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Via email: uri.reichman@nih.gov

Re: "Prospective Grant of Exclusive Patent License: Capsid-Free AAV Vectors, Compositions, and Methods for Vector Production and Gene Delivery," 84 FR 51171

Dear Dr. Reichman:

Knowledge Ecology International (KEI) and the Union for Affordable Cancer Treatment (UACT) are writing to object to the prospective licenses described in the Federal Register Notice, "Prospective Grant of Exclusive Patent License: Capsid-Free AAV Vectors, Compositions, and Methods for Vector Production and Gene Delivery," located at 84 FR 51171[1] (the "Notice").

The Notice concerns two prospective licenses in a new gene therapy platform discovered by National Institute of Health (NIH) and French scientists. The first is a fully exclusive license to Generation Bio, Inc., a company that was founded by Robert Kotin, one of the NIH inventors of the technology. The second is a co-exclusive license to Generation Bio and Spark Therapeutics.

Gene therapies have attracted public attention, due to their innovative nature and high cost. Spark Therapeutics's Luxturna costs $850,000. Zolgensma, a gene therapy to treat a rare pediatric disorder known as spinal muscular atrophy, costs $2.1 million. Generation Bio's website and Twitter handle discuss the company's plans to develop gene therapies to treat rare pediatric disorders. The prospective licenses will likely present similar price and access issues. We also note the potential stifling effect of granting exclusive licenses in a gene therapy platform, and question whether the NIH has properly analyzed whether exclusive licensing was necessary.

[1] 84 Federal Register 51171 (Sept. 27, 2019), available at https://www.federalregister.gov/documents/2019/09/27/2019-20992/prospective-grant-of-exclusive-patent-license-capsid-free-aav-vectors-compositions-and-methods-for.

We support the development of new biomedical inventions to cure genetic disorders. When, however, the NIH expends $40 billion dollars of taxpayer money each year to support such research and development, it must act as a responsible steward of the public's investment.

The NIH views its mission as promoting the commercialization of taxpayer-sponsored research - without regard for other concerns. Yet Congress limited the NIH's authority to transfer the fruits of public research to the private sector, per the criteria outlined in Section 209 of the Bayh-Dole Act. The NIH may not ignore those limits, rewrite them to serve its interests, or selectively apply them.

We object to the proposed licenses on the following grounds:

1. We have concerns about the timing of the license and selection of Generation Bio as licensee;
2. Our correspondence with the NIH concerning the prospective licenses indicates that the NIH has not faithfully applied the criteria in 35 U.S.C. § 209 and 37 C.F.R. § 404, and, in particular, that it has not properly considered the reasonableness and necessity of granting an exclusive license in a platform technology for expansive fields of use;
3. The NIH has withheld information about the license on the basis of inapplicable confidentiality provisions; and
4. The NIH apparently has not sought the antitrust advice of the U.S. Attorney General regarding the license, as required by 40 U.S.C. § 559.

In the event that the NIH grants the license over our objections, we request that the license agreement incorporates provisions designed to safeguard the public interest and effectuate the policy objectives of the Bayh-Dole Act and the governing principles of the Public Health Service (PHS) Technology Transfer Policy Manual.

Background

The Federal Register Notice "Prospective Grant of Exclusive Patent License: Capsid-Free AAV Vectors, Compositions, and Methods for Vector Production and Gene Delivery" concerns two prospective licenses in one federally-owned invention - a non-viral, eukaryotic, vector-based gene therapy.

The invention is claimed in U.S. Patent No. 9,598,703, "Capsid-free AAV vectors, compositions, and methods for vector production and gene delivery" (the "'703 patent"), which lists as inventors, Luis Garcia and Cyriaque Beley of France, Thomas Voit of Great Britain, and Robert Kotin and Lina Li of Maryland (NIH).

The NIH Office of Technology Transfer (OTT) assigned the invention NIH Reference No. E-241-2010, "Capsid-Free AAV Vectors for Gene Delivery and Their Use for Gene Therapy."

The invention consists of a "linear nucleic acid molecule comprising in this order: a first adeno-associated virus (AAV) terminal repeat (ITR), a nucleotide sequence of interest, and a second AAV ITR, wherein said nucleic acid molecule is devoid of AAV capsid protein coding sequences."[2] It is referred to, in a PubMed article written by its inventors, as close-ended DNA.[3]

The OTT webpage for E-241-2010 lists the following competitive advantages of the invention:

Competitive Advantages

- The AAV vectors described in the invention devoid the AAV capsid proteins and thus are not exposed to the adverse effects caused by immunogenicity.
- In contrast to the use of plasmid DNA for gene delivery, the AAV DNA of the invention seems to confer greater stability in cell nuclei, allowing prolonged expression compared to plasmid DNA.
- The vector DNA of the invention is not limited in size to the packageable size genome.
- The production of the AAV DNA vector is economical, simple and provides high yields.

Source: https://www.ott.nih.gov/technology/e-241-2010.

Similarly, the Notice describes the invention's advantages over existing AAV gene therapies as follows:

> They are advantageous over conventionally used AAV vectors, as they are non-immunogenic. They are also advantageous over plasmid-based expression constructs since they are of eukaryotic origin and thus devoid of the bacterial-type DNA methylation as typically present in plasmids.

The non-immunogenic nature of the invention could, indeed, offer a significant advantage over existing AAV gene therapies, whose potential to prompt adverse immune system reactions have been a major concern, especially after the controversial death of a pediatric clinical trial participant, Jesse Gelsinger, due to an adverse immune system response to an AAV therapy.

Argument

1. We have concerns about the selection of Generation Bio as exclusive licensee, and the NIH's response to our question about potential conflicts of interest have not allayed those concerns.

We noticed some peculiarities when researching the proposed licenses as they relate to Generation Bio, a biotech platform company that was founded in 2016 by Robert Kotin and Mark Angelino. Kotin was a Senior Investigator within the NIH Intramural Research Program

[2] https://www.ott.nih.gov/technology/e-241-2010
[3] https://www.ncbi.nlm.nih.gov/pubmed/23936358

when he helped discover the subject invention. In addition to founding Generation Bio, Kotin has been described as the company's "Head of Discovery" and "Advisor."

While we understand that NIH scientists may go on to pursue careers in the private sector, we are concerned that the NIH may have ignored the requirement in the Bayh-Dole Act to explore non-exclusive licensing of the invention, in a case where an NIH employee seeks not only to profit from invention he made while drawing a salary from the NIH, but to gain exclusive rights over an invention, blocking the ability of others to use the invention and driving up the costs of using these tools in the development of new medicines, a perverse outcome for the NIH.

Generation Bio's business platform is centered around a gene therapy that appears to be identical to the subject invention, and the company has publicized its relationship with Kotin and Kotin's role in developing its technology. In a January 4, 2018 press release, Generation Bio writes:

> Our unique **capsid-free technology** enables the development of genetic medicines that can be titrated and maintained to optimally impact each patient's disease over a lifetime. In addition, it **avoids the immunogenicity associated with viral vector-based gene therapies** that limits the number of patients who can be treated and prevents re-dosing.
>
> The company's core technology was discovered by **Generation Bio scientific founder and Head of Discovery, Robert Kotin**, Ph.D.
>
> As a **senior investigator at the National Institutes of Health**, Dr. Kotin discovered a novel modality for non-viral gene transfer, known as **closed-ended DNA, or ceDNA**. This eukaryotic DNA has a unique ability to translocate from the cytoplasm of the cell to the nucleus **without the use of a viral capsid**. Once in the nucleus, **ceDNA** forms stable, non-integrating episomes that result in high levels of long-term gene expression.[4]

We have observed many other similarities between the description of Generation Bio's ceDNA in the January 2018 press release and the "capsid-free AAV vectors" claimed in the '703 patent and described on the NIH OTT webpage and Federal Register Notice. The titles of the Licensing Opportunity webpage for the invention and the Federal Register Notice both contain the phrase "Capsid-Free AAV Vectors", while the press release describes a "capsid-free technology." The press release, OTT webpage, Notice, and the '703 patent all describe an invention that avoids the immunogenicity associated with viral vector-based gene therapies. The OTT webpage links to a PubMed Article titled "Production and Characterization of Novel Recombinant Adeno-Associated Virus Replicative-Form Genomes: A Eukaryotic Source of DNA for Gene Transfer" (PMID: 23936358), which describes "closed-ended, linear duplex, or 'CELiD', DNA."

[4] https://generationbio.com/atlas-venture-launches-generation-bio/ (emphasis added).

KEI considered and investigated the possibility that Generation Bio could have been referring to some other invention developed by Kotin as an NIH scientist, but that does not seem to be the case. A search for all inventions associated with Kotin on the NIH Office of Technology Transfer website returned the following results:

Production of Adeno-Associated Viruses in Insect Cells
Ref: E-325-2001-1 | Updated: May 9, 2018 | NHLBI
AAV4 Vector and Uses Thereof
Ref: E-071-2000-0 | Updated: May 9, 2018 | NHLBI
AAV5 Vector for Transducing Brain Cells and Lung Cells
Ref: E-072-2000-0 | Updated: May 9, 2018 | NHLBI
AAV5 Vector and Uses Thereof
Ref: E-127-1998-0 | Updated: May 9, 2018 | NHLBI
AAV4 Vector And Uses Thereof
Ref: E-066-1996-0 | Updated: May 9, 2018 | NHLBI
Capsid-Free AAV Vectors for Gene Delivery and Their Use for Gene Therapy
Ref: E-241-2010/0 | Updated: Oct 12, 2016 | NHLBI

Only the last invention listed, "Capsid-Free AAV Vectors for Gene Delivery and Their Use for Gene Therapy," relates to the technology described in the Generation Bio press release. It is the same invention that is listed in the Federal Register license notice. Also, KEI searched the USPTO database for a patent that was assigned to the United States, lists Kotin as an inventor, and describes a "capsid-free AAV vector." The '703 patent was the only one. Finally, the instant Notice is the only Federal Register notice in which the NIH discloses a prospective exclusive patent license to Generation Bio.

How is it that Generation Bio apparently is already discussing its proprietary rights in the technology that the NIH is here proposing to license and opening to public comment?

Generation Bio was founded on October 21, 2016. The NIH listed the E-241-2010 technology as available for licensing on October 12, 2016. Kotin clearly founded a company to profit from an invention he helped discover as an NIH employee. It appears Generation Bio received preference over other companies that applied for the license.

The NIH's answers to our questions regarding these concerns were not helpful.

KEI asked Dr. Uri Reichman (the NIH contact listed on the Notice) for a list of the companies that applied for the licenses. He declined to provide one.

KEI asked Dr. Reichman whether the NIH "see[s] any potential issue in licensing an invention discovered by then-NIH-employee Robert Kotin to a company which Kotin co-founded? Why or why not?" Dr. Reichman simply responded: "No!", ignoring the second part of KEI's question.

We think the relationship between Kotin and Generation Bio as concerns the subject license warrants further scrutiny and explanation. Given the NIH's history with Kotin and the public's role in financing this technology, the public has a right to know how the NIH has ensured that no conflicts inhere in the proposed licenses. At minimum, we hope that, in responding to our comments, the NIH will provide a more circumspect answer to KEI's questions about the Kotin/Generation Bio relationship than "No!".

2. The NIH has not demonstrated that it properly evaluated the necessity of granting an exclusive license or that it has ensured that the scope of rights will not be broader than reasonably necessary to induce the investment needed to commercialize the subject technology.

Before granting an exclusive license in federally-owned technology, the agency proposing the license must find both that granting an exclusive license is a reasonable and necessary incentive and "that the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application[.]" 35 U.S.C. § 209(a)(1)-(2).

We are concerned, based on Dr. Reichman's answers to our questions, that the NIH has not properly applied the limitations set forth at 35 U.S.C. § 209(a)(1)-(2).

Necessity of Exclusivity

"A Federal agency may grant an exclusive or partially exclusive license on a federally owned invention . . . only if-- [among other things] (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[.]" 35 U.S.C. § 209(a)(1).

Consistent with Section 209(a)(1), PHS's " Best Practices for the Licensing of Genomic Inventions" announces a preference for non-exclusive licenses in genomics. It states:

> Whenever possible, non-exclusive licensing should be pursued as a best practice. A non-exclusive licensing approach favors and facilitates making broad enabling technologies and research uses of inventions widely available and accessible to the scientific community.

> When a genomic invention represents a component part or background to a commercial development, non-exclusive freedom-to-operate licensing may provide an appropriate and sufficient complement to existing exclusive intellectual property rights.[5]

KEI asked Dr. Reichman "on what basis did the NIH conclude that an exclusive (as opposed to non-exclusive or partially exclusive) license to Generation Bio was a necessary incentive under 35 U.S.C. § 209(a)(1)?". He responded: "The license application is legally protected as confidential to the company."

His argument about the confidentiality of license applications precluding him from addressing our question was misplaced. KEI was simply asking Dr. Reichman to articulate how the NIH determined that exclusivity was a reasonable and necessary incentive. KEI did not ask NIH to disclose any confidential elements of a license application.

Before concluding that an exclusive license is warranted, some analysis should be undertaken, such as consideration of the incentives provided by law, such as test data protection, Orphan Drug exclusivity, priority review vouchers, and the likely case that the developer can bring other patented inventions into the project, for which exclusivity exists.

Generation Bio and Spark Therapeutics appear likely to receive incentives such as the priority review voucher, orphan drug exclusivity, and test data protection for the invention, if the invention is used in connection with a drug, vaccine or cell or gene therapy.

Generation Bio seems intent on pursuing such indications as would grant them those incentives. An article on its website discusses how "the greatest therapeutic opportunity and unmet need" for gene therapies resides in pediatric patients and how "drug development programs in other pediatric orphan disorders" can track the success of Spinraza in treating SMA.[6] Likewise, in an article titled, "Genetic Diseases Steal Too Many Kids' Futures. It Doesn't Have To Be This Way[,]" Generation Bio argues that Orphan Drug Act incentives should be used to spur investment in rare pediatric diseases.[7]

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[5] *Best Practices for the Licensing of Genomic Inventions: Final Notice*, 70 Fed. Reg. 18,413 (Apr. 11, 2005), available at https://www.govinfo.gov/content/pkg/FR-2005-04-11/pdf/05-7247.pdf.

[6] https://generationbio.com/re-generation/right-from-the-beginning-returning-to-the-origins-of-the-orphan-drug-movement/

[7] https://www.wbur.org/cognoscenti/2018/06/08/pediatric-genetic-therapies-geoff-mcdonough

Spark Therapeutics received Priority Review, Breakthrough Therapy, an dOrphan Drug designations and a Rare Pediatric Disease priority review voucher for Luxturna, an AAV gene therapy to treat a form of blindness caused by a mutation in the RPE65 gene.[8]

We also note that Roche is seeking to acquire Spark for $4.8 billion, largely on the basis of the company's rights in NIH-funded patents and the Luxturna gene therapy.

The co-exclusive license to Spark and Generation Bio appears to be directed toward the development of a gene therapy to treat Stargardt Disease, a disease affecting 8,000 to 10,000 people worldwide. Both Spark and Generation Bio list a gene therapy to treat Stargardt as part of their product pipelines.[9] Generation Bio also lists, as a product in development, a gene delivery system to treat LCA10, a genetic disorder that causes childhood blindness in two to three per 100,000 people worldwide.[10]

Rare Pediatric Disease Priority Review Vouchers are a valuable incentive for biotech companies: Spark sold the voucher it was granted for Luxturna for $110 million.[11] So, too, are Orphan drug status and FDA market exclusivity valuable to biotech companies. Orphan Drug status provides seven years of market exclusivity, commencing the day the FDA issues marketing approval on the drug. FDA-approved biologics receive 12 years test data exclusivity.

In the NIH's response to our comments, please explain if and how the NIH weighed these incentives when determining that an exclusive and co-exclusive license were necessary.

PHS has recognized that exclusive licenses are not always necessary to achieve commercial application, because companies "frequently are able to add their own proprietary technologies to the technology licensed from the government to ultimately achieve some level of uniqueness and exclusivity for the final product."[12]

Generation Bio's business model appears to be centered around its " proprietary GeneWave technology, which delivers high levels of durable gene expression and can be re-dosed to titrate and sustain effect."[13] Please explain if NIH considered the

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[8] https://www.fda.gov/news-events/press-announcements/fda-approves-novel-gene-therapy-treat-patients-rare-form-inherited-vision-loss

[9] https://generationbio.com/programs/; https://sparktx.com/scientific-platform-programs/

[10] https://generationbio.com/programs/

[11] http://ir.sparktx.com/news-releases/news-release-details/spark-therapeutics-sells-priority-review-voucher-110-million

[12] PHS Technology Transfer Policy Board, PHS Licensing Policy (October 25, 1995) at p. 3.

[13] https://generationbio.com/atlas-venture-launches-generation-bio/

possibility that the proprietary rights in GeneWave could have provided sufficient market exclusivity.

Scope of the License

Nor does it appear, from Dr. Reichman's comments in response to our questions, that the NIH has properly considered the appropriate scope of the licenses.

Before granting an exclusive license in federally-owned technology, the agency proposing the license must find "that the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application[.]" 35 U.S.C. § 209(a)(2).

The scope of a license in federally-sponsored technology may vary along the following (non-exhaustive) parameters:

- The period of exclusivity - how long the licensee may claim a monopoly on the right to market and sell the invention (i.e., five years, ten years, life of patent, etc.);
- Territorial reach (worldwide or limited to the U.S. or a particular geographic region); and
- Field of use (i.e., targeted diseases).

The scope of a license must be not greater than necessary to incentivize a licensee to commercialize a government-owned invention. There are at least seven factors that should be considered when evaluating the necessary incentive:

1. The costs of financing research and development and bringing the invention to market, including obtaining FDA approval;
2. The government's investment in R&D and the development stage of the technology;
3. Any expected additional subsidies from governments or charities, including, for example, the Orphan Drug Tax Credit or additional grants or continued or new collaborations with the NIH or other government agencies;
4. The existence of other incentives, including, for example, test data protection, Orphan Drug exclusivity and awards of priority review vouchers;
5. The anticipated cost to manufacture the resultant invention; and
6. The expected post-market entry profitability of the invention, by year.

To apply 35 U.S.C. § 209(a)(2) with respect to a proposed exclusive license, the NIH must weigh the costs and risks associated with commercializing the government-owned technology against the probable benefits of doing so, and adjust the terms of the license accordingly.

When, for example, developing a publicly-owned invention would be a relatively less attractive prospect for investors, it may be more appropriate for the NIH to create additional incentives

through granting broad exclusive rights. On the other hand, when the risks and costs associated with developing the technology are relatively low compared to incentives that are relatively high, the NIH should negotiate a narrower license and more favorable terms for the American public.

In any event, the analysis regarding the scope of the license should be a fact-specific, case-by-case determination. If, in every instance, the NIH gives away a "sweetheart deal" in licenses in publicly-owned inventions to private companies, it is not complying with Section 209.

From what we can tell, the NIH is, once again, planning to grant the broadest possible rights in the patented invention.

Attractiveness of the Investment

Commercial development of the subject technology appears to be a highly attractive prospect to investors. Generation Bio has already raised upwards of $125 million in investment capital based on the promises of its ceDNA.[14] Moreover, the potential patient population for the invention is large. Generation Bio is pursuing "a diverse portfolio of programs for diseases of the liver," and "delivery systems for additional tissues, including the eye, muscle and brain."[15] On its website, Generation describes how its technology "can extend the benefits of gene therapy to large diseases and global populations."[16] In addition to broad disease indications, Generation envisions a large manufacturing scale: in a June 2019 presentation, CEO Geoffrey McDonough described how the company's "[u]pstream scale unlocks production for millions of patients[.]"[17]

Given the lucrative potential of this technology, the breadth of its possible applications, and its potential importance to patients, the NIH should negotiate a narrower scope of rights - if it grants exclusivity in the first place. That does not appear to be the case, however, as explained below.

Duration of exclusivity

Perhaps the most important licensing provision, in terms of impact on price and access, is the duration of exclusivity, because it determines the length of time that the licensee can claim a monopoly on the patented invention and set whatever price the market can bear. This is a particularly sensitive concern in the area of life-threatening diseases, such as cancer, where the demand for a life-extending drug or biologic is especially inelastic, and rare diseases, where competition is limited.

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[14] https://www.biospace.com/article/generation-bio-raises-100-million-series-b-to-finance-non-viral-gene-therapy-program/

[15] https://generationbio.com/programs/

[16] https://generationbio.com/approach/

[17] https://www.jefferies.com/CMSFiles/Jefferies.com/files/Generation%20Bio.pdf

KEI asked whether, for the proposed licenses, "[t]he period of exclusivity [or co-exclusivity] is to be life of patent or less than life of patent?" Dr. Reichman answered: "It will be negotiated. Typically exclusive licenses are for the term of the patent."

Dr. Reichman's statement that "[t]ypically exclusive licenses are for the term of the patent[]" is consistent with KEI's experience with the NIH (but not with other federal agencies), and life of patent is the default period of exclusivity in NIH's Model Exclusive Patent License Agreement.[18]

The NIH may not, as a routine practice, grant exclusivity for life-of-patent, without regard to whether a shorter period of time would suffice. Such a practice would violate the requirement that the scope of the license is not greater than reasonably necessary. Each invention to be licensed presents unique circumstances. If the NIH always negotiates licenses with a term of life of patent, that would strongly indicate that NIH is not accounting for those individualized circumstances.

Field of Use

We have significant concerns about the proposed fields of use for the licenses.

The Federal Register Notice for the prospective licenses lists the following fields of use:

> *Exclusive field*: Electroporation-mediated delivery of DNA-based vectors to express therapeutic molecules for the treatment or prevention of human diseases.
>
> *Co-exclusive field*: The treatment or prevention of cancer by administration of DNA-based vectors (with the exception of electroporation mediation) to express therapeutic molecules.

Because the phrases "treatment or prevention of human diseases" and "treatment or prevention of cancer" can be fairly characterized as vague, KEI asked: "What diseases fall within the field of use for the exclusive license to Generation Bio?" Dr. Reichman answered: "This is the broadest possible scope."

We are concerned that the broadness of these fields of use will inhibit competition and innovation in a type of technology that has so far commanded extraordinarily high prices, limiting public access. This is inconsistent with Section 209(a)(2) and PHS's own technology transfer policies.

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18 https://www.ott.nih.gov/sites/default/files/documents/pdfs/NIH-Patent-License-Exclusive-model-102015.pdf

The PHS Technology Transfer Policy Manual, Ch. 300, stipulates that PHS:

> seeks to ensure that a licensee obtains the appropriate scope of rights necessary to develop a potential application of the invention. This enables as many companies as possible to obtain commercial development rights, resulting in the concurrent development of many potential applications and the further promotion of the invention's utilization by the public.

Similarly, PHS's Best Practices for Licensing of Genomic Inventions states that "[i]n those cases where exclusive licensing is necessary to encourage research and development by private partners, best practices dictate that exclusive licenses should be appropriately tailored to ensure expeditious development of as many aspects of the technology as possible."[19]

We question how granting the "broadest possible field of use" in a platform gene therapy complies with Section 209(a)(2), facilitates that PHS's Technology Transfer Policy for ensuring "the appropriate scope of rights," and is consistent with Best Practices for Licensing Genomic Inventions. How do the fields of use proposed allow "concurrent development of many potential applications"?

There is widespread consensus that granting exclusive rights for the broadest possible field of use in a platform technology is bad for innovation and is certainly a bad policy for the NIH.

Territorial Reach

The Federal Register notice states that "the prospective exclusive license territory may be worldwide" -- the broadest possible territorial reach.

The PHS Technology Transfer Policy Manual states that "PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries."

We question how worldwide rights in the subject technology facilitates that policy and call on the NIH to articulate its rationale for concluding that worldwide rights satisfy Section 209 and the Technology Transfer Policy quoted above.

3. The NIH has not been fully transparent about the license, impeding the public's right to comment under 35 U.S.C. 209(e).

[19] *Best Practices for the Licensing of Genomic Inventions: Final Notice*, 70 Fed. Reg. 18,413 (Apr. 11, 2005), available at https://www.govinfo.gov/content/pkg/FR-2005-04-11/pdf/05-7247.pdf.

A federal agency may not grant an exclusive license in government-owned technology without first notifying the public of the prospective license, allowing a minimum 15-day period for the public to comment, and considering all timely submitted comments. 35 U.S.C. § 209(e).

In order for the public to meaningfully participate in the notice-and-comment process, it must have basic information about the licenses.

The NIH has, without any legal justification, erected several barriers that prevent the public from obtaining information necessary to comment effectively on proposed exclusive licenses.

In response to many of our questions, the NIH has stated that the requested information is confidential or that the terms of a license are yet to be determined. Neither assertion is a valid basis for denying the public basic information about the licenses.

The NIH's reference to the confidentiality of license applications is not sound. Federal law and regulations make only part - not all - of a license application confidential.

The federal regulation governing confidentiality of license applications states:

37 C.F.R. § 404.14 Confidentiality of information.

> Title 35, United States Code, section 209, requires that any plan submitted pursuant to § 404.8(h) and any report required by § 404.5(b)(6) shall be treated as commercial or financial information obtained from a person and privileged and confidential and not subject to disclosure under section 552 of Title 5 of the United States Code.

37 C.F.R. § 404.14 refers to "any **plan** submitted pursuant to § 404.8(h)[.]" 37 C.F.R. § 404.14 (emphasis added). 37 C.F.R. § 404.8 lists 11 different components of a license application, of which only one, 37 C.F.R. § 404.8(a)(8), refers to a plan - "A detailed description of applicant's plan for development or marketing of the invention, or both[.]" The other components, listed at 37 C.F.R. § 404.8(a)(1)-(7) and (9)-(11), are not "plans" and thus are nonconfidential under § 404.14.

Section 209 of the Bayh-Dole Act refers to the confidentiality of a licensee's "plan for development or marketing of the invention" (35 U.S.C. § 209(f)) and "periodic reporting on utilization of the invention, and utilization efforts, by the licensee" (35 U.S.C. § 209(d)(2)).

The plain language of the federal law and regulations governing exclusive licenses are clear: only the license application's development plan and the licensees' periodic utilization reports are confidential.

KEI emailed its interpretation of 37 C.F.R. § 404.14 as it pertains to Section 209 license applications to Dr. Reichman and to Mark Rohrbaugh, Special Advisor for Technology Transfer, NIH, and asked the NIH to explain if and why our interpretation was wrong. Neither Dr. Reichman nor Mr. Rohrbaugh responded, even after KEI submitted a follow-up request for a response.

We thus object to the licenses on the grounds that the NIH has withheld relevant information without a valid basis for doing so, impeding the public's right of comment under Section 209(e).

4. The NIH apparently has not sought the antitrust advice of the U.S. Attorney General regarding the licenses, as required by 40 U.S.C. 559.

We object to the license unless the NIH first obtains the antitrust advice of the United States Attorney General, who confirms that the license would not be anticompetitive.

Under the Federal Property and Administrative Services Act, 40 U.S.C. §§ 101 *et seq.*, "[a]n executive agency shall not dispose of property to a private interest until the agency has received the advice of the Attorney General on whether the disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law." 40 U.S.C. § 559(b)(1).

This includes when the NIH proposes to grant an exclusive license in federally-owned technology. "Property" is defined at 40 U.S.C. § 102 to mean "any interest in property," with certain exceptions that do not include patents. Similarly, Section 559 creates certain exceptions that do not include patents.

41 C.F.R. § 102-75.270 supports the notion that the term "property" in Section 559 includes intellectual property rights such as patents.

41 C.F.R. § 102-75.270 - Must antitrust laws be considered when disposing of property?

Yes, antitrust laws must be considered in any case in which there is contemplated a disposal to any private interest of -

(a) Real and related personal property that has an estimated fair market value of $3 million or more; or

(b) Patents, processes, techniques, or inventions, irrespective of cost.

KEI asked Dr. Reichman whether the NIH requested the advice of the U.S. Attorney General concerning the licenses. He did not answer. In the past, the NIH has asserted its position with respect to 40 U.S.C. § 559 as follows:

> "The statute you reference is directed to the disposal (assignment) of government property. It has little relevance to our patent licensing activities, which are principally government by the Bayh-Dole Act and its regulations."

The NIH's interpretation of 40 U.S.C. § 559 is incorrect.

The Bayh-Dole Act expressly incorporates federal antitrust laws. 35 U.S.C. § 209(a)(4) allows a federal agency to grant an exclusive license only if the license "will not tend to substantially lessen competition or create or maintain a violation of the Federal antitrust laws." 35 U.S.C. § 211 provides that "[n]othing in this chapter shall be deemed to convey to any person immunity from civil or criminal liability, or to create any defenses to actions, under any antitrust law[.]" The Bayh-Dole Act sets out the areas in which the statute "shall take precedence over any other Act which would require a disposition of rights in subject inventions[,]" 35 U.S.C. § 210, and mentions 21 separate statutes, but not the FPASA.

Second, the term "disposal" is not a defined term under 40 U.S.C. § 102 of the FPASA, and is not limited to "assignment" or "sale." In fact, there are many examples of regulations and laws that include licensing amongst dispositions, either explicitly or by implication.

If NIH grants a fully-exclusive license to a federally-owned invention for life of patent, and allows termination of the license only in narrow, vaguely-defined circumstances, then it is effectively disposing of a government property interest so as to trigger 40 U.S.C. § 559.

This is a particularly important issue in these licenses, where non-exclusive licenses to the patented inventions can and should be available to any firm developing gene therapies. The NIH is creating a monopoly where a monopoly should not exist.

5. In the event that the NIH decides to grant the licenses over our objections, we recommend that the NIH includes a series of provisions designed to safeguard the public interest and ensure that the licenses implement the governing principles in the PHS Technology Transfer Manual.

In the event that the NIH proceeds with the licenses, KEI requests that it includes the following provisions to protect the public's interest in NIH-funded technology:

1. **Price discrimination.** Any medical technology using the patented invention should be available in the United States at a price that does not exceed the median price in the seven largest economies by GDP that have at least 50 percent of the GNI per capita as the United States, using the World Bank Atlas method. This is a modest safeguard.

2. **Low and middle income countries.** The exclusive licenses should not extend to countries with a per capita income less than 30 percent of the United States, in order to

ensure that the patents do not lead to restricted and unequal access in developing countries. If the NIH rejects this suggestion, it needs to provide something that will give effect to the policy objective in the "United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy," which states the following: "PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries."

3. **Global registration and affordability.** The licenses should require Generation Bio and Spark Therapeutics to disclose the steps they will take to enable the timely registration and availability of the medical technology at an affordable price in the United States and in every country with a demonstrated need, according to the Centers for Disease Control and Prevention (CDC) and/or the World Health Organization (WHO), either by supplying a country directly at an affordable, publicly disclosed price and with sufficient quantities, or by providing technology transfer and rights to all intellectual property necessary for third parties to do so.

4. **Medicines Patent Pool.** The NIH should retain a right to grant the WHO, the Medicines Patent Pool or other governments the rights to use the patent rights to procure the medical technology from competitive suppliers, including technology transfer, in developing countries, upon a finding by HHS or the WHO that people in these markets do not have sufficient access to the medical technology.

5. **Years of exclusivity.** We propose the license reduce the years of exclusivity when revenues are large. The NIH has many options, including by providing an option for non-exclusive licensing, such as was done in the ddI case. We propose that the exclusivity of the license be reduced when the global cumulative sales from products or services using the inventions exceed certain benchmarks. For example, the period of exclusivity in the license could be reduced by one year for every $500 million in global cumulative revenue after the first one billion in global sales. This request is consistent with the statutory requirements of 35 U.S.C. § 209, which requires that "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application."

6. **Transparency of R&D outlays.** The licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product or service that uses the inventions, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions. Reporting on actual R&D outlays is important for determining if the NIH is meeting the requirements of 35 U.S.C. § 209, that "the

proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application." Specifically, having data on actual R&D outlays on each clinical trial used to obtain FDA approval provides evidence that is highly relevant to estimating the risk adjusted costs of bringing NIH licensed inventions to practical application.

Conclusion

We object to the licenses for the reasons stated herein. If the NIH proceeds with the licenses over our objections, we urge that it incorporate the provisions listed herein that are designed to protect the public's investment in this gene therapy platform.

Sincerely,

Knowledge Ecology International
Union for Affordable Cancer Treatment