Summary of proposed changes, rationale and actions required

Agent	**Approved List 2004 status**	**EC Biological Agents Directive 2000/54/EC classification**	**Swiss FOEN 2011 classification**	**Result of initial consultation with ACDP virology experts**	**Proposed Approved List 2012 status** (latest Approved List page number)	**Actions required from ACDP**
Lujo virus	Not listed	Not listed	Not listed	Suggested inclusion in List and proposed HG4 classification	HG4 (p26)	Agree classification
Lymphocytic choriomeningitis LCMV	Listed as Lymphocytic choriomeningitis as HG3	HG2	LCMV as HG2; 'LCMV neurotropic strains' as HG3	It was agreed that we should have a separate entry in the Approved List for LCM-Armstrong strain with Hazard Group 2 classification	p26. Now have LCMV (all strains other than Armstrong) as HG3 and LCMV Armstrong as HG2	Agree separate entries and classifications
"Other LCM-Lassa complex viruses"	HG2	HG2	No catch all or named agents listed	Three examples (Kodoko, Morogoro, Merino Walk) now given in notes section,	HG2 p27	Do you agree with placing the named agents in notes under catch-all or should they be listed?

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				newly listed by name. It was agreed that they are all HG2 and can be listed in this 'catch-all' category.		
Whitewater Arroyo	Not listed	Not listed	Not listed	New agent included at ACDP recommendation. It was agreed as being HG2 and evidence in EID 2011 paper suggests homology with LCMV	HG2 p27	To agree classification as HG2
Chapare	Not listed	Not listed	Not listed	Recently described pathogenic new world arenavirus. (Plos pathol 2008 Apr 18)	HG3 or 4? p27	Paper cites close relatedness to Machupo, Guanarito and Sabia which are all HG4, therefore suggesting HG4. Action required to agree inclusion

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				suggested for inclusion.		as HG4
"Other new world arenaviruses"	Not listed	'Other Tacaribe complex viruses' listed as HG2	No catch alls in list; Tacaribe listed as HG2	Six examples (Allpahuayo, Bear Canyon, Cupixi, Oliveros, Pirital, Tacaribe) now given in notes section, newly listed by name. It was agreed that they are all HG2 and can be listed in this 'catch-all' category.	HG2 with notes p27	Do you agree with placing the named agents in notes under catch-all or should they be listed?
Andes	Not listed	Not listed	Not listed	New agent included at ACDP recommendation. HG3 classification agreed	HG3 p28	Agree classification
"Other	HG2	HG2	No catch all in	2004 List	Other	Agree revised List descriptor

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hantaviruses"			list	descriptor "other hantaviruses" has been replaced in 2011 by a 'catch-all' for whole family named "Other Bunyaviridae not listed above" and given Hazard Group 2	Bunyaviridae not listed above HG2 p29	
Dugbe, Ganjam and Nairobi Sheep	Not listed	Not listed	All three listed as HG3	New agents included at ACDP recommendation. HG3 classifications proposed for Dugbe, Ganjam and Nairobi sheep. All 3 related viruses do infect humans	HG3 p28	Agree classification

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				– infection appears to be mild but considered reasonable to use precautionary principle.		
La Crosse	Not listed	Not listed	HG2	New agent included at ACDP recommendation. HG2 classification agreed.	HG2 p29	Agree classification
Ngari	Not listed	Not listed	Not listed	New agent included at ACDP recommendation. HG3 classification agreed. Published	HG3 p29	Agree classification

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				evidence in 2004 of human infection and person to person transmission		
Snowshoe hare virus	Not listed	Not listed	Not listed	New agent included at ACDP recommendation. Initial assessment suggests no evidence of need for greater than HG2, but question raised as it does cause human infection, and is it less severe than Nairobi sheep which is proposed at HG3?	HG2 or HG3 p29	Agree classification as either HG2 or 3

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Chinese Bunyavirus (severe fever with thrombocytopoenia syndrome; SFTS)	Not listed	Not listed	Not listed	New agent included at ACDP recommendation [N. Eng journal, April 21 2011] Evidence from this paper would classify it as HG3	HG3 p29	Agree classification and name – is 'Chinese Bunyavirus' a recognised name or should it be listed as SFTS?
Punta Toro	Not listed	Not listed	HG2	New agent included at ACDP recommendation. HG2 classification agreed.	HG2 p29	Agree classification
Ebola Cote d'Ivoire virus	Not listed	Not listed; only lists Ebola genus	HG4	New agent included at ACDP recommendation. HG4 classification	HG4 p30	Agree classification

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				agreed.		
Ebola Siena	HG4	Not listed; only lists Ebola genus		Taxonomic change – no change to Hazard Group Taxonomically now listed as Ebola Reston strain Siena therefore now listed as Ebola Reston (HG4) with a note saying 'includes strain Siena'	HG4 p30	Agree revised entry with note
Alkhurma haemorrhagic fever virus	Not listed	Not listed	Not listed	New agent included at ACDP recommendation. HG4 classification agreed.	HG4 p31	Agree classification
Central European	Not included	HG3 V	Not listed	Missing from	HG3 vaccine	Agree classification and

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tick-borne encephalitis virus		(vaccine available)		2004 List - HG3 classification compatible with EC and vaccine confirmed as available in UK	available p31	vaccine status
Influenza types A, B and C	HG2	HG2	HG2	Suggestion made that note be added regarding assessment and classification of pandemic strains	HG2 (no change) p33	To agree wording of note
Human bocavirus	Not listed	Not listed	Not listed	New agent included at ACDP recommendation. No evidence for greater than HG2 classification.	HG2 p35	Agree classification
Human partetravirus (Parv4/Parv5)	Not listed	Not listed	Not listed	New agent included at ACDP recommendation.	HG2 p35	Agree classification

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				No evidence for greater than HG2 classification		
Parechoviruses	Not listed	Not listed	HG2	New agent included at ACDP recommendation. No evidence for greater than HG2 classification	HG2 p36	Agree classification
Elephantpox	Cowpox (HG2) had footnote 'including strains isolated from elephants'	HG2	Not listed	ACDP recommended include as listed entry; HG2 classification as supported by EU Directive	HG2 p36	Agree entry in List
Rabbitpox	Vaccinia (HG2) had footnote 'including strains originally classified as rabbitpox'	HG2	HG2	ACDP recommended include as listed entry; HG2 classification as supported by EU Directive	HG2 p36	Agree entry in List

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Human rotaviruses A, B, C				Suggested addition of note that vaccine available for group A	HG 2 (no change) p38	Agree note
Ibaraki virus	Not listed	Not listed	HG3	New agent included at ACDP recommendation. HG2 classification agreed.	HG2 p38	Agree classification – note that Swiss List is at HG3
Xenotropic murine leukemia virus-related virus	Not listed	Not listed	Not listed	New agent included at ACDP recommendation. HG2 classification agreed on basis that there is now a significant body of evidence that this is not a human pathogen	HG2 p38	Agree classification

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				although it might nonetheless infect human cells. If high titre virus is being cultured RA should reflect potential risk.		
Australian bat lyssavirus; European bat lyssaviruses 1 and 2; Lagos bat virus; Mokola virus	None listed	None listed	HG3	All four recommended for listing by ACDP, agreed to be classified as HG3 and consistency with other lyssavirus species.	HG3 p38-39	Agree classification

Briese T, Paweska JT, McMullan LK, Hutchison SK, Street C, et al. (2009) Genetic Detection and Characterization of Lujo Virus, a New Hemorrhagic Fever– Associated Arenavirus from Southern Africa. PLoS Pathog 5(5): e1000455. doi:10.1371/journal.ppat.1000455

Lujo virus (LUJV), a new member of the family Arenaviridae and the first hemorrhagic fever–associated arenavirus from the Old World discovered in three decades, was isolated in South Africa during an outbreak of human disease characterized by nosocomial transmission and an unprecedented high case fatality rate of 80% (4/5 cases). Unbiased pyrosequencing of RNA extracts from serum and tissues of outbreak victims enabled identification and detailed phylogenetic characterization within 72 hours of sample receipt. Full genome analyses of LUJV showed it to be unique and branching off the ancestral node of the Old World arenaviruses. The virus G1 glycoprotein sequence was highly diverse and almost equidistant from that of other Old World and New World arenaviruses, consistent with a potential distinctive receptor tropism. LUJV is a novel, genetically distinct, highly pathogenic arenavirus.

Mary Louise Milazzo, Grant L. Campbell, and Charles F. Fulhorst Novel Arenavirus Infection in Humans, United States. Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 17, No. 8, August 2011

Immunoglobulin G against Whitewater Arroyo virus or lymphocytic choriomeningitis virus was found in 41 (3.5%) of 1,185 persons in the United States who had acute central nervous system disease or undifferentiated febrile illnesses. The results of analyses of antibody titers in paired serum samples suggest that a North American Tacaribe serocomplex virus was the causative agent of the illnesses in 2 persons and that lymphocytic choriomeningitis virus was the causative agent of the illnesses in 3 other antibody positive persons in this study. The results of this study suggest that Tacaribe serocomplex viruses native to North America, as well as lymphocytic choriomeningitis virus, are causative agents of human disease in the United States.

Delgado S, Erickson BR, Agudo R, Blair PJ, Vallejo E, et al. (2008) Chapare Virus, a Newly Discovered Arenavirus Isolated from a Fatal Hemorrhagic Fever Case in Bolivia. PLoS Pathog 4(4): e1000047. doi:10.1371/journal.ppat.1000047

A small focus of hemorrhagic fever (HF) cases occurred near Cochabamba, Bolivia, in December 2003 and January 2004. Specimens were available from only one fatal case, which had a clinical course that included fever, headache, arthralgia, myalgia, and vomiting with subsequent deterioration and multiple hemorrhagic signs. A non-cytopathic virus was isolated from two of the patient serum samples, and identified as an arenavirus by IFA staining with a rabbit polyvalent antiserum raised against South American arenaviruses known to be associated with HF (Guanarito, Machupo, and Sabia´). RT-PCR analysis and subsequent analysis of the complete virus S and L RNA segment sequences identified the virus as a member of the New World Clade B arenaviruses, which includes all the pathogenic South American arenaviruses. The virus was shown to be most closely related to Sabia´ virus, but with 26% and 30% nucleotide difference in the S and L segments, and 26%, 28%, 15% and 22% amino acid differences for the L, Z, N, and GP proteins, respectively, indicating the virus represents a newly discovered arenavirus, for which we propose the name Chapare virus. In conclusion, two different arenaviruses, Machupo and Chapare, can be associated with severe HF cases in Bolivia.

Rémi N. Charrel, Shamsudeen Fagbo, Gregory Moureau, Mohammad Hussain Alqahtani, Sarah Temmam, and Xavier de Lamballerie. Alkhurma Hemorrhagic Fever Virus in *Ornithodoros savignyi* Ticks Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 13, No. 1, January 2007

Alkhurma hemorrhagic fever virus (AHFV) is a recently described virus within the genus *Flavivirus*. AHFV was discovered in 1995 in a patient with hemorrhagic manifestations and fever in Saudi Arabia (*1*). Subsequently, ≈20 symptomatic patients infected with this virus have been documented by virus isolation in this country. The clinical picture is extremely severe and the case-fatality rate is >30%, which makes AHFV one of the most deadly flaviviruses (*2*). Previous studies have determined that AHFV is a variant genotype of *Kyasanur Forest disease virus*, another biosafety level (BSL) 4 virus that causes viral hemorrhagic fever in certain regions of India (*3*). Accordingly, AHFV is classified as a BSL-3 or BSL-4 agent, depending on country regulations.

Xue-Jie Yu, M.D., Ph.D., Mi-Fang Liang, M.D., Shou-Yin Zhang, Ph.D. et al. Fever with Thrombocytopenia Associated with a Novel Bunyavirus in China N Engl J Med 2011;364:1523-32.

Background
Heightened surveillance of acute febrile illness in China since 2009 has led to the identification of a severe fever with thrombocytopenia syndrome (SFTS) with an unknown cause. Infection with *Anaplasma phagocytophilum* has been suggested as a cause, but the pathogen has not been detected in most patients on laboratory testing.
Methods
We obtained blood samples from patients with the case definition of SFTS in six provinces in China. The blood samples were used to isolate the causal pathogen by inoculation of cell culture and for detection of viral RNA on polymerase-chainreaction assay. The pathogen was characterized on electron microscopy and nucleic acid sequencing. We used enzyme-linked immunosorbent assay, indirect immunofluorescence assay, and neutralization testing to analyze the level of virus-specific antibody in patients' serum samples.
Results
We isolated a novel virus, designated SFTS bunyavirus, from patients who presented with fever, thrombocytopenia, leukocytopenia, and multiorgan dysfunction. RNA sequence analysis revealed that the virus was a newly identified member of the genus phlebovirus in the Bunyaviridae family. Electron-microscopical examination revealed virions with the morphologic characteristics of a bunyavirus. The presence of the virus was confirmed in 171 patients with SFTS from six provinces by detection of viral RNA, specific antibodies to the virus in blood, or both. Serologic assays showed a virus-specific immune response in all 35 pairs of serum samples collected from patients during the acute and convalescent phases of the illness.
Conclusions
A novel phlebovirus was identified in patients with a life-threatening illness associated with fever and thrombocytopenia in China. (Funded by the China Mega-Project for Infectious Diseases and others.)

Charles F. Fulhorst, Mary Louise Milazzo, Lori R. Armstrong, et al Hantavirus and Arenavirus Antibodies in Persons with Occupational Rodent Exposure, North America Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 13, No. 4, April 2007

Rodents are the principal hosts of Sin Nombre virus, 4 other hantaviruses known to cause hantavirus pulmonary syndrome in North America, and the 3 North American arenaviruses. Serum samples from 757 persons who had worked with rodents in North America and handled neotomine or sigmodontine rodents were tested for antibodies against Sin Nombre virus, Whitewater Arroyo virus, Guanarito virus, and lymphocytic choriomeningitis virus. Antibodies against Sin Nombre virus were found in 4 persons, against Whitewater Arroyo virus or Guanarito virus in 2 persons, and against lymphocytic choriomeningitis virus in none. These results suggest that risk for infection with hantaviruses or arenaviruses usually is low in persons whose occupations entail close physical contact with neotomine or sigmodontine rodents in North America.

Sonja R. Gerrard, Li Li, Alan D. Barrett, and Stuart T. Nichol Ngari Virus Is a Bunyamwera Virus Reassortant That Can Be Associated with Large Outbreaks of Hemorrhagic Fever in Africa JOURNAL OF VIROLOGY, Aug. 2004, p. 8922–8926 Vol. 78, No. 16

Two isolates of a virus of the genus *Orthobunyavirus* (family *Bunyaviridae*) were obtained from hemorrhagic fever cases during a large disease outbreak in East Africa in 1997 and 1998. Sequence analysis of regions of the three genomic RNA segments of the virus (provisionally referred to as Garissa virus) suggested that it was a genetic reassortant virus with S and L segments derived from Bunyamwera virus but an M segment from an unidentified virus of the genus *Orthobunyavirus*. While high genetic diversity (52%) was revealed by analysis of virus M segment nucleotide sequences obtained from 21 members of the genus *Orthobunyavirus*, the Garissa and Ngari virusMsegments were almost identical. Surprisingly, the Ngari virus L and S segments showed high sequence identity with those of Bunyamwera virus, showing that Garissa virus is an isolate of Ngari virus, which in turn is a Bunyamwera virus reassortant. Ngari virus should be considered when investigating hemorrhagic fever outbreaks throughout sub-Saharan Africa.

Philip M. Armstrong* and Theodore G. Andreadis A new genetic variant of La Crosse virus (B*unyaviridae*) isolated from New England. A*m. J. Trop. Med. Hyg.,* 75(3), 2006, pp. 491–496

Abstract. La Crosse virus (LACV) is found primarily in the Midwestern and Appalachian regions of the United States where it is a leading cause of mosquito-borne encephalitis in children. To determine whether the distribution of this virus extends further east into New England, we analyzed a bunyavirus that was isolated from a pool of eastern tree-hole mosquitoes, *Ochlerotatus triseriatus* (_ *Aedes triseriatus*), collected from Fairfield, Connecticut (CT) in 2005. Nucleotide and encoded amino acid sequences from portions of the S, M, and L segments were more similar to the prototype strain of La Crosse virus than that of closely related snowshoe hare virus. Phylogenetic analysis of sequences from the M segment indicated that the CT isolate represents a distinct lineage of La Crosse virus, diverging earliest from other strains found in southeastern, central, and northeastern United States. Despite low sequence homology with other viral strains, the CT isolate was antigenically similar to the prototype strain of LACV by plaque-reduction neutralization tests with polyclonal and monoclonal antibodies. This represents the first isolation of LACV in New England to our knowledge and suggests long-term independent evolution of the CT isolate.

Detlev H. Krüger,1,* Günther Schönrich1 and Boris Klempa1,2Human pathogenic hantaviruses and prevention of infectionHuman Vaccines 7:6, 685-693; June 2011;

Hantaviruses are emerging viruses which are hosted by small mammals. When transmitted to humans, they can cause two clinical syndromes, hemorrhagic fever with renal syndrome or hantavirus cardiopulmonary syndrome. The review compiles the current list of hantaviruses which are thought to be pathogenic in humans on the basis of molecular or at least serological evidence. Whereas induction of a neutralizing humoral immune response is considered to be protective against infection, the dual role of cellular immunity (protection versus immunopathogenicity) is discussed. For immunization, inactivated virus vaccines are licensed in certain Asian countries. Moreover, several classical and molecular vaccine approaches are in pre-clinical stages of development. The development of hantavirus vaccines is hampered by the lack of adequate animal models of hantavirus-associated disease. In addition to active immunization strategies, the review summarizes other ways of infection prevention, as passive immunization, chemoprophylaxis and exposition prophylaxis.

Table 1. Hantaviruses reported to be pathogenic in humans[a]

Disease/ continent	Virus[b]	Abbreviation	Rodent host	Severity of disease	Case fatality	Patient-derived sequence available in GenBank
HFRS/Europe						
	Dobrava-Belgrade[c]	DOBV				
	DOBV-Aa		*Apodemus agrarius*	mild/moderate	0.5–0.9%	yes
	DOBV-Af		*A. flavicollis*	severe	up to 10%	yes
	DOBV-Ap		*A. ponticus*	moderate	up to 10%	yes
	Saaremaa[c]	SAAV	*A. agrarius*	?[d]		no
	Puumala[c]	PUUV	*Myodes glareolus*	mild	0.1–0.4%	yes
	Tula[c]	TULV	*Microtus arvalis*	?[d]		no
			M. agrestis			
			M. rossiaemeridionalis			
HFRS/Asia						
	Hantaan[c]	HTNV	*Apodemus agrarius*	severe	up to 10%	yes
	Amur/Soochong		*A. peninsulae*	severe?		yes
	Seoul[c,e]	SEOV	*Rattus spp.*	mild	<1%	yes
	Thailand[c]	THAIV	*Bandicota indica*	?[d]		no
HFRS/Africa						
	Sangassou or related viruses[f]	SANGV	*Hylomyscus simus*	?[d]		no
HCPS/Americas						
	Andes[c]	ANDV	*Oligoryzomys longicaudatus*	severe	25–35%	yes
	Orán	ORNV	*O. longicaudatus*			yes
	Bermejo	BMJV	*O. chacoensis*			yes
	Lechiguanas	LECV	*O. flavescens*			yes
	Rio Mamore[c]	RIOMV	*O. microtis*			no[g]
	Choclo	CHOV	*O. fulvescens*			yes
	Maciel	MCLV	*Necromys benefactus*			no
	Laguna Negra[c]	LNV	*Calomys laucha*			yes
	Araraquara	ARAV	*Bolomys lasiurus*			yes
	Hu39694		unknown			yes
	Castelo dos Sonhos	CASV	unknown			yes
	Juquitiba	JUQV	*O. nigripes*			yes
	Bayou[c]	BAYV	*Oryzomys palustris*			yes
	Black Creek Canal[c]	BCCV	*Sigmodon hispidus*			no
	Sin Nombre[c]	SNV	*Peromyscus maniculatus*	severe	25–35%	yes
	New York[c]	NYV	*P. leucopus*			yes
	Monongahela	MGLV	*P. maniculatus nubiterrae*			no

[a]Compiled from Hammerbeck, et al.[12] Jonsson, et al.[21] Kariwa, et al.[20] Krüger & Klempa[10] Muranyi, et al.[19] [b]Viruses are grouped according to rather strict species definition criteria recently proposed by Maes et al.[22] [c]Species listed in the latest report of the International Committee for Taxonomy of Viruses, see Fauquet, et al.[23] and www.ictvonline.org/virusTaxonomy.asp [d]Not to be estimated since only few patients are described. [e]Probably world-wide distributed. [f]Low anti-SANGV neutralizing antibodies detected in patients which can be also caused by infection with a related African hantavirus. [g]Designated as Anajatuba virus in GenBank but probably RIOMV.