

## **Summary of the WHO Position Paper on Vaccines against Hepatitis E Virus (HEV)**

### **Background**

This is the first WHO position paper on hepatitis E vaccination. It focuses primarily on the available evidence concerning the single hepatitis E vaccine that is currently licensed.

Hepatitis E virus (HEV) is a leading cause of acute viral hepatitis in developing countries. There are 4 genotypes of HEV: genotypes 1 and 2 primarily infect humans, whereas genotypes 3 and 4 mainly infect mammalian animals with occasional cross-species transmission to humans. It is estimated that genotypes 1 and 2 account for approximately 20.1 million HEV infections, 3.4 million symptomatic cases, 70 000 deaths, and 3 000 stillbirths annually. Hepatitis E occurring sporadically or as disease outbreaks has been identified in at least 63 countries. Data also suggests that HEV infection may be endemic in some countries.

The overall burden of disease due to hepatitis E is greatest in parts of the world where clean drinking water is scarce, as faecal contamination of drinking water is a major route of HEV transmission. In developing countries, the disease mainly affects young adults (aged 15–39 years), predominantly male adults. During waterborne outbreaks, children may develop severe hepatitis E as a result of co-infection with Hepatitis A virus, and probability of symptomatic disease increases with age. Infections from genotype 1 result in high mortality rates among persons with pre-existing chronic disease and among pregnant women. Infection during pregnancy is also associated with poor fetal outcomes including miscarriage, premature delivery, and stillbirths

Currently, there are no WHO guidelines on treatment of hepatitis E. Treatment for acute hepatitis E is generally supportive.

There are two experimental vaccines that have progressed to clinical trials in humans, of which only one vaccine, Hecolin<sup>®</sup>, has been developed and manufactured. It is currently only licensed for use in China in China for use in people 16-65 years of age, who are at high risk for HEV infection based on occupation or lifestyle.

This vaccine, based on a 239 amino acid recombinant HEV peptide, is highly immunogenic. It protects against symptomatic HEV infection, with a very high efficacy rate against HEV genotype 4. Data on its protection against genotype 1 is very limited and against genotypes 2 and 3 are not available. However, there is data to show that HEV 239 may be expected to protect against infection from all four genotypes. With regards to asymptomatic infection, this vaccine can effectively lower, but not eliminate this risk.

Long-term efficacy, duration of protection, and the need and timing for a potential booster dose of the vaccine remain to be determined. Furthermore, no data is as yet available on its effectiveness.

Serious adverse events following hepatitis E vaccination are rare. The cost-effectiveness of hepatitis E vaccination programmes in outbreak settings has yet to be studied.

### **WHO Position**

WHO recognizes the importance of hepatitis E as a public health problem in many developing countries, particularly among special populations such as pregnant women and individuals living in

camps for displaced persons and in outbreak situations. The one currently licensed hepatitis E vaccine (HEV 239 vaccine, Hecolin®) is considered a promising vaccine which has shown a high degree of efficacy against hepatitis E disease in 16–65 year-old healthy subjects in China. However, data on the incidence of hepatitis E virus infection and disease worldwide, and the contribution of hepatitis E to mortality in the general population where infection is common, are limited.

In the absence of sufficient information at this time, WHO does not make a recommendation on the introduction of the vaccine for routine use in national programmes in populations where epidemic and sporadic hepatitis E disease is common. However, national authorities may decide to use the vaccine based on the local epidemiology.

Due to the lack of sufficient information on safety, immunogenicity and efficacy in the following population subgroups, WHO does not recommend routine use of the vaccine in children below 16 years of age, pregnant women, chronic liver disease patients, and patients on organ transplant waiting lists, and travellers.

There may be special situations such as outbreaks where the risk of hepatitis E or of its complications or mortality is particularly high. The current WHO position concerning routine programmes should not preclude the use of the vaccine in these specific situations. In particular, the use of the vaccine to mitigate or prevent outbreaks of hepatitis E should be considered as well as the use of the vaccine to mitigate consequences in high risk groups such as pregnant women.

To address the information gaps about the vaccine, WHO recommends the pre-emptive design of a research protocol that would be used to study safety and immunogenicity of the vaccine in outbreak situations, among pregnant women, in patients with chronic liver disease, and in immunosuppressed persons, including those awaiting or having received solid organ transplantation.