5. Summary of Data Reported and Evaluation

5.1 Exposure data

Hepatitis D virus (HDV) exists as a satellite agent of hepatitis B virus (HBV). The viral genome is a circular RNA molecule about 1700 bases long, and HDV antigen is the only known protein that it encodes. The antigen is required for viral replication in hepatocytes. Because hepatitis B surface antigen forms the envelope of HDV, HBV infection is a prerequisite for formation of HDV particles. HDV infection has been detected only in humans, although the agent can be transmitted to HBV-infected chimpanzees and to woodchucks infected with woodchuck hepatitis virus.

HDV infection can be identified in serum by detecting antibody to HDV (anti-HD) and/or HDV RNA; HDV antigen can also be detected immunohistochemically in hepatocytes. In co-infection, HDV RNA and immunoglobulin M class anti-HD appear, followed by the transient appearance of immunoglobulin G class anti-HD. Superinfection usually results in chronic infection, viraemia and persistence of anti-HD.

In countries where endemicity for HBV is low, the prevalence of HDV infection is low, except among intravenous drug users and recipients of blood products. In areas of intermediate and high endemicity for HBV, the prevalence of HDV infection is highly variable: In general, it is rare in Asia, but up to one-half of individuals with chronic HBV infection in parts of southern Europe, the Middle East, Africa, the Pacific Basin and the Amazon region may be infected with HDV. Marked variations in the prevalence of HDV infection are found within countries and sometimes between ethnic groups.

The predominant route of transmission in countries of high endemicity is unknown, that in countries of low endemicity appears to be parenteral. Sexual transmission also occurs.

HDV co- or superinfection generally results in a more severe clinical course than HBV infection alone. HDV superinfection is associated more frequently with progressive liver disease and cirrhosis than HBV infection alone.

Immunoprophylaxis with HBV vaccine is presumed to protect the individual against co-infection but cannot protect HBV carriers against superinfection with HDV. Immune globulin does not protect against HDV superinfection, and no specific HDV vaccine is available.

5.2 Human carcinogenicity data

Several case series showed no evidence of HDV infection among cases of hepatocellular carcinoma, while others reported high levels of infection.

In two case-control studies of hepatocellular carcinoma and HDV infection among subjects seropositive for hepatitis B surface antigen, there were no anti-HD-seropositive individuals among cases or controls. Three further case-control studies suggested a positive association but had limited statistical power.

5.3 Animal carcinogenicity data

No adequate data were available to the Working Group.

5.4 Other relevant data

Case series suggest that chronic hepatitis and cirrhosis develop more rapidly in patients infected with both HBV and HDV than in those infected with HBV alone.

5.5 Evaluation[1]

There is *inadequate evidence* in humans for the carcinogenicity of infection with hepatitis D virus.

There is *inadequate evidence* in experimental animals for the carcinogenicity of infection with hepatitis D virus.

Overall evaluation

Infection with hepatitis D virus *is not classifiable as to its carcinogenicity to humans (Group 3).*

[1]For definition of the italicized terms, see Preamble, pp. 30–34.