New inhalable measles vaccine may lead to vaccines for other diseases

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A team of researchers led by the University of Colorado at Boulder believe a dry powder, inhalable vaccine developed for measles prevention and slated for human clinical trials later this year in India will lead to other inhalable, inexpensive vaccines for illnesses ranging from tuberculosis to cervical cancer.

The inhalable measles vaccine, developed by a team led by CU-Boulder chemistry and biochemistry Professor Robert Sievers, involves mixing "supercritical" carbon dioxide with a weakened form of the measles virus. The process produces microscopic bubbles and droplets that are dried to make the inhalable powder, which is dispensed into the mouths of patients using a small, cylindrical plastic sack with an opening like the neck of a plastic water bottle.

According to the World Health Organization, measles is one of the leading causes of death among young children. In 2008 there were an estimated 164,000 measles deaths in children worldwide -- nearly 450 deaths a day -- and India accounts for about two-thirds of global measles deaths in infants and children. "Clinical trials are the next vital step in making this vaccine widely available," he said.

"One of our primary goals of this project is to get rid of needles and syringes, because they frighten some people, they hurt, they can transmit diseases and there are issues with needle disposal," he said. With the new technology, the inhaled powder is sent directly into the lungs, a good target since measles attacks through the respiratory tract, said Sievers.

"A person taking a deep breath from the sack is effectively vaccinated."

Sievers will give a presentation on the subject at the Eighth European Conference on Supercritical Fluid Applications to be held May 9-12 in Graz, Austria.

Phase One of the clinical trials to test the safety and efficacy of the measles inhalant product are slated to start this summer in Pune, India, and will involve about 180 people, said Sievers. Phase Two of the India clinical trials are expected to involve a larger number of patients.

Sievers, also a fellow at CU's Cooperative Institute for Research in Environmental Sciences, said the measles vaccine development idea grew out of atmospheric chemistry research he and his students were conducting. The team was attempting to determine the chemistry of specific air pollutants in particular regions of the world and how people inhale and process tiny airborne droplets of pollutants.

As part of the measles project, Sievers and his students and colleagues invented and patented a device known as the Carbon Dioxide Assisted Nebulization with a Bubble Dryer, or CAN-BD, in which two mixed streams of fluid are rapidly expanded to atmospheric pressure where the tiny bubbles and droplets are dried by mixing them with warm nitrogen. The resulting, inhalable-sized vaccine bits are embedded in micro-particles of sugars and amino acids, he said.

Aktiv-Dry is a Boulder spinoff company Sievers co-founded in 2002 with Professor John Carpenter of the University of Colorado School of Pharmacy and Brian Quinn, current president of Aktiv-Dry. The company, which employs about 10 people including former CU-Boulder students, currently is developing CAN-BD for the marketplace.

"This project came out of the University of Colorado, and Aktiv-Dry is

partially owned by the university through the University of Colorado Technology Transfer Office," said Sievers. "I've had 40 CU-Boulder students who have earned their doctorates under me through the years, and it was those students and their work that really positioned us at the right time to gain significant funding for this project."

The $20 million Aktiv-Dry research effort is funded by the Grand Challenges in Global Health Initiative, which was created by the Bill and Melinda Gates Foundation through the Foundation for The National Institutes of Health. Sievers' project addresses one of the 14 Grand Challenges -- the needle-free administration of vaccines by pulmonary or nasal aerosols.

David H. McAdams, a CU-Boulder doctoral student in the chemistry and biochemistry department working with Sievers, said he switched his academic focus from atmospheric chemistry particle analytics to participate in the measles project. "I saw an opportunity to use the analysis of such particulates to benefit mankind and to help save children by using inhalable vaccines."

The CU team recently tested the durability of the inhalant vaccine by shipping a batch from the Serum Institute of India to CU-Boulder, then shipping the same batch two months later to the East Coast and back to Boulder. The vaccine proved to be stable throughout the shipping process, indicating it likely would be effective under challenging environmental conditions encountered in developing nations, Sievers said.

The cost of an inhalant dose for measles developed by Sievers and his team is about 26 cents -- roughly the cost for an injectable form of the dose. As a practical matter, said Sievers, the treatment of patients with novel technologies should not be more expensive than standard treatment costs.

The new technology could potentially be used to deliver tiny antibiotics particles to treat people with multi-resistant tuberculosis, said Sievers. While the antibiotic inhalant would likely be combined with oral doses and injections, the use of CAN-BD would direct the antibiotic directly to the lungs where the disease is focused, said Sievers.

Another potential use for the CAN-BD technology is treating human papilloma virus, a sexually transmitted disease that causes cervical cancer. "More women in India today die of cervical cancer than from breast cancer, which is a much bigger killer in the United States," he said. Current treatment for papilloma virus is a three-dose injection regimen that costs about $300 -- a cost Sievers and his group would like to lower significantly for it to be distributed to women who need it in developing nations.

Provided by University of Colorado at Boulder