# Chikungunya virus – should we think now about a vaccine?

**LONDON, UK----25th June 2009----ExpertREACT.** Recent research released by **VacZine Analytics** investigates latest trends/dynamics regarding Chikungunya virus and its global disease burden. The research questions whether manufacturers should think seriously about restarting the development of a preventative vaccine and investigates potential commercial viability relative to other priorities.

Chikungunya virus (CHIK) is an RNA alphavirus (*Togaviridae*) first described in the early 1950s during an epidemic in East Africa **(1).** The virus is spread by mosquitoes of the *Aedes* family including *Aedes aegypti, albopictus* or *vigilax.* The same vectors are responsible for the transmission of dengue, another well known virus endemic to South-east Asia which has similar symptoms. Unlike dengue, CHIK infection is rarely fatal but can cause debilitating joint pain, high fever, nausea, rash and fatigue. On occasions these symptoms can be prolonged and recurrent causing significant morbidity especially during large epidemics. Vulnerable members of the population including the immunocompromised and very old or young are at heightened risk for CHIK infection. In addition there is evidence suggesting CHIK can be passed through the placenta from the mother to foetus **(2).** Currently, there is no specific treatment for CHIK infection or a licensed preventative vaccine.

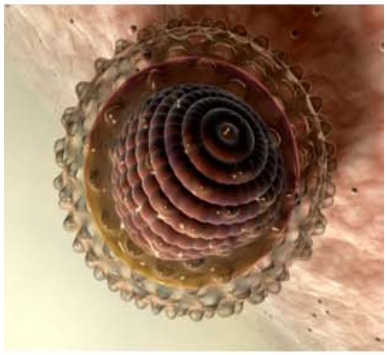
CHIK has become of concern because in recent decades there have been large-scale explosive outbreaks in endemic areas. The most notable are those which occurred in the Indian Ocean islands of La Reunion (France) and other such as Comorros, Mayotte and the Seychelles. In Reunion, 35-40% of the population (~260,000) were infected with around 250 deaths (Case Fatality: 1/1000) mostly in >70 yrs group. Further afield in India (2006), 1.4 million suspected CHIK cases were reported to the Indian National Vector Borne Disease Control Program (INVBDCP) **(3).** Based on the Indian experience, it is challenging to estimate the true burden of CHIK as many actual cases are not reported, confused with other endemic diseases or simply not laboratory tested to confirm the true presence of the virus. For the India 2006 epidemic, when normalising to population seroprevalence it is estimated that around 148,000 of the 1.4 million suspected cases are likely to have been due to CHIK. Investigators state that around 3,000 excess deaths occurred in the epidemic although not all attributable to CHIK **(4).**

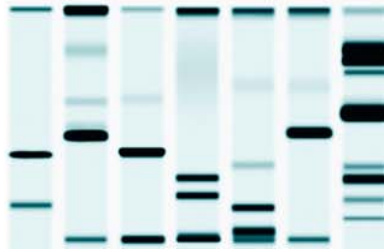
CHIK causes explosive epidemics due to its high attack rate and absence of herd immunity in the population. Also in the Indian epidemic of 2006, which was the first major outbreak since 1973 **(5),** it is speculated that viral remergence was due to human population migration from the Indian Ocean region. The isolated viral genotype was similar. In addition, the CHIK virus genome can mutate increasing its transmissibility in vectors, but also possibly an ability to cause unpredictable atypical epidemics such as that observed in La Reunion.

Increased migration, travel and spread of mosquito vectors pose the greatest threat of increased burden of CHIK on global health. These dynamics are evidenced by CHIK cases being imported to Western nations from returning travellers and the first major local outbreak which occurred in the Ravenna province of Italy, July 2007. Because *Aedes albopictus* is endemic to this region, a highly viremic traveller returning from India was able to initiate a local epidemic of 214 laboratory confirmed cases but also possibly in other parts of Italy **(6).** The importation of CHIK cases and possibility of local outbreaks has prompted some countries e.g. Singapore, Australia and Hong Kong to initiate active surveillance systems which were already established in France (2006) where CHIK is a mandatory notifiable disease. In the United States, 38 cases of CHIK were confirmed in returning travellers **(7)** (CDC MMWR), however, the disease is not notifiable despite the US having extensive temperate zones with *Aedes albopictus* distribution.

Because widespread CHIK infection is linked with the absence of population immunity (anti-CHIK IgG) and infection can confer life-long immunity, the development of a CHIK vaccine is a plausible strategy to reduce CHIK disease burden. Since the 1970s, CHIK vaccine approaches have been pursued using mainly formalin-killed and live approaches (VADIP). For example, the US military (USAMRIID) have tested a live vaccine (TSI-GSD-218) in Phase I/II where the vaccine was shown to be safe and immunogenic in 88 volunteers, although some vaccinees experienced transient arthralgia **(8).** The status of TSI-GSD-218 is currently unclear although the US government allowed French authorities to collaborate based on the situation in La Reunion.







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Newer companies involved in CHIK vaccine development are VGX Pharmaceuticals, TI Pharma (Schering-Plough/Erasmus & Nobilon) and Bharat Biotech although no candidate (as of June 2009) appears to be in human clinical testing.

However the case is made, for CHIK vaccine development it is a case of commercial viability. Conceivably, a safe and effective CHIK vaccine could be marketed to Western travellers visiting CHIK endemic regions or indeed the growing private markets of SE Asia. Such strategies are already being pursued with new vaccines for Japanese encephalitis (JEV) and dengue mainly by Sanofi Pasteur (ChimeriVAX™-dengue and JE) and Novartis vaccines (Intercell AG), Ixiaro (R). For Ixiario (R), the US ACIP committee has recently recommended the vaccine for US travellers to SE Asia which is a positive step for a market considered many considered underdeveloped. Other possibilities for a CHIK vaccine are military use or even stockpiling in Western countries having high densities of *Aedes albopictus* and travellers returning from CHIK regions.

Based on recent analysis by **VacZine Analytics** (9), a CHIK vaccine should be more viewed as a strategic entry opportunity for a newcomer rather than potential high revenue earner. It could compliment a company with an existing travel vaccine portfolio. However, of the major mosquito borne diseases CHIK is low down on the list in terms of yearly deaths and DALYS. Considering the meagre amounts spent in GAVI eligible countries on vaccines for diseases such as yellow fever (YF) it will be a challenge moving CHIK up the list unless there is a dramatic change in disease burden or maybe a significant local outbreak in the West. Neither of these events can be ruled out, especially in the longer term.



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