

KEI response to four GAO questions, June 22, 2020

1. To what extent is there a need for greater transparency about what intellectual property HHS owns and how it manages it?

There is an enormous need for greater transparency of the licensing of intellectual property that HHS owns and funds, as well as related information regarding the costs of clinical trials and the role of federal subsidies and incentives for the development of biomedical technologies.

Throughout KEI's 40 years of experience dealing with these issues, our efforts to obtain information from HHS about the intellectual property it owns and manages have been met with unjustified resistance and secrecy, and this lack of transparency has only grown worse over time, to the extent that HHS undertakes actions that protect the companies that development biomedical products and services and their investors at the expense of public.

Undermining the ability of the public to make informed comments on prospective exclusive licenses

In the course of commenting on proposed exclusive NIH patent licenses under 35 U.S.C. 209, we often reach out to NIH technology transfer officers to gain basic information that will allow us to evaluate the proposed licenses and whether or not they comply with the criteria listed at 35 U.S.C. 209(a). We ask simple, noncontroversial questions such as who are the principal officers of the licensee, how much the government spent to develop the technology, what grants and clinical trials are associated with the technology, and, most importantly, how the NIH evaluated the criteria for granting an exclusive license under 35 U.S.C. 209(a). NIH tech transfer officers refuse to answer the majority of our questions, falsely claiming that the information we are seeking is irrelevant and and/or they have already answered the questions--even though that is not true, because the questions clearly relate to the statutory criteria and are specific to a new license being proposed by the NIH.

A recent example of the NIH's lack of transparency related to its licensing activities involved a proposed license to Retargeted Therapeutics, which, according to the NIH, is incorporated in Delaware.¹ According to Delaware's online business records, however, there is no company of that name incorporated in Delaware, nor does Retargeted maintain a website, Twitter handle, or

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<https://www.federalregister.gov/documents/2020/05/22/2020-11036/prospective-grant-of-an-exclusive-patent-license-antibody-based-therapy-for-the-treatment-of-cd20>.

social media presence of any kind that would allow the public to evaluate whether the company is capable of developing a valuable publicly-owned invention into a product that will benefit patients. We repeatedly asked the technology transfer officer responsible for the license about the identity of Retargeted Therapeutics principal officers -- something that is nonconfidential and would be public knowledge had Retargeted been registered to conduct business in Delaware or any other state. She refused to answer prior to the deadline for filing comments, did not address the question in her response to our comments, and did not address the question in two emails sent to her after the close of the comment period. But this was just one of a series of cases where the NIH has been unwilling to provide information about the entities seeking exclusive license.

There are many cases where the firm has no web page, or a simple web page that provides almost no information about the company. We don't in general object to the NIH giving licenses to new start up ventures, but when the firm has almost no public presence, the NIH should be willing to share information about who owns and runs the firm. Among the questions the NIH has refused to answer are if the principals in the firm are former NIH employees.

Ownership of firms

Sometimes the NIH will refer to a licensee as a US company, when it is clearly just a local subsidiary of a company in China, Switzerland, Poland, France or elsewhere.

Trial Costs

Another typical issue concerns the secrecy around R&D costs for bringing an invention to market. For example, for one license to Gilead/Kite for a CAR T treatment, the NIH already was conducting a trial involving 76 patients, on its own campus. At that time two CAR T treatments had been approved by the NIH, one on the basis of clinical evidence from 63 patients², the other from 100 patients. The NIH refused to disclose what it was spending on the 76 patient trial. This information was relevant to the issue of how much Gilead would have to spend to obtain FDA approval for this treatment, and thus, how many years of exclusive rights were necessary as an incentive, but also, it would shed light on the R&D costs for the first two FDA approved CAR T treatments, at a time when the price was controversial. Novartis was claiming it had spent a billion on Kymriah, and access globally was limited by the high price. People often complain about the lack of transparency of R&D costs, and express frustration that companies won't share reliable data. But in this case, and in several other cases, it was the NIH, a federal agency, refusing to disclose the costs. This is appalling.

In the past, the NIH was much more forthcoming on R&D costs for trials it had funding on specific treatments. During the controversies over the prices of Taxol, a cancer drug licensed to

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<https://www.fda.gov/news-events/press-announcements/fda-approval-brings-first-gene-therapy-united-states>

Bristol Myers Squibb by the National Cancer Institute, the NIH shared data on the clinical trial costs associated with several drugs under development,³ and the National Cancer Institute used to publish, annually, the costs of trials it funded by phase, including the average per patient costs.

Even today, the National Cancer Institute (NCI) publishes annually a figure for the amount of money in its budget spent on clinical trials, in its NCI Budget Fact Book. For Fy 2017, for example, the outlay was \$806.6 million. It is unlikely that the NIH can publish such a number without more granular data on the costs of specific trials⁴.

Recently, KEI received from the Veterans Administration, from a FOIA request, data on more than 800 clinical trials it has funded, including the costs of trials, the trial identifier and title, the collaborators, phase, enrollment and six other meta data points. It defies belief that the NIH has no idea of the costs of trials that it funds, including trials it conducts on its own campus. This data is extremely important for evaluating the reasonableness of pricing and the terms of exclusivity in licenses.

BARDA has also been non-transparent, but not always. In some cases, BARDA issues press releases stating the amount of the money it will provide to conduct clinical trials, build factories or other items, for firms, in connection with specific therapies. But in response to a FOIA request for the costs of clinical trials conducted in support of the 42 or more FDA approvals for products addressing CBRN, PI, and EID threats that received support from BARDA, BARDA first promised KEI extensive disclosures, but then consulted with the NIH, and the NIH advised them to withhold almost everything. What we received was the dollar amount for several clinical trials, but BARDA redacted the type of product, and the enrollment numbers for the trial, so the information was almost worthless, and certainly useless for determining the average per patient costs in clinical trials.

Failures in reporting government rights in HHS funded inventions

Another issue with respect to what intellectual property HHS owns and how it manages is how it does not correct failure to disclose government rights to publicly-funded inventions, in patents. We have sent multiple letters to the NIH Office of Extramural Research outlining compelling evidence for why certain patents likely received government funding but do not make the required disclosures, and as far as we are aware, the NIH has never taken title to a subject invention covered in patents that failed to disclose government funding, as suggested by evidence submitted by KEI. A Briefing Note about the issue is available [here](#) and our webpage on the issue is [here](#).

³ See: Exclusive Agreements Between Federal Agencies and Bristol-Myers Squibb Co. for Drug Development: Is the Public Interest Protected? Hearings. 102nd Congress. Serial No. 102-35.

⁴ <https://www.cancer.gov/about-nci/budget/fact-book/archive>

Failures in responding to requests under the Freedom of Information Act

We have also experienced significant, unjustified obstacles to obtaining information about federally-owned or funded inventions from HHS under the Freedom of Information Act (FOIA). For example, the NIH refuses to disclose the royalties earned by NIH inventors from NIH patent licenses, and asserts that it does not maintain records that disclose the cost of NIH clinical trials, because (according to the NIH) the NIH does not allocate resources by trial. We submitted a request in September 2019 for all NIH records that disclose the NIH's recordkeeping procedures for the budgets and costs of intramural clinical trials, and the request is still outstanding. When we submitted a request to the National Cancer Institute for documents disclosing the components of the costs of intramural clinical trials, we were told that the National Cancer Institute Center for Cancer Research, as well as the National Clinical Center, both provided funding for the trials, but only the Clinical Center provided us cost information, so the information was incomplete. We appealed that decision, and the response is past due, per the FOIA statutory deadline.

Another request from Fall of 2019 for all applications for waivers of the U.S. manufacture requirement under 35 U.S.C. 204 and any decisions concerning those waivers is also still outstanding.

We are appealing a FOIA request related to 40 clinical trials that were funded by BARDA. BARDA gave us a table containing the costs of the clinical trials, the type of product, and the patient enrollment numbers. The type of product investigated in the trial and patient enrollment numbers were redacted as confidential information or trade secrets.

These are just a few examples of the barriers we face in obtaining information from HHS under the Freedom of Information Act.

2. What information about HHS-owned patents and related licenses should be made available to the public and policymakers that is currently unavailable to them?

For each biomedical exclusive license granted by a federal agency:

- An estimate of the amount of money the federal government has spent on research and development related to the patented invention, with a narrative explaining the role of government funding at each stage of development.
- An analysis of the availability of regulatory exclusivities for both test data on the treatment of FDA-defined **orphan diseases**.

- An analysis of the likelihood that a product using the invention in the licensed field of use will qualify for a U.S. FDA priority review voucher.
- An estimate of the investment required for clinical trials necessary for FDA approval.
- The identity of the principal officers and significant shareholders of any proposed exclusive patent license, when such information is not otherwise available from SEC filings or a company web site.
- The text of any unpublished patent application related to a proposed exclusive license.
- A description of the analysis the NIH performed in concluding that an exclusive license is a necessary incentive under 35 U.S.C. 209(a)(1).
- A description of the analysis the NIH performed in concluding that the scope of exclusivity is not broader than the necessary incentive under 35 U.S.C. 209(a)(2).
- The terms of exclusive licenses, including the years of exclusivity, the geographic scope of exclusivity naming the all countries where the NIH intends to file patent applications and license them to the prospective licensee, and the terms of royalty payments to the NIH. The NIH should disclose the proposed material terms of prospective exclusive patent licenses, especially the years of exclusivity, in the Federal Register notice proposing the licenses. Once the licenses are granted, it should publish the full license text.
- The identity of applicants for the license.

Also:

- All applications for waivers of the U.S. manufacturing requirement under 35 U.S.C. 204 and all determinations concerning those waivers.
- A list of all CRADAs executed by HHS, with metadata such as the year executed, collaborating company, and CRADA number.
- The text of all “Other Transactions” executed by NIH and BARDA, with any provisions regarding the allocation of rights in intellectual property and data unredacted.

Public Notice Requirements

The notice and comment period under 35 U.S.C. 209(e) should be a minimum of 60 days, which was the original minimum for the Bayh-Dole Act until 2000, unless there is a compelling reason for a shorter period.

The changes to the minimum days for public notice on licenses was included in the November 1, 2000, Public Law 106-404, titled, the Technology Transfer Commercialization Act Of 2000. The act also eliminated the public notice requirement for inventions made under a cooperative research and development agreement (CRADA). In recent years, federal agencies in HHS have used this discretion to eliminate public notice of exclusive licenses on CRADA inventions.

CRADA notices

The NIH and other federal agencies have also largely stopped providing notices of the opportunity for or for the public to comment on the prospective offer of a CRADA. The agency sometimes names and provides commentary on a handful of CRADAs in the OTT annual reports, but does not publish a list of such agreements. The NIH has required KEI to submit FOIA requests for the names of the CRADAs, and initially refused to provide such a list on the grounds that the NIH would have to generate the record from its iEdison system, and was not required to do so under FOIA. KEI told the NIH that a failure to provide a list of CRADAs would leave KEI no choice but to FOIA all of the CRADAs. When the NIH continued to block the least of a list of the CRADAs, KEI FOIAed all of the CRADAs. That FOIA was then rejected on the grounds that we could have FOIAed a list of the CRADAs, before asking for all of them. KEI shared information with the FOIA office from Mark Rohrbaugh, refusing to prove such a list, and the NIH subsequently has provided a list, which KEI updates from time to time, with considerable delays in FOIA processing, and publishes here: <http://drugdatabase.info/cradas/>.

The sharp decline in NIH Federal Register notices regarding CRADA is illustrated in Tables 1 and 2.

Table 1: NIH notices by calendar and fiscal year, and executed Standard CRADAs by fiscal year

| Year | Notices, Calendar Year | Notices, Fiscal Year | NIH Standard CRADAs, reported by OTT as executed, by fiscal year |
|-------------|---------------------------------------|---------------------------------|---|
| 1995 | 9 | 9 | 32 |
| 1996 | 11 | 10 | 44 |
| 1997 | 15 | 16 | 32 |
| 1998 | 17 | 11 | 43 |
| 1999 | 19 | 23 | 48 |
| 2000 | 20 | 22 | 34 |
| 2001 | 17 | 17 | 44 |
| 2002 | 5 | 4 | 34 |
| 2003 | 4 | 6 | 36 |
| 2004 | 10 | 7 | 43 |
| 2005 | 16 | 20 | 39 |
| 2006 | 2 | 2 | 22 |
| 2007 | 2 | 2 | 23 |
| 2008 | 4 | 4 | 33 |

| | | | |
|------|---|---|----|
| 2009 | 2 | 1 | 33 |
| 2010 | 3 | 4 | 39 |
| 2011 | 3 | 2 | 40 |
| 2012 | 0 | 1 | 57 |
| 2013 | 4 | 4 | 46 |
| 2014 | 1 | 1 | 45 |
| 2015 | 0 | 0 | 73 |
| 2016 | 4 | 2 | 89 |
| 2017 | 1 | 3 | 93 |
| 2018 | 0 | 0 | 63 |
| 2019 | 0 | 0 | 74 |

Table 2 summarizes the declines in NIH notices on CRADAs as a percentage of NIH executed CRADAs since 1995⁵, in five-year periods.

Table 2: Percentage of NIH CRADA notices to number of executed CRADAs, per 5 year period

| 5 year period | Notices, Calendar Year | Notices, Fiscal Year | NIH CRADAs, reported by OTT, as executed, by fiscal year* | Notices / CRADAs (fiscal years) |
|---------------|------------------------|----------------------|---|---------------------------------|
| 1995 to 1999 | 71 | 67 | 199 | 34% |
| 2000 to 2004 | 56 | 56 | 191 | 29% |
| 2005 to 2009 | 26 | 29 | 150 | 19% |
| 2010 to 2014 | 11 | 12 | 227 | 5% |
| 2015 to 2019 | 5 | 5 | 392 | 1% |

Note that Dr. Francis Collins became the Director of the NIH on August 17, 2009, and the frequency of notices subsequently declined sharply.

Notices of patents issued under CRADA agreements

When asked about the fact that since 2016, the NIH has executed more exclusive patent licenses than are noticed in the Federal Register, Mark Rohrbaugh explained that the exclusive licenses granted included patents related to CRADAs, and the NIH was not obligated to notice

⁵ The searchable FederalRegister.Gov has limited copies of CRADA notices prior to 1995.

licenses for CRADA related patents. Rohrbaugh also stated that the elimination of the requirement for notice and comment on the exclusive licenses was one of the attractions of the CRADAs themselves. From fy 2016 to fy 2019, there were 23 more exclusive patent licenses granted than public notices and requests for comments on exclusive patent licenses. This can be compared to the period from fy 2006 to fy 2015, when there were 84 more notices than executed exclusive patent licenses.

There are several reasons for the public to be aware of exclusive licenses granted by the NIH when there is a CRADA, and also to have the opportunity to comment on the grant and terms of the license. The federal agency has the discretion to license on a non-exclusive basis, when at least one of the inventors is a federal employee, to limit the years of exclusivity, and to include other provisions in the license that will protect the public, such as provisions on pricing, which the agency has in fact used, in the past, as well also provisions relating to the field of use, geographic scope of the license, and the research uses permitted. It would be better if the public was given the opportunity to comment on proposed exclusive licenses relating to CRADAs, particularly in cases where the government has performed significant development work, where the inventions possibly relate to multiple products, and where the affordability of and access to the invention is important.

3. What are the benefits of disclosing this information and what is the harm to the public interest in not having it in the public domain?

Benefits of Transparency over HHS Licensing Activities:

Having information about NIH patent licenses is vital to an understanding of whether or not NIH technology transfer activities comply with the statutes governing them, including but not limited to the Bayh-Dole Act. Section 209 of the Bayh-Dole Act permits exclusive licenses of federally-owned inventions only when exclusivity is a necessary incentive and requires that the scope of exclusivity is not broader than the incentive needed to induce a company to bring the patented invention to market. 35 U.S.C. § 209(a)(1)-(2). 35 U.S.C. § 209(e) obligates federal agencies that intend to grant an exclusive patent license to notify the public, allow a period of time to comment, and consider all timely comments. The public's ability to meaningfully comment on proposed licenses will be limited if NIH is allowed to continue to withhold pertinent information from the public, including such obvious details as the identify of the persons controlling and owning the firm seeking the license, the proposed years of exclusivity, royalties, field of use and geographic scope of the license, and provisions if any (including greater transparency and clarity regarding the lack of measures if there are none), relating to the statutory requirement that the benefits of the invention be made "available to the public on reasonable terms."

The interests in enabling the public to make informed assessments of NIH's licensing activities is compelling, because NIH licenses are skewed toward the interests of the pharmaceutical industry by maximizing the scope of rights given to companies, which will enlarge the monopolies that companies can claim on publicly-funded inventions, leading to higher prices and delaying the entry of generic competition.

HHS maintains a position that is not supported by the text of the Bayh-Dole Act, which is that its only obligation when conducting technology transfer is to ensure that inventions are developed into products that are available to the public, regardless of the terms on which they are made available. This issue has received more public attention in the context of march-in requests, but it translates toward HHS's attitude and conduct toward exclusive licenses under 35 U.S.C. 207 and 209. 35 U.S.C. 209(a)(1)-(2) states in pertinent part as follows:

- (a) Authority.—A Federal agency may grant an exclusive or partially exclusive license on a federally owned invention under section 207(a)(2) only if—
 - (1) granting the license is a reasonable and necessary incentive to—
 - (A) call forth the investment capital and expenditures needed to bring the invention to practical application; or
 - (B) otherwise promote the invention's utilization by the public;
 - (2) the Federal agency finds that the public will be served by the granting of the license, as indicated by the applicant's intentions, plans, and ability to bring the invention to practical application or otherwise promote the invention's utilization by the public, and that the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application, as proposed by the applicant, or otherwise to promote the invention's utilization by the public[.]

This is clearly a limited authority, and allows NIH to grant exclusivity only when it is a necessary incentive. Despite that clear directive, NIH technology transfer officers assert that the NIH may grant an exclusive license whenever exclusivity will help ensure that an invention is brought to market. That does not comport with the statutory standard, which is "necessary," not "helpful."

35 U.S.C. 209(a) also mandates a case-specific analysis, because every invention is unique and has a different value to investors. In other words, the necessary incentive to bring one invention to market, which is in its very early stages of development, would be very different from the incentive needed to induce a company to bring an invention to market that is being tested in a clinical trial sponsored or conducted by the NIH.

The NIH fails to conduct the necessary case specific analysis. No matter the development stage of the technology or other relevant factors, **the result from the NIH is always the same.** It grants the broadest possible rights to inventions. The NIH substitutes unfounded assumptions for the statutorily-required analysis. Mark Rohrbaugh, Special Advisor for Technology Transfer to the NIH, issued to KEI a letter in which he stated that the ***NIH always grants exclusive licenses, for life of patent, because companies require those terms.*** NIH technology

transfer officers have told us that they are not aware of instances in which NIH granted a license for a term of exclusivity shorter than life of patent.

As originally enacted, the Bayh-Dole Act only allowed exclusivity for 5 years, and in the past the NIH has granted licenses for shorter than life of patent and used the licensee's desire for an extension as leverage to exact valuable concessions for the public. For example, the cancer drug cisplatin (cisplatinum) was licensed to Bristol-Myers Squibb (BMS).⁶ BMS petitioned HHS for and was granted an extension of the original exclusivity period to five years from the first commercial sale. Before that exclusivity period expired, BMS requested a seven-year extension from HHS. Several other companies competed for the license. HHS negotiated a five-year extension of the license term with BMS, but in return BMS was required to lower the price of cisplatin by 30 percent and contribute \$35 million to cancer research directed by the NIH staff. HHS explained its rationale for granting a five-year extension, rather than the seven years requested by BMS, as follows:

[G]iven the fact that Bristol has already had almost five years of an exclusive market for cisplatinum, and that the market for cisplatinum is expected to expand dramatically in the next few years, we believe that five years of additional exclusivity is a sufficient incentive to induce Bristol to undertake the commitments which it has offered and is the best decision in the public interest.

This is the type of analysis that the NIH is required to perform, under section 209 of the Bayh-Dole Act, but fails to engage in.

In another example involving a National Cancer Institute invention, the NIH licensed the HIV drug ddI (didanosine) to BMS. The license term was initially exclusive, but gave the NIH the option of making the license nonexclusive before the expiration of the NIH patents, which the NIH exercised in 2001. A term of exclusivity less than the life of patent did not chill investment - several companies competed for the license. Around the time of the ddI license, the NIH frequently granted 10 year periods of exclusivity.

The NIH's failure to honor its statutory obligations when licensing federally-owned inventions can lead to negative outcomes for U.S. taxpayers and consumers, when it results in unnecessary and overbroad monopolies. Transparency over its licensing activities can lead to political pressure on the NIH to bring its conduct in line with the statutory standard, or it can support legislative reforms.

Transparency over Clinical Trial Costs

Transparency over the role of public funds in the development of biomedical inventions will benefit the public because it is a foundational issue that is central to the debate over drug

⁶ 48 Fed. Reg. 53177 (Nov. 25, 1983).

prices. Many discussions of the costs of drug development cite a report from the Tufts Center for the Study of Drug Development (CSDD) stating that drug development costs on average \$2.8 billion in today's dollars, and that claim is widely accepted, although the underlying data has never been disclosed and the CSDD accepts money from the pharmaceutical industry. There is thus a need for reliable data about clinical trial costs. Publishing the costs of publicly-funded trials is not a controversial idea, does not threaten any legitimate confidential business interests, and is feasible to do. The NIH published clinical trial costs on its website for a period of time, and the California Institute of Regenerative Medicine (CIRM) discloses on its website the amount of money it spends on the clinical trials that it sponsors as well as enrollment numbers, which provides the enrollment and funding amount for each clinical trial it funds. See <https://www.cirm.ca.gov/clinical-trials>.

Issues with Current Disclosure Mechanisms

Online databases such as projectreporter.nih.gov and ClinicalTrials.gov disclose limited information related to the federal government's role in funding the development of biomedical inventions, but there are serious limitations on those databases, and they are not a reliable method of researching biomedical development costs. Annex 1 contains a detailed explanation of the limitations and issues with the current methods of tracking the public role in funding biomedical inventions.

Harm to the Public by Not Having this Information in the Public Domain

The harm to the public caused by the lack of transparency over the federal government's role in funding biomedical research and development is that the public lacks the information necessary to have a fully informed debate on these issues. Attempts at reforms are met with the threat that any meaningful restraints on the monopoly rights of the pharmaceutical industry over federally-funded biomedical products will destroy innovation. We do not disagree that some level of incentives and profitability is needed for companies to make the investments necessary to bring biomedical products to market, but without greater transparency, the public will not be able to assess if society is over incentivizing or effectively incentivizing investment.

4. What are your views on how HHS can/should balance the statutory requirements to protect proprietary information (e.g., the Trade Secrets Act) with greater transparency about its management of government-owned intellectual property?

None of the information that we are seeking and that HHS has withheld is a legitimate "trade secret." Companies will always prefer non-disclosure but that preference should not be confused with protection of information that meets the legal definition of a trade secret.

HHS will assert that disclosure of any information that the pharmaceutical industry wishes to keep confidential will threaten its technology transfer program. But with the valuable incentives provided by HHS we find it highly unlikely that companies will walk away from these opportunities.

The NIH is notably less transparent in its licensing activity and in reporting R&D outlays on licensed properties, than are the companies themselves, through disclosures to the Securities and Exchange Commission (SEC), when the outlays or licensing terms are material to the value of a stock. The SEC disclosure requirements are designed to serve the interests of investors in publicly traded stocks, and do not require disclosure for companies that are not publicly traded, or when the outlays on R&D or terms of licenses are not significant enough to influence share prices, as may be the case for some larger firms, so the HHS policies on disclosures are important. The fact that under Generally Accepted Accounting Principles (GAAP) companies are required to make disclosures of trial costs and the costs of acquiring licenses to compounds, know-how and patented inventions, and reporting income streams by product and geographic area, when these are material to the value of the stock, not to mention the compensation of executives and board members, and principal shareholders, illustrates the hostility of the NIH toward transparency, when the public is funding the R&D.

Annex 1, Limitations in Public Databases Disclosing Information Relevant to the Public Role in Funding Biomedical Inventions.

Searching Clinical Trial Costs on RePORTER

Searching for clinical trials costs, or at least the total cost of the NIH grants that funded clinical trials, on NIH's RePORTER search engine is a difficult if not an impossible task. Often, RePORTER does not allow a researcher to match a clinical trial to only the NIH grants that funded the trial. In other words, there will not be a direct, one to one correlation between the grant and the trial. Also, while RePORTER allows users to search by National Clinical Trial (NCT) number, a search for one trial often returns a large number of grant results, many of which bear no relation to the trial number searched, making it impossible to isolate the funding that supported a particular trial.

The table below illustrates the challenges in using RePORTER to obtain data on trial costs, for five clinical trials. In one egregious example, a search for projects related to NCT00004070, "Gene Therapy in Treating Patients With Unresectable, Recurrent, or Refractory Head and Neck Cancer," returned **960** matching grants, most of which had nothing to do with that trial. If RePORTER were accurate, and all 960 grant results associated with NCT00004070 actually funded the trial, then a single, year-long clinical trial consisting of only seven patients received \$244,699,874 in NIH funds - an absurd result.

Example: Searches for specific clinical trials and projects matching that search criteria

| Trial Searched | Number of Grant Results | Total Cost |
|----------------|-------------------------|---------------|
| NCT00004070 | 960 | \$244,699,874 |
| NCT01475058 | 745 | \$239,938,136 |
| NCT03896568 | 626 | \$215,091,759 |
| NCT00002748 | 419 | \$130,331,260 |
| NCT01869270 | 154 | \$13,666,254 |

A search for NCT00004070 along with the terms “head” and “neck” in all fiscal years returns four matching results, totaling \$859,571 in grants, an amount at least remotely consistent with the expected budget of a phase 1/2 clinical trial with 7 patients enrolled. However, limiting the search results by keywords involves some level of speculation regarding which projects are relevant, and will often result in including grants that were not relevant, or missing ones that were.

It appears that RePORTER returns all core projects cross-linked to the trial number in any way, such as including grants by the same principal investigator on different topics, instead of just the specific grants that funded the clinical trial and the specific years when the trial was funded.

We ask that the clinical trial search be improved to be more precise regarding the grants that are connected to a specific trial. Ideally, of course, a search using the ClinicalTrials.gov ID search field should only return as results the projects that were directly related to that trial.

Budget for clinical trials that are active

As of November 2019, RePORTER listed 20,859 unique clinical trials funded by the NIH. Of these trials, 13,201 appeared as either completed (12,019), suspended (97), or terminated (1,086). There were 6,621 trials collectively referred to here as “active” clinical trials since they were either active, not recurring (1,888), enrolling by invitation (286), recruiting (3,798), or available (2) at the time this research was conducted. The remaining are mostly trials that were withdrawn, withheld, or their status is unavailable.

The NIH Project RePORTER only provides information about costs that have been incurred in ongoing or previous fiscal years. For this reason, the RePORTER database is of little use to estimate the cost of active clinical trials, even if we are able to match one trial to one specific grant. The vast majority of NIH grants that fund clinical trials are multi-year grants, and for active clinical trials it is difficult to verify, based on a project RePORTER search, whether the NIH will continue to allocate funds under that specific grant or what is the full amount that will be allocated under that grant once it has concluded.

The NIH can add a field in RePORTER reflecting the amount of money in the grant that is the estimated budget for grants that fund clinical trials. With this information, if a trial is still active we could still be able to estimate projected cost per patient, based on its budget and targeted enrollment.

But even if the searches are better designed to match trials with costs, many grants cover both expenditures that are relevant to a trial and those that are not, and also do not report on co-funding of trials by others, and may lack information about the expected future costs of ongoing trials.

Given the challenges of and limits to providing the public with accurate trial cost information through RePORTER, the NIH should maintain a separate database reporting on the trials it funds in whole or in part.

Searching for clinical trial cost data using ClinicalTrials.Gov

Another NIH online database containing information about trials is ClinicalTrials.gov. Trial listings on clinicaltrials.gov contain a section titled “More information,” which includes information about “U.S. NIH Grant/Contract[s]” related to a specific trial, a core project, and a link to RePORTER.

The hyperlink, for example, for NCT00004070, directs one to the 960 matching results in RePORTER. Again, the number and the description of most of the results make it clear that this is not targeted in a useful way to the clinical trial identified as NCT00004070.

We expect that fixing the problem described in the previous section would also narrow down the number of projects hyperlinked to RePORTER from ClinicalTrials.gov. That would be helpful. Ideally, however, the ClinicalTrials.gov website should itself have information about the cost of clinical trials. This is possible under current statutory authority in 42 U.S.C. § 282(j).

42 U.S.C. § 282(j), inserted by Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA), creates the core standard for the registration of certain clinical trials on ClinicalTrials.gov. The information subject to reporting requirements is specified under 42 U.S.C. § 282(j)(2)(A)(ii), and comprises: a) descriptive information, such as a brief summary and study design; b) recruitment information, including eligibility criteria and recruitment status; c) location and contact information, such as the name of the sponsor; and d) administrative data, including a unique protocol identification number. Currently, 42 U.S.C. § 282(j)(2)(A)(ii) does not require reporting information on the cost of the clinical trials. Importantly, 42 U.S.C. § 282(j)(2)(A)(iii) authorizes the Secretary of the Department of Health and Human Services to modify the clinical trial information disclosure requirements if it provides “a rationale for why such a modification improves and does not reduce such clinical trial information.”

A modification to include information regarding the budget or actual outlays for a clinical trial will clearly be useful, and highly relevant to those studying the economics of research and development of medical technologies and the justification of prices for those technologies.

Searching for patents using RePORTER

RePORTER allows users to perform searches based on over 20 different search fields. None of those fields allows users to perform searches based on patent numbers. RePORTER does have information about patents, however. Users performing a search with any other search criteria can review the “Patents” tab in the search results to determine if there are any patent numbers associated with the term searched. For example, a query based on project number R01AI069350 will return four patents related to that project: 10179112, 9782357, 9163248, and 8449875. Conversely, a search using any of these four patent numbers will not return the project number R01AI069350. Although RePORTER provides a text search field, we have performed several searches using patent numbers that we know are related to specific projects listed in RePORTER, and these searches have not generated any hits.

One way to make RePORTER more helpful is allowing searchers by patent number.

We are aware that the ExPORTER Data Catalog provides a dataset with patents and NIH project numbers. This dataset is a useful resource, and we value the fact that the NIH has made it available in an open data format. However, we believe many users are not aware that this dataset exists, and do not have the skills to use it. Moreover, although the ExPORTER data file makes it possible to locate patents and a related project number, users have to perform additional steps in RePORTER to obtain further information. For example, ExPORTER does not identify the fiscal year of the grant associated with a patent. Some grants extend over 20 years.

Incomplete Patent Information Reported by the iEdison

All patents reported through the iEdison system and available at RePORTER should also have government interest statements disclosed on the patents themselves. Nevertheless, we are aware of hundreds of patents available in the RePORTER database that lack government interest statements, both in the text searchable version and in the certificates of correction. The table below shows examples of patents and related government grants that lack government interest statements. We are able to provide a larger list with hundreds of patents, if necessary.

Example: Patents listed in RePORTER, without government interest statements

| Patent ID | Project ID | Patent Assignee | Grant Disclosed in Text GOVT | Grant Disclosed in CofC GOVT |
|--------------------------|-------------|---------------------------------------|------------------------------|------------------------------|
| 10222392 | R21CA120742 | The Johns Hopkins University, Pioneer | No | No |

| | | | | |
|--------------------------|-------------|---|----|----|
| | | Hi-Bred International | | |
| 10213503 | U54AI057156 | University of Texas System | No | No |
| 10209325 | R01EB007829 | Siemens Healthcare GmbH The Johns Hopkins University | No | No |
| 10196392 | R01GM118557 | Vanderbilt University | No | No |
| 10196369 | R03MH097522 | Sanford Burnham Prebys Medical Discovery Institute | No | No |

The fact that there are hundreds of patents that are listed in RePORTER but that lack government interest statements (something that could be verified by searching for these patents in U.S. Patent and Trademark Office (USPTO) databases), is indicative of how little effort the NIH puts into enforcing the disclosure provisions in the Bayh-Dole Act.

We have asked the NIH to provide us with information about their efforts to enforce the Bayh-Dole Act reporting requirements, including the actions the NIH is taking to make sure that patents reported via the iEdison system and listed in the RePORTER database also have government interest statements listed in the patent texts.

KEI has also asked the NIH to what extent, the NIH is in collaboration with the USPTO to ensure that patents disclosed in the RePORTER database also have government interest statements.