-1 or S1-CRADA. NIH negotiated terms with companies for research studies such as: (1) basic research that led to greater understanding of biological processes, (2) applied research with the goal of determining whether a drug or vaccine candidate appeared to be safe and effective in animals or human clinical trials, (3) development and testing of devices, and (4) research with a company's proprietary materials, such as a drug candidate, antibody, or biological factor, without the company's participation in the research itself.

NIH developed a more compact CRADA template, the M-CRADA, for receiving companies' proprietary materials in anticipation of a greater demand after the reasonable pricing clause was removed from CRADAs. The M-CRADA format shortened the time needed to negotiate final terms because there was no longer a need to remove through negotiation the irrelevant terms in the S-CRADA template used for joint research collaborations. The S2-CRADA model at the time included 64 terms over 13 pages; whereas, the M-CRADA model amounted to 20 terms on three pages. After FY1995, all other collaborations were still based on the longer format without the pricing clause, which we refer to here as Standard-2- or S2-CRADAs.



NIH CRADAs by category

Type	Early 90s	Late 90s	Fold increase Early to Late	Late 90s S2-CRADA	Late 90s M-CRADA	%M
Company	153	676	4.4	209	467	69%
Non-Profit*	6	21	3.5	9	12	57%
Multi-Party	3	14	4.7	14	0	0%
TOTAL	162	711	4.4	232	479	67%

*Includes universities, hospitals, research centers, and government

Number of Individual Companies with CRADAs

Early '90s (S1-CRADAs)	Late '90s (S2- or M- CRADAs)	Fold Increase	Late '90s S2-CRADA	Late '90s M-CRADA	Both S- & M-CRADAs
104	246	2.4	154	130	38

Q: Could the introduction of the M-CRADA explain the large increase in CRADAs after FY1995?
Multiple factors including the introduction of the M-CRADA format may have contributed to the increase in CRADAs after FY1995, but the NIH analysis suggests that the M-CRADA was probably not the primary cause. Unlike fully collaborative research projects, companies may perceive only a modest benefit in providing materials of interest to NIH researchers. In the early 1990s, the pricing provision likely tipped the scale against providing materials because the reasonable pricing clause increased companies' risk in the event NIH made an invention and the company licensed and developed into a product subject to pricing limitations.

Of the 246 individual companies that held CRADAs in the late 1990s, 210 (85%) were new collaborators, two-fold more than all the individual companies with CRADAs in the early 1990s. These new collaborators held 155 S2-CRADAs and 217 M-CRADAs in the late 1990s. The removal of the reasonable pricing clause is the most likely explanation for this large increase in new entrants to CRADAs collaborating under both M-CRADAs and S2-CRADAs.