SAM HOUSTON STATE UNIVERSITY
Notification of Use (NOU)
Biological Agents, Recombinant Materials, CDC and USDA Regulated Agents

The purpose of this document is to ensure adequate review of occupational health and safety precautions and the procedures for use, handling, storage and disposal of biohazardous agents. The Principal Investigator (P.I.) or Supervisor must be fully aware of the potential hazards associated with the agent(s) used in the work area.

NOU(s) expire after 5 years. Continuing reviews must be submitted annually [form sent by Environmental Health and Safety (EHS)]. Amendments to the NOU do not change the renewal date, the original approval dates apply. No human or animal pathogen can be studied without prior written approval of the Institutional Biosafety Committee.

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Type of Submission: ☐ New ☐ Renewal ☐ Amendment (NOU #: _____)

Type of Agent: ☐ Biological agent, list agent(s): _____
☐ Recombinant material

Animals: ☐ Yes ☐ No ☐ Creation of transgenic animals

Arthropods: ☐ Yes ☐ No ☐ Creation of transgenic arthropods

Biosafety Level at which this agent will be used: ☐ BSL1 ☐ BSL2
(One biosafety level per NOU.)

Select the Risk Group (RG) for this agent: ☐ RG1 ☐ RG2
(RG definitions: https://osp.od.nih.gov/biotechnology/nih-guidelines/)

I am familiar with and agree to comply with the SHSU Safety Manual, the SHSU Risk Management, the CDC/NIH *Biosafety in Microbiological and Biomedical Laboratories* (current edition) and the NIH *Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.*

The information provided in this document is accurate to the best of my knowledge. I agree to abide by the provisions set forth in this plan as approved by the Sam Houston State University Institutional Biosafety Committee.

I acknowledge if an unexpected increase in virulence is observed, I will notify EHS immediately. I accept responsibility for providing all lab personnel with a copy of this NOU, and providing training for all lab personnel involved in the research project described in this NOU before commencement of work.

P.I. (Signature)	Title	Extension	Date Submitted
P.I. (Printed Name, Credentials)	SHSU ID#	Department	Route

Institutional Biosafety Committee Use Only

Date Approved _____ **Date for Resubmission** _____ **NOU Number** _____

DURC ☐ **Yes** ☐ **No**

☐ **A** ☐ **B** ☐ **C** ☐ **D1** ☐ **D2** ☐ **D3** ☐ **D4** ☐ **D5** ☐ **D6** ☐ **D7** ☐ **E** ☐ **F**
NIH categories

IBC Chairman Signature _____ **Print Name** _____

SECTION I: General information

1. **List agent(s) (include strains or generation; no abbreviations):**

Attach a copy of the pathogen safety data sheet if available, or supporting safety information (eg, manufacturer safety, data or fact sheet).
(eg, http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/index-eng.php, https://www.cdc.gov/az/a.html)

2. **Goal of the project (1-2 sentences):**

3. **Description of use (include techniques used for in-vitro, in-vivo and vector work. Do not copy detailed protocols or grant information; this section should be ¼ to ½ page long):**

4. **Location:**

Building(s)/Room Number(s): _____

5. Occupational Health

a. Are all personnel enrolled in the Employee Occupational Health Program?
☐ No ☐ Yes

b. Can this agent infect humans?
☐ No (proceed to question 6)
☐ Yes
☐ Unknown

c. Is the infection associated with replication in humans or is it abortive (no infectious progeny, for example viral replicons or defective adenoviral vectors)?
☐ Abortive (proceed to question 6)
☐ Unknown
☐ Replicative

i. Can the agent cause disease in healthy humans? ☐ No ☐ Yes ☐ Unknown

- If yes and no are both checked (e.g., multiple agents are listed in #1), provide an explanation:

ii. Can the agent cause disease in immunocompromised humans? ☐ No ☐ Yes ☐ Unknown
- If yes and no are both checked (e.g., multiple agents are listed in #1), provide an explanation:

d. Is medical surveillance recommended for the agent(s) prior to commencement of work, and/ or ongoing during project?

☐ No ☐ Yes

e. If yes, what type of surveillance is recommended?

☐ **Initial** ☐ **Ongoing**

Please explain:

f. Is a vaccine available for the agent?
☐ No (proceed to question 6)
☐ Yes ☐ FDA approved ☐ Internationally available ☐ Experimental (IND)
List vaccine:

g. Is immunization recommended by the ACIP at the listed biosafety level?(Advisory Committee on Immunization Practices (ACIP) at www.cdc.gov) ☐ No ☐ Yes

6. Agent Assessment (Answers are to be based on this scope of work *in-vitro*)

a. Provide the following:

i. Maximum volume to be cultured/handled at one time per container (e.g. flask, tubes, roller bottles): _____

ii. Maximum number of containers cultured/handled at one time: _____

If agent is abortive, skip to b.

iii. Maximum concentration to be cultured/handled at one time (units eg, pfu/mL):

iv. Will the agent be concentrated prior to experimental use? ☐ No ☐ Yes:

- Final total volume: _____
- Final concentration: _____
- Describe use of the concentrated material: _____

b. Will infectious material be manipulated outside of primary containment (eg., BSC)?

☐ No

☐ Yes, provide scientific justification:

c. Describe agent stability in the environment

i. Agent stability in regards to spill, fomites, survival outside of host:

ii. Susceptibility to decontamination as it pertains to the lab (heat, chemical inactivation):

d. Describe potential routes of lab transmission (including recombinant material).

☐ Inhalation ☐ Mucous membrane ☐ Ingestion ☐ Sharps (including needle sticks) ☐ Other: _____

e. What is the origin of the infectious material and from where will you specifically receive the agent?

☐ Existing stock
☐ Clinical isolate location:
☐ Field sample location:
☐ Commercially purchased
☐ Collaborator
☐ Other:

f. In the box below, describe pathogenicity for each agent, including disease incidence and severity in humans.

☐ Not infectious (proceed to question 7)

g. What is the infectious dose for each agent in humans? Provide reference. (If unknown, state whether or not the dose being used can be expected to cause infection and an explanation.)

h. If human data is not available, summarize from the most appropriate animal model studies (pathogenicity, infectivity and route of shedding from animals)?

7. Agent Inactivation

a. Will the project involve inactivating agent or samples?

☐ No (proceed to question 8)
☐ Yes

b. Reason for agent/sample inactivation

☐ To work at the same biosafety level
☐ To work at a lower biosafety level or on bench-top
☐ For shipment
☐ Other: Please describe below.

c. Inactivation and Verification Procedure(s)

No samples will be brought to a lower biosafety level prior to inactivation validation.

Please provide a detailed SOP* of the inactivation procedure(s) and validation procedure(s) for complete inactivation. This should also include the frequency of validation testing.

***Note: this must be attached to your IBC protocol documentation or available during inspection.**

9. Evaluation of Dual Use potential experiments of concern (US Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern). If answer is "yes", please explain in detail.

a. Is it likely that the harmful consequences of the agent will be enhanced?

☐ No

☐ Yes, explain in detail:

b. Is it likely that the immunity or effectiveness of an immunization against the agent without clinical and/or agricultural justification will be disrupted?

☐ No

☐ Yes, explain in detail:

c. Is it likely that:

i. resistance to clinically and/or agriculturally useful prophylactic or therapeutic interventions will be conferred to the agent?

☐ No ☐ Yes, explain in detail:

ii. the agent's ability to evade detection methodologies will be facilitated?

☐ No ☐ Yes, explain in detail:

d. Is it likely that the stability, transmissibility, or the ability to disseminate the agent will be increased?
☐ No ☐ Yes, explain in detail:

e. Is it likely that the host range or tropism of the agent will be altered?
☐ No ☐ Yes, explain in detail:

f. Is it likely that the susceptibility of a host population to the agent will be enhanced?
☐ No ☐ Yes, explain in detail:

g. Is it likely that an eradicated or extinct agent will be generated or reconstituted?
☐ No ☐ Yes, explain in detail:

10. Agent Propagation

a. Will agent(s) be propagated on this study?
☐ No
☐ Yes

b. What systems (cells and bacteria) will be used with the agent(s) listed (e.g. propagation, transduction, etc.)?
☐ N/A (e.g. broth or agar)
i. Cells of arthropod or animal origin: _____
ii. Cells of human or nonhuman primate origin: _____
Human or nonhuman primate product NOU approval number(s): _____
iii. Bacteria: _____

11. Check the personal protective equipment (PPE) worn when handling agent(s) in-vitro:

☐ Lab coat or gown/gloves/eye & face protection as needed (BSL1)
☐ Lab coat/gloves/eye & face protection as needed (BSL2)

12. Respiratory Protection

N95 respirator explain when and why this is worn:

13. Additional PPE

☐ Face Shield, explain when and why this is worn: _____
☐ Surgical mask, explain when and why this is worn: _____

14. Check lab equipment used when handling agent(s) in-vitro:

☐ Centrifuge (Sealed lid and cups/bucket) Building/Room: _____
☐ Blender
☐ Homogenizer, type: _____
☐ Sonicator
☐ Shaker Building/Room: _____
☐ Chemical Fume Hood: Building/Room: _____
☐ Biological Safety Cabinet (BSC): Building/Room: _____
☐ Other specify: _____

15. Method for disposal of biohazardous waste:

☐ Placed in red bag for disposal.
☐ Autoclaved, then placed in the biohazard trash.
☐ Chemically disinfected, then placed in the biohazard trash.
☐ Chemical disinfection or autoclave of bulk liquid, then disposed of based on MSDS
☐ Autoclaved, then packaged for incineration. [for only ABSL-1/ABSL-2]
☐ Other: _____

16. List disinfectant(s) used for surface decontamination and spills:

☐ CaviCide ☐ MicroChem
☐ Bleach ☐ Other _____ %

17. If you are planning recombinant or synthetic nucleic acid molecules work, please fill out Section II ☐ **N/A**

If you are planning any animal work, please fill out Section III ☐ **N/A**

If you are planning any arthropod vector work, please fill out Section IV ☐ **N/A**

SECTION II: Recombinant Material

https://osp.od.nih.gov/biotechnology/nih-guidelines/

Definition of recombinant and synthetic nucleic acid molecules per NIH-OBA guidelines

In the context of the NIH Guidelines, recombinant and synthetic nucleic acids are defined as: (i) molecules that are constructed by joining nucleic acid molecules that can replicate in a living cell, or (ii) nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, or (iii) molecules that result from the replication of those described in (i) or (ii) above.

1. **Goal of the project involving recombinant work:**

2. **Description of recombinant work:**

3. **Location:**

Building(s)/Room Number(s): _____

4. **Will synthetic DNA <u>other than primers</u> be used, or will material be sent to be synthesized?**
   ☐ No ☐ Yes, please explain:

5. **Clone manipulation**
   a. **Will there be clone modification performed in your lab?**
      ☐ N/A, there will be no clone manipulation performed. Proceed to question 7.
      ☐ Yes, please explain:

   b. **At what biosafety level will you be conducting the <u>cloning portion</u> (not rescue) of your research:**
      ☐ BSL1 ☐ BSL2

   c. **Will full-length clones be created?**
      ☐ No
      ☐ Yes, please explain:

6. **Gene editing**
   a. **Are you using gene editing, transcription, genome modification, or similar technology (CRISPR, TALENs, zinc fingers, etc.)?**
      ☐ No (proceed to question 7)
      ☐ Yes, please explain

   b. **Are guide RNA and Cas9 in the same construct?**
      ☐ Yes ☐ No ☐ N/A

   c. **Will a germline be modified?**
      ☐ No, proceed to d.
      ☐ Yes
      i. What organism(s) is being modified?
         ☐ Human ☐ Other, please specify: _____

d. What organism(s)/cell type is being modified/silenced? _____

e. Delivery system:
☐ Expressed guide RNA ☐ Purified ☐ N/A

f. Describe how the CRISPR will be dosed (viral vector, plasmid, liposome, etc.).

g. Describe the function of the gene(s) being modified/silenced:

h. Describe the expected function/loss-of-function of the gene(s) once modified/silenced:

i. CRISPR Information: Discuss the desired effect of gene editing on the animal or cell line. An example of a source for understanding the transgene being silenced or over-expressed is GENE CARDS (http://www.genecards.org/).

i. Is the guide RNA sequence specific to animals, arthropods, humans, or could it affect any combination thereof?
☐ No ☐ Yes, describe any homology between human and animal guide sequences:

ii. Describe what is known about off-target effects with the system you are using:

7. Answer the following questions.	
a. Does the inserted gene encode a known oncogene?	☐ Yes ☐ No
b. Does the viral DNA integrate into the host genome?	☐ Yes ☐ No
c. Does the inserted gene have the potential for altering the cell cycle?	☐ Yes ☐ No
d. Is there a probability of generating replication-competent viruses?	☐ Yes ☐ No
If yes to any of the above, please explain:	

8. Are you cloning risk group 2-4 nucleic material into a risk group 2-4 agent? (D1)

☐ No
☐ Yes, please provide the following information:

a. List the agent used to provide the inserted nucleic material: _____
   i. List the region of the insert: _____
b. List the agent used as a backbone: _____
   i. List the region of the insertion: _____

9. Are you creating point mutation in a risk group 2-4 agent? (D1)

☐ No
☐ Yes, please provide the following information:

a. List the location of the point mutations: _____
b. Indicate the expected outcome of the mutation(s): _____

10. Are you cloning risk group 2-4 nucleic material into nonpathogenic prokaryotic or lower eukaryotic host-vector systems? (eg., *E. coli)* (D2)

☐ No
☐ Yes, please provide the following information:

a. List prokaryote/eukaryote strain used: _____
b. List the vector(s) used: _____
c. If the DNA is from a Risk Group 4 agent, does the recombinant material contain a totally and irreversibly defective fraction of the agent's genome?
   ☐ No ☐ Yes ☐ N/A
d. Are you only using E. coli to express a protein (end of recombinant work)
   ☐ No ☐ Yes, list proteins expressed: _____

11. Are you propagating the recombinant <u>virus</u> in tissue culture? (D3)

☐ No

☐ Yes, please provide the following information:

a. Will a helper virus be used?

☐ No ☐ Yes, list proteins expressed: _____

b. Is there a probability of generating replication-competent viruses?

☐ No ☐ Yes

12. Are you going to inoculate animals and/or arthropods with the proposed recombinant material? (D4)

☐ No ☐ Yes

13. Are you going to creating transgenic animals by stable introduction of the proposed recombinant material to alter the animal's genome?

☐ No

☐ Yes, please provide the recommended biosafety level:

☐ BSL2 (D4)

☐ BSL1, used in rodents (E3)

☐ BSL1, not used in rodents

14. Will this work involve the deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally (other than *Escherichia coli* cloning selection)? Could this acquisition compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture?	☐ Yes ☐ No ☐ Yes ☐ No	**A-1a**
15. Will this experiment involve the cloning of toxin molecules with LD_{50} of less than 100 nanograms per kilogram body weight (e.g., microbial toxins such as the botulinum toxins, tetanus toxin, diphtheria toxin, and *Shigella dysenteriae* neurotoxin)?	☐ Yes ☐ No (proceed to C-1)	**B-1**
a. Provide LD_{50} ng/kg of body weight:		
b. Is this molecule lethal to vertebrates at 100 ng to 100 mg per kg body weight?	☐ Yes ☐ No	
c. Is the cloning done in *Escherichia coli* K-12?	☐ Yes ☐ No	
16. Will this experiment involve the deliberate transfer of recombinant or synthetic nucleic acid molecules, or DNA/RNA derived from recombinant or synthetic nucleic acid molecules, into one or more human research participants.	☐ Yes ☐ No	**C-1**
17. Will this experiment involve using Risk Group 2, Risk Group 3, Risk Group 4, or restricted agents as host-vector systems?	☐ Yes ☐ No	**D-1**
If yes, please explain:		

18. Will this experiment involve the use of whole plants?	☐ Yes ☐ No	**D-5 / E-2**
19. Will this experiment involve more than 10 liters of culture?	☐ Yes ☐ No	**D-6**
20. Will this experiment involve work with influenza virus? **Experiments with influenza viruses generated by recombinant or synthetic methods (e.g., generation by reverse genetics of chimeric viruses with re-assorted segments, introduction of specific mutations) shall be conducted at the biosafety level corresponding to the risk group of the virus that was the source of the majority of segments in the recombinant or synthetic virus.**	☐ Yes ☐ No (proceed to E-1)	**D-7**
21. Will experiments involve work with the following influenza viruses? **a. Human H2N2 (1957-1968)-**virus containing H2 hemagglutinin (HA) gene in cold-adapted, live attenuated vaccine strains (e.g., A/Ann Arbor/6/60 H2N2) in which the segments with mutations conferring temperature sensitivity and attenuation are not altered in the recombinant virus. **b. Human H2N2 (1957-1968)-**virus containing genes from human H2N2 other than the HA gene.	☐ Yes ☐ No ☐ Yes ☐ No	**D-7a**
c. Highly Pathogenic Avian Influenza H5N1 strains (within the Goose/Guangdong/96-like H5 lineage (HPAI H5N1) containing a minority of genes and/or segments from a HPAI H5N1 influenza virus. **d. Highly Pathogenic Avian Influenza H5N1 strains (within the Goose/Guangdong/96-like H5 lineage (HPAI H5N1) containing a majority of genes and/or segments from a HPAI H5N1 influenza virus.**	☐ Yes ☐ No ☐ Yes ☐ No	**D-7b**
e. Influenza viruses containing any gene or segment from 1918 H1N1.	☐ Yes ☐ No	**D-7c**
f. Will the experiment involve work with an influenza virus containing genes from one of 1918 H1N1, HPAI H5N1, and human H2N2 (1957-1968) viruses that is resistant to both classes of current antiviral agents, adamantanes and neuraminidase inhibitors? If yes, contact EHS before submission	☐ Yes ☐ No	**D-7d (if yes, mark A-1 yes also)**
22. Will this experiment involve the formation of recombinant or synthetic nucleic acid molecules containing more than two-thirds of the genome of any eukaryotic virus?	☐ Yes ☐ No	**E-1**
23. Will this experiment involve the use of arthropods or small animals with recombinant or synthetic nucleic acid molecule-modified microorganisms? **24. Will this experiment involve the use of recombinant DNA-modified arthropods or small animals associated with plants?**	☐ Yes ☐ No ☐ Yes ☐ No	**E-2-b-5**

Exempt Experiments. The following recombinant or synthetic nucleic acid molecules are exempt from the NIH Guidelines. If the answer for questions 8-24 were No, then registration with the Institutional Biosafety Committee (IBC) is not required.

25. Will the experiment include synthetic nucleic acids that:		
a. Can either replicate or generate nucleic acids that can replicate in any living cell?	☐ Yes ☐ No	**F-1**
b. Are designed to integrate into DNA?	☐ Yes ☐ No	
c. Produce a toxin that is lethal for vertebrates at an LD_{50} of less than 100 nanograms per kilogram body weight?	☐ Yes ☐ No	
26. Will the experiment include recombinant or synthetic nucleic acids that are not in organisms, cells or viruses and that have not been modified or manipulated (e.g., encapsulated into synthetic or natural vehicles) to render them capable of penetrating cellular membranes?	☐ Yes ☐ No	**F-2**
27. Will the experiment include recombinant or synthetic nucleic acids that consist solely of the exact recombinant or synthetic nucleic acid sequences from a single source that exists contemporaneously in nature?	☐ Yes ☐ No	**F-3**
28. Will the experiment include recombinant or synthetic nucleic acids that that consist entirely of nucleic acids from a prokaryotic host, including its indigenous plasmids or viruses when propagated only in that host (or a closely related strain of the same species), or when transferred to another host by well-established physiological means?	☐ Yes ☐ No	**F-4**
29. Will the experiment include recombinant or synthetic nucleic acids that consist entirely of nucleic acids from a eukaryotic host including its chloroplasts mitochondria, or plasmids (but excluding viruses) when propagated only in that host (or a closely related strain of the same species)?	☐ Yes ☐ No	**F-5**
30. Will the experiment include recombinant or synthetic nucleic acids that consist entirely of DNA segments from different species that exchange DNA by known physiological processes, though one or more of the segments may be a synthetic equivalent? See Section IV-C-1-b-(1)-(c), *Major Actions*), as determined by the NIH Director, with the advice of the RAC, and following appropriate notice and opportunity for public comment. See Appendices A-I through A-VI, *Exemptions under Section III-F-6* for a list of natural exchangers that are exempt from the *NIH Guidelines*.	☐ Yes ☐ No	**F-6**
31. Will this experiment include genomic DNA molecules that have acquired a transposable element, provided the transposable element does not contain any recombinant and/or synthetic DNA?	☐ Yes ☐ No	**F-7**
32. Will the experiment include recombinant or synthetic nucleic acids that do not present a significant risk to health or the environment? See Section IV-C-1-b-(1)-(c), *Major Actions*, as determined by the NIH Director, with the advice of the RAC, and following appropriate notice and opportunity for public comment. See Appendix C, *Exemptions under Section-III-F-8* for other classes of experiments which are exempt from the *NIH Guidelines.*	☐ Yes ☐ No	**F-8**

If you are planning any animal work, please fill out Section III ☐ **N/A**

If you are planning any arthropod vector work, please fill out Section IV ☐ **N/A**