Biological Risk Assessment

# Agent/ Toxin Information

|  |
| --- |
| Agent name(s): Click or tap here to enter text.  Risk Group: Choose an item.  This is a(n): Choose an item.  Host Range: Choose an item. |

## Questions:

1. Is the agent/toxin a known Dual Use Research of Concern (DURC) agent/ toxin?

No

Yes

1. Is the agent/toxin a known Select Agent or Toxin?

No

Yes

1. Is the agent an infectious agent/viral vector pose a risk of infecting other animals besides humans or non-human primates?

No

Yes

1. What are the modes of transmission of this agent/ toxin (select all that apply)?

Direct contact with blood or body fluid

Fomite transmission (i.e. doorknobs, countertops, lab equipment, etc.)

Aerosol

Droplet (secretions from eyes, nose, mouth)

Water

Soil

Biological Vector

Mechanical Vector

Other (specify): Click or tap here to enter text.

1. Does the agent/ toxin possess any of the following characteristics?

Spore Former

Exotic Agent

Hard to kill

Low infectious dose

Easy to Acquire

1. Will a large quantity (> 10L in one container) and/or high concentration of agent/ toxin be made or used in work?

No

Yes

1. Is there a vaccine or other prophylactic treatment available?

No

Yes

1. Is there a treatment available if infected with this agent/ toxin (i.e. antibiotic)?

No

Yes

1. Will you be using a viral vector?

No

Yes- answer the following:

* 1. What is the Parent virus? Click or tap here to enter text.
  2. What is the host range (select from below)?

Xenotropic

Amphotropic (envelope/ pseudotype)

* 1. What is the source of the vector?

Commerical (specify): Click or tap here to enter text.

Lab Made (specify lab): Click or tap here to enter text.

Colleague (name of colleague): Click or tap here to enter text.

Other (specify): Click or tap here to enter text.

* 1. Where was the vector produced?

Propagated in a laboratory

Purification methods used by your laboratory

Purification methods used by a supplier

Helper virus

Other (specify):

* 1. What are the safety features of this vector?

Split genome in multiple plasmids

Deleted structures

Self-inactivating

Gutless

Other (specify): Click or tap here to enter text.

* 1. Is this a replication competent virus?

No

Yes

If yes, have there been any modifications and/ or has it been tested?

Click or tap here to enter text.

1. Will any live animals be used in any part of the research?

No

Yes- answer questions below.

1. Animal type: Click or tap here to enter text.
2. Species: Click or tap here to enter text.
3. Existing transgenic or creating a new strain?

No

Yes

1. Will a viral vector be used in the animal or will it be exposed to an infectious agent?

No

Yes- describe below:

Click or tap here to enter text.

1. Is this a permissive species (humanized, immune deficient, carry endogenous adventitious agents, viruses, or sequences such as retroviral LTR)?

No

Yes

1. Will this animal be used for xenograft or tumor studies?

No

Yes

1. Will cell cultures be used in any part of the research?

No

Yes- answer questions below.

1. Will human cells, non-human primate (NHP) cells, stem cells, or primary cell culture be used?

No

Yes

1. Will the cells be transformed, transfected, or developed into a cancer (tumor) cell line?

No

Yes

1. Do the cell cultures contain endogenous adventitious agent/ viruses/ viral sequences?

No

Yes

1. Are the cells a host for an expression system, virus packaging cell line, or virus propagation?

No

Yes

Are the cells for *in vitro* use only or *in vivo* for transplant/allograft/xenograft studies?

*In vitro* only

*In vivo*

1. Will the insect virus *Baculovirus* be used in this research in an insect cell line?

No

Yes

1. Plant hosts used in any part of research?
   1. Plant common name and species: Click or tap here to enter text.
   2. Will the plant be infected with Agrobacterium and/or plant viral vectors or significant agricultural microorganism?

No

Yes

* 1. Is this plant a noxious weed?

No

Yes

1. Are bacteria, fungi, or parasitic agent or other microorganism used as a host?
   1. Is the host from an RG-1, such as *E. coli* K-12 strain, *Saccharomyces, Kluyveromyces,* or asporogenic strains of *B.subtilis* or *B.licheniformis*?

No

Yes (specify): Click or tap here to enter text.

* 1. Is the host any of the following (select all that apply):

Opportunistic pathogen

RG-2 agent

RG-3 agent

RG-4 agent

Select Agent

DURC

Agriculturally or environmentally significant

* 1. Will the virulence or pathogenicity of the host be modified?

No

Yes

* 1. Will a toxin be produced?

No

Yes (specify): Click or tap here to enter text.

* 1. Will this effect currently used medical treatment for this agent/ toxin?

No

Yes

* 1. Can a surrogate organism, killed organism, or attenuated strain be used in place of the selected host?

No

Yes

1. Are you using a gene or sequence (including synthetic) in your procedure?

No

Yes- answer below.

* 1. If genes are being used in research, does the gene or sequence (including synthetic) originate from any of the following?

Opportunistic pathogen

RG-2 agent

RG-3 agent

RG-4 agent

Select Agent

DURC

Agriculturally or environmentally significant

* 1. Are any of the following risks associated with inserting this gene/ sequence into host? (select all that apply)

No risks known

Up-regulation/ Silencing Expression

Regain of Function

Oncogenes

Virulence factors

Toxins

Expanded Host Range

Immune Suppression

* 1. Would insertion of the gene/ sequence change sensitivity of the host to the following:

No changes known

Antibiotics

Pesticides

Bactericides

Viricides

Fungicides

Insecticides

## Risk Assessment and Comments:

Click or tap here to enter text.

# NIH Guidelines Section

Please read each part carefully, and select any boxes that apply this risk assessment. If your procedure involves any recombinant or synthetic nucleic acid molecules (DNA, RNA, synthetic) you need to determine which section(s) of the NIH Guidelines apply to your work. Most work done at UWM falls under Sections III-D, III-E, or III-F of the NIH Guidelines, but there may be certain cases in which research falls under III-A, III-B, or III-C, which will require additional approvals and considerations. If the agent being used is a low risk, requiring only BSL-1 containment, and it doesn’t really fit in III-D or III-F, then it is covered in III-E.

If you are working with animals, the BSL containment is ABSL-1, ABSL-2, or ABSL-3 per the BMBL. If you are working with plants, containment levels are BSL1-P, BSL2-P, BSL3-P, as outlined in Appendix P of the NIH Guidelines. If your work is done with large scale quantities (>10L in a culture vessel), this is designated at BSL1-LS, BSL2-LS.

A complete risk assessment will be based on the risk group of the agent, the risks associated with the agents and genes, the quantity or concentration of the recombinant materials or vectors, the source of genes and/ or vectors, the procedures and equipment used in the research, the facility(ies) used in the research, PPE, and training/ experience of the lab personnel.

## NIH Guidelines Checklist

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Select if Applicable** | **Topic** | **NIH Guidelines Reference and Additional Resources** | **Requires Approval of:** | **When Does it Need to be Approved?** |
|  | **Major Actions: Transfer of Drug Resistant Trait.** Protocol involves the deliberate transfer of a drug-resistance trait to microorganisms that are not currently known to acquire the trait naturally if this acquisition could impede that use of current medical treatments used to control disease agents in humans, veterinary medicine, or agriculture | Section III-A | NIH Director, RAC, IBC | Before commencing research |
|  | **Cloning of toxin molecules with an LD50 < 100 ng/kg body weight**. Protocol involves rDNA/ synthetic nucleic acids containing genes for the biosynthesis of a biotoxin with an LD50 < 100ng/kg body weight. Cloning of toxin molecules in *E.coli* K-12 strains, segments for the biosynthesis of toxin molecules with vertebrate LD50 between 100ng/ kg body weight and 100 g/kg body weight may be included in specific experiments already approved by the NIH OBS in this section but require consultation with the NIH OBA. | Section III-B | NIH/ OBA, IBC | Before commencing research |
|  | **Deliberate transfer of recombinant or synthetic nucleic acids into human research participants. (all)** | Section III-C | NIH/ OBA, RAC, IRB, IBC | Before commencing research |
|  | **Use of infectious agents (RG-2, RG-3, RG-4)** If an RG-2, RG-3, or RG-4 infectious agent is used as part of a host-vector system, with the exception of Influenza (see Section III-D-7) it falls in this category. | Section III-D-1 | IBC | Before commencing research |
|  | **Cloning DNA from Infectious Agents.** Includes use of recombinant/ synthetic NA molecules from RG-2, RG-3, RG-4 or Select Agent cloned into non-pathogenic prokaryotic or lower eukaryotic Host-Vector System. (transformed/transduced cells, vectors, siRNA, microorganisms) | Section III-D-2 | IBC | Before commencing research |
|  | **Viral Vectors in Cell Culture.** Includes use of infectious viruses or defective viruses in the presence of a helper virus in tissue culture. | Section III-D-3 | IBC | Before commencing research |
|  | **Viral Sequences in Cell Culture**. Includes use of recombinant synthetic NA molecules containing < to < eukaryotic viral genome propagated and maintained in tissue culture (no helper virus) | Section III-D-3 | IBC | Before commencing research. |
|  | **Cloning DNA using a RG-1 Host.** Includes use of recombinant/ synthetic NA molecules from RG-1 agent cloned into a non-pathogenic prokaryotic RG-1 agent. | Section III-E or Section III-F-8  Review Appendix C for Host-Vector Systems that are Exempt | BSO or IBC | Exempt- notify IBC when starting research |
|  | **Transgenic Animals.** Includes creation or use of transgenic animals, including the introduction of recombinant/ synthetic NA, GMOs, or GM cells. | Section III-D-4  Section III-E-3  Section III-E-2 | BSO or IBC | Some cases are exempt, except when infecting animal |
|  | **Transgenic Plants.** Includes use or creation of transgenic plants, including algae, or the introduction of recombinant/ synthetic NA, or GMOs | Section III-D-5  Section III-E-2 | BSO or IBC | Some cases are exempt, check w/ BSO |
|  | **Propagating modified organisms with culture volumes exceeding 10 liters.** This involves producing large single batch quantities of genetically modified organisms. | Section III-D-6 | IBC | Before commencing research |
|  | **Experiments involving influenza virus** (H2N2, HPAI H5N1, 1918 H1N1). Involves influenza viruses generated by recombinant or synthetic methods (e.g., generation by reverse genetics of chimeric viruses with reasserted segments, introduction of specific mutations). | Section-III-D-7 | IBC | Before commencing research |
|  | **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) | Section III-E-1 | BSO (just to register, approval not required) | Simultaneous with start of research (does not require approval) |
|  | **Use of RG-1 Host-Vector systems & genes not covered elsewhere, may be conducted using BSL-1 containment** | Section III-E | BSO (just to register, approval not required) | Simultaneous with start of research (does not require approval) |
|  | **De novo generation of transgenic/knockout Rodents requiring ABSL-1 containment** | Section III-E-3 | BSO (just to register, approval not required)  IACUC | Simultaneous with start of research (does not require approval) |
|  | **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. | Section III-F-1 | BSO (just to register, approval not required) | Simultaneous with start of research (does not require approval) |
|  | **Use of recombinant NA that is not in organisms or viruses and not modified to penetrate cell membranes, or consists of DNA segments from a single nonchromosomal or viral DNA source.** | Section III-F-2 or  Section III-F-3 | BSO (just to register, approval not required) | Simultaneous with start of research (does not require approval) |
|  | **Consist entirely of nucleic acids from a prokaryotic host propogated in the same or closely related strain.** | Section III-F-4 | BSO (just to register, approval not required) | Simultaneous with start of research (does not require approval) |
|  | **Consist entirely of nucleic acids from a eukaryotic host (except viruses) propagated in the same or closely related strain of the same species.** This includes breeding transgenics with only genes from that species manipulated; no foreign sequences. | III-F-5 | BSO (just to register, approval not required) | Simultaneous with start of research (does not require approval) |
|  | **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 sublist) | III-F-6 Appendix A | BSO (just to register, approval not required) | Simultaneous with start of research (does not require approval) |
|  | **Genomic DNA that has acquired a transposable element if it does not contain any recombinant or synthetic DNA** | III-F-7 | BSO (just to register, approval not required) | Simultaneous with start of research (does not require approval) |
|  | **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 | BSO (just to register, approval not required) | Simultaneous with start of research (does not require approval) |
|  | ***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 | BSO (just to register, approval not required) | Simultaneous with start of research (does not require approval) |
|  | ***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 | BSO (just to register, approval not required) | Simultaneous with start of research (does not require approval) |
|  | ***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 | BSO (just to register, approval not required) | Simultaneous with start of research (does not require approval) |
|  | **The purchase or transfer of transgenic rodents requiring ABSL-1 containment** | III-F-8 Appendix  C-VII | BSO (just to register, approval not required)  IACUC | Simultaneous with start of research (does not require approval) |
|  | **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 | BSO (just to register, approval not required)  IACUC | Simultaneous with start of research (does not require approval) |

A risk assessment should be conducted prior to submission of a Biosafety Protocol. For additional assistance with Biological Risk Assessments, including training, please contact the biological safety program.

**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 ; Appendix C, F, G, I, K, P and Q](http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines)

[BMBL: Sections III, IV, and V and Appendix A, E, and I](https://www.cdc.gov/biosafety/publications/bmbl5/)