IBC Reviewer Checklist for Risk Assessment and *NIH Guidelines* rDNA #_____ BS#_____

Agent or Vector: risk factors

- ☐ Agent name(s) and risk group(s): _____
- ☐ Infectious material, pathogen, opportunistic pathogen, biological toxin, human/NHP body fluid, cells, or tissue
- ☐ Host range: human, broad/multi-host, environmentally or agriculturally important
- ☐ Infectious agent/viral vector pose a risk of infecting other animals: horizontal versus vertical transmission
- ☐ Unusual characteristics, spore former, exotic agent
- ☐ Hard to kill or easy to acquire, low infectious dose
- ☐ Mode of transmission: aerosol
- ☐ Large quantity and/or high concentration of agent made or used in work
- ☐ Prophylaxis or treatment available or recommended
- ☐ Viral vector
  - ☐ Parent virus_____
  - ☐ host range: xenotropic, amphotropic (envelope/pseudoytpe)
  - ☐ vector : commercial, lab made, colleague, core facility
  - ☐ vector production: propagated in lab, purification methods used by lab or supplier, helper virus
  - ☐ safety features; split genome in multiple plasmids, deleted structures, self-inactivating, gutless
  - ☐ replication competent virus: modifications, has it been tested

Host: risk factors

- ☐ Animal used in any part of the research
  - ☐ Species: rodent, fish, fly, nematode, etc
  - ☐ Existing transgenic or creating new strains
  - ☐ Viral vector or infectious agent challenge/exposure
  - ☐ Permissive species: humanized, immune deficient, carry endogenous adventitious agents, viruses, or sequences such as retroviral LTR
  - ☐ Used for xenograft or tumor studies
- ☐ Cell culture used in any part of the research
  - ☐ Human cells, non-human primate cells, stem cells, or primary cell culture
  - ☐ Transformed, transfected, or cancer (tumor) cell line
  - ☐ Cells contain endogenous adventitious agents/viruses/viral sequences
  - ☐ Host for expression system, virus packaging cell line, or virus propagation
  - ☐ *In vitro* use only or *in vivo* for transplant/allograft/xenograft studies
- ☐ Insect cell lines used?
  - ☐ Baculovirus
- ☐ Plant hosts used in any part of research?
  - ☐ Agrobacterium and/or plant viral vectors or significant agricultural microorganism
  - ☐ Noxious plant
- ☐ Bacteria, fungi, virus, or parasitic agent used as host?
  - ☐ Risk Group 1: *E. coli* K-12 strain, *Saccharomyces, B. subtilis,* etc. cloning/expression systems only
  - ☐ Risk group: opportunistic pathogen or RG-2, RG-3, or RG-4
  - ☐ Cloning/expression between natural exchangers or within same species or closely related strain
  - ☐ Will the virulence or pathogenicity of host be modified
  - ☐ Can a surrogate organism, attenuated strain, or killed organism be used?

Genes Manipulated: risk factors

- ☐ Is the gene or *sequence (*including synthetic) from RG-2, RG-3, or RG-4 agent, or biological toxin
- ☐ Are the genes or *sequences to oncogenes, virulence factors, toxins, or cause immune suppression
- ☐ Does the gene/*sequence change sensitivity to antibiotics, pesticides, or insecticides that would be used to control the host

Risk Assessment and Comments:

NIH Guidelines Sections:

Please Check all that apply in the boxes below: *Recombinant or synthetic nucleic acid molecules (rsNA) apply to all *Guideline* sections. Synthetic sequences are considered the same as RNA, DNA, recombinant RNA/DNA and use RG of host/gene in sequence.			**NIH Guidelines reference**:
a.	☐	**Transfer of Drug Resistance trait to microorganisms** i.e., a drug used to treat disease caused by the biological agent under study if compromises ability to control disease agent - NIH/OSP and IBC and NIH Director approval.	III-A-1-a
b.	☐	**Cloning of toxin molecules with an LD_{50} < 100 ng/kg body weight** -Requires NIH/OSP and IBC approval	III-B
c.	☐	**Deliberate transfer of rsNA or DNA or RNA derived from rsNA into humans** -IBC approval	III-C
d.	☐	**Use of Risk Group 2, 3, 4 or restricted agent as Host-Vector Systems**	III-D-1
e.	☐	**Administration of rsNA material into animals** (transformed/transduced cells, vectors, siRNA, microorganisms)	III-D-1, III-D-4
f.	☐	**Experiments involving transgenic/knockout animals requiring ABSL-2 containment or higher**	III-D-1, III-D-4-b
g.	☐	**Cloning genes from a Risk Group 2, 3, 4 or restricted agent into a nonpathogenic prokaryotic or lower eukaryotic Host-Vector System** except toxins with an LD_{50} < 100 ng/kg BW -Requires IBC approval	III-D-2
h.	☐	**Use of infectious DNA or RNA viruses or defective DNA or RNA viruses in the presence of helper virus in a tissue culture system**	III-D-3, or III-E-1
i.	☐	***De novo* generation of transgenic/knockout animals requiring ABSL-1 containment**	III-D-4-a
j.	☐	***De novo* generation of transgenic/knockout animals requiring ABSL-2 containment or higher**	III-D-4-b
k.	☐	**Experiments involving whole plants including algae, creating transgenic plants**	III-D-5 or III-E-2
l.	☐	**Propagating modified organisms with culture volumes exceeding 10 liters**	III-D-6
m.	☐	**Experiments involving influenza virus** (H2N2, HPAI H5N1, 1918 H1N1)	III-D-7
n.	☐	**Use of cells/cell lines containing <2/3 eukaryotic viral genome** (cells must lack helper virus if using defective virus if propagated and maintained in culture)	III-E-1
o.	☐	**Use of RG-1 Host-Vector systems & genes not covered elsewhere, may be conducted using BSL-1 containment**	III-E
p.	☐	**De novo generation of transgenic/knockout Rodents requiring ABSL-1 containment**	III-E-3
q.	☐	**Synthetic nucleic acid molecules that:** (1) can neither replicate nor generate nucleic acids that can replicate in any living cell (synthetic nucleic acids that do not contain an origin of replication or contain elements known to interact with either DNA or RNA polymerase), and (2) are not designed to integrate into DNA and (3) do not produce a toxin that is lethal for vertebrates at an LD50 of < 100 ng/ kg body weight.	III-F-1
r.	☐	**Use of rDNA/SNA that is not in organisms or viruses and not modified to penetrate cell membranes, or consists of DNA segments from a single non chromosomal or viral DNA source**	III-F-2 or III-F-3
s.	☐	**Consist entirely of nucleic acids from a prokaryotic host including indigenous plasmids or viruses when propagated in that host**	III-F-4
t.	☐	**Consist entirely of nucleic acids from a eukaryotic host propagated in that host**	III-F-5
u.	☐	**Consist entirely of DNA molecules segments from different species exchange DNA by a known physiological process** (see Appendix A for qualified natural exchangers exempt species sub list)	III-F-6 Appendix A
v.	☐	**Genomic DNA that has acquired a transposable element if it does not contain any rDNA/SNA**	III-F-7
x.	☐	**Use of cells/cell lines containing <1/2 eukaryotic viral genome of RG-1 or RG-2 viruses** (propagated and maintained in culture)	III-F-8 Appendix C-I
x.	☐	***E. coli* K-12 Host-Vector Systems for cloning/expression** except if *E. coli* host contains: (i) conjugation proficient plasmids or generalized transducing phages, (ii) lambda/lambdaoid/Ff bacteriophages or non-conjugative plasmids used as vectors (iii) >10L cultures, (iv) cloning of DNA from RG-3, RG-4, restricted organisms, biotoxins	III-F-8 Appendix C-II
y.	☐	***S. cerevisiae, S. uvarum,* or *Kluyveromyces* Host-Vector Systems for cloning/expression** (except (i) >10L cultures, (ii) cloning of DNA from RG-3, RG-4 or restricted organisms or biotoxins)	III-F-8 Appendix C-III III-F-8 Appendix C-IV
z.	☐	***B. subtilis or B. licheniformis* Host-Vector Systems (asporogenic strains) for cloning/expression** (except (i) >10L cultures, (ii) cloning of DNA from RG-3, RG-4 or restricted organisms or biotoxins)	III-F-8 Appendix C-V
aa.	☐	**The purchase or transfer of transgenic rodents requiring ABSL-1 containment**	III-F-8 Appendix C-VII
ab.	☐	**Transgenic rodent colony maintenance, breeding, crossing strains to create a new strain requiring ABSL-1 containment** except if either parent strain or progeny requires ABSL-2 and neither parent strain contains genetic modifications of (i) incorporation of >1/2 exogenous eukaryotic virus genome; or (ii) incorporation of transgene under control of gammaretroviral LTR, and progeny is not expected to contain >1/2 exogenous eukaryotic virus genome	III-F-8 Appendix C-VIII

Considerations for Assessing Risk in the Biological Research Laboratory

Review of rDNA and Biosafety protocols submitted to the IBC should include a risk assessment of the biohazardous materials used including pathogens, toxins, human cells and tissue, animal use, host, vector, and gene, the facilities and methods that will be used in the project. Synthetic sequences are considered the same as RNA, DNA, recombinant RNA/DNA and use RG of host/gene in sequence. *NIH Guidelines* Section II provides guidance for performing a comprehensive risk assessment and determining the appropriate containment conditions. Additional resources referenced are: the *Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th ed.* and the Occupational Safety and Health Administration (OSHA) regulation, 29CFR 1910.1030 and OSHA publication 3127.

Risk Assessment References: *NIH Guidelines*: Section II-A and Appendix A, B, C, and E. *BMBL*: Sections I, II, and VIII, and Appendix D, F, and H **Physical and Biocontainment Conditions References:** *NIH Guidelines*: Sections III-D, III-E, and III-F have work specific minimum containment conditions and described in Appendix C, F, G, I, K, P and Q. *BMBL*: Sections III, IV, and V and Appendix A, E, and I