This form should be used for all taxonomic proposals. Please complete all those modules that are applicable (and then delete the unwanted sections). For guidance, see the notes written in blue and the separate document "Help with completing a taxonomic proposal"

Please try to keep related proposals within a single document; you can copy the modules to create more than one genus within a new family, for example.

MODULE 1: **TITLE, AUTHORS, etc**

Code assigned:	***2011.004aV***	(to be completed by ICTV officers)

Short title: New species Murid herpesvirus 7 in the genus Rhadinovirus, subfamily Gammaherpesvirinae, family Herpesviridae, order Herpesvirales
(e.g. 6 new species in the genus *Zetavirus*)

Modules attached (modules 1 and 9 are required)	**1** ☒	**2** ☒	**3** ☐	**4** ☐	**5** ☐
	6 ☐	**7** ☐	**8** ☐	**9** ☒	

Author(s) with e-mail address(es) of the proposer:

Andrew Davison (a.davison@mrcvu.gla.ac.uk) & James Stewart (j.p.stewart@liv.ac.uk)

List the ICTV study group(s) that have seen this proposal:

A list of study groups and contacts is provided at http://www.ictvonline.org/subcommittees.asp . If in doubt, contact the appropriate subcommittee chair (fungal, invertebrate, plant, prokaryote or vertebrate viruses)	Herpesvirales Study Group

ICTV-EC or Study Group comments and response of the proposer:

All comments during the SG discussion period were positive and the proposal was unanimously approved by the SG (voting period ended 2/11/2011).

Date first submitted to ICTV:	April 19, 2010
Date of this revision (if different to above):	February 11, 2011 (differs only in the addition of the SG activity) October 12, 2011 (addition of phylogenetic tree)

MODULE 2: **NEW SPECIES**

creating and naming one or more new species.

If more than one, they should be a group of related species belonging to the same genus. All new species must be placed in a higher taxon. This is usually a genus although it is also permissible for species to be "unassigned" within a subfamily or family.

Code	***2011.004aV***	(assigned by ICTV officers)

To create 1 new species within:

Genus:	***Rhadinovirus***
Subfamily:	***Gammaherpesvirinae***
Family:	***Herpesviridae***
Order:	***Herpesvirales***

Fill in all that apply.

- If the higher taxon has yet to be created (in a later module, below) write "**(new)**" after its proposed name.
- If no genus is specified, enter "**unassigned**" in the genus box.

And name the new species:	**GenBank sequence accession number(s) of reference isolate:**
Murid herpesvirus 7	GQ169129

Reasons to justify the creation and assignment of the new species:

- Explain how the proposed species differ(s) from all existing species.
  - If species demarcation criteria (see module 3) have previously been defined for the genus, **explain how the new species meet these criteria**.
  - If criteria for demarcating species need to be defined (because there will now be more than one species in the genus), please state the proposed criteria.
- Provide accession numbers for genomic sequences
- Further material in support of this proposal may be presented in the Appendix, Module 9

Two isolates of a novel relative of murine gammaherpesvirus 68 (MHV68; species *Murid herpesvirus 4*, genus *Rhadinovirus*, subfamily *Gammaherpesvirinae,* family *Herpesviridae*, order *Herpesvirales*) have been reported. The first was made in Brest, France, ostensibly from a white-toothed shrew, *Crocidura russula* (Chastel *et al.*, 1994). The second was made from several wood mice, *Apodemus sylvaticus*, in Cheshire, UK (Hughes *et al.*, 2010). These viruses have been named Brest herpesvirus (BRHV) and wood mouse herpesvirus (WMHV), respectively. The complete genome sequence of WMHV has been published (GQ169129; 120108 bp, consisting of the unique region plus one copy of the terminal repeats), along with a 71913 bp region of the BRHV genome at left end of the unique region. In the comparable regions, these viruses share 99.2% DNA sequence identity, indicating that they are two strains of the same virus.

Herpesviruses are defined as distinct species if (a) their genomes differ in a readily assayable and distinctive manner across the entire genome (e.g. restriction endonuclease cleavage site patterns obtained with many enzymes) and not merely at a specific site (e.g. small number of genes or small number of restriction endonuclease sites) and (b) if the virus can be shown to have distinct epidemiologic and biologic characteristics.

(a) Genome relatedness. As no formal sequence identity values exist for classifying herpesvirus species, arguments in this regard are based on precedent. As described in Hughes *et al.* (2010), the WMHV and MHV68 genomes share a mean nucleotide sequence identity of 85% (not counting gaps), with greatest similarity in the first 10 kbp at the left end of the unique region, which contains 4 protein-coding and 8 tRNA-like genes that are specific to these viruses. Within individual coding regions, amino acid sequence identity ranges from 60 to 98%. The nucleotide sequence identity value is close to that between viruses in species *Human herpesvirus 1* and *Human herpesvirus 2* (NC_001806 and NC_001798), which has been cited as 83% (Dolan *et al.*, 1998). The corresponding value between viruses in species *Bovine herpesvirus 1* and *Bovine herpesvirus 5* (NC_001847, Schwyzer *et al.*, 1996; NC_005261, Delhon *et al.*, 2003), is significantly higher, being calculated by us at 96%. A phylogenetic tree for the viral DNA polymerase is shown in Module 9.

(b) Biological properties. MHV68 is studied almost exclusively in a laboratory mouse (*Mus musculus*) model, but its natural host is predominantly the yellow-necked field mouse (*Apodemus flavicollis*) (Ehlers *et al.*, 2007). However, the virus has also been detected in wood mice (*A. sylvaticus*). This has been interpreted as *A. flavicollis* hosting MHV68 and *A. sylvaticus* hosting WMHV, with some crossover (Hughes *et al.*, 2010). The isolation of BRHV from a host in a different order (Insectivora) from that of WMHV and MHV68 (Rodentia) is at odds with co-evolution between herpesviruses and their hosts. It seems probable that the virus that was isolated actually originated from a rodent, either by cross-infection in the wild or in the laboratory, since isolation included passage in mouse brains. WMHV and MHV68 exhibit similar biological characteristics in the wood mouse model (Hughes *et al.*, 2010). However, differences are apparent in the ability to grow in the lungs, to develop iBALT (perivascular and peribronchial, B cell-rich lymphocyte infiltration with evidence of lymphatic follicle formation) and, perhaps, to reactivate from latency in splenic leukocytes.

We conclude that WMHV and BRHV meet the criteria to be classified into a new species, and recommend the name *Murid herpesvirus 7*, being added to the existing members in the genus *Rhadinovirus,* namely *Ateline herpesvirus 2, Ateline herpesvirus 3, Bovine herpesvirus 4, Human herpesvirus 8, Macacine herpesvirus 5, Murid herpesvirus 4* and *Saimiriine herpesvirus 2*.

MODULE 9: **APPENDIX**: supporting material

additional material in support of this proposal

References:

Chastel, C., Beaucournu, J. P., Chastel, O., Legrand, M. C. & Le Goff, F. (1994). A herpesvirus from an European shrew (Crocidura russula). Acta Virol. 38, 309.

Delhon, G., Moraes, M.P., Lu, Z., Afonso, C.L., Flores, E.F., Weiblen, R., Kutish, G.F. & Rock, D.L. (2003). Genome of bovine herpesvirus 5. J. Virol. 77, 10339-10347.

Dolan, A., Jamieson, F.E., Cunningham, C., Barnett, B.C. & McGeoch, D.J. (1998). The genome sequence of herpes simplex virus type 2. J. Virol. 72, 2010-2021.

Ehlers, B., Kuchler, J., Yasmum, N., Dural, G., Voigt, S., Schmidt-Chanasit, J., Jakel, T., Matuschka, F. R., Richter, D., Essbauer, S., Hughes, D. J., Summers, C., Bennett, M., Stewart, J. P. & Ulrich, R. G. (2007). Identification of novel rodent herpesviruses, including the first gammaherpesvirus of Mus musculus. J Virol 81, 8091-8100.

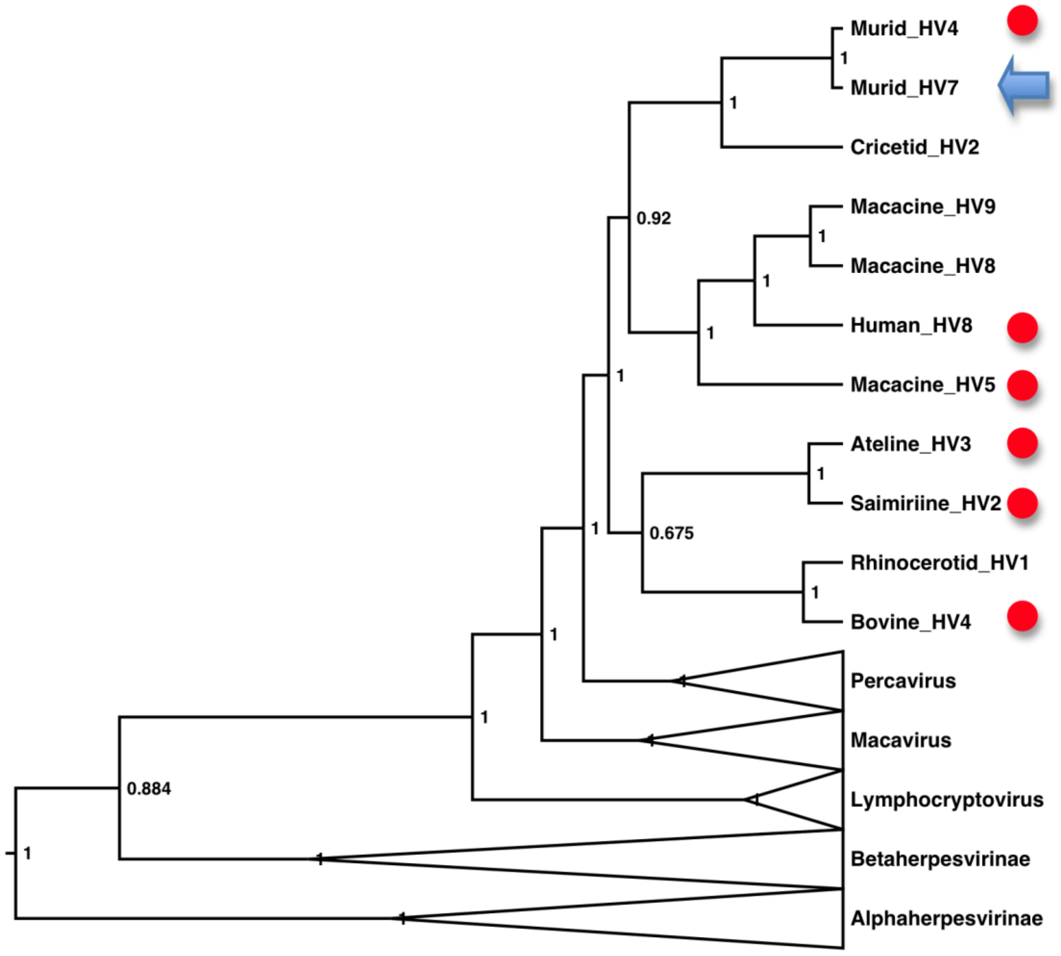
Hughes, D. J, Kipar, A., Milligan, S. G., Cunningham, C., Sanders, M., Quail, M. A., Rajandream, M. A., Efstathiou, S., Bowden, R. J. , Chastel, C., Bennett, M., Sample, J. T, Barrell, B., Davison, A. J. & Stewart, J. P. (2010). Characterization of a novel wood mouse virus related to murid herpesvirus 4. J. Gen. Virol. 91, 867-879.

Schwyzer, M. & Ackermann, M., 1996. Molecular virology of ruminant herpesviruses. Vet. Microbiol. 53, 17-29.

Annex:

Include as much information as necessary to support the proposal, including diagrams comparing the old and new taxonomic orders. The use of Figures and Tables is strongly recommended but direct pasting of content from publications will require permission from the copyright holder together with appropriate acknowledgement as this proposal will be placed on a public web site. For phylogenetic analysis, try to provide a tree where branch length is related to genetic distance.

Phylogenetic tree for herpesvirus DNA polymerases. Amino acid sequences were aligned by using ClustalW under default settings. The Bayesian analysis program BEAST utilized the Jones-Taylor-Thornton model, with among-site rate heterogeneity modelled by a gamma distribution with 5 categories plus an invariant sites (JTT+G+I). The program was run for 10 million iterations, with a relaxed uncorrelated lognormal clock model and a speciating Yule process as a tree prior. 75% of the trees were discarded as burn-in, and the consensus tree was based on the final 25% of trees generated. Posterior probability values are shown at the nodes. Branches for the subfamilies *Alphaherpesvirinae* and *Betaherpesvirinae* and the genera *Lymphocryptovirus*, *Macavirus* and *Percavirus* in the subfamily *Gammaherpesvirinae* are shown collapsed. The noncollapsed branches show members (marked by red dots) or potential members of the genus *Rhadinovirus* in the subfamily *Gammaherpesvirinae*. WMHV (murid HV7) is marked by a blue arrow, alongside MHV68 (murid HV4).


Murid_HV4
Murid_HV7
Cricetid_HV2
Macacine_HV9
Macacine_HV8
Human_HV8
Macacine_HV5
Ateline_HV3
Saimiriine_HV2
Rhinocerotid_HV1
Bovine_HV4
Percavirus
Macavirus
Lymphocryptovirus
Betaherpesvirinae
Alphaherpesvirinae
1
1
0.92
1
1
1
1
1
0.675
1
1
1
1
0.884
1