

## Speaker Abstracts

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#### Ethics Case Study: Dengue

**Background:** Dengue is the most common mosquito-borne viral illness world-wide. There are four different dengue virus (DENV) serotypes, each capable of causing the full spectrum of disease. Dengue is unique in that antibody to one of the 4 serotypes can enhance the severity of disease of a heterotypic DENV upon subsequent secondary DENV infection. This has been termed antibody dependent enhancement of infection and it is thought that the heterotypic antibody can bind to the DENV without inducing neutralization. The antibody-virus complex then enters Fc R bearing cells leading to higher viremia and more severe disease. Epidemiologic studies have identified the greatest risk factor for severe dengue is a second, heterotypic DENV infection.

**Challenges:** Treatment for DENV infection consists only of supportive care; licensed anti-viral agents for DENV do not exist. In addition, experimentally infecting subjects with a monovalent DENV could potentially put them at risk for more severe dengue should that experience a secondary, heterotypic infection. The risk of this is greater in dengue endemic areas. In addition, there is a risk to third parties if CHIM studies are conducted in areas in which the vector is present.

**Proposed Approach:** Prior to the conduct of a dengue challenge study the virulence of the proposed challenge virus must be characterized. Two models for dengue challenge exist: a controlled human infection model and a disease model. The objectives of the study should justify the use of a disease model over that of an infection model. Appropriate clinical care must be available to subjects and the risk of mosquito-borne transmission must be mitigated.

**Conclusions:** Dengue human challenge can be safely and ethically conducted if the risks to volunteers and the risk of transmission to third parties is adequately mitigated.

