May 19, 2017

Commander
U.S. Army Medical Research and Materiel Command
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Dear Command Judge Advocate:

We write to you to appeal your decision of 21 April, 2017, wherein you responded to comments previously submitted by the undersigned groups, and stated that the Army intends to grant an exclusive patent license to Sanofi Pasteur, Inc. ("Sanofi").

This Appeal Satisfies the Requirements of 37 CFR 404.11(a)(3)

This appeal is timely made under 37 CFR 404.11(a)(3), submitted within thirty calendar days of receiving knowledge of the basis for the appeal. The undersigned represent patients, consumers, and taxpayers, including many in the Gulf region and elsewhere who would be eligible recipients for a Zika vaccine and who will be significantly affected by the proposed license.

> **The American Federation of State, County and Municipal Employees** (AFSCME) is the largest public employee union in the United States, with over 1.6 million members. AFCSME has approximately 3,400 local unions and 58 councils and affiliates in 46 states, the District of Columbia, and Puerto Rico.
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> **Knowledge Ecology International** (KEI) is a non-governmental organization that advocates for access to affordable medicines, with a focus on human rights and social justice.
>
> **People of Faith for Access to Medicines** (PFAM) builds on the foundation established by faith-based organizations playing a central role in U.S. health care, culture, and politics, the strengths of the existing access to medicines movement, and the historic legacy of faith communities making essential contributions to social movements. PFAM conducts outreach, education, and organizing at both the levels of individual congregations and at the highest levels of faith denominations.
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> **Social Security Works** (SSW) is a non-profit organization that advocates for the economic security of disadvantaged and at-risk populations, and those who depend

upon Social Security. SSW convenes Strengthen Social Security, a coalition of over 300 national and state organizations representing over 50 million Americans.

Universities Allied for Essential Medicines (UAEM) is a global network of university students who advocate for global access to public health goods.

Public Citizen is a consumer advocacy organization with more than 400,000 members and supporters.

Dean Baker is an economist and co-founder of the Center for Economic and Policy Research (CEPR) in Washington, D.C.

The decision to grant Sanofi an exclusive license without pricing conditions will damage the health of individuals represented by the undersigned, because there is a high likelihood that Sanofi will charge a high price for U.S. residents, including but not limited to persons who benefit from government funded programs funded by U.S. taxpayers, and because the high prices will also result in limited access to the Zika vaccine, which will have adverse impacts including avoidable birth defects and high costs of caring for children born with the health issues that are a consequence of the Zika virus.

Sanofi's recent history of discriminatory pricing and fraud

High prices for an exclusively-licensed Zika vaccine are not only made more likely by virtue of the exclusion of market competition, but also by Sanofi's history of high prices and bad acts in the United States.

To illustrate the issue of pricing that discriminates against U.S. residents, consider the case of the multiple sclerosis drug Aubagio (INN: Teriflunomide). Sanofi charges U.S. residents four to eight times more than other high-income industrialized countries[1]:

Source	Local Currency	Exchange Rate	USD	Ratio of GoodRx Price to Source Price
U.S., GoodRx, Safeway Pharmacy With Coupon (Apr. 28, 2017)	$6,074.40	--	--	--
U.S., Medicare (2015)	$5,276.60	--	--	1.15
Australia, Pharmaceutical Benefits Scheme (PBS) (2017)	AUS$1,836.73	1.34	$1,370.69	4.43

[1] http://keionline.org/node/2759

France, Ministère des Affaires sociales et de la Santé, Before Tax (2017)	€667.27	0.92	$725.29	8.38
France, Ministère des Affaires sociales et de la Santé, After Tax (2017)	€793.04	0.92	$862.00	7.05
United Kingdom, The National Institute for Health and Care Excellence (NICE) (2014)*	£1,037.84	0.77	$1,347.84	4.51
New Zealand, PHARMAC (2017)	NZ$1,582.62	1.46	$1,083.99	5.60
Ireland, National Centre for Pharmacoeconomics (NCPE), Ex-Factory Price (2014)**	€1,250.41	0.92	$1,359.14	4.47

We also note that on April 3, 2017, the Department of Justice announced that Sanofi was required to repay $19.8 million to the Department of Veteran Affairs for overcharges.[2]

An Exclusive License of the Zika Vaccine to Sanofi Violates 35 U.S.C. § 209(a)(1)

The proposed exclusive license of the Zika vaccine to Sanofi would violate the requirements of the Bayh-Dole Act under 35 U.S.C. 209(a)(1), for being neither reasonable nor a necessary incentive to bring the invention to the public given the significant taxpayer dollars already spent on the R&D, other incentives available to the vaccine such as the priority review voucher, and the likelihood of higher prices foisted upon consumers by virtue of the exclusivity (as opposed to a non-exclusive license).

35 U.S.C. § 209(a)(1) provides that:

> (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

[2] Department of Justice, press release: "Sanofi Pasteur Agrees to Pay $19.8 Million to Resolve Drug Overcharges to the Department of Veterans Affairs," April 3, 2017. https://www.justice.gov/opa/pr/sanofi-pasteur-agrees-pay-198-million-resolve-drug-overcharges-department-veterans-affairs

(B) otherwise promote the invention's utilization by the public;

The Exclusive License is Neither Reasonable nor Necessary Incentive Where U.S. Taxpayers Have Already Funded the Research and Development of the Riskiest Clinical Trials

As pointed out in previous comments, and as pointed out below, U.S. taxpayers have paid for all of the research and development of this vaccine thus far, including the preclinical discovery phase, a government funded and sponsored Phase 1 trial, and have entered into an agreement with Sanofi to fund Phase 2 and 3 trials. Sanofi also stands to receive further incentives that create entry barriers for generic vaccines and have significant market value as a tradeable asset.

The Army has undervalued the role of the federal funding, and overstated the risks and costs faced by Sanofi. As such it cannot be said that an exclusive license to Sanofi is a reasonable and necessary incentive to bring the invention to practical application.

The role of the federal government and federal resources in this vaccine has been extensive, and is documented in Sanofi press releases:[3]

- The Phase I clinical trials are being conducted by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

- The Phase II clinical trials are funded through a $43.2 million BARDA grant to Sanofi, with an option of $130 million in additional funding for continued support through the Phase III trials.

Other incentives that the Zika vaccine would be eligible for include:

- A rare disease priority review voucher under 21 U.S.C. § 360n. Note that in February 2017, a priority review voucher was sold by Sarepta Therapeutics to Gilead, for $125 million. [4]

- Exclusive rights in test data from the U.S. government-funded clinical trials on the vaccine, for 12 years, under 42 U.S.C. § 262(i) and 42 U.S.C. § 262(k)(7)(A). If Sanofi

[3] See:
http://www.sanofipasteur.com/en/articles/Sanofi-Pasteur-Signs-Research-Agreement-for-Zika-Vaccine.aspx
and
http://www.sanofipasteur.com/en/articles/Sanofi-Pasteur-Signs-Research-Agreement-for-Zika-Vaccine.aspx.
[4] Alexander Gaffney, RAC, Michael Mezher, Zachary Brennan, Regulatory Explainer: Everything You Need to Know About FDA's Priority Review Vouchers, The Regulatory Affairs Professionals Society (RAPS), 28 April 2017.
http://www.raps.org/Regulatory-Focus/News/2015/07/02/21722/Regulatory-Explainer-Everything-You-Need-to-Know-About-FDA%E2%80%99s-Priority-Review-Vouchers/

> can prevent use of the test data by competitors seeking to gain marketing approval, it will have a regulatory monopoly even without an exclusive license to the patents.

The Army does not refer to the significant federal funding or to these other incentives once in its letter of 21 April, even while justifying the exclusive license because of the "high risk and high cost involved in advanced vaccine development," and stating that "exclusivity is needed to incentivize a company to enter a crowded and competitive preclinical marketplace, especially when the cost of clinical trials is substantial." Nowhere does the Army acknowledge the role that U.S. taxpayer dollars has played in getting through the most difficult stages of the vaccine development.[5]

In the letter, you stated that the Army will consider a number of factors, including:

> (1) the number of other competing vaccine development efforts currently underway around the world;
>
> (2) the substantial cost required to fully develop, produce, and distribute an FDA-approved vaccine, which necessitates commercial investment;
>
> (3) the potential risks assumed by the vaccine developer in moving a vaccine through the regulatory process; and
>
> (4) willingness of other vaccine developers to license, develop, and commercialize our nascent invention.

An assessment of these factors should include analysis of the risks associated with the different phases of clinical trials, recognizing that the earlier phases are riskier, and should include an assessment of how the "substantial cost" has been offset by federal funding. The absence of discussion of this in your letter suggests that you have not done so. As it stands, the public does not know what Sanofi will spend moving forward, but we do know that the company's expenditures have been minimal to none thus far.

With regard to the willingness of other vaccine developers to license, develop, and commercialize the Zika vaccine, the Army should acknowledge that it will certainly be easier to find willing partners after the riskiest trials have been completed, as opposed to earlier in the R&D, when the path to viability seems more daunting.

The Army has the option of offering an exclusive license at a later date, after evidence is available from the clinical trials the U.S. government is already funding or offering to fund. The extent of interest in selling the vaccine will be far greater for a vaccine that has success in

[5] For explanation of the risk-adjustments of the different phases of clinical trials, see, for example, James Love, "The 2016 Tufts Estimates of the Risk-Adjusted Out-of-Pocket Costs To Develop a New Drug," April 10, 2016, available at http://keionline.org/node/2464.

Phase 1, 2, and certainly 3 trials, and the government's leverage in negotiating license terms will also be far stronger. But, the Army has proposed the license to Sanofi even before having results from the Phase 1 trials the government was doing itself.

The potential demand for a Zika vaccine is very large. As we have previously pointed out, industry executives recognize the tremendous market potential for the vaccine, and the size of that market also was not mentioned in your letter and does not seem to be considered in the context of analyzing the costs and risks. An article in the *Wall Street Journal* described the situation and quoted one executive:

> Companies pursuing Zika vaccines are hoping public demand for widespread immunization will create a commercial market similar to the vaccine for rubella, another disease that causes birth defects. Any Zika vaccine wouldn't likely be aimed at pregnant women because of potential risks, but instead administered more broadly to young people.
>
> Hundreds of millions of people are at risk, said Thomas Monath, chief operations officer of the infectious-disease division at NewLink Genetics Corp., which is developing two Zika vaccines.
>
> Zika, he said, "is the biggest opportunity for a new vaccine that's come along in my career, and I've been in vaccines for 40 years."[6]

The Zika virus is of pressing concern for everyone in the Gulf of Mexico, Caribbean, and Latin American regions, including nearly 35,000 already affected by Zika in Puerto Rico, and many others throughout the United States who travel to and from those regions and who live where Zika is likely to spread.

The Governor of Louisiana stated in a letter of 10 May, 2017 to Acting Secretary of the Army Robert Speer (attached) that an exclusive license without price constraints on the vaccine could "cripple state budgets and threaten public health," and estimated that, "As many as 540,000 Louisiana residents on Medicaid alone could benefit from an effective Zika vaccine, but all my constituents deserve access in the event of local transmission."[7] Similar assertions could be made for any of a number of states in the Gulf region.

There is no going back once the exclusive license is granted. We dispute the legality of proceeding without an accurate and honest assessment of the costs and risks that heavily

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[6] Betsy McKay and Peter Loftus, " America's Next Defense Against Zika and Other Foreign Invaders - Experimental DNA vaccines could shield against infectious-disease outbreaks that now spread around the world with alarming speed," *Wall Street Journal*, December 16, 2016. http://www.wsj.com/articles/americas-next-defense-against-zika-and-other-foreign-invaders-1481810402

[7] Letter from Governor John Bel Edwards to Acting Secretary of the Army Robert Speer, May 10, 2017. Available at http://keionline.org/sites/default/files/may-2017-LA-gov-to-army-zika-letter.pdf. Letter enclosed.

weighs existing U.S. taxpayer contributions, and the logic of proceeding without assessing the viability of finding willing partners at a later stage rather than before even the Phase I trials are complete.

We note also the February 16, 2017 memorandum by Diane Singhroy, PhD., titled "Notes on Zika Manufacturing Capacity," which had been provided to the Army during the public comment period, and offered this comment on the challenges of manufacturing the ZPIV vaccine:

> Generally, the biggest roadblock to developing an inactivated vaccine, is finding a reliable way to grow stocks of the virus in the lab. This would involve finding the proper organism to grow the virus so that is can be harvest, inactivated and turned into a vaccine. Ideally, researchers would try to grow the virus in a cell line, since this it is the most cost effective solution. Unfortunately some viruses are difficult to grow in cell culture rendering the whole process very time consuming and tedious. This is the case for influenza, for example, since it has to be manufactured in fertilized chicken eggs! Fortunately ZPIV can be grown in a standard cell line called vero cells.
>
> Because these techniques are straightforward and relatively standard in a virologist's tool box, many drug companies would be capable of manufacturing inactivated whole virus vaccines, provided they had access to the particular parameters needed to effectively produce the vaccine and test its inactivation.

Dr. Singhroy also identified 158 firms that can manufacture a vaccine in the United States.[8]

Addressing Price Concerns is Feasible and Within the Army's Authority

In your letter, you indicated that the Army "lacks the means, expertise, and authority to define, implement, and enforce 'affordable prices' or to set price controls for a potential vaccine that will require great investment and face high risk of failure…" This argument is incredulous, particularly since the proposals put forth in the comment period require no extensive training in economics or any other academic discipline.

The December 21, 2016 comment by KEI on the proposed license included a suggestion of a simple 49-word sentence in the license to ensure that the United States did not pay more than other high income countries. It read as follows:

> "The [agency] will normally expect the licensee to make products available to the public in the United States at prices no higher than the median price charged in the seven countries with the largest GDP, that have per capita incomes of at least half that of the United States."

[8] http://keionline.org/sites/default/files/Note-on-Zika-vaccine-manufacturing.pdf

That proposal, as with the others including limiting the term of exclusivity, requiring transparency regarding R&D costs and other data, or requiring concessions of affordability in developing countries, can be contractually obligated under the Army's existing authority to license, and requires only the means and expertise in contract drafting that the Army's attorneys already have.

"Practical Application" Under the Bayh-Dole Act Requires Reasonable Pricing

If the license is granted, the Bayh-Dole Act requires that the Zika vaccine be made available to the public on reasonable terms, including at a reasonable price.

KEI noted in a previous submission (which we have attached as an appendix to this appeal) that the term "practical application" appears seven times in 35 U.S.C. § 209 as a condition for the grant of an exclusive license on a federally-owned patents.[9] "Practical application" is defined under 35 U.S.C. § 201(f) as follows:

> (f) The term "practical application" means to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and *that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms.* (Emphasis added.)

Our submission discussed the statutory history of the Bayh-Dole Act and relevant case law in the United States, patent law in the United Kingdom and South Africa, and other interpretations of "reasonable terms" in fora such as the World Trade Organization. We argued that contrary to the arguments made by Senators Birch Bayh and Bob Dole during their post-Senate careers as lobbyists, "reasonable terms" includes "reasonable price" in the context of the legislative history of the Bayh-Dole Act and arguments made by Senator Bayh during the 1997 CellPro march-in case. U.S. case law also supports the position that reasonable terms, in the context of various industries and statutes, includes reasonable price.

We also noted as further persuasive evidence that the U.K. government officially interprets the term "reasonable terms" in its patent statute to include reasonable price, based upon various decisions related to compulsory licenses in British courts. South African law has similar provisions. Finally, we noted that in a World Trade Organization dispute with Mexico, the United States interpreted reasonable terms to include a reasonable price.

Finally, how else could the Army interpret the mandate to have the invention available "to the public on reasonable terms", if that did not include the price? Are there conditions other than the price that "the public" is expected to be confronted with when a vaccine is available?

[9] http://keionline.org/node/2742

We attach the comments by KEI on the definition of “practical application,” the technical submission by Diane Singhroy, and the letter by the Governor of Louisiana, for consideration in the context of this appeal.

Conclusion

The U.S. Army should not grant an exclusive license to Sanofi at this time, given the absence of evidence that an exclusive license is a “reasonable and necessary” incentive for development, noting that this issue can be revised later, after evidence is available from the Phase 1, 2 and 3 government funded trials. And, if a license is granted, it should provide assurances that the vaccine will “be available to the public on reasonable terms,” explicitly including reasonable prices.

Sincerely,

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Signed on behalf of the following:

Knowledge Ecology International
People of Faith for Access to Medicines
Public Citizen
Dean Baker
Social Security Works
American Federation of State, County and Municipal Employees
Universities Allied for Essential Medicines

Annexes:

- KEI Comments re: Practical Application
- Letter from Louisiana Governor John Bel Edwards to Acting Secretary of the Army Robert Speer, May 10, 2017
- Diane Singhroy, Notes on Zika Manufacturing Capacity