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Doctors Without Borders/ Médecins Sans Frontières (MSF) Comments to the Department of Defense Notice of Intent to Grant an Exclusive License of U.S. Government-Owned Patents on a Zika Vaccine Candidate

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Doctors Without Borders/Médecins Sans Frontières (MSF) provides the following comments regarding the Notice from the Department of the Army of the United States Department of Defense *of its 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.* Notice appeared in 81 FR 89087 on Friday, December 9, 2016.

MSF objects to the grant of an exclusive patent license and urges the United States government to consider the negative impact an exclusive agreement will have on the development, affordability and availability of a Zika vaccine, which is urgently needed for people affected by the Zika virus in the United States and worldwide. We ask the U.S. government to consider instead granting an open non-exclusive patent license with appropriate and publicly available terms and conditions to help ensure that further development of this U.S. government funded-technology will prioritize all health needs and ensure sustainable and affordable access of any resulting vaccine.

Overview

MSF is an international medical humanitarian organization working in nearly 70 countries. Every year, MSF vaccinates tens of thousands of children, delivering more than 3.9 million doses of vaccines and immunological products in 2014 alone. We need biomedical innovations that improve medical outcomes and are accessible and affordable, including for prevention and treatment of global health emergencies. We hope to use an effective Zika vaccine in our medical operations in the future. MSF, Ministries of Health and people around the world will only be able to benefit from the U.S. government investment if the resulting vaccine is effective, safe, available, affordable and suitably adapted to the resource-limited settings where most people affected by Zika virus live. Through our work, MSF witnesses the everyday impact of having limited or no access to medicines, diagnostics and vaccines, due to the lack of innovation on essential, suitably adapted and affordable medical tools in the contexts and populations where they are most needed.

We recognize the need to reward innovation and finance research and development (R&D). We thank the U.S. government for its funding and leadership in Zika vaccine research. The acceleration¹ of research on Zika vaccine candidates almost a year after the World Health Organization declared the epidemic a global health emergency is very welcomed.

However, an exclusive license to a single pharmaceutical company is unnecessary to promote innovation and instead has the potential of hindering innovation as well as future access to this promising vaccine candidate. The need for an open public health-driven innovation approach is even more important given that this medical technology has been fully funded and is owned by the United States government. The licensing of this technology should ensure full public return on the public investment that U.S. taxpayers have made and are continuing to make.

A vaccine that is not appropriately developed or a vaccine without appropriate measures to ensure access is insufficient and would be a missed opportunity to make maximal use of limited US government resources. The next step in the Zika vaccine development process, including its licensing and technology transfer strategy, needs to ensure that U.S. government funding and leadership in vaccine R&D results in a vaccine that is effective and accessible for all patients in need in the U.S. and globally, including the most neglected. As the latest Ebola outbreak in West Africa should constantly remind us, diseases have no borders in a globalized world. Without a global research and access strategy for the Zika vaccine, Zika will not be fully stopped.

Exclusive patent licensing is not a necessary or appropriate strategy to further develop this Zika vaccine candidate.

MSF objects to the granting of this exclusive license for development of Zika vaccine candidates for the following reasons:

1. The grant of exclusivity is not a reasonable and necessary incentive to promote innovation and further development of a Zika vaccine.

We agree with comments submitted by Knowledge Ecology International and others² that argue that the Army proposal to grant an exclusive license to patents on a Zika vaccine to Sanofi Pasteur (Sanofi) is contrary to the provisions of 35 U.S.C. 209(a)(1). According to U.S. law, the United States government 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 inventions utilization by the public.” In other words, the U.S. government cannot grant exclusive licenses in cases where the exclusive rights are not reasonable and necessary for the practical application and utilization of the invention.

Before an exclusive license is granted, Sanofi or any other potential recipient of an exclusive license and the U.S. Army have the burden of proving that these exclusive rights are necessary. Pharmaceutical companies usually argue that exclusivity is necessary to recoup investments and risk associated with the research and development process, as well the opportunity cost to work on a given technology, but we argue that this exclusivity is unnecessary to promote innovation and the further development of the vaccine candidate given:

- a. The significant funding and resources that the U.S. government has already dedicated to this vaccine candidate, including more than \$40 million in BARDA grant funding to Sanofi.³

- b. Sanofi and any other vaccine developer that further develops this vaccine candidate are also eligible to receive additional funding, incentives and subsidies from the U.S. government, including the likely lucrative Food and Drug Administration (FDA) Priority Review Voucher (PRV) for neglected diseases, without any product access conditions attached, if a vaccine is successfully registered with the FDA⁴, as well as potentially the different tax credits and exclusivities attached to an orphan drug designation. The FDA voucher itself has been valued on the open market at at least 350 million USD through recent reported transactions.
- c. Sanofi and other vaccine developers may also receive other resources provided by other countries. For example, the funds and resources that will be made available to accelerate vaccine development for emerging infectious diseases with the recently launched Coalition for Epidemic Preparedness Innovations (CEPI) that multiple governments, philanthropies like the Bill & Melinda Gates Foundation and the Wellcome Trust, and MSF are members of.
- d. There is no publicly available information on the investment that Sanofi has made or will need to make to complete development of this vaccine. The financial risk and investment that Sanofi will need to make is limited and predictable, but the potential profitability is considerable. There is an expected profitable commercial market for this vaccine that will provide appropriate incentives for recovering any potential additional investment that Sanofi or any other vaccine developers may need to make to further develop this technology.

2. The grant of patent exclusivity can hinder innovation for Zika vaccines and doesn't allow research strategies that promote collaboration and focus on neglected medical needs.

The grant of exclusive rights in the US government-owned patents is not the best tool to promote innovation and can hinder innovative efforts on Zika vaccine development. Even where government funding does lead to important advances in biomedical innovation, these investments still do not necessarily lead to effective prioritization of further R&D and successful outcomes driven by patients and public health needs if the appropriate licensing and technology strategy is not pursued.

- a. An exclusive license will give Sanofi a monopoly in the research, manufacturing and sale of the technology and will allow Sanofi to exclude competition in the clinical development as well as in the manufacturing and pricing of this technology.
- b. The grant of exclusivity does not ensure that the Zika vaccine development process will target the populations most in need. Sanofi will be allowed to pursue research strategies to maximize use of the vaccine candidate in profitable markets, like the U.S. or the travel market, limiting or excluding clinical development of competing research agendas that should include a broader and diverse geographical scope to ensure any resulting vaccine is effective and useful in the full range of populations who may need this vaccine, including neglected patients in Africa and other neglected regions.⁵
- c. The grant of exclusivity does not ensure that a vaccine will be developed or that it will adhere to a timely development process. The recent announcement on promising results of clinical trials of rVSV Ebola vaccine that MSF supported shows the importance of government funding and leadership for vaccine development. It also shows how the Canadian government's exclusive licensing was unnecessary and tragically delayed urgently needed innovation. It was thanks to initial studies at a Canadian government laboratory that the VSV-EBOV vaccine was confirmed as potentially effective against Ebola. Despite the fact that the government licensed this vaccine to a U.S. company, NewLink, four years before the West African Ebola outbreak, the project stalled and the vaccine was not made available to people at risk for more than five years. If at least Phase

If clinical trials had been conducted prior to the most recent outbreak, the vaccine could have been deployed during the emergency and potentially helped save lives. This wasted opportunity and failure to advance the vaccine's development nevertheless netted NewLink more than \$63.5M profit when they sold the rights to pharmaceutical company Merck during the most critical phase of the outbreak. A non-exclusive license could have allowed the Canadian government, either prior to or during the outbreak, to take more decisive action to encourage or require the timely testing and development of the vaccine.

3. An exclusive license can be a barrier to ensuring a Zika vaccine will be available and affordable to all who need it.

The high price of vaccines is already a key medical and operational challenge for MSF and many governments. By 2014 the price to fully vaccinate a child in the poorest countries of the world was 68 times more expensive⁶ than it was in 2001. The price in other countries is even higher. Many countries, especially countries considered middle-income economies, are often unable to afford new high-priced vaccines that prevent countless deaths from vaccine-preventable diseases such as childhood pneumonia.

Before granting a license on U.S. government-owned rights, the U.S. government should ensure that the license will ensure that the "benefits" of the invention will be "available to the public on reasonable terms," a requirement of 35 U.S.C. §201(f). Granting an exclusive license to a vaccine manufacturer will not only fail to ensure any resulting vaccine is available on reasonable terms, but can also become a significant barrier to the future availability and affordability of the vaccine.

As the vaccine development has been publicly financed by the U.S. government, the price of any resulting vaccine should be closely aligned with production costs. Yet, an exclusive license to Sanofi will allow the company to charge high prices based on what their targeted markets will bear regardless of actual costs. Based on our experience, leaving these decisions exclusively to a pharmaceutical company may not lead to appropriate public health outcomes. We hope Sanofi commits to and implements an appropriate access and manufacturing strategy, but it is relevant for the U.S. government to know that when left to decide strategy without government oversight, Sanofi has failed previously and currently to ensure uninterrupted manufacturing, supply and affordability of essential medical tools for which they are the sole supplier. For example, Sanofi's pricing strategies for its inactivated polio vaccine⁷ and dengue vaccine⁸ are a barrier to access for many middle-income countries.

While MSF continues to be challenged by high prices of medical tools, we know that high prices are avoidable and affordable innovation is possible. In 2001, high prices left MSF limited in our ability to save the lives of people living with HIV. At the time pharmaceutical companies charged MSF, governments and patients an astronomical US \$10,000 per person, per year for antiretroviral medicines used to treat HIV. This meant that MSF and governments, in the face of thousands of people dying daily from AIDS-related illnesses, could only provide treatment to a very limited number of people. In response, affected governments and civil society applied legal safeguards to remove patent barriers and foster generic competition. HIV treatment costs fell, virtually overnight, to one US dollar a day per person.⁹ As a result of competition among generic medicines producers, prices for first-line HIV medicines have continued to fall and today more than 18 million people receive treatment,¹⁰ including through U.S. government-funded programs such as the President's Emergency Plan For AIDS Relief (PEPFAR) and the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund). In 2012, generics accounted for 96 percent of all treatments purchased by donor-funded programs such as the Global Fund.¹¹

An exclusive license will also be barrier to competition in the manufacturing and supply of the technology, as it will allow Sanofi to exclude other manufacturers from producing and selling the technology. Promoting competition is the best tool to ensure affordability as well as ensuring sufficient manufacturing and supply

of any resulting vaccine. MSF and patients have repeatedly experienced the consequences of what happens when a single supplier discontinues manufacturing of an effective and needed product for conditions affecting neglected populations. For example, in 2010, due to limited profitability, Sanofi decided to stop manufacturing an important antivenom to treat deadly snake bites. The company did not reveal this decision until 2013, resulting in a worldwide supply shortage of a critical antivenom before a replacement product can be launched.¹²

A better way to promote U.S. government funded innovation: open non-exclusive licenses with terms and safeguards for patient-driven innovation and future affordable access

An exclusive license fails to address the need for an innovation strategy that put the needs of all patients and vaccine providers at the center of the biomedical innovation system. Instead, MSF recommends that the U.S. government consider an open licensing and technology transfer strategy to allow Sanofi and a variety of vaccine developers and researchers to test and further develop this vaccine, promoting a variety of scientific, research, development, business and delivery approaches. The licensing of this technology should include the creation of terms and conditions that will act as safeguards to ensure that the development will be patient-driven and that any resulting vaccine will be safe, effective, appropriately available and affordable to all people in need. We also recommend that the U.S. government make the terms and conditions of the license publicly available to allow for appropriate review, accountability and implementation of the safeguards created.

Granting an open non-exclusive license with the appropriate terms and conditions will have at least the following positive public health impact:

1. An open license can help promote timely development of the vaccine candidate.

An open, non-exclusive license not only ensures that multiple companies can move towards developing the product, but can ensure that if one company fails to meet milestones or advance development, the patent holder (the US government) can move on to others and not have their hands tied. A non-exclusive license allows several vaccine developers to pursue different research, regulatory and development strategies of the vaccine candidate, and also can reduce the negative health impact of research stalled or delayed by a single researcher strategy. For example, in the case of the rVSV Ebola vaccine highlighted above, had the Canadian government granted an open license, governments and medical service providers such as MSF would not have been dependent on the development timeline of only one company.

2. An open license will allow interested companies to test the safety and efficacy of the vaccine candidate in a variety of populations and contexts.

An open license allows several companies and vaccine researchers to test the effectiveness and safety of the technology in a variety of settings, including pursuing research strategies that target the needs of neglected populations due to expectation of limited profitability and/or knowledge gaps on Zika epidemiology in Africa.

3. An open license will help ensure stable supply.

An open license allows several companies to manufacture a resulting vaccine and reduces the public health liability created by a single manufacturer that decides to stop manufacturing or is not able to meet the global demand of a successfully developed Zika vaccine.

4. An open license will help ensure affordable access.

An open license may facilitate the emergence of competition in the manufacturing and supply of Zika vaccines, which is ultimately the best tool to promote affordability.

U.S. government can lead the way on creating new models for research and development for essential medical tools

The reliance on the creation and granting of exclusivities to pharmaceutical companies in R&D of essential medical technologies is a flawed paradigm for funding and promoting innovation. This often leads to limited access while failing to stimulate open and patient-driven innovation. It is even less rational when the United States is already funding and de-risking the development of the medical technology as is the case with the Zika vaccine.

New approaches are needed not only to avoid US taxpayers paying twice¹³ – first by paying a significant percentage of the R&D costs and second by paying high prices – but also to ensure that the vaccine development and manufacturing process will be public health-driven and benefit all in need, especially for essential medical tools like vaccines needed for emergencies and epidemics.

MSF has for years raised the alarm about the challenges of high prices and need for new incentives to promote innovation that do not rely on monopolies and exclusivities. In our experience, both as a medical provider and funder of innovation,¹⁴ competition and open access to essential medical technologies is a useful tool to reduce prices and promote supply security and therefore increase access to resulting technologies. MSF recently published a report on biomedical innovation, “Lives on the Edge: Time to align medical research and development with people’s health needs,”¹⁵ that provides an overview of some the challenges with the current innovation system and our proposals on steps governments need to take to improve it.

New approaches to promote medical innovation, including approaches that MSF and others have supported, are demonstrating that affordable and accessible medical breakthroughs are possible. This is particularly true when intellectual property is openly pooled, like with the UNITAID-Medicines Patent Pool – which the US National Institutes of Health was the first to join, to promote competition in the HIV/AIDS drug development¹⁶ – and when incentives break the link between the cost of R&D and the price and sale of the end product.

There are ongoing efforts in international fora to consider how this could be achieved, including in the commitments made by the United States and other governments on new models for biomedical innovation that de-link R&D costs from prices in recent years at the World Health Assembly following the Report of the Consultative Expert Working Group on R&D Financing and Development (CEWG report) and most recently through the 2016 UN Political Declaration on Antimicrobial Resistance. In the same direction, the recently released report of the UN Secretary General’s High Level Panel on Access to Medicines made a variety of recommendations,¹⁷ including increasing transparency and reforming incentives for innovation, especially for the licensing of publicly funded research.

Conclusion

At a time when the high price of life-saving medical tools, including hepatitis drugs, biologics and vaccines, is becoming a barrier to effective medical care worldwide and medicines are being rationed because of high prices in the U.S. and around the world, it is very concerning to see the U.S. government considering locking in a development deal that will limit innovation and will not safeguard affordable access to the resulting

vaccine. Instead of creating new exclusivities for pharmaceutical companies by giving away exclusive rights on publicly funded innovation, the U.S. government should pursue R&D strategies that promote open and collaborative innovation and ensure affordable access to resulting products.

¹ Thomas K. The Race for a Zika Vaccine. New York Times. 19 November 2016. Available from: <https://www.nytimes.com/2016/11/20/business/testing-the-limits-of-biotech-in-the-race-for-a-zika-vaccine.html> and, Pellerin C. Human Trials Begin for Army-Developed Zika Vaccine. US Department of Defense. 8 November 2016. Available from: <https://www.defense.gov/News/Article/Article/999584/human-trials-begin-for-army-developed-zika-vaccine>

² Comments by KEI and others. 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). Submitted 12 January 2017. Available from: <http://keionline.org/sites/default/files/Zika-12Jan2016-KEI-AFSCME-PFAM-UAEM-BAKER-35USC209a1.pdf>

³ Pellerin C. Army Researchers, Sanofi Pasteur to Co-Develop Zika Virus Vaccine. Department of Defense. 7 July 2016. Available from: <https://www.defense.gov/News/Article/Article/830751/army-researchers-sanofi-pasteur-to-co-develop-zika-virus-vaccine>, and Sagonowsky E. Sanofi grabs \$43M in U.S. government funds to advance Zika vaccine into Phase I. FiercePharma. 26 September 2016. Available from: <http://www.fiercepharma.com/vaccines/sanofi-grabs-43m-u-s-government-funds-for-zika-vaccine-r-d>

⁴ Brock W, Cohen R, Cone J, McKenna L. The Zika loopholes. Politico. 25 March 2016. Available from: <http://www.politico.com/agenda/story/2016/03/the-right-way-to-encourage-companies-to-develop-a-treatment-for-zika-000079>

⁵ Adams P, Nutt C. A Zika Vaccine, but for Whom? New York Times. 28 December 2016. Available from: https://www.nytimes.com/2016/12/28/opinion/a-zika-vaccine-but-for-whom.html?_r=0

⁶ MSF. The Right Shot: Bringing down barriers to affordable and adapted vaccines, 2nd ed. January 2015. Available from: <https://www.msfaccess.org/our-work/vaccines/article/2345>

⁷ MSF. MSF responds to inactivated polio vaccine price announcement. 4 March 2014. Available from: <https://www.msfaccess.org/content/msf-responds-inactivated-polio-vaccine-price-announcement>

⁸ Coconuts Manila. DOH: We can't afford to give free dengue vaccine to everyone. 22 February 2016. Available from <http://manila.coconuts.co/2016/02/22/doh-we-cant-afford-give-free-dengue-vaccine-everyone>

⁹ Médecins Sans Frontières. Untangling the Web of Antiretroviral Price Reductions, 17th edition. July 2014. Available from: http://www.msfaccess.org/sites/default/files/MSF_UTW_17th_Edition_4_b.pdf

¹⁰ UNAIDS. Fact sheet November 2016. Available from: <http://www.unaids.org/en/resources/fact-sheet>

¹¹ UNITAID. HIV Medicines Technology and Market Landscape. March 2014. Available from: <http://www.unitaid.eu/images/marketdynamics/publications/HIV-Meds-Landscape-March2014.pdf>

¹² MSF. Snakebite: How Sanofi slithered its way out of the neglected antivenom market. July 2015. Available from: https://www.msfaccess.org/sites/default/files/NTDs_Brief_FavAfrique_ENG_2015.pdf

¹³ An exclusive license will undermine existing United States domestic and global commitments towards the fight against zika. The Congressionally approved Zika funding totals at least \$1.1 billion in 2016. Source: The Status of Funding for Zika: The President's Request, Congressional Proposals, & Final Funding - <http://kff.org/global-health-policy/issue-brief/the-status-of-funding-for-zika-the-presidents-request-congressional-proposals-final-funding/>

¹⁴ See for example, http://www.dndi.org/wp-content/uploads/2009/03/DNDi_Modelpaper_2013.pdf and MSF's proposal for a better model for TB R&D regime development: <http://www.msfaccess.org/spotlight-on/3p-project-new-approach-developing-better-treatments-tb>

¹⁵ MSF. Lives on the Edge: Time to align medical research and development with people's health needs. May 2016. Available from: <http://www.msfaccess.org/content/report-lives-edge-time-align-medical-research-and-development-people%E2%80%99s-health-needs>

¹⁶ Chen H. US Government First to Share Patents with Medicines Patent Pool. The White House. 30 September 2010. Available from: <https://www.whitehouse.gov/blog/2010/09/30/us-government-first-share-patents-with-medicines-patent-pool>

¹⁷ Full report and submissions to the UN Secretary General High Level Panel on Access to Medicines, available from: <http://www.unsgaccessmeds.org/>