

APPENDIX B. CLASSIFICATION OF HUMAN ETIOLOGIC AGENTS ON THE BASIS OF HAZARD

This appendix includes those biological agents known to infect humans as well as selected animal agents that may pose theoretical risks if inoculated into humans. Included are lists of representative genera and species known to be pathogenic; mutated, recombined, and non-pathogenic species and strains are not considered. Non-infectious life cycle stages of parasites are excluded.

This appendix reflects the current state of knowledge and should be considered a resource document. Included are the more commonly encountered agents and is not meant to be all-inclusive. Information on agent risk assessment may be found in the *Agent Summary Statements* of the CDC/NIH publication, [Biosafety in Microbiological and Biomedical Laboratories](#) (see [Sections V-C, V-D, V-E, and V-F](#), *Footnotes and References of Sections I through IV*). Further guidance on agents not listed in Appendix B may be obtained through: [Centers for Disease Control and Prevention](#), Biosafety Branch, Atlanta, Georgia 30333, Phone: (404) 639-3883, Fax: (404) 639-2294; National Institutes of Health, Division of Safety, Bethesda, Maryland 20892, Phone: (301) 496-1357; Biosafety Manager, National Animal Disease Center, U.S. Department of Agriculture - ARS, Ames, Iowa 50010, Phone: (515) 337-7772.

Appendix B - Table 1. Basis for the Classification of Biohazardous Agents by Risk Group (RG)

Risk Group 1 (RG1)	Agents that are not associated with disease in healthy adult humans
Risk Group 2 (RG2)	Agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are <i>often</i> available
Risk Group 3 (RG3)	Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions <i>may be</i> available (high individual risk but low community risk)
Risk Group 4 (RG4)	Agents that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are <i>not usually</i> available (high individual risk and high community risk)

Appendix B-I. Risk Group 1 (RG1) Agents

RG1 agents are not associated with disease in healthy adult humans. Examples of RG1 agents include asporogenic *Bacillus subtilis* or *Bacillus licheniformis* (see [Appendix C-IV-A](#), *Bacillus subtilis* or *Bacillus licheniformis* Host-Vector Systems, Exceptions); adeno- associated virus (AAV – all serotypes); and recombinant or synthetic AAV constructs, in which the transgene does not encode either a potentially tumorigenic gene product or a toxin molecule and are produced in the absence of a helper virus. A strain of *Escherichia coli* (see [Appendix C-II-A](#), *Escherichia coli* K-12 Host Vector Systems, Exceptions) is an RG1 agent if it (1) does not possess a complete lipopolysaccharide (*i.e.*, lacks the O antigen); and (2) does not carry any active virulence factor (*e.g.*, toxins) or colonization factors and does not carry any genes encoding these factors.

Those agents not listed in Risk Groups (RGs) 2, 3 and 4 are not automatically or implicitly classified in RG1; a risk assessment must be conducted based on the known and potential properties of the agents and their relationship to agents that are listed.

Appendix B-II. Risk Group 2 (RG2) Agents

RG2 agents are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are *often* available.

Appendix B-II-A. Risk Group 2 (RG2) - Bacterial Agents Including Chlamydia

- Acinetobacter baumannii* (formerly *Acinetobacter calcoaceticus*)
- Actinobacillus*
- Actinomyces pyogenes* (formerly *Corynebacterium pyogenes*)
- Aeromonas hydrophila*
- Amycolata autotrophica*
- Archanobacterium haemolyticum* (formerly *Corynebacterium haemolyticum*)
- Arizona hinshawii* - all serotypes
- Bacillus anthracis*
- Bartonella henselae*, *B. quintana*, *B. vinsonii*
- Bordetella* including *B. pertussis*
- Borrelia recurrentis*, *B. burgdorferi*
- Burkholderia* (formerly *Pseudomonas* species) except those listed in Appendix B-III-A (RG3)
- Campylobacter coli*, *C. fetus*, *C. jejuni*
- Chlamydia psittaci*, *C. trachomatis*, *C. pneumoniae*
- Clostridium botulinum*, *C. chauvoei*, *C. haemolyticum*, *C. histolyticum*, *C. novyi*, *C. septicum*, *C. tetani*
- Coxiella burnetii* – specifically the Phase II, Nine Mile strain, plaque purified, clone 4
- Corynebacterium diphtheriae*, *C. pseudotuberculosis*, *C. renale*
- Dermatophilus congolensis*
- Edwardsiella tarda*
- Erysipelothrix rhusiopathiae*
- Escherichia coli* - all enteropathogenic, enterotoxigenic, enteroinvasive and strains bearing K1 antigen, including *E. coli* O157:H7
- **Francisella tularensis* specifically **F. tularensis* subspecies *novicida* [aka *F. novicida*], strain Utah 112; **F. tularensis* subspecies *holarctica* LVS; **F. tularensis* biovar *tularensis* strain ATCC 6223 (aka strain B38)
- *For research involving high concentrations, BL3 practices should be considered (see [Appendix G-II-C-2. Special Practices \(BL3\)](#)).
- Haemophilus ducreyi*, *H. influenzae*
- Helicobacter pylori*
- Klebsiella* - all species except *K. oxytoca* (RG1)
- Legionella* including *L. pneumophila*
- Leptospira interrogans* - all serotypes
- Listeria*
- Moraxella*
- Mycobacterium* (except those listed in [Appendix B-III-A](#) (RG3)) including *M. avium* complex, *M. asiaticum*, *M. bovis* BCG vaccine strain, *M. chelonae*, *M. fortuitum*, *M. kansasii*, *M. leprae*, *M. malmoense*, *M. marinum*, *M. paratuberculosis*, *M. scrofulaceum*, *M. simiae*, *M. szulgai*, *M. ulcerans*, *M. xenopi*
- Mycoplasma*, except *M. mycoides* and *M. agalactiae* which are restricted animal pathogens
- Neisseria gonorrhoeae*, *N. meningitidis*
- Nocardia asteroides*, *N. brasiliensis*, *N. otitidiscaviarum*, *N. transvalensis*
- Pseudomonas aeruginosa*
- Rhodococcus equi*
- Salmonella* including *S. arizonae*, *S. choleraesuis*, *S. enteritidis*, *S. gallinarum-pullorum*, *S. meleagridis*, *S. paratyphi*, A, B, C, *S. typhi*, *S. typhimurium*
- Shigella* including *S. boydii*, *S. dysenteriae*, type 1, *S. flexneri*, *S. sonnei*
- Sphaerophorus necrophorus*
- Staphylococcus aureus*

--*Streptobacillus moniliformis*

--*Streptococcus* including *S. pneumoniae*, *S. pyogenes*

--*Treponema pallidum*, *T. carateum*

--*Vibrio cholerae*, *V. parahaemolyticus*, *V. vulnificus*

--*Yersinia enterocolitica*

--*Yersinia pestis* specifically *pgm*⁽⁻⁾ strains (lacking the 102 kb pigmentation locus) and *lcr*⁽⁻⁾ strains (lacking the LCR plasmid)

Appendix B-II-B. Risk Group 2 (RG2) - Fungal Agents

--*Blastomyces dermatitidis*

--*Cladosporium bantianum*, *C. (Xylohypha) trichoides*

--*Cryptococcus neoformans*

--*Dactylaria galopava* (*Ochroconis gallopavum*)

--*Epidermophyton*

--*Exophiala (Wangiella) dermatitidis*

--*Fonsecaea pedrosoi*

--*Microsporum*

--*Paracoccidioides braziliensis*

--*Penicillium marneffe*

--*Sporothrix schenckii*

--*Trichophyton*

Appendix B-II-C. Risk Group 2 (RG2) - Parasitic Agents

--*Ancylostoma* human hookworms including *A. duodenale*, *A. ceylanicum*

--*Ascaris* including *Ascaris lumbricoides suum*

--*Babesia* including *B. divergens*, *B. microti*

--*Brugia* filaria worms including *B. malayi*, *B. timori*

--*Coccidia*

--*Cryptosporidium* including *C. parvum*

--*Cysticercus cellulosae* (hydatid cyst, larva of *T. solium*)

--*Echinococcus* including *E. granulosus*, *E. multilocularis*, *E. vogeli*

--*Entamoeba histolytica*

--*Enterobius*

--*Fasciola* including *F. gigantica*, *F. hepatica*

--*Giardia* including *G. lamblia*

--*Heterophyes*

--*Hymenolepis* including *H. diminuta*, *H. nana*

--*Isospora*

--*Leishmania* including *L. braziliensis*, *L. donovani*, *L. ethiopia*, *L. major*, *L. mexicana*, *L. peruviana*, *L. tropica*

--*Loa loa* filaria worms

--*Microsporidium*

--*Naegleria fowleri*

--*Necator* human hookworms including *N. americanus*

--*Onchocerca* filaria worms including, *O. volvulus*

--*Plasmodium* including simian species, *P. cynomolgi*, *P. falciparum*, *P. malariae*, *P. ovale*, *P. vivax*

--*Sarcocystis* including *S. sui hominis*

--*Schistosoma* including *S. haematobium*, *S. intercalatum*, *S. japonicum*, *S. mansoni*, *S. mekongi*

--*Strongyloides* including *S. stercoralis*

--*Taenia solium*

--*Toxocara* including *T. canis*

--*Toxoplasma* including *T. gondii*

--*Trichinella spiralis*

--*Trypanosoma* including *T. brucei brucei*, *T. brucei gambiense*, *T. brucei rhodesiense*, *T. cruzi*
--*Wuchereria bancrofti* filaria worms

Appendix B-II-D. Risk Group 2 (RG2) - Viruses

Adenoviruses, human - all types

Alphaviruses (Togaviruses) - Group A Arboviruses

--Chikungunya vaccine strain 181/25
--Eastern equine encephalomyelitis virus
--Venezuelan equine encephalomyelitis vaccine strains TC-83 and V3526
--Western equine encephalomyelitis virus

Arenaviruses

--Junin virus candid #1 vaccine strain
--Lymphocytic choriomeningitis virus (non-neurotropic strains)
--Tacaribe virus complex
--Other viruses as listed in the reference source (see [Section V-C, Footnotes and References of Sections I through IV](#))

Bunyaviruses

--Bunyamwera virus
--Rift Valley fever virus vaccine strain MP-12
--Other viruses as listed in the reference source (see [Section V-C, Footnotes and References of Sections I through IV](#))

Caliciviruses

Coronaviruses

Flaviviruses - Group B Arboviruses

--Dengue virus serotypes 1, 2, 3, and 4
--Japanese encephalitis virus strain SA 14-14-2
--Yellow fever virus vaccine strain 17D
--Other viruses as listed in the reference source (see [Section V-C, Footnotes and References of Sections I through IV](#))

Hepatitis A, B, C, D, and E viruses

Herpesviruses - except Herpesvirus simiae (Monkey B virus) (see [Appendix B-IV-D, Risk Group 4 \(RG4\) - Viral Agents](#))

--Cytomegalovirus
--Epstein Barr virus
--*Herpes simplex* types 1 and 2
--*Herpes zoster*
--Human herpesvirus types 6 and 7

Orthomyxoviruses

--Influenza viruses types A, B, and C (except those listed in [Appendix B-III-D, Risk Group 3 \(RG3\) - Viruses and Prions](#))
--Tick-borne orthomyxoviruses

Papilloma viruses

--All human papilloma viruses

Paramyxoviruses

- Newcastle disease virus
- Measles virus
- Mumps virus
- Parainfluenza viruses types 1, 2, 3, and 4
- Respiratory syncytial virus

Parvoviruses

- Human parvovirus (B19)

Picornaviruses

- Coxsackie viruses types A and B
- Echoviruses - all types
- Polioviruses - all types, wild and attenuated
- Rhinoviruses - all types

Poxviruses - all types except Monkeypox virus (see [Appendix B-III-D](#), Risk Group 3 (RG3) - Viruses and Prions) and restricted poxviruses including Alastrim, Smallpox, and Whitepox (see [Section V-L](#), Footnotes and References of Sections I through IV)

Reoviruses - all types including Coltivirus, human Rotavirus, and Orbivirus (Colorado tick fever virus)

Rhabdoviruses

- Rabies virus - all strains
- Vesicular stomatitis virus non exotic strains: VSV-Indiana 1 serotype strains (e.g. Glasgow, Mudd-Summers, Orsay, San Juan) and VSV-New Jersey serotype strains (e.g. Ogden, Hazelhurst)

Rubivirus (Togaviruses)

- Rubella virus

Appendix B-III. Risk Group 3 (RG3) Agents

RG3 agents are associated with serious or lethal human disease for which preventive or therapeutic interventions *may be* available.

Appendix B-III-A. Risk Group 3 (RG3) - Bacterial Agents Including Rickettsia

- Bartonella*
- Brucella* including *B. abortus*, *B. canis*, *B. suis*
- Burkholderia* (*Pseudomonas*) *mallei*, *B. pseudomallei*
- Coxiella burnetii* (except the Phase II, Nine Mile strain listed in [Appendix B-II-A](#), Risk Group 2 (RG2) - Bacterial Agents Including Chlamydia)
- Francisella tularensis* (except those strains listed in [Appendix B-II-A](#), Risk Group 2 (RG2) - Bacterial Agents Including Chlamydia)
- Mycobacterium bovis* (except BCG strain, see [Appendix B-II-A](#), Risk Group 2 (RG2) - Bacterial Agents Including Chlamydia), *M. tuberculosis*
- Orientia tsutsugamushi* (was *R. tsutsugamushi*)
- Pasteurella multocida* type B - "buffalo" and other virulent strains
- Rickettsia akari*, *R. australis*, *R. canada*, *R. conorii*, *R. prowazekii*, *R. rickettsii*, *R. siberica*, *R. typhi* (*R. mooseri*)
- Yersinia pestis* (except those strains listed in [Appendix B-II-A](#), Risk Group 2 (RG2) - Bacterial Agents Including Chlamydia)

Appendix B-III-B. Risk Group 3 (RG3) - Fungal Agents

- Coccidioides immitis* (sporulating cultures; contaminated soil)
- Histoplasma capsulatum*, *H. capsulatum* var. *duboisii*

Appendix B-III-C. Risk Group 3 (RG3) - Parasitic Agents

None

Appendix B-III-D. Risk Group 3 (RG3) - Viruses and Prions

Alphaviruses (Togaviruses) - Group A Arboviruses

- Chikungunya virus (except the vaccine strain 181/25 listed in [Appendix B-II-D](#) Risk Group2 (RG2) – Viruses)
- Semliki Forest virus
- St. Louis encephalitis virus
- Venezuelan equine encephalomyelitis virus (except the vaccine strains TC-83 and V3526, see [Appendix B-II-D](#) (RG2) – Viruses)
- Other viruses as listed in the reference source (see [Section V-C](#), *Footnotes and References of Sections I through IV*)

Arenaviruses

- Flexal
- Lymphocytic choriomeningitis virus (LCM) (neurotropic strains)

Bunyaviruses

- Hantaviruses including Hantaan virus
- Rift Valley fever virus

Coronaviruses

- SARS-associated coronavirus (SARS-CoV)
- Middle East respiratory syndrome coronavirus (MERS-CoV)

Flaviviruses - Group B Arboviruses

- Japanese encephalitis virus (except those strains listed in [Appendix B-II-D](#) Risk Group2 (RG2) - Viruses)
- West Nile virus (WNV)
- Yellow fever virus
- Other viruses as listed in the reference source (see [Section V-C](#), *Footnotes and References of Sections I through IV*)

Orthomyxoviruses

- Influenza viruses 1918-1919 H1N1 (1918 H1N1), human H2N2 (1957-1968), and highly pathogenic avian influenza H5N1 strains within the Goose/Guangdong/96-like H5 lineage (HPAI H5N1).

Poxviruses

- Monkeypox virus

Prions

- Transmissible spongiform encephalopathies (TSE) agents (Creutzfeldt-Jacob disease and kuru agents)(see [Section V-C](#), *Footnotes and References of Sections I through IV*, for containment instruction)

Retroviruses

- Human immunodeficiency virus (HIV) types 1 and 2

- Human T cell lymphotropic virus (HTLV) types 1 and 2
- Simian immunodeficiency virus (SIV)

Rhabdoviruses

- Vesicular stomatitis virus (except those strains listed in [Appendix B-II-D Risk Group2 \(RG2\) - Viruses](#))

Appendix B-IV. Risk Group 4 (RG4) Agents

RG4 agents are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are *not usually* available.

Appendix B-IV-A. Risk Group 4 (RG4) - Bacterial Agents

None

Appendix B-IV-B. Risk Group 4 (RG4) - Fungal Agents

None

Appendix B-IV-C. Risk Group 4 (RG4) - Parasitic Agents

None

Appendix B-IV-D. Risk Group 4 (RG4) - Viral Agents

Arenaviruses

- Guanarito virus
- Lassa virus

- Junin virus (except the candid #1 vaccine strain listed in [Appendix B-II-D Risk Group2 \(RG2\) – Viruses](#))
- Machupo virus
- Sabia

Bunyaviruses (Nairovirus)

- Crimean-Congo hemorrhagic fever virus

Filoviruses

- Ebola virus
- Marburg virus

Flaviruses - Group B Arboviruses

- Tick-borne encephalitis virus complex including Absetterov, Central European encephalitis, Hanzalova, Hypr, Kumlinge, Kyasanur Forest disease, Omsk hemorrhagic fever, and Russian spring-summer encephalitis viruses

Herpesviruses (alpha)

- Herpesvirus simiae (Herpes B or Monkey B virus)

Paramyxoviruses

- Equine Morbillivirus (Hendra virus)

Hemorrhagic fever agents and viruses as yet undefined

Appendix B-V. Animal Viral Etiologic Agents in Common Use

The following list of animal etiologic agents is appended to the list of human etiologic agents. None of these agents is associated with disease in healthy adult humans; they are commonly used in laboratory experimental work.

A containment level appropriate for RG1 human agents is recommended for their use. For agents that are infectious to human cells, e.g., amphotropic and xenotropic strains of murine leukemia virus, a containment level appropriate for RG2 human agents is recommended.

Baculoviruses**Herpesviruses**

- Herpesvirus ateles
- Herpesvirus saimiri
- Marek's disease virus
- Murine cytomegalovirus

Papilloma viruses

- Bovine papilloma virus
- Shope papilloma virus

Polyoma viruses

- Polyoma virus
- Simian virus 40 (SV40)

Retroviruses

- Avian leukosis virus
- Avian sarcoma virus
- Bovine leukemia virus
- Feline leukemia virus
- Feline sarcoma virus
- Gibbon leukemia virus
- Mason-Pfizer monkey virus
- Mouse mammary tumor virus
- Murine leukemia virus

- Murine sarcoma virus

- Rat leukemia virus

Appendix B-V-1. Murine Retroviral Vectors

Murine retroviral vectors to be used for human transfer experiments (less than 10 liters) that contain less than 50% of their respective parental viral genome and that have been demonstrated to be free of detectable replication competent retrovirus can be maintained, handled, and administered, under BL1 containment.
