Proposed Changes to Appendix B of the *NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)*

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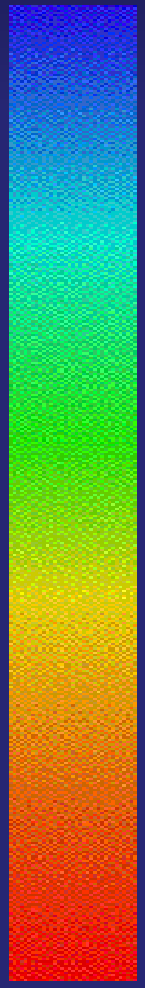
Outline

- What are Appendix B and Risk Groups
- What is the Role of Appendix B in the Risk Assessment
- Impetus for Updating Appendix B
- Proposed Changes
- Comments Received
- Next Steps

Appendix B of the *NIH Guidelines*

Appendix B specifies the risk group (RG) classification of an agent based upon its ability to cause disease in healthy adults and the availability of treatment for that disease

Risk Groups - *NIH Guidelines*



- **Risk Group (RG)1 - Agents that are not associated with disease in healthy adult humans**
- **RG2 - Agents that *are associated with human disease* which is rarely serious and for which preventive or therapeutic interventions are *often* available**
- **RG3 - Agents that are associated with *serious or lethal human disease* for which preventive or therapeutic interventions *may be* available (high individual risk but low community risk)**
- **RG4 - Agents that are associated with *serious or lethal human disease* for which preventive or therapeutic interventions *are not usually* available (high individual risk and high community risk)**

Role of Appendix B in the Risk Assessment

- **The risk group of an organism is a key component of the risk assessment to determine containment under the *NIH Guidelines*; therefore, it is important to list an organism in its appropriate risk group**
  - **IBCs can always increase containment for experiments under the *NIH Guidelines***
  - **In general, IBCs must consult with OBA to lower containment**

Impetus for updating Appendix B: Risk Groups

- *NIH Guidelines* current classification of organisms into risk groups does not include many attenuated strains used in recombinant research
  - A risk assessment to determine the appropriate containment for many of these attenuated strains has been conducted by NIH and the Centers for Disease Control and Prevention (CDC) during the periodic revisions of the CDC/NIH BMBL
- In addition, some circulating viruses are not specifically listed: e.g. West Nile Virus, a RG3 Flavivirus

Proposed Updates to Risk Groups

The following are proposed to be added to the list of RG2 Bacteria:

- ***Coxiella burnetii*** **Nine Mile strain, plaque purified clone 4**
- ***Francisella tularensis*** **subspecies***
  - ***novicida*****, Utah 112**
  - ***holartica*** **LVS**
  - **biovar tularensis strain ATCC 6223 (also known as strain B38)**

***For research involving high concentrations of these attenuated *F. tularensis* strains, biosafety level 3 practices should be considered**

Proposed Updates to Risk Groups

The following are proposed to be added to the list of RG2 Bacteria (cont'd):

- ***Yersinia Pestis, pgm*$^{(-)}$ (lacking the 102 kb pigmentation locus) and *lcr*$^{(-)}$ (lacking the LCR plasmid)**

Proposed Updates to Risk Groups (cont'd)

The following are proposed to be added to the list of RG2 Viruses:

- **Chikungunya vaccine strain 181/25**
- **Junin virus candid #1 vaccine strain**
- **Venezeula equine encephalitis vaccine strain V3526**
- **Japanese encephalitis virus strain SA 14-14-2**

Proposed Updates to Risk Groups (cont'd)

Clarification of the description of vesicular stomatitis virus strains that are RG2 organisms:

- **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)**

Proposed Updates to Risk Groups (cont'd)

The following are proposed to be added to the list of RG3 viruses:

- **SARS-associated Coronavirus (SARS-CoV)**
- **Chikungunya virus**
- **West Nile Virus**

Process to Date

- FR notice published on July 25, 2011 (76 FR 44340) and Public Comment ended September 9, 2011.
- One comment received from the American Biological Safety Association (ABSA)

Response to Public Comments

ABSA's comments:

- **"OBA should consider adding additional information to Section II-A-3 covering the assignment of Risk Group to commonly used attenuated strains."**
  - **Section II-A-3 of the *NIH Guidelines* provides a framework for conducting a comprehensive risk assessment**

Response to Public Comments (cont'd)

OBA appreciates ABSA's comments and will add a reference to Appendix B to the last sentence of the first paragraph of Section II-A-3:

> **"Certain attenuated strains or strains that have been demonstrated to have irreversibly lost known virulence factors may qualify for a reduction of the containment level compared to the Risk Group assigned to the parent strain (see Appendix B, *Classification of Human Etiologic Agents on the Basis of Hazard* and Section V-B, *Footnotes and References of Sections I-IV*)."**

Next Steps

- **OBA seeks RAC concurrence on the changes as outlined to Appendix B and Section II-A-3 of the *NIH Guidelines***
- **A Final FR notice will be published to implement these changes**