

Malaria vaccine plant takes a gamble

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By Maggie Fox, Health and Science Editor

ROCKVILLE, Maryland (Reuters) - In a nondescript office park tucked between a hospital and a strip mall thrive hundreds of thousands of the most infectious malaria-carrying mosquitoes ever born.

They will be dissected for the motherlode that they carry -- baby malaria parasites, fodder for a new malaria vaccine.



The insects' suburban Maryland home is owned by Sanaria Inc., which cut the ribbon on Friday on its new facility. Founder and chief executive officer Dr. Stephen Hoffman is taking a gamble that he can do what has been impossible -- make a vaccine against malaria.

"We know it is going to work," Hoffman says as he offers a tour of the 23,500-square-foot (2,183-sq-metre) building. "I am quite confident and I am staking my career on it."

Malaria, caused by a parasite carried by mosquitoes, kills more than 1 million people every year and makes 300 million seriously ill -- mostly young children in Africa.

Experts agree that a vaccine is the best way to fight the disease, but this has proven near-impossible. The Plasmodium falciparum parasite has a complex life cycle inside mosquitoes and the human body, which helps it evade the immune system.

Last week GlaxoSmithKline Plc reported that its experimental vaccine had protected 65 percent of infants from infection, but it reduced illness by just 35 percent after six months.

In contrast, Hoffman's vaccine has been shown to provide more than 90 percent protection against malaria, lasting for at least 10 months.

But no one thought he could produce it, because it required the use of a particular stage of the *P. falciparum* parasite called a sporozoite. This is the stage in the one-celled parasite's life when it leaves the mosquito's salivary glands to enter the human bloodstream.

For his early experiments Hoffman used live mosquitoes, but that would not work for large-scale vaccination. He had to figure out how to get the sporozoites out of the mosquitoes' salivary glands, clean them up and use them to make a vaccine.

Sanaria has raised \$45 million in grants to do this, including \$9 million from the U.S. National Institutes of Health, \$30 million from the Bill and Melinda Gates Foundation via the PATH Malaria Vaccine Initiative and \$4 million from the U.S. Army Military Infectious Diseases Research Program.

VETERAN TEAM

Hoffman, a retired Navy captain who once headed the malaria program at the U.S. Naval Medical Research Center, hopes to be testing vaccine in human volunteers by 2008. He has assembled a team of biotech veterans to help him.

Vaccines work using antigens -- proteins that activate the body's immune system. In this case, the antigen will be a whole *Plasmodium* sporozoite, weakened, or attenuated, so it cannot infect the liver as normal parasites do.

Sanaria must create sterile mosquitoes -- itself a proprietary process -- infect them with *P. falciparum* parasites and use the mosquitoes as living bioreactors.

"We now, at the end of this, are going to have the world's most highly infectious mosquitoes," Hoffman said. They are kept locked behind five doors, at the facility outside Washington.

About 44 days after infecting the mosquitoes, Sanaria workers can harvest the sporozoites -- a fussy process that requires technicians in sterile cover-ups to sit for hours at microscopes to remove the mosquitoes' salivary glands.

Some experimental malaria vaccines use just one or two genes from the *Plasmodium* parasite. Hoffman believes priming the body to recognize the whole organism is a more effective approach, and many vaccine experts agree.

"This clearly is quite promising," NIAID director Dr. Anthony Fauci said in an interview.

"The technical advances that he made, getting enough sporozoites out to make substantial numbers of vaccines, makes me feel very optimistic ... If anyone can pull this off, Steve can."

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