January 7, 2019

Peter Soukas, J.D.
Technology Transfer and Patent Specialist
Technology Transfer and Intellectual Property Office
National Institute of Allergy and Infectious Diseases
National Institutes of Health, 5601 Fishers Lane, Suite 6D
Rockville, MD 20852-9804
Via Email: ps193c@nih.gov

Re: 83 FR 65696. Prospective Grant of Exclusive Patent License: Production of Live Respiratory Syncytial Virus and Parainfluenza Virus Vaccines to Medigen Vaccines Biologics Corp. (Medigen), having a place of business in Zhubei, Taiwan.

Dear Peter Soukas,

We are writing to express opposition to the grant of an exclusive license for U.S. Provisional Patent Application Number 62/661,320, filed April 23, 2018 and entitled "Chimeric Vaccines," [HHS Reference No. E-018-2018-0]; and U.S. and foreign patent applications claiming priority to the aforementioned application to Medigen Vaccines Biologics Corp. (Medigen), having a place of business in Zhubei, Taiwan.

According to the Federal Register notice 83 FR 65696, the intellectual property to be licensed is:

> "U.S. Provisional Patent Application Number 62/661,320, filed April 23, 2018 and entitled 'Chimeric Vaccines,' [HHS Reference No. E-018-2018-0]; and U.S. and foreign patent applications claiming priority to the aforementioned applications."

A search for this application using several patent databases does not return any provisional application with that number. An email received on January 7, 2019, from Peter Soukas, J.D., to Knowledge Ecology International (KEI) confirmed that the patent application has not been published.

We note that the provisional application was filed in April 2018, and the USPTO normally does not publish such applications for 18 months, pursuant to 35 U.S.C. § 122.

KEI and Doctors without Borders/Médecins Sans Frontières (MSF) have asked your office for a copy of the patent application, but one was not provided.

Although the notice states that the license will also cover "foreign patent applications claiming priority to the aforementioned applications," and states that the geographical scope of the license "may be worldwide," the notice does not have information regarding which specific

countries will be included in this license. Because the provisional patent application was filed in April 2018, it is still well within the deadline to file for a PCT application or additional direct national filings. For the purpose of analysing the scope of a license and whether it complies with 35 U.S.C. § 209 and 37 CFR part 404, understanding which countries will be covered by the exclusive license is critically important. This information has not been provided.

The Federal Register notice 83 FR 65696 announcing the grant of this exclusive license was published on December 21, 2018, the Friday before the Christmas holiday. The deadline to file comments is January 7, 2019. While 35 U.S.C. § 209 states that public notice of the intention to grant an exclusive or partially exclusive license on a federally-owned invention has to be provided in an appropriate manner at least 15 days before the license is granted, the 15 days period is only a minimum. The NIH could grant a longer comment period, and in fact has done so with regards to other recent public notices.[1] There are no impediments to extending the deadline beyond the minimum of 15 days, and it would have been reasonable to do so given the limited amount of information provided in the notice.

According to the notice, the license will be granted to Medigen Vaccines Biologics Corp. (Medigen), having a place of business in Zhubei, Taiwan. On their website Medigen describes itself as, "an independent vaccine company developing vaccines against emerging infectious diseases and chronic diseases including cancer."[2] Medigen was founded in 2004. The subsidiary based in Taiwan was founded in 2012.[3] According to sbir.gov, Medigen has received $ 4,632,774.00 in awards from HHS and the USDA.[4]

With regard to the invention, the Federal Register notice states the following:

> "This invention relates to the use of murine pneumonia virus (MPV), a virus to which humans normally are not exposed and that is not cross-protected with RSV, as a vector to express the RSV fusion (F) glycoprotein as an RSV vaccine candidate."

Despite the fact that the Federal Register notice provides limited information regarding the live respiratory syncytial virus, we believe this is an important virus affecting patients worldwide. According to T Shi, DA McAllister, KL O'Brien, et al., *Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study,* Lancet (2017):

> "Globally, RSV is a common cause of childhood ALRI and a major cause of hospital admissions in young children, resulting in a substantial burden on health-care services.

[1] The Federal Register notice 83 FR 65696 related to a different exclusive license was also published by the NIH on December 21, 2018, but set a deadline to file comments until January 22, 2019. https://www.federalregister.gov/d/2018-27672
[2] https://medigen-usa.com/about/
[3] http://www.medigen.com.tw/en/business-activities-medigen-vaccinology-corp/
[4] https://www.sbir.gov/sbc/medigen-inc-0

> About 45% of hospital admissions and in-hospital deaths due to RSV-ALRI occur in children younger than 6 months. An effective maternal RSV vaccine or monoclonal antibody could have a substantial effect on disease burden in this age group."

According to Graham, Barney S. *Vaccines against respiratory syncytial virus: The time has finally come,* Vaccine vol. 34,30 (2016): 3535-41:

> "Respiratory syncytial virus (RSV) is the most common cause of hospitalization in children under 5 years of age. In developing countries RSV also causes substantial mortality in children under 1 year of age. All children are infected by the age of 3 and people are repeatedly infected throughout life. In otherwise healthy children over 5 years of age and in adults, RSV typically causes an upper respiratory syndrome sometimes complicated by sinusitis and otitis media. In individuals with T cell deficiencies like Severe Combined Immunodeficiency (SCID) or following allogenic bone marrow transplantation or lung transplantation, RSV can cause a life-threatening progressive pneumonia. In addition, RSV infection in the frail elderly is associated with excess mortality at frequencies comparable to influenza virus infection. Infections tend to be seasonal in temperate climates, but in tropical climates can be detected throughout the year."

> "Approximately 20 per 1000 infants less than six months of age are hospitalized with severe RSV illness, and in the institutionalized elderly about 1–2 per 1000."

The Federal Register notice provides almost no information on parainfluenza, or why this virus will also be covered by the license, but we believe that this is also a virus with an important global disease burden. According to Sato M, Wright PF. *Current status of vaccines for parainfluenza virus infections*, Pediatr Infect Dis J. (2008) October 27 (10 Suppl):S123-5:

> "Because PIVs account for 17% of hospitalized illness associated virus isolation, the development of PIV vaccine would be a major advance in preventing lower respiratory tract infection in infants and young children."

In the event that the NIH decides to grant this exclusive license to a company based in Zhubei, Taiwan, we ask that the following safeguards be placed on the license.

1. Any vaccine 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. The exclusive license does 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.

3. Medigen must agree to disclose the steps it will take to enable the timely registration and availability of the vaccine at an affordable price in the United States and in every county with a demonstrated need, according to the Centers for Disease Control and Prevention (CDC)/ 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. 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 vaccine 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 vaccine.

5. Reduce term of exclusivity when revenues are large. 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. This request is consistent with the statutory requirements of 35 USC § 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." There are a number of ways the NIH could implement this in practice. We would be pleased to discuss ideas further.

6. 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 grant of an exclusive patent license and urge the United States government to consider the negative impact an exclusive agreement will have on the development, affordability and availability of potential RSV or parainfluenza virus vaccines for people affected by these viruses in the United States and worldwide.

1. There is a lack of transparency regarding the proposed technology to be licensed, and the extent the public sector has already and will going forward subsidize the development of one or more vaccines covered by the license. The patent application is not public.

2. The notice period covering 10 business days and two public holidays including Christmas and New Years Day is insufficient time to evaluate the potential of the technology included in the license and the impact an exclusive license may have on ensuring appropriate further development of resulting candidate vaccines, or access and affordability of resulting vaccine products.

3. The NIH has not provided any information to establish that there is an appropriate justification for the grant of an exclusive license, and if so, that the scope of the rights granted have been limited to that which is reasonably necessary, under the standards set out in 35 U.S.C. § 209.

4. If the NIH does proceed with an exclusive license, the license should at a minimum include provisions to safeguard affordable access, and limit the scope of the exclusive rights to those reasonably necessary to induce the necessary investment to bring the inventions into practical application, as defined in 35 U.S.C. § 201(f).

Based upon the objections described herein, and the lack of sufficient information provided in the Federal Register notice, we request that the NIH consider a non-exclusive license or provide additional information relevant to evaluating this proposed licensing agreement and provide opportunities to consider the proposed license based on this information through a hearing or subsequent comment period.

Sincerely,

Knowledge Ecology International (KEI)

Doctors Without Borders/Médecins Sans Frontières USA