IBC MEETING COMMENTS

June 18, 2025 – Zoom Conference Call

Attendance – IBC Committee			
Present	Name	Expertise	Role
	Paul Gulig	Microbiology	Member
x	Luis Martinez	Microbiology	Member
x	Jason Clements		Member
x	Norman Beatty	Infectious Diseases	Member
x	Steeve Boulant	Virology	Member Left at 1:30pm
	Sanford L. Boye	Virology	Member
	Amber Duren		Community Member
	Mariola Ferraro	Microbiology	Member
x	Dean Gabriel	Plants	Member
x	Gary Heil		Member
	Michael McIntosh	Virology	Member
x	John D. McVay	Plants	Community Member
x	Mark Moehle	Microbiology	Member
x	Kamal A. Mohammed	Microbiology	Member
	Christopher Overend		Member
x	[redacted]	Animals	Member
	Elias J. Sayour	Clinical Trials	Member
x	Clay Smith	Virology	Chair
	Daniel R. Swale	Insects	Member
	Amy Vittor	Infectious Diseases	Member

Attendance – Staff and Guests		
Present	Name	Affiliation/Position
x	[redacted]	PI Guest
x	Pratibha Srivastava	UF EHS
x	Kindra Kelly-Quagliana	UF EHS
x	Pat Glenton	PI Guest
x	Anna Gioseffi	UF EHS
x	Laura Castillo	UF EHS
x	Craig Moneypenny	UF EHS
x	[redacted]	PI Guest
x	Alek Aranyos	UF EHS
x	Jennifer Jackson	UF EHS
x	Erica Gonzaga	UF EHS
x	Savannah Hardiman	UF EHS
x	Laurence Prunetti	UF EHS

Agenda:

	Full Committee Projects	PI
1	Decoding protein synthesis	Kotaro Fujii – Renewal BIO5785
2	investigating beta-adrenergic regulation of mucin synthesis in airways	[redacted]
3	A Phase 1, Randomized, Double-blind, Placebo-controlled, Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of the Antisense Oligonucleotide AMX0114 Administered to Adult Participants with Amyotrophic Lateral Sclerosis	James Wymer
4	Mollicutes Studies	[redacted]
	Amendments	**PI**
1	Study of oncogenic driver mutations (e.g. PIK3CA, KDR, and etc.) in canine hemangiosarcoma and human angiosarcoma tumorigenesis.	[redacted]
2	Investigation and Mitigation of Pathogen Persistence in Food Systems using Artificial Intelligence and Multi-Omics	Boce Zhang
3	Canine Inducible-Insulin	[redacted]
4	Leveraging Immunological Mechanisms to Mediate Tumor response	[redacted]
5	Chemoimmunomodulation in Metastatic Cancers	[redacted]

6	3rd Generation Lenti Viral infusion into LentiX 293 T cells Amendment 2-21-24 - Novel antibody therapy for muscarinic receptor (M3r) autoantibody in Sjogrens Disease Amendment 2-21-24 – Use of Gene therapy in Sjogren Mouse Model, B6NOD-Aec1/2 Amendment 9-9-24- Using beneficial probiotics as therapy in Sjogren Mouse Model, B6NOD-Aec1/2	[redacted]
7	Membranes of the Dental Pathogen Streptococcus mutans	L Brady
8	"A Phase 1/2 Dose-escalation Study Evaluating the Safety, Tolerability, and Efficacy of VX-522 in Subjects 18 Years of Age and Older With Cystic Fibrosis and a CFTR Genotype Not Responsive to CFTR Modulator Therapy"	Cesar Trillo-Alvarez
9	Serotonin Systems in Pain, Psychiatric disorders, Neurodevelopmental disorders, and Alzheimer's Disease	[redacted]

Minutes

Meeting was called to order at: 1:02pm

Project Review

Principal Investigator: Kotaro Fujii

Project Title: Decoding protein synthesis

Renewal BIO5785

Vector/Agent(s) to be used: Plasmids

Name and Function of Transcribed Nucleic Acids:

- Firefly luciferase, untranslated regions (UTRs) of signaling transcripts (Ptch1, Smo, Gli1, Gli3, NF2, Lets2, Sav1, Scrib, Taz, Yap, Hbb). Genes are expressed from SV40 promoter. Function of Genes: luciferase (enzymes that produce bioluminescence).
- Renilla luciferase; Renilla is expressed from SV40 promoter.
- S1 aptamer, 5'UTRs of gene of interest; RNA with S1 aptamer will be *in vitro* transcribed from SP6 promoter.
- Firefly luciferase, Renilla luciferase; Genes are expressed from CMV promoter. Function of Genes: luciferase (enzymes that produce bioluminescence).

- ribosomal DNA (rDNA) encoding ribosomal RNA (rRNA); Genes are expressed from RNA polymerase 1 promoter. Gene encode ribosomal RNAs, which are components of ribosome.
- MAP1, MAP2, NAT1; Genes of interest will be transcribed from own promoter.
- CRISPR, guide RNA to the MAP1, MAP2 genes; CRISPR will be expressed from GAP promoter and cleave target DNA sites.
- CRISPR, guide RNA to the 5'UTR of Ptch1 gene; CRISPR will be expressed from GAP promoter and cleave target DNA sites.

Host(s) to be used: *E. coli* DH5α, rodent cell line, human cell line; *S.cerevisiae*

NIH Guidelines:

This project falls under the following applicable sections of the NIH Guidelines:

- III-E for the use of Cas9 technology in *E. coli, S. cerevisiae* and rodent cells.
- III-F-8, appendices C-I for the use of recombinant/synthetic nucleic acids in tissue culture.
- III-F-8, appendices C-II for the use of K-12 lineage *E. coli* (DH5α).
- III-F-8, appendices C-III for work involving *Saccharomyces*.

Biosafety Level and Any Additional Requirements:

- BSL-1 for the *in vitro* use of Cas9 editing in mammalian cells and use of plasmids in K-12 *E. coli* (DH5α), *S. cerevisiae* and rodent cells.
- BSL-2 for all work involving the use of human derived cell lines.

Training: All training completed

Approval: Conditional approval pending BSC certification (Yes-11, No-0, Abstain-0)

Principal Investigator: [redacted]

Project Title: investigating beta-adrenergic regulation of mucin synthesis in airways

BIO number not yet assigned

Vector/Agent(s) to be used: RNAi or CRISPR/Cas Technologies

Name and Function of Transcribed Nucleic Acids: p38/MAPK14; to inhibit the messenger RNA (mRNA) of p38/MAPK14. airway beta 2 adrenergic receptor; to inhibit the mRNA of beta 2 adrenergic receptor.

Host(s) to be used: Rodent airway p38/MAPK14; Rodent airway beta 2 adrenergic receptor

NIH Guidelines: III-F-1 Experiments involving synthetic nucleic acids that are 1) non-replicative, 2) do not contain an origin of replication, 3) do not contain elements known to interact with either DNA or RNA polymerase, 4) do not integrate in DNA, and 5) do not produce a toxin with LD50 < 100 Nanograms/Kilogram Body Weight.

Biosafety Level and Any Additional Requirements: ABSL-1 for *in vivo* rodent work.

Training: All training completed

Approval: Conditional approval pending the addition of a section to the risk mitigation to better describe the risks. (Yes-11, No-0, Abstain-0)

Principal Investigator: James Wymer

Project Title: A Phase 1, Randomized, Double-blind, Placebo-controlled, Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of the Antisense Oligonucleotide AMX0114 Administered to Adult Participants with Amyotrophic Lateral Sclerosis

BIO number not yet assigned

Vector/Agent(s) to be used: RNAi or CRISPR/Cas Technologies

Name and Function of Transcribed Nucleic Acids: calpain-2; gene silencing via ribonuclease degradation of mRNA targeted by the ASO.

Host(s) to be used: human patients

NIH Guidelines: III-C-1s for the administration of recombinant/synthetic nucleic acids to human patients.

Biosafety Level and Any Additional Requirements: Handling the AMX0114, investigational product is approved at BSL-1.

All study personnel must complete initial and annual Bloodborne Pathogens training.

Training: All training completed

Approval: All approved as recommended (Yes-10, No-0, Abstain-0)

Principal Investigator: [redacted]

Project Title: Mollicutes Studies

BIO number not yet assigned

Vector/Agent(s) to be used: Nucleic Acid/Gene Removal/Mutation

Name and Function of Transcribed Nucleic Acids: Various genes/nucleic acids. Functions include: Signaling & cellular processes; Environmental information processing; Metabolism; Genetic information processing; undefined function by Kegg Orthology and transcription factor, repressor.

Host(s) to be used: *Galleria mellonella*

NIH Guidelines: III-D-1-a for cloning nucleic acids from risk group 2 agents into lower eukaryotes and III-D-2-a for the use of the transposon insertion using the mini-Tn4001tetM plasmid pTF20 generated mutant mycoplasma strains being added to the *G. mellonella*.

Biosafety Level and Any Additional Requirements: BSL-2 biosafety containment practices for the use of handlining risk group 2 (RG2) agents and ACL-2 for the injection of RG2 into the arthropod wax worm larva *G. mellonella*.

Training: All training completed

Approval: All approved as recommended (Yes-11, No-0, Abstain-0)

Amendments

Principal Investigator: [redacted]

Title: Study of oncogenic driver mutations (e.g. PIK3CA, KDR, and etc.) in canine hemangiosarcoma and human angiosarcoma tumorigenesis.

BIO6830

Summary: This amendment adds two more cell lines, personnel changes, and additional CRISPR and *in vivo* rodent studies.

This work falls under the following NIH guidelines:

- III-D-3a (a or b) for packaging lentiviral vectors in the presence of a packaging system
- III-D-4-a for experiments involving use of recombinant nucleic acids inrodents

- III-E-1 for formation of recombinant or synthetic nucleic acids containing no more than 2/3 of the genome of any eukaryotic virus;
- III-F-8 (appendix C-II?) for use of recombinant nucleic acids in *E. coli* strains (DH5alpha); and application of genome editing in eukaryotic hosts (such as CRISPR/Cas-9 technologies).

The work can be safely done with the following biosafety containments and practices:

- BSL-2+ containment and practices for work with human cell lines and lentiviral vectors. Extra (+) precautions emphasize the use of mucous membrane protection, the use of safe sharps, and the substitution of glassware with plasticware, initial and annual BBP training.for work with human derived cells
- ABSL-2 for injections of human cells/modified human cells into rodents.
- ABSL-1+Hu for animal housing after injection of unmodified human cells and human cells receiving plasmids.

Training: All training completed

Approval: All approved as recommended (Yes-10, No-0, Abstain-0)

Principal Investigator: Boce Zhang

Title: Investigation and Mitigation of Pathogen Persistence in Food Systems using Artificial Intelligence and Multi-Omics

BIO6140

Summary: This amendment updates the personnel list, adds one additional plasmid, and adds fermented beverages as new food matrices for studying pathogen survival. Project remains approved at BSL-2 for work with RG2 pathogens and BSL-1 for experiments utilizing nonpathogenic strains under Sections III-E and III-F-8 Appendix C-II of the NIH Guidelines.

Training: All training completed

Approval: All approved as recommended (Yes-10, No-0, Abstain-0)

Principal Investigator: [redacted]

Title: Canine Inducible-Insulin

BIO6785

Summary: This amendment adds cross dosing of gene vectors (rAVV and Hcad). Both vectors (rAAV and Hcad) have been modified with 10 base pair changes in the coding sequence. These changes do not affect the amino acid sequence of the human Lispro protein, nor do they alter the ligand. The dosage of both HCAd and AAV9 remains unchanged. In addition to this, Adenovirus and AAV vectors have been added to the study.

This amendment does not change the applicable NIH Guidelines (III-D-4-a) nor the approved biosafety levels (BSL-1/BSL-2/ABSL-1/ABSL-1+).

- III-D-4-a, for the use of AAV and adenovirus in animals.
- BSL-1 practices and containment are appropriate for *in vitro* work with rAAV vectors.
- BSL-2 containment and practices for work with adenoviral vectors and ABSL-2+ for inoculations and wiping post-injection site with ABSL-2 for subsequent housing.
- ABSL-1+ is recommended for animal inoculations using both AAV, with safe sharps handling, post-injection site wiping, and ABSL-1 for subsequent housing.

Initial and annual Bloodborne Pathogens training is required for all project personnel.

Training: All training completed

Approval: All approved as recommended (Yes-10, No-0, Abstain-0)

Principal Investigator: [redacted]

Title: Leveraging Immunological Mechanisms to Mediate Tumor response

BIO6653

Summary: A human-derived cell line is being added as an amendment to this study. This amendment proposes lowering the safety level from ABSL-2 to ABSL1-i and ABSL1-Hu+ for the housing of animals inoculated with unmodified cell lines under this project.

The relevant sections of the NIH Guidelines that cover this work remain unchanged by this amendment:

- III-D-4-b, for the use of recombinant modified cell lines in rodents.
- III-E-1, for cell line transduction by lentiviruses.
- III-F-8 Appendix C-1 for the maintenance of genetically modified cells in culture.

The biosafety containment levels and practices under which the work was originally approved to be conducted also remain unchanged, with the addition of ABSL1-i and ABSL1-Hu+.

- BSL-2+ is recommended for the work with transduced cell lines and in vitro experiments with LVV. The "+" practices require mucous membrane protection and substituting plastic labware for glassware where possible, and initial and annual Bloodborne Pathogens training.
- ABSL-2+ for animal inoculations with transduced cell lines (requires the use of mucous membrane protection, safe sharps and wiping of the injection site) and
- ABSL-2 for subsequent housing.

NOTE: For rodents treated with stably transduced cell lines, housing may be reduced to ABSL-1 if data is provided to the biosafety office demonstrating that the cell lines do not produce replication competent virus.

- ABSL1-i for housing rodents inoculated with non-transduced cell lines, including inactivation of bedding materials for the first 72 hours post-inoculation in rodents, followed by bedding disinfection.
- ABSL1-Hu+ for human cell lines.
- Label "Use of Human Cells in Animals" on caging and at the entrance of the room.
- Initial and annual Bloodborne Pathogens training is required for all project personnel.

Training: All training completed

Approval: Conditionally approved. The DC2.4 cell line needs to be added to the nucleic acids sub-form.

Additional comments: Reduction in ABSL containment for cells stably transduced with lentivirus will require data demonstrating absence of replication competent virus. Human cell lines not modified can be used in rodents at ABSL-1+hu; recombinantly modified human cells will require ABSL-2+

(Yes-9, No-0, Abstain-1)

Principal Investigator: [redacted]

Title: Chemoimmunomodulation in Metastatic Cancers

BIO6977

Summary: Technical and Personnel changes. The technical changes include adding two new cell lines and two new lentiviral vectors.

These changes require the following safety and containment practices:

- BSL-2 for culturing human cell lines and *in vitro* manipulation of CRISPRi in mammalian cell lines

- BSL-2+ for experiments involving lentivirus work in mammalian cell lines. The "+" designates the use of mucous membrane protection and substituting plastic labware for glassware where possible. Required personal protective equipment (PPE) includes a Laboratory coat, disposable gloves, and mucous membrane protection. A proper protocol for inactivation/decontamination of biohazard waste is emphasized. Annual bloodborne pathogens training is also required.
- ABSL-2+ for lentiviral vector injections into rodents with subsequent ABSL-2 housing. The "+" designates the use of mucous membrane protection, substituting plastic labware for glassware where possible, use of safe sharps, and wiping of the injection site. Required personal protective equipment (PPE) includes a Laboratory coat, disposable gloves, and mucous membrane protection. A proper protocol for inactivation/decontamination of biohazard waste is emphasized. Annual bloodborne pathogens training is also required.
- Animal containment could be lowered to ABSL-1+/ABSL-1 if negative RCL testing is performed and data provided and approved by the Biosafety Office.

These changes update the applicable NIH guidelines as follows:

- III-D-3-a for packaging lentiviral vectors in the lab
- III-D-4-b for injection of lentiviral vectors into rodents
- III-E for the use of CRISPRi technology in mammalian cells
- III-E-1 for lentiviral transfection and transduction of mammalian cell lines

Training: All training completed

Approval: All approved as recommended (Yes-10, No-0, Abstain-0)

Principal Investigator: [redacted]

Title: 3rd Generation Lenti Viral infusion into LentiX 293 T cells Amendment 2-21-24 - Novel antibody therapy for muscarinic receptor (M3r) autoantibody in Sjogrens Disease Amendment 2-21-24 – Use of Gene therapy in Sjogren Mouse Model, B6NOD-Aec1/2 Amendment 9-9-24- Using beneficial probiotics as therapy in Sjogren Mouse Model, B6NOD-Aec1/2

BIO5697

Summary: Personnel and technical changes. Adding a new *E.coli* Nissel strain with an empty plasmid vector that includes an antibiotic-resistant cassette into the gut microflora of our genetically engineered rodent model.

This work can safely be performed at the following biosafety containment practices:

- BSL-2 for the work involving working with human *in vitro* cell culture and production/packaging of lentiviral vectors
- ABSL-1-i for the adding the*E. coli* Nissel carrying the **pACYC184 plasmid** by gavage to rodents

This work falls under the following NIH guidelines:

- III-D-3-a for the packaging of LLV *in vitro*
- III-D-4-a for the administration of recombinant nucleic acid modified *E. coli* to animals
- III-E for the propagation of the non K12 E. coli Nissel strain carrying a plasmid
- III-F-8 appendix C-I for transfecting mammalian cells with r/sNA, maintaining genetically modified cells in culture

Training: All training completed

Approval: All approved as recommended (Yes-11, No-0, Abstain-0)

Principal Investigator: L Brady

Title: Membranes of the Dental Pathogen *Streptococcus mutans*

BIO6945

Summary: Personnel Update and technical change. Technical Change: Includes *Streptococcus pneumoniae* to the study.

This amendment does not alter the previously applicable NIH Guidelines (Sections III-D-1-a and III-D-2-a) or the approved biosafety levels (BSL-1/BSL-2). Instead, it adds Sections III-E and III-F-8 Appendix C-II.

The project falls under the following NIH guidelines:

- III-D-1-a for use of Risk Group 2 agent as Host-Vector Systems
- III-D-2 -a for DNA From Risk Group 2 agents cloned into Nonpathogenic Prokaryotes
- III-E for work involving non-exempt *E. coli* strains (BL-21)
- III-F-8 Appendix C-II for work with *E. coli* K-12 strains.

BSL-1 containment and practices for plasmid maintenance in *E. coli* K-12 and non-K-12 strains.

BSL-2 containment and practices for work with *Streptococcus pneumoniae, mutans, sanguinus, and agalactiae.*

- All samples centrifuged using a sealed rotor must be opened only in a biosafety cabinet.
- Personnel must complete initial and annual take bloodborne pathogens training.

Training: All training completed

Approval: All approved as recommended (Yes-10, No-0, Abstain-0)

Principal Investigator: Cesar Trillo-Alvarez

Title: "A Phase 1/2 Dose-escalation Study Evaluating the Safety, Tolerability, and Efficacy of VX-522 in Subjects 18 Years of Age and Older With Cystic Fibrosis and a CFTR Genotype Not Responsive to CFTR Modulator Therapy"

BIO6543

Summary: INFORMATIONAL AMENDMENT: This amended project was previously approved on 07/17/2024 at BSL-1 and BSL-2 containment and practices with section III-C-1 of the NIH Guidelines applying. On 6/18/2025, the IBC noted that the sponsor has requested a pause on recruiting and enrolling because of two adverse advents at other investigational sites. A new amendment will be submitted with additional mitigation protocols and informed consent once the sponsor has determined the appropriate parameters.

The relevant section of the NIH Guidelines that covers this work and the biosafety containment levels and practices under which the work was originally approved to be conducted remain unchanged by this amendment.

- Section III-C-1 for use of recombinant/synthetic nucleic acids in human subjects

The work was previously approved to be conducted using the following biosafety containment and practices:

- BSL-1 containment and practices for the handling and administration of the drug product, while patient samples must be handled in accordance with BSL-2 containment and practices.

All project personnel must complete Bloodborne Pathogens (BBP) training.

Training: All training completed

Approval: No vote, for informational purposes only.

Principal Investigator: [redacted]

Title: Serotonin Systems in Pain, Psychiatric disorders, Neurodevelopmental disorders, and Alzheimer's Disease

BIO7484

Summary: Personnel and technical changes. An AAV is being added to the registered materials list. These changes do not affect the previously approved biosafety and containment practices:

- BSL-1 for the handling of prepared AAVs and siRNAs
- ABSL-1+ for injections of AAVs and siRNAs into rodents. The '+' designation designates the use of mucous membrane protection and safe sharps. Subsequent ABSL-1 housing is appropriate.

These changes also do not affect NIH guidelines:

- III-D-4-a for the injection of AAVs into rodents
- III-F-1 for the intracerebral or intracranial injection of siRNA into rodents

Training: All training completed

Approval: All approved as recommended (Yes-11, No-0, Abstain-0)

The meeting adjourned at 2:13pm