The VSV Ebola vaccine study: facts on the VSV-ZEBOV vaccine for interested persons

The purpose of this fact sheet is to provide targeted information efficiently. This text is not exhaustive and does not provide sufficient information for a volunteer considering participation in the clinical trial.

What does the VSV-Ebola vaccine contain? The vaccine is made from a modified *vesicular stomatitis virus* (VSV), a virus that usually infects livestock. To make the vaccine, the envelope of the natural VSV virus has been replaced by the envelope from the Zaire strain of the Ebola virus (ZEBOV), the strain that is causing the current Ebola outbreak. Like the measles or yellow fever vaccine, this VSV-Ebola vaccine is "live": once injected, it multiplies for a few days before being eliminated and thus could trigger a strong immune response

How may this vaccine protect against Ebola? This vaccine has been extensively tested in mice and monkeys. In these animals, the VSV-Ebola vaccine induced the production of antibodies directed against the Ebola virus. Twenty monkeys were exposed to a lethal dose of Ebola virus after having received the VSV-Ebola vaccine: all were protected, whereas all control animals died. This vaccine only protected animals against the Zaire strain of the Ebola virus, not against other strains. Thus, the vaccine stimulates the immune system in a specific manner. *The ability of the VSV-Ebola vaccine to protect humans against the Ebola virus has not been tested and cannot be inferred: receiving a dose of vaccine does not imply protection.*

What are the risks related to the VSV portion of the vaccine? VSV infection is rare in humans: the natural VSV virus essentially causes a flu-like illness lasting a few days; complications (sore throat with throat vesicles) are rare. VSV has been used for decades in research laboratories in Switzerland and abroad without complications. The vaccine version of VSV has been "attenuated" to cause even fewer symptoms. The safety of the combination of the vaccine VSV version and the Ebola envelope is only beginning to be tested in humans and has not been tested large-scale in monkeys; supplemental studies are ongoing. In vaccinated animals, the VSV-Ebola vaccine was very well tolerated with no observed side effects, including by monkeys with a weakened immune system.

What are the possible side effects of the vaccine? As the vaccine includes an attenuated form of VSV, it may cause inflammation. The intensity of this inflammation is likely to vary from nothing to a "flu-like illness" with fever, loss of appetite, muscle aches, etc. We expect this not to last more than a few days (1-3). As with any medication, this vaccine could cause an allergic reaction. Other adverse effects have not been seen in animal experiments but cannot be ruled out in humans. We can therefore not exclude the risk of an unexpected or severe adverse event.

What are the possible risks for my contacts? No vaccine virus was identified in the saliva or urine of immunized monkeys or health care workers. However, there is yet no formal demonstration that infectious vaccine virus is never found transiently in the body fluids of vaccinees. This will thus be monitored and, purely as a precaution, certain measures will be requested to protect contacts.

Is it absolutely sure that the VSV-Ebola vaccine does not include an Ebola virus that may infect people vaccinated with it? Yes. First, the VSV-Ebola vaccine is not made out of Ebola virus but out of VSV virus. Thus it cannot be contaminated by the Ebola virus. VSV-Ebola only includes the envelope of the Ebola virus and none of its other molecules which would be necessary for its multiplication. Any risk of getting Ebola virus infection from VSV-Ebola is thus ruled out. In an Ebola virus infection, the natural Ebola envelope can play a role in hemorrhage. To reduce this risk, the envelope used in the vaccine has been modified. While vaccination in humans requires prudent follow-up, no serious side effects were observed in the monkeys and humans already vaccinated.

Who has already received the VSV-Ebola vaccine? This vaccine is only just beginning to be tested in humans. Three humans have received the vaccine after having been possibly exposed to Ebola virus through needlestick injuries. One person had no side effects at all and two had one day of fever. All are doing well. *The ability of the VSV-Ebola vaccine to protect humans against Ebolavirus has not been tested and cannot be inferred: receiving a dose of vaccine does not imply that you will be protected and does not permit the relaxation of measures required to reduce the risk of exposure.* Similarly, should you be exposed to Ebola virus, an enhanced risk of infection or of a more severe infection cannot yet be formally excluded.

This text has been approved by Swissmedic (2014GT1010) and the Ethics Committees of WHO (RPC-696) and the Canton of Geneva (14-221).