An exclusive license to patents on a new Zika vaccine to Sanofi is contrary to the provisions of 35 U.S.C. 209(a)(1)

To: Commander, U.S. Army Medical Research and Materiel Command,
ATTN: Command Judge Advocate, MCMR-JA,
504 Scott Street, Fort Detrick, MD 21702-5012.
Via fax: +1.301.619.5034

CC: Barry M Datlof, CIV,
USARMY MEDCOM USAMRMC (US)
barry.m.datlof.civ@mail.mil

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The following organizations and individuals are providing the following comments on the Department of the Army proposed exclusive license for patents on a vaccine for the Zika virus.

Knowledge Ecology International (KEI)
American Federation of State, County and Municipal Employees (AFSCME)
People of Faith for Access to Medicines (PFAM)
Public Citizen (PC)
Social Security Works (SSW)
Universities Allied for Essential Medicines (UAEM)
Dean Baker, Washington, DC

Background: On December 9, 2016, the U.S. Department of the Army published a notice in the Federal Register, titled: “Intent To Grant an Exclusive License of U.S. Government-Owned Patents.” See: 81 FR 89087. The notice concerned:

> intent to grant an exclusive, royalty-bearing, revocable license to pending United States Provisional Patent Application 62/343,315, entitled, “Zika Virus Vaccine and Methods of Production” filed May 31, 2016 and an exclusive, royalty-bearing, revocable license to pending United States Provisional Patent Application 62/370,260, entitled, “Zika Vaccine and Methods of Preparation” filed August 3, 2016 to Sanofi Pasteur, Inc.

According to the WHO:

> WHO has concluded that Zika virus infection during pregnancy is a cause of congenital brain abnormalities, including microcephaly; and that Zika virus is a trigger of Guillain-Barré syndrome. Intense efforts are continuing to investigate the link between Zika virus and a range of neurological disorders, within a rigorous research framework.

According to the CDC:

> Zika is linked to birth defects. Zika infection during pregnancy can cause a serious birth defect called microcephaly that is a sign of incomplete brain development. Doctors have also found other problems in pregnancies and among fetuses and infants infected with Zika virus before birth.

The Zika virus is spreading, and if an effective vaccine is available, the number of persons who will benefit from the vaccine, including in particular women of childbearing age, will be large. Access to the vaccine will depend in part on the price. The grant of exclusive rights in the patents for a vaccine invented by the federal government and developed on federal government grants and research and development contracts runs the risk of high prices that will be unaffordable for many patients, and will impose large costs on society when vaccines are reimbursed by public or private sector entities.

These comments focus on the requirements of 35 U.S.C. 209(a)(1), which prohibits the use of exclusive licenses in cases where the exclusive rights are not reasonably necessary for the practical application of the invention.

Joint Comments on the Proposed Exclusive License

In our opinion, the Army proposal to grant an exclusive license to patents on a new Zika vaccine to Sanofi is contrary to the provisions of 35 U.S.C. 209(a)(1). According to the statute, a Federal Agency may grant an exclusive or partially exclusive license "only if" the exclusivity is "a reasonable and necessary incentive to call forth the investment capital needed to bring the invention to practical application; or otherwise promote the invention's utilization by the public" (emphasis added).

The grant of the exclusive rights in the patent is an unnecessary incentive to bring the invention to practical application because of the significant federal funding in the clinical trials and the grant of additional exclusivities and subsidies.

1. **The development of the Zika vaccine is financed by the federal government.**

While the Army has been unwilling to share information on the federal government's funding of the vaccine development, there are facts available to the public that are directly relevant. In support of the notion that the federal government is financing the development of this vaccine, consider the following news stories and press releases.

- Sanofi Pasteur press release: "Sanofi Pasteur Signs Research Agreement For Zika Vaccine: Walter Reed Army Institute of Research to transfer technology." July 6, 2016.

http://www.sanofipasteur.com/en/articles/Sanofi-Pasteur-Signs-Research-Agreement-for-Zika-Vaccine.aspx

Sanofi and its vaccines global business unit Sanofi Pasteur announced today a Cooperative Research and Development Agreement (CRADA) with the Walter Reed Army Institute of Research (WRAIR) on the co-development of a Zika vaccine candidate. According to the terms of the agreement, WRAIR will transfer its Zika purified inactivated virus (ZPIV) vaccine technology to Sanofi Pasteur, opening the door for a broader collaboration with the U.S. government.

The agreement also includes Sanofi Pasteur's production of clinical material in compliance with current GMP (Good Manufacturing Practices) to support phase II testing, optimization of the upstream process to improve production yields, and characterization of the vaccine product. Sanofi Pasteur will also create a clinical development and regulatory strategy.

WRAIR will share data related to the development of immunologic assays designed to measure neutralizing antibody responses following natural infection and vaccination with ZPIV, biologic samples generated during the performance of non-human primate studies, and biologic samples generated during the performance of human safety and immunogenicity studies using ZPIV. WRAIR, the National Institute of Allergy and Infectious Diseases (NIAID)--part of the U.S. National Institutes of Health (NIH), and the Biomedical Advanced Research and Development Authority (BARDA)--part of the Health & Human Services (HHS) Office of the Assistant Secretary of Preparedness and Response--have been coordinating pre-clinical development of the candidate encouraged by new, pre-clinical research conducted by WRAIR and the Beth Israel Deaconess Medical Center[1]. NIAID will sponsor a series of phase 1 ZPIV trials while the technology transfer process is occurring.

- Sanofi Pasteur Press Release, BARDA Grants $43.2 Million USD To Sanofi Pasteur For Zika: Funds will be used for phase II development and manufacturing, September 26, 2016.
  http://sanofipasteurus.mediaroom.com/2016-09-26-BARDA-Grants-43-2-million-USD-to-Sanofi-Pasteur-for-Zika

This press release states the following:

"Sanofi Pasteur is in the process of creating a clinical development and regulatory strategy while WRAIR and the National Institute of Allergy and Infectious Diseases (NIAID)--part of the U.S. National Institutes of Health (NIH)—are conducting a series of phase I ZPIV trials. Beyond the funding provided by BARDA for the two phase I/II clinical trials, there is an option in the contract that BARDA can exercise for continuing support through Phase III industrial and clinical development. . . .

> The Biomedical Advanced Research and Development Authority (BARDA), within the Office of the Assistant Secretary for Preparedness and Response in the U.S. Department of Health and Human Services, provides an integrated, systematic approach to the development and purchase of the necessary vaccines, drugs, therapies, and diagnostic tools for public-health medical emergencies. The project has been funded with Federal funds from BARDA under Contract HHSO100201-6000039C."

See also:

- Cheryl Pellerin, Army Researchers, Sanofi Pasteur to Co-Develop Zika Virus Vaccine, *DoD News*, Defense Media Activity, July 7, 2016 https://www.defense.gov/News/Article/Article/830751/army-researchers-sanofi-pasteur-to-co-develop-zika-virus-vaccine

- Katie Lange, Army specialist aids in development of potential Zika vaccine, July 22, 2016, *DoD News.* https://www.army.mil/article/172025/army_specialist_aids_in_development_of_potential_zika_vaccine

- Col. Nelson L. Michael and Col. Stephen J. Thomas, Army researchers developing Zika vaccine, Walter Reed Army Institute of Research, August 3, 2016 https://www.army.mil/article/172733/army_researchers_developing_zika_vaccine

- Bill Berkrot, "Zika vaccine race spurred by crisis and profit potential," October 4, 2016. Reuters story. http://finance.yahoo.com/news/zika-vaccine-race-spurred-crisis-051317237.html

The Reuters story focuses on the potential profits from the vaccine:

> Although Zika infections are mild or asymptomatic in most people, demand for a vaccine is expected to be strong because it can cause devastating birth defects, pharmaceutical executives and disease experts said.
>
> The most lucrative market is seen in travelers seeking inoculation against the virus that has moved rapidly across the Americas and is the only mosquito-borne disease also spread through sex.
>
> "It scares people," said Scott Weaver, a virologist with the University of Texas and chairman of the Zika task force for the Global Virus Network. "Europeans and Americans can pay a pretty high price for these kinds of vaccines."

"If you consider just a portion of the U.S. traveler population, we can conservatively envision a Zika market opportunity exceeding $1 billion" a year, said Joseph Kim, chief executive of Inovio Pharmaceuticals (INO.O), a Pennsylvania company that is farthest along in the development path with human testing of a vaccine candidate underway in hard hit Puerto Rico.

- Cheryl Pellerin, Human trials begin for Army-developed Zika vaccine, *DoD News,* Defense Media Activity, November 9, 2016, https://www.army.mil/article/178087/human_trials_begin_for_army_developed_zika_vaccine

- 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." December 16, 2016. *Wall Street Journal.* http://www.wsj.com/articles/americas-next-defense-against-zika-and-other-foreign-invaders-1481810402

The McKay and Loftus article includes this comment on the commercial market for the vaccine:

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."

- Ed Silverman, "US Army license being awarded to Sanofi for a Zika vaccine raises questions", *Stat News,* December 22, 2016. https://www.statnews.com/pharmalot/2016/12/22/zika-vaccines-army-sanofi/

The Silverman article provided this relevant quote from Sanofi, which indicates that Sanofi anticipates the federal funding of the vaccine development will continue through late stage testing, and it notes that Sanofi has not even created its own commercial plan for development:

> “A Sanofi Pasteur spokeswoman tells us that the vaccine maker has not yet created a commercial plan and could not say what price may eventually be charged or when the vaccine might become available. Late-stage testing has not begun. She did say the company expects to ask BARDA for more funding.”

- Patrick Adams And Cameron Nutt, A Zika Vaccine, but for Whom? New York Times. December 28, 2016. https://mobile.nytimes.com/2016/12/28/opinion/a-zika-vaccine-but-for-whom.html

The Adams and Nutt op-ed focuses on concerns about access to the vaccine in Africa:

> In September, Congress allocated $1.1 billion to combat Zika in the United States. That’s compared with the $2 million raised by the African Development Bank to support the World Health Organization’s Zika surveillance in parts of Africa. Moreover, to help pay for the American domestic response, Congress cut $109.5 million previously dedicated to strengthening laboratory capacity in parts of West Africa devastated by Ebola — funding that might have helped to define and address the threat of Zika in Africa.
>
> The paradox is that while the development of a Zika vaccine relies heavily on knowledge acquired from Africa, Zika vaccines are unlikely to be prioritized for use there — largely because we have been content to accept flimsy assumptions as scientific facts. Like other diseases before it, the data on Zika seems to matter only when it helps those of us in rich countries protect ourselves. Yet it’s this double standard that allows outbreaks to become pandemics, and that imperils public health — in Africa and everywhere.

- Eric Sagonowsky, U.S. Army's planned Zika vax license to Sanofi raises nonprofit's ire. FiercePharma, January 10, 2017. http://www.fiercepharma.com/vaccines/u-s-army-s-zika-vax-license-to-sanofi-gets-nonprofit-s-ire

> A Sanofi spokesperson said the company is "sharing inherent risks" by partnering with the government on Zika, adding that, even with tax-funded support, the drug giant is "still assuming financial and opportunity risks by devoting human and other resources to this project that otherwise would be working on other projects."
> "We have been informed of the objections and welcome the opportunity to respond," according to the spokesperson.
>
> Sanofi says it has "modeled various scenarios" for the virus and its prevalence, adding that the "nature of the epidemiology and spread of the virus will impact the degree of profitability." Sanofi said it's "way too early" to talk about pricing or when the vaccine candidate might be available.

The January 10, 2017 story by Sagonowsky does not explain or quantify the financial investments by Sanofi in the Zika vaccine. The quotes from Sanofi can be read as a claim that even when the federal government is paying for the research and development, Sanofi could have directed its own staff to work on other projects, so there was a undefined opportunity cost for Sanofi's attention to Zika. But in any event, it is the responsibility of the Army to determine if granting exclusive rights are a necessary incentive for the development of the vaccine, when the company's financial contributions are minor, and when the company will benefit from two other policy mechanisms that act as robust incentives, given Sanofi's minimal financial risks and contributions.

2. **Sanofi will benefit from exclusive rights in test data granted under the CRADA agreement.**

Biologic products benefit from 12 years of exclusive rights that prevent a potential competitor from gaining marketing approval through reliance upon evidence that a vaccine is safe and effective.

42 U.S.C. 262(i) defines biologic products to include vaccines.

42 U.S.C. 262(k)(7)(A) creates 12 years of exclusive rights in the test data.

The 12 years of exclusive rights in test data are, wholly apart from any patent protection that may or may not exist, a significant barrier for entry by a biosimilar product, and would require a follow on biosimilar product to replicate costly and time consuming clinical trials. See, for example:

- Emerging Health Care Issues: Follow-on Biologic Drug Competition, Federal Trade Commission Report, June 2009

3. **Sanofi will benefit from the FDA Priority Review Voucher.**

In 2016, Zika was added to the number of diseases eligible for the FDA Priority Review Voucher (PRV) by the Congress. Public Law 114-147, which amended 21 U.S.C. § 360n(a)(3)(R).

- U.S. President Obama Signs Bill Adding Zika Virus To FDA List Of Diseases For Priority Review Voucher Program, Kaiser Daily Global Health Policy Report. April 20, 2016 http://kff.org/news-summary/u-s-president-obama-signs-bill-adding-zika-virus-to-fda-list-of-diseases-for-priority-review-voucher-program/

See also: Tropical Disease Priority Review Vouchers - Guidance for Industry

U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), October 2016, which includes this statement:

> Q2. What diseases are considered tropical diseases for priority review voucher purposes?
>
> A tropical disease is any of the following diseases (see section 524(a)(3) of the FD&C Act):
> * Tuberculosis
> * Malaria
> * Blinding trachoma
> * Buruli Ulcer
> * Cholera
> * Dengue/Dengue haemorrhagic fever
> * Dracunculiasis (guinea-worm disease)
> * Fascioliasis
> * Human African trypanosomiasis
> * Leishmaniasis
> * Leprosy
> * Lymphatic filariasis
> * Onchocerciasis
> * Schistosomiasis
> * Soil transmitted helminthiasis
> * Yaws
> * Filovirus Diseases
> * **Zika Virus Disease**
> * Any other infectious disease for which there is no significant market in developed nations and that disproportionately affects poor and marginalized populations, designated by order of the Secretary.

The PRV is a valuable incentive in itself. For example, in 2015, United Therapeutics sold an FDA PRV to AbbVie for $350 million. Reuters, “AbbVie buys special review voucher for $350 million,” Aug. 29, 2015, http://www.reuters.com/article/us-abbvie-priorityreview-idUSKCN0QO1LQ20150819.

Concluding comments on 35 USC 209(a)(1).

It is the combination of federal funding on the R&D and the incentives already provided for in the 12 years of exclusive rights to use test data for marketing approval, and the FDA Priority Review Voucher that make an exclusive license on the patents unnecessary and unlawful under 35 USC 209(a)(1).

Signed:

Knowledge Ecology International is a non-profit non-governmental organization that advocates for access to affordable medicines, with a focus on human rights and social justice.

AFSCME is the American Federation of State, County and Municipal Employees with 1.6 million members who provide the vital services that make America happen. AFSCME advocates for fairness in the workplace, excellence in public services and prosperity and opportunity for all working families.

People of Faith for Access to Medicines 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.

Public Citizen is a consumer advocacy organization with more than 400,000 members and supporters. Areas of organizational focus include medical technology safety and access, among others.

Social Security Works (SSW) is a non-profit organization. Its mission is to protect and improve the economic security of disadvantaged and at-risk populations, safeguard the economic security of those dependent, now or in the future, on Social Security, and maintain Social Security as a vehicle of social justice.

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

Dean Baker is an economist and co-founder of the Center for Economic and Policy Research.

Annex I, statutes referenced

35 U.S.C. 209(a)

United States Code, 2011 Edition
Title 35 - PATENTS
PART II - PATENTABILITY OF INVENTIONS AND GRANT OF PATENTS
CHAPTER 18 - PATENT RIGHTS IN INVENTIONS MADE WITH FEDERAL ASSISTANCE

Sec. 209 - Licensing federally owned inventions

§209. Licensing federally owned inventions

(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;

(3) the applicant makes a commitment to achieve practical application of the invention within a reasonable time, which time may be extended by the agency upon the applicant's request and the applicant's demonstration that the refusal of such extension would be unreasonable;

(4) granting the license will not tend to substantially lessen competition or create or maintain a violation of the Federal antitrust laws; and

(5) in the case of an invention covered by a foreign patent application or patent, the interests of the Federal Government or United States industry in foreign commerce will be enhanced.

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42 U.S.C. 206 (i) and (k)(7)(A)

United States Code, 2010 Edition
Title 42 - THE PUBLIC HEALTH AND WELFARE
CHAPTER 6A - PUBLIC HEALTH SERVICE

SUBCHAPTER II - GENERAL POWERS AND DUTIES
Part F - Licensing of Biological Products and Clinical Laboratories
subpart 1 - biological products
Sec. 262 - Regulation of biological products

§262. Regulation of biological products

(i) "Biological product" defined

In this section:

(1) The term "biological product" means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.

(k) Licensure of biological products as biosimilar or interchangeable

(7) Exclusivity for reference product

(A) Effective date of biosimilar application approval

Approval of an application under this subsection may not be made effective by the Secretary until the date that is 12 years after the date on which the reference product was first licensed under subsection (a)

Annex II, Zika virus statistics

CDC Case counts, as of January 4, 2017 (5 am EST)

US States

Locally acquired mosquito-borne cases reported: 216
Travel-associated cases reported: 4,618
Laboratory acquired cases reported: 1
Total: 4,835
Sexually transmitted: 38
Guillain-Barré syndrome: 13

US Territories

Locally acquired cases reported: 35,021
Travel-associated cases reported: 131
Total: 35,152*
Guillain-Barré syndrome: 50

CDC data on Zika virus disease cases, by area, as of January 4, 2017

Laboratory-confirmed Zika virus disease cases reported to ArboNET by state or territory — United States, 2015–2017 (as of January 4, 2017)§

States	Travel-associated cases* No. (% of cases in states) (N=4,619)	Locally acquired cases† No. (% of cases in states) (N=216)
Alabama	30 (1)	0 (0)
Arizona	51 (1)	0 (0)
Arkansas	15 (<1)	0 (0)
California	393 (9)	0 (0)

Colorado	49 (1)	0 (0)
Connecticut	58 (1)	0 (0)
Delaware	17 (<1)	0 (0)
District of Columbia	30 (1)	0 (0)
Florida	825 (18)	210 (97)
Georgia	106 (2)	0 (0)
Hawaii	16 (<1)	0 (0)
Idaho	4 (<1)	0 (0)
Illinois	90 (2)	0 (0)
Indiana	51 (1)	0 (0)
Iowa	21 (<1)	0 (0)
Kansas	19 (<1)	0 (0)
Kentucky	29 (1)	0 (0)
Louisiana	35 (1)	0 (0)
Maine	13 (<1)	0 (0)

Maryland	129 (3)	0 (0)
Massachusetts	115 (2)	0 (0)
Michigan	64 (1)	0 (0)
Minnesota	64 (1)	0 (0)
Mississippi	23 (1)	0 (0)
Missouri	35 (1)	0 (0)
Montana	7 (<1)	0 (0)
Nebraska	13 (<1)	0 (0)
Nevada	19 (<1)	0 (0)
New Hampshire	12 (<1)	0 (0)
New Jersey	173 (4)	0 (0)
New Mexico	9 (<1)	0 (0)
New York	989 (21)	0 (0)
North Carolina	86 (2)	0 (0)
North Dakota	2 (<1)	0 (0)

Ohio	80 (2)	0 (0)
Oklahoma	29 (1)	0 (0)
Oregon	42 (1)	0 (0)
Pennsylvania††	166 (4)	0 (0)
Rhode Island	50 (1)	0 (0)
South Carolina	54 (1)	0 (0)
South Dakota	2 (<1)	0 (0)
Tennessee	59 (1)	0 (0)
Texas	287 (6)	6 (3)
Utah	20** (<1)	0 (0)
Vermont	10 (<1)	0 (0)
Virginia	106 (2)	0 (0)
Washington	61 (1)	0 (0)
West Virginia	11 (<1)	0 (0)
Wisconsin	48 (1)	0 (0)

Wyoming	2 (<1)	0 (0)
Territories	**Travel-associated cases* No. (% of cases in territories) (N=131)**	**Locally acquired cases† No. (% of cases in territories) (N=35,021)**
American Samoa	1 (1)	114 (<1)
Puerto Rico	128 (98)	34,045*** (97)
US Virgin Islands	2 (2)	862 (3)

§Only includes cases meeting the probable or confirmed CSTE case definition and does not include asymptomatic infections unless the case is a pregnant woman with a complication of pregnancy
*Travelers returning from affected areas, their sexual contacts, or infants infected in utero
†Presumed local mosquito-borne transmission
††One additional case acquired through laboratory transmission
**Includes one case with unknown route of person-to-person transmission.
***The Puerto Rico Department of Health is retroactively reporting cases, resulting in larger than normal increases in cases in recent weeks.