

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Recombinant DNA Advisory Committee; Notice of Meeting

Pursuant to Public Law 92-463, notice is hereby given of a meeting of the Recombinant DNA Advisory Committee on June 8-9, 1995. The meeting will be held at the National Institutes of Health, Building 31C, 6th Floor, Conference Room 6, 9000 Rockville Pike, Bethesda, Maryland 20892, starting on June 8, 1995, at approximately 9 a.m., and will recess at approximately 6 p.m. The meeting will reconvene on June 9, 1995, at approximately 8:30 a.m. and will adjourn at approximately 5 p.m. The meeting will be open to the public to discuss Proposed Actions under the NIH Guidelines for Research Involving Recombinant DNA Molecules (59 FR 34496) and other matters to be considered by the Committee. The Proposed Actions to be discussed will follow this notice of meeting. Attendance by the public will be limited to space available. Members of the public wishing to speak at this meeting may be given such opportunity at the discretion of the Chair.

Dr. Nelson A. Wivel, Director, Office of Recombinant DNA Activities, National Institutes of Health, MSC 7052, 6006 Executive Boulevard, Suite 323, Bethesda, Maryland 20892-7052, Phone (301) 496-9838, FAX (301) 496-9839, will provide materials to be discussed at this meeting, roster of committee members, and substantive program information. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should contact Dr. Wivel in advance of the meeting. A summary of the meeting will be available at a later date.

OMB's "Mandatory Information Requirements for Federal Assistance Program Announcements" (45 FR 39592, June 11, 1980) requires a statement concerning the official government programs contained in the Catalog of Federal Domestic Assistance. Normally NIH lists in its announcements the number and title of affected individual programs for the guidance of the public. Because the guidance in this notice covers not only virtually every NIH program but also essentially every Federal research program in which DNA recombinant molecule techniques could be used, it has been determined not to be cost effective or in the public interest to

attempt to list these programs. Such a list would likely require several additional pages. In addition, NIH could not be certain that every Federal program would be included as many Federal agencies, as well as private organizations, both national and international, have elected to follow the NIH Guidelines. In lieu of the individual program listing, NIH invites readers to direct questions to the information address above about whether individual programs listed in the Catalog of Federal Domestic Assistance are affected.

Dated: May 15, 1995.

Susan K. Feldman,

Committee Management Officer, NIH.

[FR Doc. 95-12406 Filed 5-19-95; 8:45 am]

BILLING CODE 4140-01-M

Recombinant DNA Research: Proposed Actions Under the Guidelines

AGENCY: National Institutes of Health (NIH), PHS, DHHS.

ACTION: Notice of Proposed Actions Under the NIH Guidelines for Research Involving Recombinant DNA Molecules (59 FR 34496).

SUMMARY: This notice sets forth proposed actions to be taken under the NIH Guidelines for Research Involving Recombinant DNA Molecules (59 FR 34496). Interested parties are invited to submit comments concerning these proposals. These proposals will be considered by the Recombinant DNA Advisory Committee at its meeting on June 8-9, 1995. After consideration of these proposals and comments by the Recombinant DNA Advisory Committee, the Director of the National Institutes of Health will issue decisions in accordance with the NIH Guidelines.

DATES: Comments received by June 1, 1995, will be reproduced and distributed to the Recombinant DNA Advisory Committee for consideration at its June 8-9, 1995, meeting.

ADDRESSES: Written comments and recommendations should be submitted to Dr. Nelson A. Wivel, Director, Office of Recombinant DNA Activities, National Institutes of Health, MSC 7052, 6006 Executive Boulevard, Suite 323, Bethesda, Maryland 20892-7052, or sent by FAX to 301-496-9839.

All comments received in timely response to this notice will be considered and will be available for public inspection in the above office on weekdays between the hours of 8:30 a.m. and 5 p.m.

FOR FURTHER INFORMATION CONTACT:

Background documentation and additional information can be obtained from the Office of Recombinant DNA Activities, National Institutes of Health, MSC 7052, 6006 Executive Boulevard, Suite 323, Bethesda, Maryland 20892-7052, Phone 301-496-9838, FAX to 301-496-9839.

SUPPLEMENTARY INFORMATION: The NIH will consider the following actions under the NIH Guidelines for Research Involving Recombinant DNA Molecules:

I. Addition to Appendix D of the NIH Guidelines Regarding a Human Gene Transfer Protocol/Drs. Curiel and Alvarez

In a letter dated January 5, 1995, Drs. David T. Curiel and Ronald D. Alvarez of the University of Alabama, Birmingham, Alabama, submitted a human gene transfer protocol entitled: A Phase I Study of Recombinant Adenovirus Vector-Mediated Delivery of an Anti-erbB-2 Single-Chain (sFv) Antibody Gene for Previously Treated Ovarian and Extraovarian Cancer Patients to the Recombinant DNA Advisory Committee for formal review and approval at its March 6-7, 1995, meeting. Due to reviewers' comments before the March 1995 meeting, the protocol was not forwarded to the committee.

In a letter dated April 12, 1995, Drs. David T. Curiel and Ronald D. Alvarez of the University of Alabama, Birmingham, Alabama, submitted a revised protocol to the Recombinant DNA Advisory Committee for formal review and approval at its June 8-9, 1995, meeting.

II. Addition to Appendix D of the NIH Guidelines Regarding a Human Gene Transfer Protocol/Dr. Curiel

In a letter dated April 13, 1994, Dr. David Curiel of the University of Alabama, Birmingham, Alabama, submitted the human gene transfer protocol entitled: Phase I Trial of a Polynucleotide Vaccine to Human Carcinoembryonic Antigen in Patients with Metastatic Colorectal Cancer to the Recombinant DNA Advisory Committee for formal review and approval at its June 9-10, 1994, meeting. During the June 1994 meeting, the committee approved the protocol by a vote of 10 in favor, 4 opposed, and no abstentions. Approval was contingent on the review and approval by the primary reviewers of a revised Informed Consent document (as approved by the Institutional Review Board). On June 29, Dr. Curiel submitted an Institutional Review Board approved Informed Consent Document. The primary reviewers approved the revised

Informed Consent Document. On September 17, 1994, Dr. Nelson Wivel, Office of Recombinant DNA Activities, National Institutes of Health, informed Dr. Curiel that Dr. Harold Varmus, Director, National Institutes of Health, concluded that the protocol should be reviewed again by the committee when additional preclinical data are available.

In a letter dated April 12, 1995, Dr. David T. Curiel of the University of Alabama, Birmingham, Alabama, submitted a revised protocol to the Recombinant DNA Advisory Committee for formal review and approval at its June 8-9, 1995, meeting.

III. Addition to Appendix D of the NIH Guidelines Regarding a Human Gene Transfer Protocol/Drs. Paulson and Lyerly

In a letter dated March 31, 1995, Drs. David F. Paulson and H. Kim Lyerly of Duke University Medical Center, Durham, North Carolina, submitted a human gene transfer protocol entitled: A Phase I Study of Autologous Human Interleukin-2 Gene Modified Tumor Cells in Patients with Locally Advanced or Metastatic Prostate Cancer to the Recombinant DNA Advisory Committee for formal review and approval.

IV. Addition to Appendix D of the NIH Guidelines Regarding a Human Gene Transfer Protocol/Drs. Berchuck and Lyerly

In a letter dated April 10, 1995, Drs. Andres Berchuck and H. Kim Lyerly of Duke University Medical Center, Durham, North Carolina, submitted a human gene transfer protocol entitled: A Phase I Study of Autologous Human Interleukin 2 (IL-2) Gene Modified Tumor Cells in Patients with Refractory Metastatic Ovarian Cancer to the Recombinant DNA Advisory Committee for formal review and approval.

V. Addition to Appendix D of the NIH Guidelines Regarding a Human Gene Transfer Protocol/Drs. Steiner and Holt

On April 13, 1995, Drs. Mitchell S. Steiner and Jeffrey T. Holt of Vanderbilt University School of Medicine, Nashville, Tennessee, submitted a human gene transfer protocol entitled: Gene Therapy for the Treatment of Advanced Prostate Cancer by In Vivo Transduction with Prostate-Targeted Vectors Expressing Antisense c-myc RNA to the Recombinant DNA Advisory Committee for formal review and approval.

VI. Addition to Appendix D of the NIH Guidelines Regarding a Human Gene Transfer Protocol/Dr. McIvor

In a letter dated April 12, 1995, Dr. R. Scott McIvor of the Institute of Human Genetics, University of Minnesota, Minneapolis, Minnesota, submitted a human gene transfer protocol entitled: Gene Therapy for Purine Nucleoside Phosphorylase Deficiency to the Recombinant DNA Advisory Committee for formal review and approval.

VII. Addition to Appendix D of the NIH Guidelines Regarding a Human Gene Transfer Protocol/Drs. Scardino, Thompson, Woo

In a letter dated April 11, 1995, Drs. Peter T. Scardino, Timothy C. Thompson, and Savio L.C. Woo of Baylor College of Medicine, Houston, Texas, submitted a human gene transfer protocol entitled: Phase I Study of Adenoviral Vector Delivery of the HSV-tk Gene and the Intravenous Administration of Ganciclovir in Men with Local Recurrence of Prostate Cancer After Radiation Therapy to the Recombinant DNA Advisory Committee for formal review and approval.

VIII. Addition to Appendix D of the NIH Guidelines Regarding a Human Gene Transfer Protocol/Dr. Whitley

In a letter dated April 12, 1995, Dr. Chester B. Whitley of the Institute of Human Genetics, University of Minnesota, Minneapolis, Minnesota, submitted a human gene transfer protocol entitled: Gene Therapy for Scheie Keratopathy to the Recombinant DNA Advisory Committee for formal review and approval.

IX. Addition to Appendix D of the NIH Guidelines Regarding a Human Gene Transfer Protocol/Drs. Munshi and Barlogie

In a letter dated April 13, 1995, Drs. Nikhil C. Munshi and Bart Barlogie of the University of Arkansas, Little Rock, Arkansas, submitted a human gene transfer protocol entitled: Thymidine Kinase (TK) Transduced Donor Leukocyte Infusions as a Treatment for Patients with Relapsed or Persistent Multiple Myeloma after T-cell Depleted Allogeneic Bone Marrow Transplant to the Recombinant DNA Advisory Committee for formal review and approval.

X. Addition to Appendix D of the NIH Guidelines Regarding a Human Gene Transfer Protocol/Drs. Fox and Urba

In a letter dated April 12, 1995, Drs. Bernard A. Fox and Walter J. Urba of Chiles Research Institute, Providence Portland Medical Center, Portland,

Oregon, submitted a human gene transfer protocol entitled: Adoptive Cellular Therapy of Cancer Combining Direct HLA-B7/β2-Microglobulin Gene Transfer with Autologous Tumor Vaccination for the Generation of Vaccine-Primed Anti-CD3 Activated Lymphocytes to the Recombinant DNA Advisory Committee for formal review and approval.

XI. Addition to Appendix D of the NIH Guidelines Regarding a Human Gene Transfer Protocol/Dr. Hwu

In a letter dated April 12, 1995, Dr. Patrick Hwu of the National Institutes of Health, Bethesda, Maryland, submitted a human gene transfer protocol entitled: Treatment of Patients with Advanced Epithelial Ovarian Cancer using Anti-CD3 stimulated Peripheral Blood Lymphocytes Transduced with a Gene Encoding a Chimeric T-cell Receptor Reactive with Folate Binding Protein to the Recombinant DNA Advisory Committee for formal review and approval.

XII. Addition to Appendix D of the NIH Guidelines Regarding a Human Gene Transfer Protocol/Dr. Marasco

In a letter dated April 12, 1995, Dr. Wayne A. Marasco of the Dana-Farber Cancer Institute, Boston, Massachusetts, submitted a human gene transfer protocol entitled: Intracellular Antibodies Against HIV-1 Envelope Protein for AIDS Gene Therapy to the Recombinant DNA Advisory Committee for formal review and approval.

XIII. Addition to Appendix D of the NIH Guidelines Regarding a Human Gene Transfer Protocol/Dr. Verfaillie

In a letter dated April 12, 1995, Dr. Catherine Verfaillie of the University of Minnesota, Minneapolis, Minnesota, submitted a human gene transfer protocol entitled: Autologous Marrow Transplantation for Chronic Myelogenous Leukemia Using Stem Cells Obtained After In Vivo Chemotherapy Cytokine Priming to the Recombinant DNA Advisory Committee for formal review and approval.

XIV. Proposed Amendments to Appendix B of the NIH Guidelines Regarding Updating the Classification of Microorganisms/Fleming

In a letter dated June 24, 1993, Dr. Diane Fleming, President of the Mid-Atlantic Biological Safety Association requested updating Appendix B, Classification of Microorganisms on the Basis of Hazard. The Mid-Atlantic Biological Safety Association submitted an updated list of the classification of microorganisms for the Committee to

review which included the latest taxonomy and agent risk group classifications as defined by the Centers for Disease Control and Prevention. This request was published for public comment in the **Federal Register** (August 18, 1994, 58 FR 44098).

During the September 9–10, 1993, meeting, the Recombinant DNA Advisory Committee recommended by consensus that the current classification of etiologic agents described in the Biosafety in Microbiological and Biomedical Laboratories, 3rd edition, May 1993, U.S. Department of Health and Human Services, should be endorsed by the Committee. The Committee retains the option to adopt any modification to the CDC listing. The Committee recommended that the revised Appendix B, Classification of Microorganisms on the Basis of Hazard, submitted by Dr. Fleming should not be adopted until the Committee received letters of concurrence from both the Centers for Disease Control and Prevention and the NIH Division of Safety.

In a telephone call on October 20, 1994, Dr. Fleming stated that Appendix B, Classification of Microorganisms on the Basis of Hazard, would be reviewed by experts from the Centers for Disease Control and Prevention and the American Society for Microbiology. The revised Appendix B was submitted to the Recombinant DNA Advisory Committee December 1–2, 1994, meeting for review and discussion. During the December 1994 meeting, the Committee recommended publishing the revised Appendix B in the **Federal Register** for public comment, with further review of this proposal and possible approval during the March 6–7, 1995, meeting.

During the March 6–7, 1995 meeting, the Recombinant DNA Advisory Committee deferred approval of the proposed amendments to Appendix B pending additional revisions to the remaining appendices of the NIH Guidelines that are required to adequately accommodate the revised Appendix B. The motion for deferral included a recommendation that a subcommittee consisting of Dr. Straus, Office of Recombinant DNA Activities staff, and *ad hoc* experts would meet for one day to develop the required modifications. The motion passed by a vote of 17 in favor, 0 opposed, and no abstentions.

The Appendix B Subcommittee met on May 5, 1995. The proposed Appendix B reads as follows:

Appendix B. Points to Consider in the Assessment of Risk for Research and Production Involving Human Etiologic Agents and Oncogenic Viruses

Note: Appendix B includes only those biological agents known to infect humans. Information regarding restricted animal and plant pathogens is available from: U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services, Import-Export Products Staff, Room 756, Federal Building, 6505 Belcrest Road, Hyattsville, Maryland 20782; Phone: (301) 436-7830; Fax: (301) 436-8226.

Appendix B reflects the current state of knowledge and should be considered as guidance for establishing an initial, qualitative assessment regarding the safe handling of specific etiologic agents and oncogenic viruses and is not intended to replace a thorough assessment of the potential risk associated with such agents. Although Appendix B is considered to be comprehensive, this information should not be considered all-inclusive. A Task Force of the American Society of Microbiologists (ASM) will conduct an annual review of Appendix B and its recommendations will be presented to the Recombinant DNA Advisory Committee (RAC) as proposed amendments to the NIH Guidelines. The nomenclature reflects conformity with the most recent international agreements on taxonomy and nomenclature of agents at this time.

Appendix B-I. Qualitative Risk Assessment

Appendix B should be considered in conjunction with Appendices G and K in making an initial determination regarding the appropriate level of physical containment necessary to ensure the safe conduct of research or production. Appendix G specifies physical containment for standard laboratory experiments involving healthy adult individuals and defines Biosafety Level 1 (BL1) through Biosafety Level 4 (BL4). Appendix K supersedes Appendix G for large scale (over 10 liters) research or production involving healthy adult individuals and defines Good Large Scale Practice (GLSP) through Biosafety Level 3—Large Scale (BL3—LS).

Appendix B-II. Quantitative Risk Assessment

Appendix B-II-A. An initial qualitative risk assessment should be followed by a thorough quantitative risk assessment of the specific agent strain, immune status of the host relative to the agent in question, and potential agent-host-activity interactions, e.g., potential for aerosol production.

Appendix B-II-B. In the event that additional information is available regarding a specific strain listed in Appendix B, the Principal Investigator (PI) must make an initial qualitative risk assessment. The Institutional Biosafety Committee (IBC) must also make a quantitative risk assessment for experiments described in Section III-A, Experiments that Require IBC Approval, RAC Review, and NIH Approval, and Section III-C, Experiments that Require IBC Approval Before Initiation.

Appendix B-III. Risk Assessment Criteria

Factors to be considered in determining the level of containment include agent factors such as: virulence, pathogenicity, stability, route of spread, communicability, operations(s), quantity, and availability of vaccines or treatment. Changes to the agent which enhance or remove virulence factors should be considered by the PI and IBC which has the authority to raise or lower the containment level for that particular agent (see Sections III-C-2-a and V-B). For strains in which there is increased risk potential, the level of physical containment should be increased over the level that is recommended for the parent strain.

Appendix B-III-A. Agent-Specific Considerations. The following criteria should be considered when making a risk assessment determination for a specific strain:

Appendix B-III-A-1. Any strain isolated directly from a human or animal should be treated as a potentially pathogenic organism until proven otherwise.

Appendix B-III-A-2. Any strain that is known to be more hazardous than the parent (wild-type) strain, e.g., introduction of a drug-resistance trait to a strain that is not known to acquire that trait naturally, if such acquisition could compromise the use of the drug to control that agent, should be handled at a higher containment level (see Section III-A-1).

Appendix B-III-A-3. For any strain that has been genetically modified and is not specifically listed in Appendix B, the PI must make an initial determination regarding the potential risk of the genetically modified agent. The Institutional Biosafety Committee (IBC) must also make a quantitative risk assessment for experiments described in Section III-A, Experiments that Require IBC approval, RAC Review, and NIH Approval, and Section III-C, Experiments that Require IBC Approval Before Initiation.

Appendix B-III-A-4. For agents where more than one species is known

to be pathogenic for humans, Appendix B may include the genus name as well as individual species which are known to be pathogenic. When such a genus is listed in Appendix B, non-pathogenic species and strains are excluded. For parasites, non-infectious life cycle stages are excluded.

Appendix B-III-A-5. Certain attenuated strains or strains that have been demonstrated to have lost known virulence factors, e.g., genes, and that are to be used as: (1) a product, (2) part of a product, (3) or for prophylactic or therapeutic purposes, may qualify for a reduction in containment compared to the Risk Group (RG) assigned to the parent strain (see Sections III-C-2-a and V-B).

Appendix B-III-A-6. Careful consideration should be given to the application of some Risk Group 2 (RG2) agents. RG2 agents may be cultured at BL2 containment, e.g., dengue virus; however, when such agents are used for animal inoculation work or transmission studies, BL3 containment is recommended. Similarly, RG3 agents, e.g., monkey pox, Venezuelan equine encephalitis, and yellow fever viruses should be handled at BL4 containment for animal inoculation and transmission studies.

Appendix B-III-A-7. Individuals working with HIV, SIV, or other bloodborne pathogens should consult the Occupational Exposure to Bloodborne Pathogens, Final Rule (see Appendix B-VI-J). BL2 containment is recommended for activities involving all blood-contaminated clinical specimens, body fluids, and tissues from all humans or from HIV- or SIV- infected or inoculated laboratory animals. Activities such as producing research-laboratory scale quantities of HIV or SIV, manipulating concentrated virus preparations, and conducting

procedures that may produce droplets or aerosols, are performed in a BL2 facility, but using the additional practices and containment equipment recommended for BL3. Activities involving industrial-scale volumes or preparation of concentrated HIV or SIV are conducted in a BL3 facility, using BL3 practices and containment equipment (see Appendix B-VI-D).

Appendix B-III-A-8. Specific strains may fall into either a more hazardous Risk Group (RG) or a less hazardous risk group depending on genetic background and natural history. Appendix B is derived from information regarding the parent (wild-type) strain (see Appendices B-VI-B through B-VI-D).

Appendix B-III-B. Laboratory Personnel Considerations. Appendix B is based on the potential effect of a biological agent on healthy adult humans and does not account for instances in which an individual may have increased susceptibility to such agents, e.g., preexisting disease, medications, compromised immunity, pregnancy, or breast feeding.

Appendix B-IV. Classification of Etiologic Agents and Oncogenic Viruses by Risk Group (RG)

The World Health Organization recommends the use of the term Risk Group (RG) to indicate qualitative risk assessment based on agent characteristics (see Appendix B-VI-E). Appendix B is intended to serve as guidance in determining RG classification. The characteristics used for the qualitative risk assessment of biohazardous agents by RG are defined in Appendix B-IV-A. RG are categorized according to their potential risk, i.e., Risk Group 1 (RG1) corresponds to the lowest level of risk and Risk Group 4 (RG4) corresponds to the highest level of risk (see Appendix B-VI-E). Appendix B-IV-B summarizes

RG1 through RG4 and the relationship of these categories to Appendix G (see Appendix B-VI-E).

Certain strains specified in RG2, are known to represent minimal risk to humans; therefore, such organisms may be classified within RG1 and handled at BL1 (see Appendices III-C-2-a and V-B). Certain attenuated strains that are commonly used for live vaccines or that have an extensive history of safe laboratory use without harmful effect, may be placed in a lower RG than the parent strain (see Appendices B-VI-C and B-VI-D).

Risk assessment is ultimately a subjective process. Strains that are not listed in RG2 through RG4 are not implicitly classified in RG1; therefore, the PI must make an initial risk assessment determination. The Institutional Biosafety Committee (IBC) must also make a quantitative risk assessment for experiments described in Section III-A, Experiments that Require IBC approval, RAC Review, and NIH Approval, and Section III-C, Experiments that Require IBC Approval Before Initiation. Further guidance regarding the assessment of risk for agents not specifically listed in Appendix B is available from: Centers for Disease Control and Prevention, Biosafety Branch, Office of Health and Safety, Mail Stop F-05, 1600 Clifton Road, N.E., Atlanta, Georgia 30333; Phone: (404) 639-3883; Fax: (404) 639-2294. Biosafety in Microbiological and Biomedical Research Laboratories (see Appendix B-VI-D) and Control of Communicable Diseases in Man (see Appendix B-VI-B) provide additional guidance for determining appropriate containment conditions for specific etiologic agents and oncogenic viruses.

Appendix B-IV-A. Classification of Biohazardous Agents by Risk Group (RG) (see Appendix B-VI-E).

APPENDIX B-IV-A—CLASSIFICATION OF BIOHAZARDOUS AGENTS BY RISK GROUP (RG)

Risk Group 1 (RG1)	No/very low individual risk No/very low community risk.	An agent that is unlikely to cause human disease. Well characterized agents not known to cause disease in healthy adult humans and of minimal potential hazard to laboratory personnel and the environment.
Risk Group 2 (RG2)	Moderate individual risk Low community risk.	Agents which can cause human disease but are unlikely to be a serious hazard to workers, the community or the environment; percutaneous exposure, ingestion, or mucous membrane exposure may cause serious infection; however, effective treatment and preventive measures are available and the risk of spread of infection is limited.
Risk Group 3 (RG3)	High individual risk Low community risk.	Indigenous or exotic agents which usually cause serious human disease but do not ordinarily spread from one infected individual to another. Effective treatment or preventive measures are available.
Risk Group 4 (RG4)	High individual risk High community risk.	Dangerous/exotic agents which can cause serious human disease and can be readily transmitted directly or indirectly from one individual to another. Effective treatment and preventive measures are not usually available.

Appendix B-IV-B. Relationship Between Risk Group (RG) and Appendix G (see Appendix B-VI-E).

Note. Special consideration will be given to large-scale (greater than 10 liters of culture) and aerosol producing operations which may

pose additional significant risks and thus may require additional containment (see Appendix K).

APPENDIX B-IV-B—RELATIONSHIP BETWEEN RISK GROUP (RG) AND APPENDIX G (SEE APPENDIX B-VI-E)

Risk group (RG)	Biosafety level	Examples of laboratories	Laboratory practices	Safety equipment
Risk Group 1 (RG1).	Biosafety Level 1 (BL1) (Appendix G-II-A).	Basic teaching laboratories	Good microbiological practices (Appendix G-II-A-1).	Generally not required (Appendix G-II-A-4).
Risk Group 2 (RG2).	Biosafety Level 2 (BL2) (Appendix G-II-B).	(1) primary health services; (2) primary level hospitals; (3) diagnostic, teaching, and research laboratories.	Good microbiological practices, protective clothing, biosafety sign when special provisions required (Appendix G-II-B-2).	Open bench plus biosafety cabinet (Class I,II) for potential aerosols (Appendices G-II-B-3 and G-III-L).
Risk Group 3 (RG3).	Biosafety Level 3 (BL3) (Appendix G-II-C).	Special diagnostic laboratories	Good microbiological practices, protective clothing, biosafety sign, special clothing, controlled assess, directional air flow (Appendix G-II-C-2).	Biosafety cabinet (Class I,II,II) and/or other primary containment for all activities (Appendices G-II-C-3 and G-III-L).
Risk Group 4 (RG4).	Maximum Containment/Biosafety Level 4 (BL4) (Appendix G-II-D).	Dangerous pathogens units	Good microbiological practices, protective clothing, biosafety sign, special clothing, controlled assess, directional air flow, airlock entry, shower exit, special waste disposal (Appendix G-II-D-2).	Biosafety cabinet (Class III) or Class I or II in combination with positive pressure suits ventilated by life-support system, double-door autoclave (Appendices G-II-D-4 and G-II-L).

Appendix B-IV-C. Risk Group 1 (RG1) Agents

Note. It is not appropriate to assume that an unassessed agent belongs in RG1, e.g., vaccine strains which have undergone multiple *in vivo* passages are not considered to be avirulent based only on the fact that they are vaccine strains.

RG1 agents are usually not placed on a list but are assumed to include all bacterial, fungal, viral, rickettsial, chlamydial, and parasitic agents which have been assessed for hazard and that are not included in higher RG. RG1 agents can be used for undergraduate and secondary educational training and teaching laboratories and other facilities in which work is conducted with defined and characterized strains of viable microorganisms that are: (1) not known to cause disease in healthy adult humans, and (2) represent minimal potential hazard to laboratory personnel or the environment under standard conditions. RG1 agents can be handled safely in the laboratory without special apparatus or equipment using techniques generally acceptable for nonpathogenic materials. RG1 includes the following agents: asporogenic *Bacillus subtilis* or *Bacillus licheniformis* (see exceptions in Appendix C-IV-A); *Escherichia coli*-K12 (see exceptions in Appendix C-II-A); *Saccharomyces cerevisiae* and *Saccharomyces uvarum* (see exceptions in Appendix C-III-A); Baculovirus vectors (see exceptions in Appendix C-I-A); infectious canine hepatitis viruses;

and influenza reference strains A/PR/8/34 and A/WS/33.

Appendix B-IV-C-1. Risk Group 1 (RG1) Low-Risk Oncogenic Viruses (See Appendix B-VI-G)

- Adenovirus 7-Simian virus 40 (Ad7-SV40)
- Avian leukosis virus
- Bovine leukemia virus
- Bovine papilloma virus
- Chick-embryo-lethal orphan (CELO) virus or fowl adenovirus 1
- Dog sarcoma virus
- Guinea pig herpes virus
- Lucke (Frog) virus
- Hamster leukemia virus
- Marek's disease virus
- Mason-Pfizer monkey virus
- Mouse mammary tumor virus
- Murine leukemia virus
- Murine sarcoma virus
- Polyoma virus
- Rat leukemia virus
- Rous sarcoma virus
- Shope fibroma virus
- Shope papilloma virus
- Simian virus 40 (SV40)

Appendix B-IV-D. Risk Group 2 (RG2) Agents

RG2 includes agents that represent moderate risk to healthy human adults and the environment. RG2 agents may produce disease (varying degrees of severity) as a result of accidental inoculation, injection, or other means of cutaneous penetration. RG2 agents can generally be contained using standard laboratory practices. Some RG2 agents may cause disease as a result of direct

contact or respiratory transmission; however, such instances are self-limiting and do not result in serious illness, e.g. the common cold (rhinoviruses). RG2 agents are recommended for use only in facilities where laboratory personnel are trained in the safe handling of these agents (see Appendix G-II-B-2).

Appendix B-IV-D-1. Risk Group 2 (RG2)—Bacteria

Note. When "spp" follows the name of a genus, or "serotype" follows a species, only those species or serotypes known to be pathogenic to healthy human adults are included.

- Acinetobacter baumannii*
- Actinobacillus spp.*
- Actinomyces pyogenes*
- Aeromonas hydrophila*
- Amycolata autotrophica*
- Archanobacterium haemolyticum*
- Arizona hinshawii*—all serotypes
- Bacillus anthracis* (BL3 practices)
- Bartonella henselae*, *B. quintana*, *B. vinsonii*
- Bordetella spp.* including *B. pertussis* (BL3 practices)
- Borrelia recurrentis*, *B. burgdorferi*
- Burkholderia* (previously *Pasteurella spp.*) except those listed in Appendix B-IV-E-1 (RG3))
- Burkholderia pseudomallei* (BL3 practices)
- Campylobacter coli*, *C. fetus spp. fetus*, *C. jejuni*
- Chlamydia psittaci* (BL3 practices)
- Chlamydia trachomatis* (BL3 practices)
- Chlamydia pneumoniae* (BL3 practices)
- Clostridium botulinum* (BL3 practices), *Cl. chauvoei*, *Cl. haemolyticum*, *Cl.*

histolyticum, *Cl. novyi*, *Cl. septicum*, *Cl. tetani*
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
Haemophilus ducreyi, *H. influenzae*
Helicobacter pylori
Klebsiella spp.
Legionella spp. including *L. pneumophila* (BL3 practices)
 Legionella-like organisms
Leptospira interrogans—all serotypes
Listeria spp.
Moraxella spp.
Mycobacterium spp. (except those listed in Appendix B-IV-E-1 (RG3)) including *M. avium* complex, *M. asiaticum*, *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 spp., except *M. mycoides* and *M. agalactiae* which are restricted animal pathogens (see Appendix B-V-B)
Neisseria gonorrhoea (BL3 practices), *N. meningitidis* (BL3 practices)
Nocardia asteroides, *N. brasiliensis*, *N. otitidiscaviarum*, *N. transvalensis*
Rhodococcus equi
Salmonella spp. and serotypes including *S. arizonae*, *S. choleraesuis*, *S. enteritidis*, *S. gallinarum-pullorum*, *S. meleagridis*, *S. paratyphi*, A, B, C, *S. typhi* (BL3 practices), *S. typhimurium*
Shigella spp. (BL3 practices) and serotypes including *S. boydii*, *S. dysenteriae*, Type 1, *S. flexneri*, *S. sonnei*
Sphaerophorus necrophorus
Staphylococcus aureus
Streptobacillus moniliformis
Streptococcus spp. including *Streptococcus pneumoniae*, *S. pyogenes*
Treponema pallidum, *T. carateum*
Vibrio cholerae, *V. parahemolyticus*, *V. vulnificus*
Yersinia enterocolitica, *Y. pestis* (BL3 practices)

Appendix B-IV-D-2. Risk Group 2 (RG2)—Fungal Agents

Note. When “spp” follows the name of a genus, or “serotype” follows a species, only those species or serotypes known to be pathogenic to healthy human adults are included.

Blastomyces dermatitidis
Cladosporium bantianum, *C. (Xylohypha) trichoides*

Cryptococcus neoformans (Droplets/aerosols require biosafety cabinet)
Dactylaria galopava (*Ochroconis gallopavum*)
Epidermophyton spp.
Exophiala (*Wangiella*) *dermatitidis*
Fonsecaea pedrosoi
Microsporium spp.
Paracoccidioides brasiliensis
Penicillium marneffeii
Sporothrix schenckii
Trichophyton spp.

Appendix B-IV-D-3. Risk Group 2 (RG2)—Parasitic Agents

Note. When “spp” follows the name of a genus, or “serotype” follows a species, only those species or serotypes known to be pathogenic to healthy human adults are included.

Ancylostoma spp. human hookworms including *A. duodenale*, *A. ceylanicum*
Ascaris spp. including *Ascaris lumbricoides suum*
Babesia spp. including *B. divergens*, *B. microti*
Brugia spp. filaria worms including *B. malayi*, *B. timori*
Coccidia spp.
Cryptosporidium spp. including *C. parvum*
Cysticercus cellulosae (hydatid cyst, larva of *T. solium*)
Echinococcus spp. including *E. granulosus*, *E. multilocularis*, *E. vogeli*
Entamoeba histolytica
Enterobius spp.
Fasciola spp. including *F. gigantica*, *F. hepatica*
Giardia spp. including *G. lamblia*
Heterophyes spp.
Hymenolepis spp. including *H. diminuta*, *H. nana*
Isospora spp.
Leishmania spp. including *L. braziliensis*, *L. donovani*, *L. ethiopia*, *L. major*, *L. mexicana*, *L. peruviana*, *L. tropica*
Loa loa filaria
Microsporidium spp.
Naegleria fowleri
Necator spp. human hookworms, including *N. americanus*
Onchoerca spp. filaria including, *O. volvulus*
Plasmodium spp. including simian species, *P. cynomologi*, *P. falciparum*, *P. malariae*, *P. ovale*, *P. vivax*
Sarcocystis spp. including *S. sui hominis*
Schistosoma spp. including *S. haematobium*, *S. intercalatum*, *S. japonicum*, *S. mansoni*, *S. mekongi*
Strongyloides spp. including *S. stercoralis*
Taenia solium
Toxocara spp. including *T. canis*
Toxoplasma spp. including *T. gondii*

Trichinella spiralis
Trypanosoma spp. including *T. brucei brucei*, *T. brucei gambiense*, *T. brucei rhodesiense*, *T. cruzi*
Wuchereria bancrofti (filaria)

Appendix B-IV-D-4-a. Risk Group 2 (RG2)—Viruses and Prions (See Appendices B-IV-D-4-b and B-IV-D-4-c)

Note. When “spp” follows the name of a genus, or “serotype” follows a species, only those species or serotypes known to be pathogenic to healthy human adults are included.

Adenoviruses, human—all types
 Arboviruses (see Appendix B-IV-D-4-b)
 Arenaviruses (see Appendix B-IV-D-4-b)
 Bunyamwera virus
 Coronaviruses
 Coxsackie A and B viruses
 Creutzfeldt-Jacob disease agent (prion)
 Echoviruses—all types
 Encephalomyocarditis virus (EMC)
 Encephalomyelitis viruses (droplets/aerosols require BL3 practices) (see Appendix B-IV-D-4-b)
 Hepatitis A, B (BL3 practices), C (BL3 practices), D, E viruses
 Herpesviruses (BL3 practices) including Cytomegalovirus, Epstein Barr, *Herpes simplex* types 1 and 2, and *Herpes zoster*, except Herpesvirus simiae (Monkey B virus) (see Appendix B-IV-F-4 (RG4))
 Human Immunodeficiency Virus (HIV) all serotypes (see Appendices B-VI-A-7 and B-IV-J for special requirements)
 Human T cell lymphotropic viruses (HTLV) types 1 and 2 (BL3 practices)
 Influenza viruses
 Kuru (prion)
 Lymphocytic choriomeningitis virus (BL3 practices—except neurotropic strains)
 Lymphogranuloma venereum agent
 Measles virus
 Molluscum contagiosum virus
 Mumps virus
 Orf virus
 Papovaviridae including human papilloma viruses
 Parainfluenza virus
 Paravaccinia virus
 Polioviruses—all types, wild and attenuated
 Poxviruses—all types such as Cowpox (biosafety cabinet and immunization required), Monkeypox (biosafety cabinet and immunization required) or Vaccinia (biosafety cabinet and immunization required), Camelpox, Milker—s node virus, Molluscum contagiosum virus, Orf, Rabbitpox, Tanapox, and Yabapox except Alastrim, Smallpox, and Whitepox (see Appendices B-V-B and B-VI-H)

Rabies virus (biosafety cabinet and immunization required)—all strains including fixed/attenuated virus except Rabies street virus

Reoviruses—all types

Respiratory syncytial virus

Rhinoviruses—all types

Rubella virus

Simian viruses—all types including simian immunodeficiency virus (BL3 practices), except Herpesvirus simiae (Monkey B virus) and Marburg virus (see Appendix B-IV-F-4 (RG4))

Transmissible Spongiform

Encephalopathies (TME)—prions (Creutzfeldt-Jacob; Kuru)

Vesicular Stomatitis Virus, lab adapted strains: VSV-Indiana, San Juan, and Glasgow

Appendix B-IV-D-4-b. Arboviruses and Arenaviruses Assigned to Biosafety Level 2

Note. When laboratory work is conducted with biological agents for which epidemiology and etiology are unknown or incompletely understood, it is presumed that the work presents a biohazard similar to related agents until further information can be provided. This method of risk assessment was used by the American Committee on Arthropod-Borne Viruses (ACAV) Subcommittee on Arbovirus Laboratory Safety for work with arboviruses for which risk information is inadequate or unavailable (see Appendix B-VI-D).

Acado

Acara

Aguacate

Alfuy

Almpiwar

Amapari

Ananindeua

Anhanga

Anhemi

Anopheles A

Anopheles B

Apeu

Apoi

Aride

Arkonam

Aroa

Aruac

Arumowot

Aura

Avalon

Abras

Abu Hammad

Aabahoyo

Bagaza

Bahig

Bakau

Baku

Bandia

Bangoran

Bangui

Banzi

Barmah Forest

Barur

Batai

Batama

Bauline

Bebaru

Belmont

Benevides

Benfica

Bertioga

Bimiti

Birao

Bluetongue

Boraceia

Botambi

Boteke

Bouboui

Bujaru

Bunyamwera

Bunyip

Burg E Arab

Bushbush

Bussuquara

Buttonwillow

Bwamba

Cacao

Cache Valley

Caimito

California enc.

Calovo

Candiru

Cape Wrath

Capim

Caraparu

Carey Island

Catu

Chaco

Chagres

Chandipura

Changuinola

Charleville

Chenuda

Chilibre

Chobar gorge

Clo Mor

Colorado tick fever

Corriparta

Cotia

Cowbone Ridge

Csiro Village

Cuiaba-D'aguilar

Dakar Bat

Dengue-1

Dengue-2

Dengue-3

Dengue-4

Dera Ghazi Khan

East. equine enc. (vaccine recommended)

Edge Hill

Entebbe Bat

Ep. Hem. Disease

Erve

Eubenangee

Eyach

Flanders

Fort Morgan

Frijoles

Gamboa

Gan Gan

Gomoka

Gossas

Grand Arbaud

Great Island

Guajara

Guama

Guaratuba

Guaroa

Gumbo Limbo

Hart Park

Hazara

Highlands J

Huacho

Hughes

Icoaraci

Ieri

Ilesha

Ilheus

Ingwavuma

Inkoo

Ippy

Irituia

Isfahan

Itaporanga

Itaqui

Jamestown Canyon

Japanaut

Jerry Slough

Johnston Atoll

Joinjakaka

Juan Diaz

Jugra

Jurona

Jutiapa

Kadam

Kaeng Khoi

Kaikalur

Kaisodi

Kamese

Kammavan pettai

Kannaman gamam

Kao Shuan

Karimabad

Karshi

Kasba

Kemerovo

Kern Canyon

Ketapang

Keterah

Keuraliba

Keystone

Kismayo

Klamath

Kokobera

Kolongo

Koongol

Kotonkan

Kowanyama

Kunjin

Kununurra

Kwatta

La Crosse

La Joya

Lagos Bat

Landjia

Langat

Lanjan

Las Maloyas

Latino

Le Dantec

Lebombo	Prospect Hill	Tyuleniy
Lednice	Puchong	Uganda S
Lipovnik	Punta Salinas	Umatilla
Lokern	Punta Toro	Umbre
Lone Star	Qalyub	Una
Lukuni	Quaranfil	Upolu
M'poko	Restan	Urucuri
Madrid	Rio Bravo	Usutu
Maguari	Rio Grande	Uukuniemi
Mahogany Hammock	Ross River	Vellore
Main Drain	Royal Farm	Venkatapuram
Malakal	Sabo	Vinces
Manawa	Saboya	Virgin River
Manzanilla	Saint Floris	VS-Indiana
Mapputta	Sakhalin	VS-New Jersey
Maprik	Salehabad	Wad Medani
Marco	San angelo	Wallal
Marituba	Sandfly f. (Naples)	Wanowrie
Marrakai	Sandfly f. (Sicilian)	Warrego
Matariya	Sandjimba	West. equine enc. (vaccine recommended)
Matruh	Sango	Whataroa
Matucare	Sathuperi	Witwatersrand
Melao	Sawgrass	Wonga
Mermet	Sebokele	Wongorr
Minatitlan	Seletar	Wyeomyia
Minnal	Sembalam	Yaquina Head
Mirim	Serra do Navio	Yata
Mitchell River	Shamonda	Yogue
Modoc	Shark River	Zaliv Terpeniya
Moju	Shuni	Zegla
Mono Lake	Silverwater	Zika
Mont. myotis leuk.	Simbu	Zingilamo
Moriche	Simian hem. fever	Zirqa
Mosqueiro	Sindbis	Appendix B-IV-D-4-c. Vaccine Strains of Risk Group 3 (RG3) and Risk Group 4 (RG4) Viruses Which May Be Handled at Biosafety Level 2
Mossuril	Sixgun City	Chikungunya, strain 131/25
Mount Elgon Bat	Snowshoe Hare	Junin, strain Candid #1
Murutucu	Sokuluk	Rift Valley fever, strain MP-12
Mykines	Soldado	Venezuelan equine encephalomyelitis, strain TC-83
Navarro	Sororoca	Yellow fever, strain 17-D
Nepuyo	Stratford	Appendix B-IV-D-4-d. Risk Group 2 (RG2)—Moderate Risk Oncogenic Viruses (see Appendix B-VI-G)
Ngainingan	Sunday Canyon	Adenovirus
Nique	Tacaiuma	Adenovirus 2—simian virus 40 (Ad2- SV40)
Nkolbisson	Tacaribe	Epstein Barr virus (EBV)
Nola	Taggert	Feline leukemia virus (FeLV)
Ntaya	Tahyna	Feline sarcoma virus (FeSV)
Nugget	Tamiami	Gibbon leukemia virus (GaLV)
Nyamanini	Tanga	Herpesvirus (HV) ateles
Nyando	Tanjong Rabok	Herpesvirus (HV) saimiri
O'nyong-nyong	Tataguine	Papovaviridae including human papilloma viruses
Okhotskiy	Tehran	Simian sarcoma virus (SSV)-1
Okola	Tembe	Yabapox virus
Olifantsvlei	Tembusu	Appendix B-IV-E. Risk Group 3 (RG3) Agents
Oriboca	Tensaw	Note. When "spp" follows the name of a genus, or "serotype" follows a species, only those species or serotypes known to be pathogenic to healthy human adults are included.
Ossa	Tete	
Pacora	Tettngang	
Pacui	Thimiri	
Pahayokee	Thottapalayam	
Palyam	Tibrogargan	
Parana	Timbo	
Pata	Timboteua	
Pathum Thani	Tindholumur	
Patois	Toscana	
Phnom-Penh Bat	Toure	
Pichinde	Tribec	
Pixuna	Triniti	
Pongola	Trivittatus	
Ponteves	Trubanaman	
Precarious Point	Tsuruse	
Pretoria	Turlock	

RG3 includes indigenous or exotic agents which may potentially cause serious or lethal disease as a result of inhalation exposure. RG3 includes agents involving special hazards to laboratory personnel or agents derived from outside the United States and require a permit for importation, unless they are specified for higher classification. RG3 includes pathogens which require special containment conditions for facilities in which laboratory personnel have received specialized training in: (1) the safe handling of hazardous agents, i.e., equal to or greater than college level microbiology laboratory training, and (2) handling the specific RG3 agent or similar pathogens that may potentially cause serious or lethal disease. Laboratory personnel shall be supervised by trained scientists who possess significant experience in the safe handling of biohazardous agents and materials.

Appendix B-IV-E-1. Risk Group 3 (RG3)—Bacterial Agents including Chlamydia and Rickettsia

Bartonella spp.

Brucella spp. including *B. abortus*, *B. canis*, *B. melitensis* (USDA restricted), *B. suis*

Burkholderia (Pseudomonas) mallei, *B. pseudomallei* (see Appendix B-VI-F)

Coxiella burnetii

Francisella tularensis

Mycobacterium bovis, *M. tuberculosis*, *Pasteurella multocida* type B—"buffalo" and others (see Appendix B-VI-F)

Rickettsia akari, *R. australis*, *R. canada*, *R. conorii*, *R. prowazekii*

R. rickettsii, *R. siberica*, *R.*

tsutsugamushi, *R. typhi* (*R. mooseri*)

Yersinia pestis (antibiotic resistant strains)

Appendix B-IV-E-2. Risk Group 3 (RG3)—Fungal Agents

Coccidioides immitis (sporulating cultures; contaminated soil)

Histoplasma capsulatum, *H. capsulatum* var. *duboisii*

Appendix B-IV-E-3. Risk Group 3 (RG3)—Parasitic Agents

None

Appendix B-IV-E-4. Risk Group 3 (RG3)—Viral Agents

Arboviruses and certain other viruses assigned to Risk Group 3 (West Nile and Semliki Forest viruses may be classified up or down depending on the conditions of use and geographical location of the laboratory (see Appendices B-IV-E-5, B-IV-E-6 and B-VI-I).

Lymphocytic choriomeningitis virus (LCM) (neurotrophic strains)

Monkey pox virus—when used *in vitro* (see Appendix B-VI-H)

Rabies Street virus

Appendix B-4-E-5. Arboviruses and Certain Other Viruses Assigned to Biosafety Level 3 (on the Basis of Insufficient Experience)

Adelaide River

Agua Preta

Alenquer

Almeirim

Altamira

Andasibe

Antequera

Araguari

Aransas Bay

Arbia

Arboledas

Babanki

Batken

Belem

Berrimah

Bimbo

Bobaya

Bobia

Bozo

Buenaventura

Cabassue (BL3 facilities/HEPA filtration of exhaust air prior to discharge, vaccine recommended)

Cacipacore

Calchaqui

Cananea

Caninde

Chim

Coastal Plains

Connecticut

Corfou

Dabakala

Douglas

Enseada

Estero Real

Fomede

Forecariah

Fort Sherman

Gabek Forest

Gadgets Gully

Garba

Gordil

Gray Lodge

Gurupi

Iaco

Ibaraki

Ife

Ingangapi

Inini

Issyk-Kul

Itaituba

Itimirim

Itupiranga

Jacareacanga

Jamanxi

Jari

Kedougou

Khasan

Kindia

Kyzylgach

Lake Clarendon

Llano Seco

Macaua

Mapuera

Mboke

Meaban

Mojui Dos Compos

Monte Dourado

Munguba

Naranjal

Nariva

Nasoule

Ndelle

New Minto

Ngari

Ngoupe

Nodamura

Northway

Odrenisrou

Omo

Oriximina

Ouango

Oubangui

Oubi

Ourem

Palestina

Para

Paramushir

Paroo River

Perinet

Petevo

Picola

Playas

Pueblo Viejo

Purus

Radi

Razdan

Resistencia

Rochambeau

Salanga

San Juan

Santa Rosa

Santarem

Saraca

Saumarez Reef

Sedlec

Sena Madureira

Sepik

Shokwe

Slovakia

Somone

Spipur

Tai

Tamdy

Telok Forest

Termeil

Thiafora

Tilligerry

Tinaroo

Tlacotalpan

Tonate (BL3 facilities/HEPA filtration of exhaust air prior to discharge, vaccine recommended)

Ttinga

Xiburema

Yacaaba

Yaounde

Yoka

Yug Bogkanova

Appendix B-IV-E-6. Arboviruses and Certain Other Viruses Assigned to Biosafety Level 3

Aino

- Akabane
 Bhanja
 Chikungunya (BL3 facilities/HEPA filtration of exhaust air prior to discharge, vaccine recommended)
 Cocal
 Dhori
 Dugbe
 Everglades (BL3 facilities/HEPA filtration of exhaust air prior to discharge, vaccine recommended)
 Flexal
 Germiston (BL3 facilities/HEPA filtration of exhaust air prior to discharge)
 Getah
 Hantaan
 Israel Turkey mening.
 Japanese enc.
 Junin (BL3 facilities/HEPA filtration of exhaust air prior to discharge, vaccine recommended)
 Kairi
 Kimberley
 Koutango
 Louping Ill (BL3 facilities/HEPA filtration of exhaust air prior to discharge) (The importation, possession, or use of this agent is restricted by USDA regulation or administrative policy) (see Appendices B-VI-D and B-VI-F)
 Mayaro
 Middelburg
 Mobala
 Mopeia (This virus is presently being registered in the Catalogue of Arboviruses)
 Mucambo (BL3 facilities/HEPA filtration of exhaust air prior to discharge, vaccine recommended)
 Murray Valley enc.
 Nairobi sheep disease (The importation, possession, or use of this agent is restricted by USDA regulation or administrative policy) (see Appendices B-VI-D and B-VI-F).
 Ndumu
 Negishi
 Oropouche (BL3 facilities/HEPA filtration of exhaust air prior to discharge)
 Orungo
 Peaton
 Piry
 Powassan
 Puumala
 Rift Valley fever (Zinga virus) (BL3 facilities/HEPA filtration of exhaust air prior to discharge, vaccine recommended) The importation, possession, or use of this agent is restricted by USDA regulation or administrative policy (see Appendices B-VI-D and B-VI-F).
 Sagiyama
 Sal Vieja
 San Perlita
 Semliki Forest
- Seoul
 Spondweni
 St. Louis enc.
 Thogoto
 Tocio (BL3 facilities/HEPA filtration of exhaust air prior to discharge)
 Turuna
 Venezuelan equine encephalitis (BL3 facilities/HEPA filtration of exhaust air prior to discharge, vaccine recommended)
 Vesicular Stomatitis (alagoas)
 Wesselsbron (BL3 facilities/HEPA filtration of exhaust air prior to discharge) (The importation, possession, or use of this agent is restricted by USDA regulation or administrative policy) (see Appendices B-VI-D and B-VI-F).
 West Nile
 Yellow fever (BL3 facilities/HEPA filtration of exhaust air prior to discharge, vaccine recommended)
 Zinga (Rift Valley Fever virus) (BL3 facilities/HEPA filtration of exhaust air prior to discharge, vaccine recommended) The importation, possession, or use of this agent is restricted by USDA regulation or administrative policy (see Appendices B-VI-D and B-VI-F).
- Appendix B-IV-F. Risk Group 4 (RG4) Agents
 RG4 includes dangerous and exotic agents that pose a high individual risk of aerosol-transmitted laboratory infections (or related agents with unknown means of transmission) which can result in life-threatening disease. RG4 agents require the most stringent containment conditions because they are extremely hazardous to laboratory personnel and may cause serious epidemic disease. RG4 agents can only be used in special facilities in which laboratory personnel have received specialized training in: (1) the safe handling of hazardous agents, i.e., equal to or greater than college level microbiology laboratory training, and (2) handling the specific RG3 agent or similar pathogens that may potentially cause serious or lethal disease. Laboratory personnel shall be supervised by trained scientists who possess significant experience in the safe handling of biohazardous agents and materials.
- Appendix B-IV-F-1. Risk Group 4 (RG4)—Bacterial Agents
 None
- Appendix B-IV-F-2. Risk Group 4 (RG4)—Fungal Agents
 None
- Appendix B-IV-F-3. Risk Group 4 (RG4)—Parasitic Agents
 None
- Appendix B-IV-F-4. Risk Group 4 (RG4)—Viral Agents
 Absettarov
 Central European encephalitis viruses
 Crimean hemorrhagic fever (Congo)
 Ebola fever virus
 Guanarito
 Hanzalova
 Hemorrhagic fever agents and viruses as yet undefined
Herpesvirus simiae (Monkey B virus)
 Hypr
 Junin (BL3 containment and practices if vaccinated)
 Kumlinge
 Kyasanur forest disease
 Lassa
 Machupo
 Marburg
 Omsk hemorrhagic fever
 Russian spring—summer encephalitis
 Tick-borne orthomyxoviridae, Dhori & Thogoto
- Appendix B-V. Restricted Pathogens
 Appendix B-V-A. Restricted Plant Pathogens
Note. See Appendix P, *Physical and Biological Containment for Recombinant DNA Research Involving Plants*.
 Non-indigenous plant pathogens may require special laboratory design, operation, and containment features not generally addressed in Biosafety in the Microbiological and Biomedical Research Laboratories (see Appendix B-VI-D). Information on the importation, possession, or use of these agents is available from: U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services, Import-Export Products Staff, Room 756, Federal Building, 6505 Belcrest Road, Hyattsville, Maryland 20782; Phone: (301) 436-7830; Fax: (301) 436-8226.
- Appendix B-V-B. Restricted Animal Pathogens
Note. See Appendix Q, *Physical and Biological Containment for Recombinant DNA Research Involving Animals*.
 Non-indigenous domestic livestock and poultry pathogens may require special laboratory design, operation, and containment features not generally addressed in Biosafety in the Microbiological and Biomedical Research Laboratories (see Appendix B-VI-D). The importation, possession, or use of these agents is prohibited or restricted by law or by the U.S. Department of Agriculture regulations and administrative policies. Animal pathogens other than those zoonotic

agents listed in Appendix B may be subject to USDA regulations. Information on the importation, possession, or use of these agents is available from: U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services, Import-Export Products Staff, Room 756, Federal Building, 6505 Belcrest Road, Hyattsville, Maryland 20782; Phone: (301) 436-7830; Fax: (301) 436-8226.

Appendix B-V-C. Organisms Which May Not Be Studied in the United States Except at Specified Facilities

Alastrim (see Appendix B-VI-H)
Small pox (see Appendix B-VI-H)
White pox (see Appendix B-VI-H)

Appendix B-VI. Footnotes and References to Appendix B

Appendix B-VI-A. Appendix B has been adapted from the RG classification recommended by the World Health Organization (see Appendix B-VI-E), the Agent Summary Statements described in Biosafety in Microbiological and Biomedical Laboratories (see Appendix B-VI-D), Control of Communicable Diseases of Man (see Appendix B-VI-B), recommendations of the Task Force of the American Society for Microbiology, and a 1982 draft document of the Centers for Disease Control and Prevention, which includes a more complete risk assessment of human pathogens (Dr. R. Knudsen—personal communication). Appendices B-IV-A and B-IV-B are derived from the World Health Organization Laboratory Biosafety Manual (see Appendix B-VI-E). Appendices B-IV-D-4-b, B-IV-D-4-c, B-IV-E-5 and B-IV-E-6 were obtained directly (electronic transmission) from the Centers for Disease Control and Prevention. The original reference for this classification was Classification of Etiologic Agents on the Basis of Hazard, 4th edition, July 1974 (see Appendix B-VI-C).

Appendix B-VI-B. Benenson, Abram S. ed., Control of Communicable Diseases in Man, 15th edition. 1990. American Public Health Association, Washington, D.C.

Appendix B-VI-C. Center for Disease Control, Office of Biosafety, Classification of Etiologic Agents on the Basis of Hazard, 4th Edition. 1974. U.S. Department of Health, Education and Welfare, Public Health Service.

Appendix B-VI-D. U.S. Department of Health and Human Services, Public

Health Service, Centers for Disease Control and Prevention and the National Institutes of Health. Biosafety in Microbiological and Biomedical Research Laboratories, 3rd edition. 1993. Copies available from: Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402 (stock # 017-040-00523-7), Phone: (202) 512-2356.

Appendix B-VI-E. World Health Organization Laboratory Biosafety Manual, 2nd edition. WHO Albany, NY ORDER FROM: WHO Publication Centre, USA, (Q Corp) 49 Sheridan Avenue, Albany, New York 12210; Phone: (518) 436-9686 (Order # 1152213) (cost \$23.40 plus \$3.00 handling).

Appendix B-VI-F. A U.S. Department of Agriculture permit, required for import and interstate transport of pathogens, may be obtained from the U.S. Department of Agriculture, ATTN: Animal and Plant Health Inspection Service, Import-Export Products Office, Room 756, Federal Building, 6505 Belcrest Road, Hyattsville, Maryland 20782. Telephone; 301-436-7830 or 8499; FAX 301-436-8226

Appendix B-VI-G. National Cancer Institute Safety Standards for Research Involving Oncogenic Viruses, October 1974. U.S. Department of Health, Education, and Welfare (Publication # (NIH) 75-790).

Appendix B-VI-H. All activities, including storage of variola and whitepox, are restricted to the single national facility (World Health Organization Collaborating Center for Smallpox Research, Centers for Disease Control and Prevention, Atlanta, Georgia).

Appendix B-VI-I. Published regulations or guidelines from Federal, State, or local governments must also be taken into account.

Appendix B-VI-J. U.S. Department of Labor, Occupational Safety and Health Administration. 1991. Occupational Exposure to Bloodborne Pathogens, Final Rule (56 FR 64175-64182).

The rest of the NIH Guidelines will have terminology changes (i.e., Class 1, 2, 3, 4 will be changed to Risk Group 1, 2, 3, 4, respectively. Class 5 will become restrictive pathogens.) Cross references will be changed accordingly to revision in Appendix B.

XV. Report From Ad Hoc Review Committee

On March 8 and May 1, 1995, the *Ad hoc* Review Committee met to discuss

three major topics for review: (1) domain and mandate of the Recombinant DNA Advisory Committee; (2) composition of the Recombinant DNA Advisory Committee; and (3) Recombinant DNA Advisory Committee's review of human gene transfer protocols. Dr. Nelson Wivel will give a status report on the *Ad hoc* Review Committee.

XVI. Presentation on Fetal Sheep Studies/Zanjani

Dr. Esmail Zanjani of the Veterans Administration Hospital Medical Center, Reno, Nevada, will be giving a presentation on Fetal Sheep Studies. Dr. Zanjani will present results of his experimental work on in utero cell transfer.

OMB's "Mandatory Information Requirements for Federal Assistance Program Announcements" (45 FR 39592, June 11, 1980) requires a statement concerning the official government programs contained in the Catalog of Federal Domestic Assistance. Normally, NIH lists in its announcements the number and title of affected individual programs for the guidance of the public. Because the guidance in this notice covers not only virtually every NIH program but also essentially every Federal research program in which DNA recombinant molecule techniques could be used, it has been determined not to be cost effective or in the public interest to attempt to list these programs. Such a list would likely require several additional pages. In addition, NIH could not be certain that every Federal program would be included as many Federal agencies, as well as private organizations, both national and international, have elected to follow the NIH Guidelines. In lieu of the individual program listing, NIH invites readers to direct questions to the information address above about whether individual programs listed in the Catalog of Federal Domestic Assistance are affected.

Effective Date: May 9, 1995.

Daryl A. Chamblee,

Acting Deputy Director for Science Policy and Technology Transfer.

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