

The number of standard and material CRADAs executed by the NIH from 1985 to 2020 and the relationship to NIH reasonable pricing clause

KEI Briefing Note 2021:3

James Love

April 5, 2021

One argument against the use by the NIH of provisions in patent licenses, CRADAs, other license and material transfer agreements or the exercise of march-in rights is that such actions will chill collaboration between the NIH and developers of new drugs or other important biomedical technology. While this may be true as a general proposition, the extent of the negative impact on collaborations is more important, as are circumstances when the NIH has sufficient leverage to obtain concessions on prices. It is not as if the NIH (or other federal agencies, such as DoD or BARDA) never have leverage on prices in any of its funding or licensing agreements (illustrated most recently by the several Operation Warp Speed Contracts with pricing provisions included.)

Some comments submitted on the proposed rules for “Rights to Federally Funded Inventions and Licensing of Government Owned Inventions” have cited statistics on CRADAs before, during and after a reasonable pricing agreement was attached, making the claim that a dramatic increase in the number of CRADA agreements after the policy was abandoned was evidence that the reasonable pricing policy harmed such collaborations. An obvious and deliberate flaw in this argument is the fact that the NIH created a new type of CRADAs, referred to as materials CRADAs that were first issued in 1996.

The NIH reports statistics separately for the “standard” and “materials” CRADAs. The materials CRADA is similar to another NIH instrument, the Material Transfer Agreement.

By lumping the statistics for the standard and the materials CRADAs together, opponents of the reasonable pricing requirement have claimed that there was a dramatic increase in the number CRADAs. For example, the Conservatives for Property Rights [submission to NIH](#) on March 22, 2021 (Docket ID: NIST-2021-0001-0001) makes this comment:

The National Institutes of Health (NIH) in 1989 started requiring a “reasonable pricing” provision in its Cooperative Research and Development Agreement (CRADA) federal contracting vehicle in order to obtain an exclusive license to NIH-funded technologies. The requirement sparked a significant drop in NIH CRADAs, from 42 in 1989 to an average of 32 the next six years. The uncertainty, diminished IP value, and weakened property rights rising from this CRADA clause led NIH to drop the provision. Then CRADAs with NIH immediately shot up to 87 agreements in 1996 and 153 in 1997. This should be a cautionary tale for NIST here.

But what really happened was quite different. In 1997, for example, the NIH issued 121 materials CRADAs, a type of CRADA that did not even exist before 1996, and 32 standard CRADAs. 32 standard CRADAs was exactly the same number of standard CRADAs executed

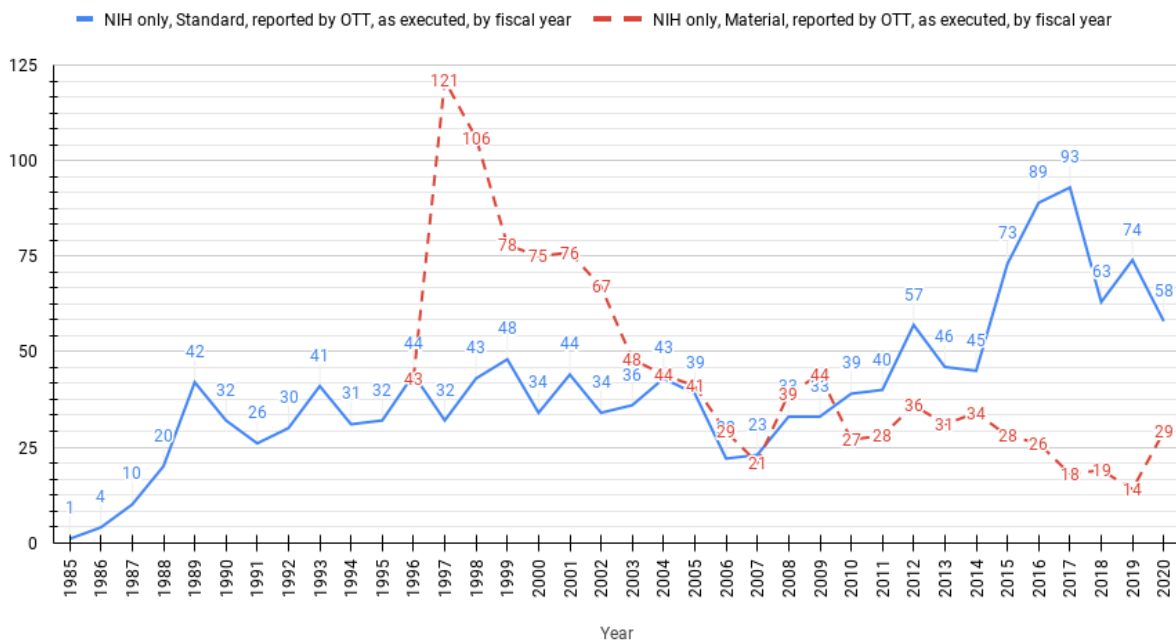
by the NIH on average from 1990 to 1994 (as cited by Conservatives for Property Rights), and the same number executed in 1995, the last year the reasonable pricing clause was used. The only thing that changed was effectively a branding and repurposing of material transfer agreements as materials CRADAs.

When one looks at the standard CRADAs themselves, which were the only type of CRADA issued before 1996, one sees a much different picture.

The number of materials CRADAs, even as a different category, also tells a much different story. The material CRADAs executed fell from 121 in 1997, to just 14 in 2019, during years when the NIH budget vastly expanded and prices for products and share prices skyrocketed.

Figure 1 shows the number of standard CRADAs executed by the NIH from 1985 to 2020, in the blue solid line, and the number of materials CRADAs issued from 1996 to 2020, in the red dashed line.

Figure 1: NIH Standard and Material CRADAs, reported by OTT as executed, by fiscal year



As illustrated above, there have been considerable variances in the number of standard CRADAs per year, including a sharp decline in 2006 and 2007, and large swings in the years 2010 to 2020, including a drop from 93 to 63 from 2017 to 2018, and a very dramatic decline of materials CRADAs from 1997 to 2007.

Every single year when the reasonable pricing clause was in effect more standard CRADAs were executed than was the case in 2006 or 2007, despite the fact that the average NIH budget

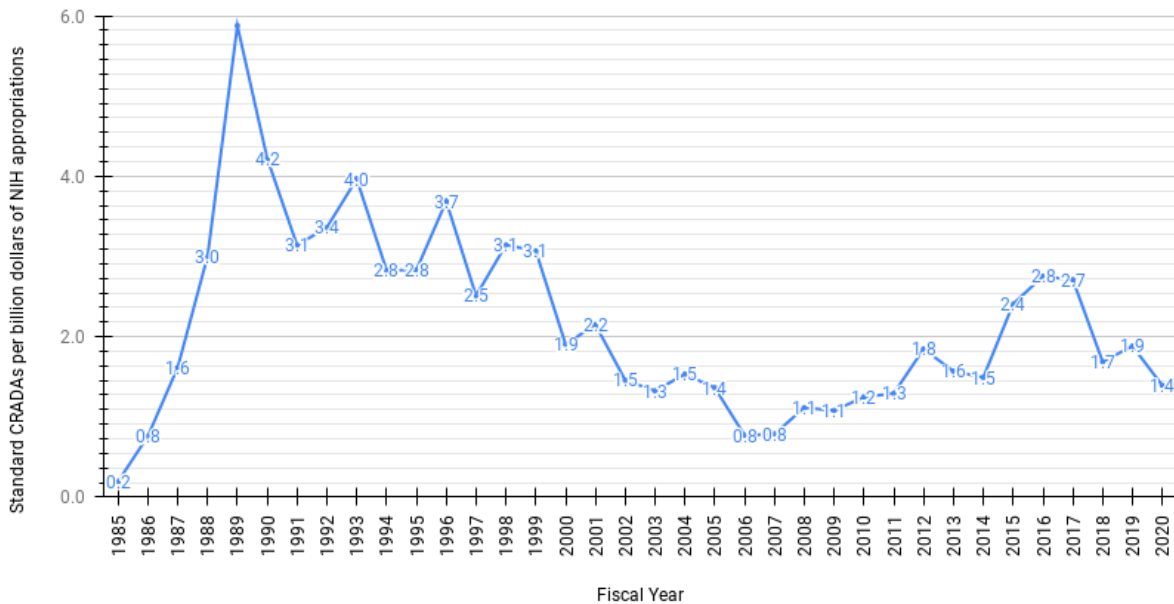
was 3.1 times as large in 2006 and 2007 than it was during the 1989 to 1995 period when the reasonable pricing clause was in effect.

Other Factors that determine the number of CRADAs executed

The number of CRADAs executed by the NIH depends upon a number of factors, including the supply of compelling collaborations available from the NIH, advances in science, and both general and sector specific economic factors.

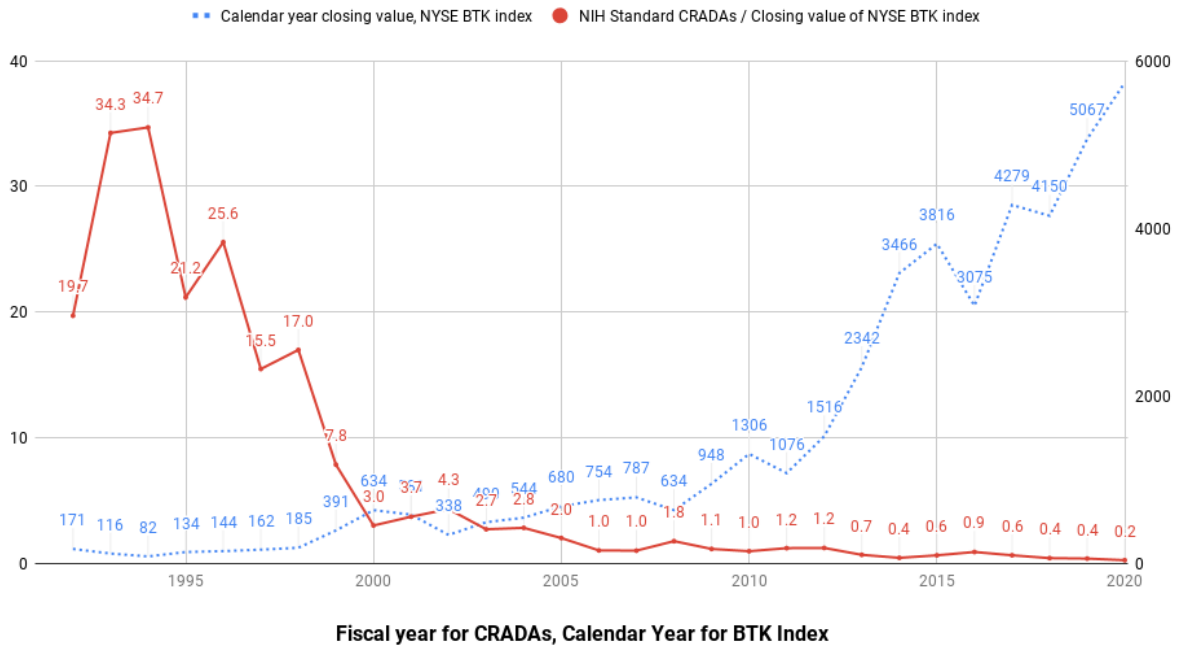
The number of NIH standard CRADAs executed from 1986 to 2020 per billion dollars appropriated to the NIH is one measure of the supply and demand for a CRADA. Through this lens, the period when the reasonable pricing clause was used had higher metrics for supply/demand, not lower.

Figure 2: Number of Standard CRADAs per billion dollars of NIH appropriations by Fiscal Year



One can also compare the number of CRADAs executed per year to the New York Stock Exchange Biotechnology Index, BTK. Figure 3 shows the number of NIH Standard CRADAs per 1000 unit of the BTK index. The closing value of the BTK index fell from 171 in 1992 to 82 in 1994, recovered, and began a sharp rise in 2012, ending at 5739 at the end of 2020. The number of standard NIH CRADAs executed, per BTK share values, was considerably higher during the period of the reasonable pricing clause. Despite significant increases in the NIH budget, the number of Standard CRADAs per stock market resources fell steadily, from 2000 to 2020.

Figure 3: NIH Standard CRADAs per 1000 value of NYSE BTK index



One can also examine the changes in the BTK index relative to changes in NIH policies. Dr. Harold Varmus signaled his interest in eliminating the reasonable pricing clause in 1994, and formally announced its elimination on April 11, 1995. Neither event moved the BTK index in any significant way. The BTK Index closed at 80.83 on January 3, 1995, the first day of trading in 1995, on 78.09 on April 10, 1995 and 78.09 on April 11, 1995, falling below 77 in following weeks.

Conclusion

The most specious claims regarding the interest in NIH CRADAs are those that add the materials CRADA numbers to the standard CRADAs to claim there was a dramatic increase in the CRADAs issues, due to the elimination of the reasonable pricing clause. The materials CRADAs were an entirely different instrument, and one almost abandoned by the NIH by 2019. Critics of march-in proceedings and the reasonable pricing clause in general have misrepresented the CRADA statistics, and ignored the body of evidence establishing that many factors determine the number of CRADAs executed, and the period when the reasonable pricing clause was in place does not provide compelling evidence regarding the chilling of collaborations.

ANNEX 1

The policy to require language in CRADA and exclusive license agreements was first implemented in 1989 by the Public Health Service (PHS), the parent organization to the NIH, under the Administration of President George HW Bush, when Bernadine Healy was the Director of the NIH. The language in CRADA and license agreements was reasonably vague, and was described by the NIH (National Institutes of Health 1994) as follows:

In 1989 the Public Health Service (PHS), NIH's parent organization, adopted a policy statement expressing concern that, because of the public investment in the research that leads to a product licensed under a CRADA, there should be "a reasonable relationship between the pricing of a licensed product, the public investment in that product, and the health and safety needs of the public." Exclusive licenses for NIH intellectual property rights may require the company to support this relationship with "reasonable evidence."

In April 1995, Dr. Varmus, then Director of the NIH under President Bill Clinton, announced that the NIH would abandon the policy and no longer include the requirement in CRADA agreements. (Leary 1995)

Bibliography

Leary, Warren E. 1995. "[U.S. Gives Up Right to Control Drug Prices.](#)" *New York Times*, April 12, 1995.

National Institutes of Health. 1994. *Reports of the NIH Panels on Cooperative Research and Development Agreements: Perspectives, Outlook and Policy Development. July 21, 1994 and September 8, 1994.*

ANNEX 2. Number of NIH CRADAs executed and NIH appropriations, by fiscal year, and closing value of BTK stock index by calendar year

Year	NIH only, Standard CRADAs, reported by OTT, as executed, by fiscal year	NIH only, Materials CRADAs, reported by OTT, as executed, by fiscal year	NIH Appropriations by FY	Calendar year close, BTK index
1985	1		\$5,149,459,000	
1986	4		\$5,262,211,000	

1987	10		\$6,182,910,000	
1988	20		\$6,666,693,000	
1989	42		\$7,144,764,000	
1990	32		\$7,576,352,000	
1991	26		\$8,276,739,000	
1992	30		\$8,921,687,000	170.6
1993	41		\$10,335,996,000	115.8
1994	31		\$10,955,773,000	81.5
1995	32		\$11,299,522,000	133.8
1996	44	43	\$11,927,562,000	144.3
1997	32	121	\$12,740,843,000	162.4
1998	43	106	\$13,674,843,000	185.1
1999	48	78	\$15,629,156,000	391.4
2000	34	75	\$17,840,587,000	634.3
2001	44	76	\$20,458,556,000	580.6
2002	34	67	\$23,321,382,000	338.2
2003	36	48	\$27,166,715,000	490.1
2004	43	44	\$28,036,627,000	544.3
2005	39	41	\$28,594,357,000	679.8
2006	22	29	\$28,560,417,000	754.3
2007	23	21	\$29,178,504,000	786.5
2008	33	39	\$29,607,070,000	634.0
2009	33	44	\$30,545,098,000	948.4
2010	39	27	\$31,238,000,000	1305.7
2011	40	28	\$30,916,345,000	1076.4
2012	57	36	\$30,860,913,000	1516.2
2013	46	31	\$29,315,822,000	2342.4
2014	45	34	\$30,142,653,000	3465.6
2015	73	28	\$30,311,349,000	3816.3
2016	89	26	\$32,311,349,000	3075.0
2017	93	18	\$34,300,999,000	4279.1
2018	63	19	\$37,311,349,000	4149.7
2019	74	14	\$39,313,000,000	5067.5
2020	58	29	\$41,636,570,000	5739.0

Number of CRADAs: <https://www.ott.nih.gov/reportsstats/technology-transfer-statistics>
NIH Appropriations: https://officeofbudget.od.nih.gov/approp_hist.html