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Swiss Expert Committee for Biosafety SECB

SECB Recommendation on

classification of activities using the viruses HBV, HCV, HDV and HGV

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Contents

1 Purpose and field of application

This document is intended to assist in the classification of activities using Group 3** hepatitis viruses (HBV and HCV), as well as other hepatitis viruses (HDV and HGV). The Recommendation takes the Containment Ordinance (ContainO) into account.

Activities using Group 3** viruses are generally assigned to Class 3. Depending on the risk assessment of an activity, however, it may be possible to work at a lower safety level. This Recommendation does not apply to activities involving the cultivation of large quantities of hepatitis viruses.

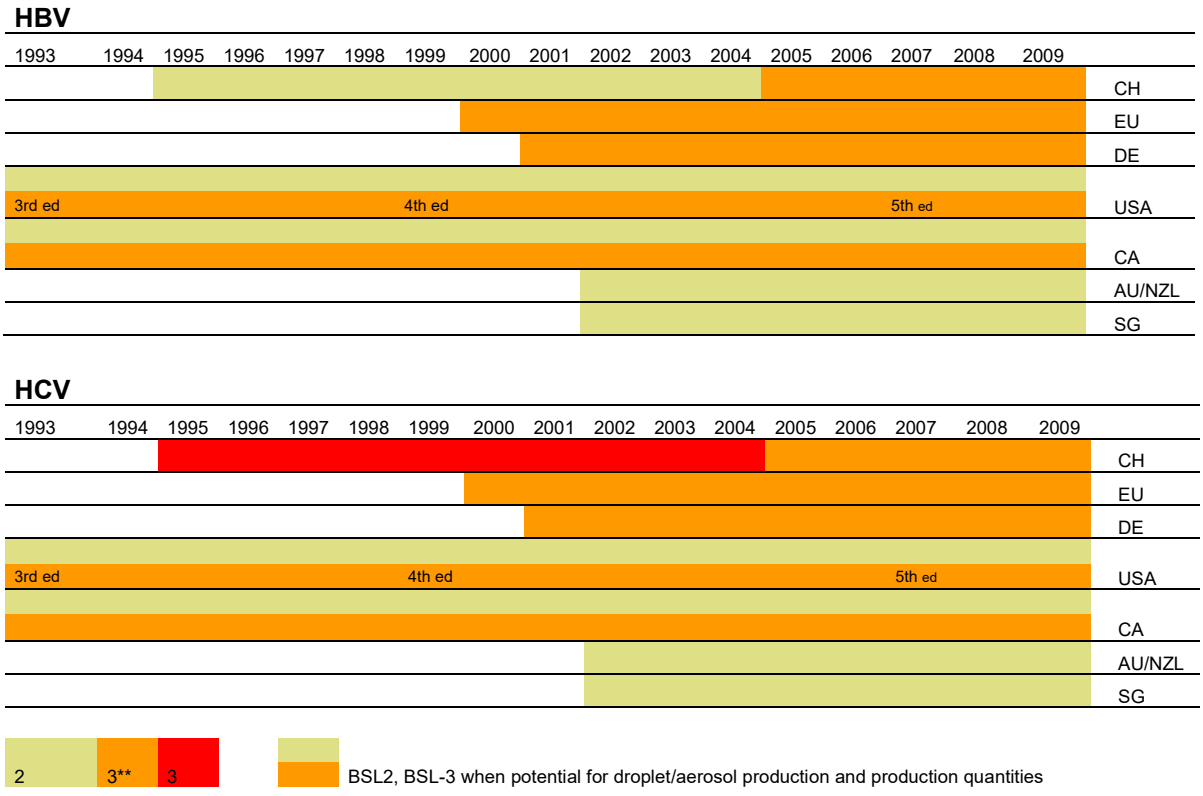
Provided a written application is submitted, the following safety measures may be altered, substituted or omitted completely for activities using Group 3** organisms:

- negative pressure,
- exhaust filtration of atmospheric air using high-efficiency mechanical filters, if the work is being carried out in a safety cabinet or a contained system,
- autoclave within the laboratory,
- general inactivation of solid and liquid wastes, provided inactivation of contaminated solid and liquid wastes is guaranteed,
- sealable work area allowing fumigation,
- staff airlock

The experience of recent years suggests that the risk of infection when working with these viruses is very low. This then raises the question of how to classify particular activities involving these viruses in the future.

2 Foundations

International classification using the example of HBV and HCV



Sources: CH: SKBS, FOEN list - EU: Directive 2000/54/EG - DE: ZKBS - USA: BMBL - CA: MSDS AU/NZL, SG: ABSA

3 Description of the different hepatitis viruses

Hepatitis B virus:

Humans are the natural host of the hepatitis B virus. Transmission takes place horizontally (parenterally or via sexual contacts) and vertically (perinatally). HBV is not known to be transmitted through the air, or through food or water. Nevertheless, particular care should be taken with any operations producing large amounts of aerosols or droplets. The incubation period varies greatly, between 3 weeks and 9 months. Outside its host the virus can remain infectious for up to seven days. All persons who work with HBV should be vaccinated against this virus without exeption. Their immune status should also be checked regularly in order to ensure they have sufficient immune protection against hepatitis B.

Hepatitis C virus:

Human hepatitis C virus causes an infectious disease that frequently becomes chronic, and which can over time lead to severe liver damage. Transmission takes place parenterally through blood. Outside its host the virus very probably remains infectious for some time, especially in dried blood. The incubation period is between 2 weeks and 6 months. There is no vaccination available as yet. A limited form of treatment is possible depending on genotype.

Hepatitis D virus:

Human delta hepatitis virus is a defective virus and has not been assigned to a family. Its natural host is humans. Infection can only take place if a person is infected with HBV. Like HBV, transmission can be horizontal and vertical, but does not occur via the air, food or water. There are no satisfactory treatments as yet. Vaccination against HBV protects indirectly against HDV. Therefore, all persons who work with HDV should without exeption be vaccinated against HBV and have their immune status checked regularly. Staff with adequate immune protection may carry out all types of work using HDV at safety level 2.

Hepatitis G virus / GBV-C:

Hepatitis G virus and the GB virus C have been isolated from patients with jaundice. However, no disease has yet been described that could be associated with infection by these two viruses. The viruses are found all over the world and 15 to 20% of the population is seropositive but shows no symptoms. Therefore, all work using HGV/GBV-C can be carried out at safety level 1.

4 New recommendation on classification

Classification of activities:

The tables below describe the classification of different activities using HBV and HCV. They are a general classification schema.

The classification of diagnostic activities is in accordance with the Guidelines on Diagnostics.

Table 1: Classification of activities using HBV

Activity		**Class**
Diagnostics	Without viral multiplication	2
Research	Activities using wildtype or infectious replication competent genetically modified viruses (e.g. viral multiplication in cell culture, development and validation of methods)	3
	Cultivation for analysis of cells that may contain HBV, but where no attempt is made at explicit multiplication of HBV	2
	Subgenomic sequences in prokaryotic and eukaryotic (incl. cell culture) expression systems	1[1]
	Subgenomic sequences in replication competent and incompetent viral expression systems	1 / 2[2]
	Whole genome in plasmids (e.g. storage, amplification in *E. coli*)	2
	Animal experiments using wildtype or infectious replication competent genetically modified viruses	3
	Animal experiments in which viral particles are no longer shed	1

Table 2: Classification of activities using HCV

Activity		**Class**
Diagnostics	Without viral multiplication	2
Research	Activities using wildtype or infectious replication competent genetically modified viruses (e.g. viral multiplication in cell culture, development and validation of methods)	3
	Cultivation for analysis of cells that may contain HCV, but where no attempt is made at explicit multiplication of HCV	2
	Subgenomic sequences in replication competent and incompetent viral expression systems	1 / 2[2]
	Whole genome in plasmids (e.g. storage, amplification in *E. coli*)	1[3]
	Transfection of subgenomic HCV replicon constructs produced in vitro in a Group 1 cell line that does not complement the defect	1
	Animal experiments using wildtype or infectious replication competent genetically modified viruses	3
	Animal experiments in which viral particles are no longer shed	1

[1] Higher classification may be possible, depending on activity and risk assessment (length or hazard potential of the sequence).

[2] According to the Group of the expression system.

[3] HCV is only infectious in its RNA form.

5 Note on safety measures

HBV, HCV, HDV and HGV are not known to be transmitted via the air. Therefore various safety measures may be altered, substituted or omitted. Such deviations must be justified on the basis of a risk assessment. The *Guideline on safety measures in human medical-microbiological diagnostics* laboratories describes criteria for deviations in diagnostic activities. This Guideline can be applied by analogy to research activities.

Unlike HBV, no protective vaccination is possible for HCV, HDV or HGV.

6 Consequences of the new classification

Current enforcement practice for Group 3** viruses has scope for some flexibility in the safety measures as a concession to research, without compromising on the safety of humans or the environment. The classification of these viruses can therefore be retained in the Swiss List of Organisms.

7 References

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