April 26, 2021

Re: Prospective Grant of an Exclusive Patent License: N-butyldeoxynojirimycin To Treat Smith-Lemli Opitz Syndrome (SLOS) and Diseases That Exhibit a Similar NPC-Like Cellular Phenotype (86 FR 18545)

Dear Dr. Hubbs:

Knowledge Ecology International (KEI) would like to offer the following comments regarding the “Prospective Grant of an Exclusive Patent License: N-butyldeoxynojirimycin To Treat Smith-Lemli Opitz Syndrome (SLOS) and Diseases That Exhibit a Similar NPC-Like Cellular Phenotype,” to SubRed Pty Ltd (“SubRed”) in Victoria, Australia.

The geographic scope of the license is worldwide, and the field of use conveys the rights to:

“[t]he use of N-butyldeoxynojirimycin in humans to treat Smith-Lemli Opitz Syndrome (SLOS) and diseases that exhibit a similar NPC-like cellular phenotype.’ This technology discloses pharmaceutical compositions and methods of use to treat SLOS and diseases having a secondary NPC like cellular phenotype or wherein the disease is an inborn error in cholesterol synthesis.”

KEI asked Dr. Hubbs questions regarding the license and the technology to be licensed. KEI greatly appreciated that Dr. Hubbs provided responses to all of our questions in a timely manner.

Dr. Hubbs noted in his responses that the technology was in the preclinical stage of development and also stated that,

“Unfortunately to date, no clinical trial of this technology has taken place. This is in part likely due to circumstances that make a trial difficult: SLOS is a very rare hereditary disease with a low patient population; and further, children with this disease have
characteristics that make it very difficult for them to participate in a clinical trial for the full period of a clinical trial, or to travel to a clinical trial site that is not near their location.”

Recognizing the difficulties of conducting trials for rare hereditary diseases, it is for this very reason - that it is a potential treatment for a rare hereditary disease - that it is crucial that the NIH ensures that the terms of this license protect equitable and affordable access to any resultant treatments. The terms included in these exclusive licenses must ensure that patients are not held hostage to high prices, particularly those without alternative treatment options.

KEI notes that the firm to receive the exclusive license is based in Australia. Per the Bayh-Dole Act, one of the requirements of granting an exclusive license is that licensees “substantially” manufacture the invention in the United States. The NIH should factor this in while negotiating terms of any exclusive license to a foreign firm and should only grant a waiver if a compelling reason is shown.

KEI asked Dr. Hubbs whether the NIH was in any concurrent negotiations to waive the domestic manufacturing requirement (35 USC 204) (in other words, whether the proposed licensee was seeking such a waiver), to which he replied that there were no negotiations underway concerning a waiver of manufacturing requirements.

Since SubRed is not based in the US, it is important that the NIH ensures license terms that will protect US patients from paying higher prices than other high income countries, for any resultant treatment. Any medical technology 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.

The above is a modest safeguard. The US government has recently incorporated similar terms in agreements related to COVID-19 vaccines and other technology contracts. For example, in the contract with Sanofi Pasteur (Sanofi) for a COVID-19 vaccine, the federal government included a term that stated that Sanofi will not sell the vaccine to any member of the G7 or Switzerland at a price lower than what the U.S. government paid. The NIH should apply this standard to its exclusive licensing practices, and prevent licensees from charging U.S. residents a higher price for products embodying the licensed invention than they charge residents of these high-income countries.

KEI also urges the NIH to include the following provisions in the terms of any license.

**Transparency**

**Transparency of R&D outlays.** The licensees 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 note that this is not a request to see a company business plan or license application. We are asking that going forward SubRed 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.

**Acknowledgement of federal funding - publication and publicity.** The licensee should be required to include, when issuing statements, press releases, and other documents describing the development of any product that includes the licensed inventions, a statement that describes the role of the licensed inventions and the total and proportionate contribution of federal funding to the research and development performed to bring the inventions to market.

**Additional transparency issues.** The license should have provisions that give effect to the transparency norms set out in WHA72.8 “Improving the transparency of markets for medicines, vaccines, and other health products”, a resolution enthusiastically supported by HHS in 2019.

**Additional Provisions to Protect the Public Interest**

**Global registration and affordability.** The licenses should require the licensee to disclose the steps that each will take to enable the timely registration and availability of the medical technology at an affordable price in the United States and in every country with a demonstrated need, according to the Centers for Disease Control and Prevention (CDC) and/or the 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.

**Medicines Patent Pool.** 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 medical technology from competitive suppliers, including technology transfer, in LMICs, upon a finding by HHS or the WHO that people in these markets do not have sufficient access to the medical technology.

**Conclusion**

It is critical that the NIH ensure that the terms of this license promote the public interest in the invention and protect patients’ equitable access to the technology, should it come to market. In the event that the NIH grants the license, KEI asks that it incorporates the provisions listed above in order to achieve those goals.
Please notify us if and when a license is granted, so we can request a copy under the Freedom of Information Act.

Sincerely,

Claire Cassedy  
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Knowledge Ecology International