Annex I

Scientific conclusions and grounds for the variation to the terms of the Marketing Authorisations

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for rabies vaccine, the scientific conclusions are as follows:

Cases of anxiety-related adverse reactions such as presyncope, syncope, loss of consciousness and anxiety were reported and demonstrated a causal relationship to the rabies vaccine administration. Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions are known to occur following, or even before, any vaccination as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance and paraesthesia. It is important that procedures are in place to avoid injury from faints. The product information of purified chick embryo cell vaccine (PCEC) vaccine was updated in this regard during the reporting interval and PRAC considered that a warning should also be added to the product information of human diploid cell culture rabies vaccine (HDVC) and purified Vero cell rabies vaccine (PVRV) vaccines.

Therefore, in view of the data presented in the reviewed PSUR(s), the PRAC considered that changes to the product information of medicinal products containing human diploid cell culture rabies vaccine (HDCV) and purified Vero cell rabies vaccine (PVRV), were warranted.

The CMDh agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for the rabies vaccine the CMDh is of the opinion that the benefit-risk balance of the medicinal products containing human diploid cell culture rabies vaccine (HDCV) and purified Vero cell rabies vaccine (PVRV) is unchanged subject to the proposed changes to the product information.

The CMDh reaches the position that the marketing authorisations of products containing human diploid cell culture rabies vaccine (HDCV) and purified Vero cell rabies vaccine (PVRV) in the scope of this single PSUR assessment should be varied. To the extent that additional medicinal products containing human diploid cell culture rabies vaccine (HDCV) and purified Vero cell rabies vaccine (PVRV) are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that such marketing authorisations are varied accordingly.

Annex II

Amendments to the product information of the nationally authorised medicinal products

Amendments to be included in the relevant sections of the Product Information (new text **underlined and in bold**, deleted text ~~strike through~~)

[For human diploid cell culture rabies vaccine (HDCV) and purified Vero cell rabies vaccine (PVRV) only]

Summary of Product Characteristics

- Section 4.4

A warning should be added as follows:

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions can occur following, or even before, any vaccination as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance and paraesthesia. It is important that procedures are in place to avoid injury from faints.

Package Leaflet

No update of the package leaflet is considered necessary.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	November CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	24 December 2016
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	22 February 2017