DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health/ NIAID

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Subject: Comments Submitted in Response to Federal Register Notice 2018-65696 (83 FR 65696), entitled "Prospective Grant of Exclusive Patent License: Production of Live Respiratory Syncytial Virus and Parainfluenza Virus Vaccines"

Dear Mr. Love:

Thank you for providing us with your comments regarding the notice of a proposed exclusive license that the National Institutes of Allergy and Infectious Diseases (NIAID) intends to grant to Medigen Vaccines Biologics Corp. (Medigen). Prior to posting such notices, the NIAID determines that the criteria set forth in 37 CFR 404.7(a)(1)(ii-iii) have been satisfied and that the company is qualified both technically and financially to be granted an exclusive license to the Government's intellectual property in the field(s) of use as specified.

The notice provides an opportunity for public comment and possible objection to the proposed license, and 35 U.S.C. § 209(e) provides that an exclusive license may be granted as long as public notice of the intention to grant such a license is provided "in an appropriate manner at least 15 days before the license is granted."

You suggest in your letter that the period to respond to the notice is too short, but this complies with the requirements of the statute, and does not appear to have affected your ability to object to the license on several grounds and provide several recommendations. These include recommendations regarding assurances of affordability, recommendations regarding limitations on the prices charged to US residents, a recommendation to limit the term of the license, a recommendation to participate in the Medicines Patent Pool, and a recommendation regarding reporting requirements.

An exclusive license is important to the successful development and commercialization of this technology. Vaccines in general have high investment costs and very low profit margins making it difficult to attract commercial partners with the capability to develop the vaccine, finance and manage clinical trials, and obtain regulatory approval in each of the relevant jurisdictions. Although the commercial market for respiratory syncytial virus (RSV) and parainfluenza virus (PIV) vaccines is relatively large, a licensee must be able to market its vaccine widely in order to obtain a return that is adequate to justify its investment in its development. There is also a great deal of competition among vaccine candidates that are currently being prepared for the RSV/PIV vaccine market (for a summary of these many candidates please see table prepared by PATH at https://vaccineresources.org/files/RSV-snapshot-

2018Dec_High%20Resolution%20V3.pdf). Our experience in licensing vaccines and other therapies in this area is extensive, and we have concluded that it is not possible to find a competent partner who will successfully bring these vaccines to market without the investment backstop that exclusivity provides.

You requested that we include certain elements in the exclusive license, including a limit on the price of a drug covered by the license for products sold in the United States. But, as NIH has emphasized in its public statements over many years[1] and in dozens of communications with your organization, we view the matter of price controls to be a question best addressed legislatively, and we respectfully decline to follow your advice on this matter.

As a point of clarification, we note that Medigen is a Taiwanese public company and, to our knowledge, has no operations in the United States. Your statement that Medigen has received grant money from the U.S. Department of Health and Human Services (HHS) and the United States Department of Agriculture (USDA) is incorrect.

With respect to your suggestions that exclusivity not extend to countries with a per capita income less than 30 percent of the United States and that NIH retain the right to grant the World Health Organization (WHO) or the Medicine Patent Pool rights to the present invention, we are aware of the problem of unequal access in developing countries to modern vaccines and therapies. Since the inception of the licensing program at NIH over thirty years ago NIH has negotiated and granted roughly 200 licenses per year for vaccines, therapies and diagnostics to large and small companies who have made them available to patients all over the world. NIH's license agreements create partnerships with companies who risk their assets to bring these drugs to market, because NIH does not have the capacity to do so itself. Without these partnerships vaccines and drugs would simply not be made, tested in clinical trials, approved by the appropriate regulatory body or made available to patients at all. Our licensing professionals, many of them with decades of experience, obtain the best terms possible in view of market and other circumstances when negotiating these agreements, which are designed to improve the chances of successful development of the licensed therapy or vaccine and its distribution to patients throughout the world.

With respect to your suggestion that exclusivity should be removed once a licensee's revenues exceed a certain threshold, this would punish a licensee for its success and certainly be counterproductive to making drugs and therapies more widely and easily available to patients.

With respect to your suggestion that a comprehensive country list be provided prior to filing and expiration of a PCT application, it is typical for NIH to file in subsets of OECD Member and Key Partner countries (http://www.oecd.org/about/membersandpartners/) and in countries where there is incidence and prevalence of RSV/PIV. The geographical scope of the license agreement will be commensurate with the development plan submitted by Medigen and NIH will take steps to ensure that the proposed terms and scope of exclusivity are not greater than reasonably necessary.

With respect to your suggestion that licensees should report the costs of their research and development including outlays for clinical trials, licensees are in fact required to report at least annually on their commercialization efforts and royalty reports are produced more frequently. However, a requirement to report costs of research and development and clinical trials would be of no utility whatsoever in an exclusivity determination. This is because typical costs of clinical trials and research and development are already well known to our experts in this field and the effort to collect and report this information would be burdensome and harmful to NIH's efforts to

[1] See, for example, in the case of Xalatan https://www.ott.nih.gov/sites/default/files/documents/policy/March-in-xalatan.pdf and in the case of Norvir https://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Norvir2013.pdf.

attract commercial partners. Such reports would include very sensitive business confidential information that would be costly to produce and to protect.

In your letter you suggest that there is a lack of transparency regarding the technology to be licensed. On the contrary, the invention was described in detail in the Federal Register Notice to which you are responding:

> 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. The RSVF ORF was codon optimized. The RSVF ORF was placed under the control of MPV transcription signals and inserted at the first (rMPV–F1), third (rMPV29F3), or fourth (rMPV–F4) gene position of a version of the MPV genome that contained a codon pair optimized L polymerase gene. There covered viruses replicated in vitro as efficiently as the empty vector, with stable expression of RSV F protein. Replication and immunogenicity of rMPV–F1 and rMPV–F3 were evaluated in rhesus macaques following administration by the combined intranasal and intratracheal routes. Both viruses replicated at low levels in the upper and lower respiratory tract, maintained stable RSV F expression, and induced similar high levels of RSV-neutralizing serum antibodies that reached peak titers by fourteen (14) days post vaccination. rMPV provides a highly attenuated yet immunogenic vector for the expression of RSV F protein, with potential application in RSV-naive and RSV experienced populations. The technology relates to live, chimeric nonhuman Mononegavirales vectors that allow a cell to express at least one protein from at least one human pathogen as well as compositions comprising the vectors, methods and kits for eliciting an immune response in a host, and methods of making the vectors.
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> Federal Register / Vol. 83, No. 245 / Friday, December 21, 2018

The science underlying this invention is described in the publication; L.G. Brock et. al., Murine Pneumonia Virus Expressing the Fusion Glycoprotein of Human Respiratory Syncytial Virus from an Added Gene Is Highly Attenuated and Immunogenic in Rhesus Macaques. *Journal of Virology*, September 2018 Volume 92 Issue 17:23-18. This publication also discusses RSV antigens in a PIV background, in addition to RSV antigens in an MPV background, which is not within the scope of this proposed license. A description of the invention was also published as a notice of licensing availability in the Federal Register on May 7, 2018: Federal Register Government-Owned Inventions; Availability for Licensing published May 7, 2018 83 FR 20084-85.

As an example of our experience in licensing technology outside OECD countries, a rotavirus vaccine strain developed by this laboratory was developed and recently launched as RotaSIIL by the Serum Institute of India. For more information on RotaSIIL, please see https://www.sabin.org/sites/sabin.org/files/sajjad_desai.pdf.

You requested a copy of U.S. provisional patent application 62/661,320. This is a provisional patent application and it has not been published. Consistent with sound patent prosecution practice, we provide unpublished patent applications under a signed Confidential Disclosure Agreement (CDA). We would be happy to provide you with the patent application under a CDA at your request.

Sincerely,

Peter Silvas

Technology Transfer and Patent Specialist