CHILDREN'S HOSPITAL BOSTON

Meeting of Boston Children's Hospital Institutional Biosafety Committee

AGENDA

11/20/2025 11:30 AM to 1:00 PM

KARP 4th Floor, Conference Room

Members Present: MM, SVH, SG, KK, CH, DC, EC, SD, BS, IJ, TW, DF, HD

Members Absent: PW, EG, JM

Guests: LS

RLSO: JF, DH, AL

SD chaired the meeting.

1 IBC Meeting Minutes

Boston Children's Hospital Institutional Biosafety Committee meeting (10/16/2025)

IBC Meeting Minute was unanimously approved by the committee.

Committee Decision:
Motion: Approved
Majority (Approved): 13
Minority (Against): 0

2 Administrative Updates

- **December Open Meeting:** December 18th, 2025.
- IBC Meeting Schedule for 2026 has been sent out to members of the committee.

3 Laboratory Events

1. **Puncture with a needle**

- **Incident summary:** A researcher sustained a needle puncture while sedating a mouse with a ketamine/xylazine solution via intraperitoneal injection.
- **Root Cause:**
    - Insufficient scuffing technique.
- **Corrective Actions:**
    - Hands-on training and practice in proper scruffing and immobilization techniques available by ARCH.

2. Puncture with a needle

- **Incident summary:** A researcher sustained a needle puncture while extracting ketamine from a vial.
- **Root Cause:**
    - Improper technique for withdrawing solution from a vial – did not insert adequate volume of air in the vial prior to withdrawing, leading to unstable handling and increased risk of needle puncture.
- **Corrective Actions:**
    - Completed training on how to extract liquid from a vial available by ARCH.

4 New submission – Clinical

IBC-P00002159 CABA-201-002 for IIM or JIIM

PI: SP

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: This is a phase 1/2 open-Label study designed to evaluate the safety and efficacy of autologous CD19-specific Chimeric Antigen Receptor T cells (CABA-201) in Subjects with Active Idiopathic Inflammatory Myopathy (IIM) or Active Juvenile Idiopathic Inflammatory Myopathy (JIIM). CABA-201 is a cell therapy product consisting of autologously derived T cells that have been genetically edited ex vivo to express human anti-CD19 with the goal of eliminating pathologic B cells while supporting the repopulation of naïve B cells to provide durable clinical responses following administration. The cell therapy product will be prepared and stored in DFCI Cell Manipulation Core Facility and transported to the inpatient room in BCH for administration via IV infusion.

Regulations Applicable to this Protocol: NIH Guidelines III-C and OSHA Bloodborne Pathogens Standard.

Motion: Modifications Required for Approval

- Majority (Approved): 13
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Revise and simplify the lay summary so that it may be understood by nonscientific members of the committee - including the study goals and biosafety precautions. Define the abbreviations used.
- The committee recommends that the high-level protocol summary be revised to more clearly reflect biosafety considerations. The submission describes a lentiviral (LV) product manufactured ex vivo and released by the manufacturer; this information should be explicitly incorporated into the summary to ensure accurate context for biosafety review.
- Include long-term follow-up procedures in the protocol, specifically addressing monitoring for potential insertional mutagenesis associated with lentiviral vector use.
- Clarify how the product will be transported (double container, with ice, etc.) to the patient room.
- Clarify if the product will the thawed by the DFCI pharmacy or at BCH, since the product needs to be infused within 60 minutes of defrost. If it is defrosted at BCH, provide details on how it is prepared prior to infusion.
- Update to include that the vials/leftover product will be disposed after infusion following BCH policies.
- All staff must complete protocol-specific training, provided by an experienced member of the group.
- Clarify the number of study subjects.

IBC-P00002156 EN-374-101: A Phase 1/2 Open-Label, Single-Ascending-Dose Study of EN-374, a Helper Dependent Adenoviral-Based Gene Therapy, in Participants with X-Linked Chronic Granulomatous Disease

PI: SP

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: This is a phase 1/2 open-label, single-ascending-dose study of EN-374, a helper dependent adenoviral-based gene therapy in participants with X-Linked Chronic Granulomatous Disease (CGD). CGD is a rare primary immune deficiency marked by recurrent bacterial or fungal infections starting in infancy due to mutations in components of the nicotinamide adenine diphosphate (NADPH) oxidase complex that result in deficient production of microbicidal superoxide anions and oxidative bursts in neutrophils. EN-374 is an in vivo approach to genetically modify hematopoietic stem cells (HSCs) to express a wild-type cytochrome β subunit gp91phox (CYBB) gene without requiring myeloablative conditioning in order to restore the NADPH complex in neutrophils and allow them to fight infections more effectively. The gene therapy product will be prepared and stored in BCH pharmacy and administered in the inpatient room via IV.

Regulations Applicable to this Protocol: NIH Guidelines III-C and OSHA Bloodborne Pathogens Standard.

Motion: Modifications Required for Approval

- Majority (Approved): 13
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- The committee recommends moving the current lay summary to the section requesting a brief high-level summary of the study.
- Rewrite the lay summary so that it may be understood by nonscientific members of the committee – including stating that this is a dual adenoviral based therapy that is being produced by a commercial manufacturer and sent to the research pharmacy. The current response references the study manual but should instead provide a concise description of the product in plain language.
- The protocol should explicitly state that two separate adenoviral subunits are required within each cell to reconstitute therapeutic activity and clarify how this dual-component approach differs from traditional adenoviral replacement therapies.
- Include a description of the use of a transposable element to integrate the wild-type CYBB gene into the genome. Also mention that integration is expected to occur at random sites, with the potential for insertional inactivation. Relevant information provided in the Recombinant DNA – Special Considerations section may be incorporated to strengthen the description.
- Spell out and provide a description of the treatment regimen - O6-benzylguanine (O6BG) and temozolomide (TMZ).

- Describe the conditioning regimen associated with the treatment as it differs from the gene therapy product itself.
- Describe the prophylactic measures for immune reactions in the protocol.
- Clarify whether the agent will be stored in the main pharmacy or IDS pharmacy.
- Include a post exposure response plan for staff handling the study product in the event of a potential needlestick injury during reconstitution of the study product in the pharmacy and preparation prior to administration.

5 New submission – Laboratory

IBC-P00002138 Comparative clam genetics and biominearlization

PI MH

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: The lab proposes to use clams as a readily available invertebrate model to study skeletal structure regeneration and repair after damage. The clam specimens will be collected from local New England waters around Boston. Gametes will be obtained by manual excision, and genetic manipulation will be assessed by electroporation of PGEM-based plasmids and CRISPR/Cas9 to evaluate editing efficiency. Plasmid preparations will be conducted at BSL-1 work practices and procedures. The electroporation into sperm of mollusks (clams) will be done at BSL-2 work practices and procedures.

Motion: Modifications Required for Approval

- Majority (Approved): 13
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Note that only updated methods should be included in the submission. The committee recommends adding a statement noting that the protocol will be amended if procedures or methods change in the future.
- List the genes contained in the pGEM-based plasmids and specify the CRISPR/Cas9 vector to be used, including the target genes for genome editing.

- Clarify which cell populations will undergo electroporation and describe the culture conditions following fertilization.
- Describe experiments involving injection of adult clams in this section as mentioned later in the protocol.
- Clarify how clams are obtained, handled, and stored in the lab. Describe the process for extracting gametes, explain whether fertilized embryos are expected to reach the larval stage, and outline the subsequent experimental steps.
- Specify the tools used to open clams, as these activities may pose safety risks.
- Clarify the planned use of syringes for injecting adult clams.
- Clarify how solid clam wastes will be discarded in the lab.
- Include the potential biohazards associated with the clams - presence of viruses and bacteria.
- Describe work done with *E.coli*.
- Provide additional details on the field collection and transport of clams. In addition to the potential biohazards associated with the clams, the protocol should describe how staff will safely collect and transport specimens (e.g., use of appropriate outdoor gear (winter weather gear, waterproof footwear etc), and whether collections are conducted individually or as a team.
- Given clams are from around Boston and may have bacteria and viruses, include the use of PPE when collecting and handling them. Toxic blue-green algal blooms can occur in local waters, include precautionary measures in the protocol, including whether investigators will monitor state advisories and avoid collecting clams during algal bloom events.
- Note that all staff involved in the shipping of biological materials must complete the Shipping training.
- Update ‘Escherichia coli - (enteroinvasive)’ to ‘Escherichia coli K12’ and include its source.
- Define the abbreviation ‘AM’.

- Check off 'III-D-8 (Experiments Involving Gene Drive Modified Organisms (Organisms generated by recombinant or synthetic nucleic acid molecules shall be conducted at a minimum of Biosafety Level 2 (BSL)-2.'
- Indicate the vectors used.
- Specify the genes that will be used with the vectors.
- Check off 'Red Biohazard Waste Container'.
- Check off 'necropsy' if tissues will be collected for histology.
- Indicate where clams be housed pre and post electroporation.
- The committee recommends evaluating alternate safety devices with the team and/or wear cut-resistant gloves when working with razor blades.
- Specify the material being transported to Marine Biological Laboratories office lab spaces.
- Specify the materials being shipped and the location.
- Include a new BSL-2 entry for work with gametes and plasmid electroporation per NIH Guidelines.

IBC-P00002061 Testing vaccine formulations in vitro using rhesus macaque white blood cells

PI: SVH

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: This protocol involves the in-vitro stimulation of cryopreserved peripheral blood mononuclear cells (PBMCs) and plasma obtained from healthy infant and adult Indochinese rhesus macaques to evaluate the immune-modulatory effects of candidate pneumococcal conjugate vaccine formulations provided by a sponsor. Vaccine formulations contain pneumococcal polysaccharides from PCV20 combined with various adjuvants, including aluminum hydroxide, aluminum phosphate, ODN-1018 (CpG), CRM197, MPLA, and QS-21. All components are sterile, GMP-manufactured. Cells will be thawed, cultured, and stimulated under BSL-2 conditions using autologous plasma or stimulated directly with vaccine formulations. For some assays, monocytes, B cells, and T cells will be FACS-sorted prior to stimulation. Downstream analyses include cytokine quantification by Luminex/Olink and flow cytometry on fixed cells. All proposed work will be conducted at BSL-2 work practices and procedures.

Regulations Applicable to this Protocol: NIH Guidelines III-F.

Motion: Modifications Required for Approval

- Majority (Approved): 12
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Indicate how solid and liquid waste is handled and disposed of. Note that all solid waste must be disposed of in a biohazard bag, sealed inside a BSC and then disposed of in a red biohazard bin. All liquid waste must be first decontaminated with final concentration of 10% bleach followed by sink disposal after 20 minutes of contact time.
- Clarify if the NHP cells will be fixed at the core facility or in the lab.
- A consultation with OHS is required for all personnel in the lab listed on the protocol due to the work with Diphtheria Toxin. An email has been sent to the lab with the attached form making an appointment with OHS to discuss the Diphtheria vaccine.
- Include PBMCs derived from the NHP blood.
- Clarify the use of a cell sorter as described in the protocol.
- Confirm whether the lab will be shipping any materials domestically or internationally. If so, note that lab members are required to complete the Shipping and Dry Ice training.
- Additional biosafety enhancements are not required per this protocol.

6 Laboratory Amendments

IBC-A00000912-2 Amendment 2 : Performing functional assays using the MA900 Multi-Application Cell Sorter

PI: LC

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: In this amendment, the laboratory will inoculate primary lymphocytes isolated from mice with M13 filamentous bacteriophages. Bacteriophages, including M13, are viruses that can only infect bacteria, not human

cells. M13 is a member of the Ff group of Inoviruses, a family of filamentous phages thatinfect Enterobacteriaceae (e.g., E. coli) without lysing the host cells. Primary lymphocytes will be harvested from mouse spleen, lungs, lymph nodes, and gut following enzymatic digestion with DNase I and Collagenase IV, and mechanical dissociation. Cell sorting of primary mouse lymphocytes incubated with M13 filamentous phages will be done at BSL-1 and mice handling will be done at ABSL-1 work practices and procedures.

Motion: Modifications Required for Approval

- Majority (Approved): 13
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Clarify if the lab will be making or amplifying the M13 phage library. If so, include *E.coli* in this section.
- Clarify whether primary lymphocytes are isolated first and then mixed with phage, or whether phage are added directly to cell suspensions from spleen and other tissues prior to sorting lymphocytes.
- Include what will be done with the phage or lymphocytes following cell sorting.
- Provide an additional sentence describing what the phage library encodes. Clarify whether the antibody fragments are of human or mouse origin, whether anything else is fused to these fragments, and whether the fragments are displayed on the phage surface.
- Clarify if the lab will perform functional assays on cells, including stimulation, as suggested by the title of the protocol and describe the experiments.
- Clarify how lymphocytes will be extracted without the use of sharps.
- Indicate 'homogenizer'.

IBC-A00001953-3 Amendment 3 : Mitochondrial Transplantation in Heart Donation after Circulatory Death: Pre-Clinical Study

PI: SE

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: The goal of the study is to enhance donor heart viability and

availability by evaluating mitochondrial transplantation for ischemic heart recovery and developing a partial heart transplantation approach using human donor valve tissue for pediatric valve replacement. This was previously evaluated using non-clinically viable human donor hearts maintained ex vivo on a perfusion system, into which viable mitochondria isolated from non-ischemic tissue were delivered to assess recovery from ischemia-reperfusion injury. In this amendment, the lab will now perform partial heart transplantation studies using human donor valve tissue that will be resected, reconstructed, and implanted into a large animal model (pigs). Animals will be observed for 4 hours after implantation during which echocardiography and pressure tissue collection. Mitochondrial isolation from cardiac cell culture, heart procurement, and ex-vivo perfusion work will be done at BSL- 2. Donor valve tissue resection, reconstruction, and implantation into animals will be performed under ABSL-2 inoculation ABSL-1 housing.

Motion: Modifications Required for Approval

- Majority (Approved): 13
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Clarify which pathogens would preclude the tissue from being used, whether the hearts or blood are tested for pathogens, and whether “implanted into the animal” refers to a subcutaneous implant.
- Describe how surgical supplies soaked in 10% bleach in the perfusion room will be handled safely to avoid cuts or lacerations and indicate whether disposable surgical tools could be used as an alternative.
- Update "procedure room" to "Surgical OR".
- Indicate what kind of transplantation will be performed.
- Clarify how surfaces will be disinfected i.e. spoklenz or clidox.
- Note that there is no BSC in the rooms specified in ARCH; consult with lab safety.
- Uncheck ‘Standard ARCH PPE’.

IBC-A00001987-2 Amendment 2 : Modeling Down Syndrome Neurogenesis

PI: BK

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: The lab seeks to understand the molecular mechanisms underlying Down syndrome, which is characterized by impaired neural stem cell proliferation, migration, and differentiation, using human induced pluripotent stem cells (hiPSCs). The hiPSCs are differentiated into neural progenitor cells (NPCs) and microglia to enable organoid assembly and model cortical development. The current research examines molecular pathways contributing to impaired NPC proliferation and migration, focusing on the aberrant activation of transposable elements (TEs) such as LINE1, using the FDA-approved nucleoside reverse transcriptase inhibitor lamivudine. In this amendment, the lab proposes to use a third- generation replication-defective lentiviral vector to deliver an shRNA construct targeting LINE1 into NPCs. Transduced NPCs will be analyzed for changes in proliferation and migration using established immunohistochemical and imaging methods. Microglial identity post hiPSC differentiation will be determined by flow cytometry. All work with human iPSCs and lentiviral vectors will be conducted at BSL-2.

Regulations Applicable to this Protocol: NIH Guidelines Section III-D.

Motion: Modifications Required for Approval

- Majority (Approved): 13
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Remove any mention of future experiments that would be addressed in subsequent amendments.
- Replace googles with safety glasses.
- Note that a staff member is approaching their due date for the annual safety training.
- Clarify why Section III-E-1 was selected and whether the lab uses PCR primers.
- Specify "Lentivirus human immunodeficiency virus 1".
- Update ‘Bleach’ to ‘70% Ethanol’.
- Indicate “Yes” as VSVg is not the native viral envelope.

- Consider adding a control vector such as a non-targeting shRNA or luciferase.
- Include flow cytometry for materials processed outside of a biosafety cabinet.
- Clarify whether the lab will ship RNA for sequencing. If so, note that staff must complete the shipping training before shipping biological materials.
- Add a BSL-1 entry to cover RNA processing from cells, microscopy, etc.
- Additional biosafety enhancements are not necessary per this protocol.

IBC-A00001178-5 Amendment 5 : Single-Cell Studies of Tissue Immunity and Inflammation

PI: JOM

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: This amendment expands the scope to include recombinant constructs for Influenza A virus, Respiratory syncytial virus (RSV), and Human rhinovirus (HRV) to investigate viral replication, gene expression, and host responses. For RSV, full-length genomes and helper plasmids will be assembled in vitro, viral RNA generated by in vitro transcription, and both reporter virus and minigenome systems are developed for controlled expression studies. For HRV, infectious clones will be built from overlapping cDNA fragments, transcribed into RNA, and transfected into HeLa cells to recover and analyze viral progeny. Subgenomic replicons expressing fluorescent (GFP) or luciferase reporters will be employed for replication assays. Human and mouse cell cultures will be experimentally infected with HRV under BSL-2 conditions, and viral replication and host responses will be evaluated via qPCR, ELISA, plaque assays, and fluorescence imaging. Lipid nanoparticles will be used to deliver mRNA or siRNA/shRNA for controlled gene expression and knockdown studies. All work involving Influenza A, HRV, RSV and LNP transfections will follow BSL-2 practices and procedures.

Regulations Applicable to this Protocol: NIH Guidelines sections III-D, III-E, and OSHA Bloodborne Pathogen Standards.

Motion: Modifications Required for Approval

- Majority (Approved): 13
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- CT has an LD50 of 250 µg/kg in humans. Specify the amount stored in the lab and the quantity transported to ARCH at one time.
- Remove the reference to "Line 32" if it was included inadvertently, as it does not appear to correspond to a specific mouse strain or cell line.
- Indicate which cell types or animals will be infected downstream with the viral constructs.
- The committee recommends using CHERP-assigned amendment numbers to avoid confusion. The proposal references amendments up to Amendment 8, but only Amendment 5 is under review.
- The protocol lists "mechanical dissociation, enzymatic and chemical digestion, mechanical digestion, and centrifugation." Clarify whether any equipment outside the tissue culture hood (e.g., bead-beater or homogenizer) is being used
- Describe the associated risks when working with a cryostat (e.g., sharps hazards, aerosol generation, exposure to infectious or recombinant materials) and outline the measures in place to mitigate these risks.
- Note that some staff members are due for the Annual Research Safety training and the Cryostat and Microtome training.
- Include details on fixation.

IBC-A00001874-3 Amendment 3 : Noninvasive imaging of immune responses

PI: MR

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: The lab focuses on understanding how the tumor microenvironment evolves in response to cancer immunotherapies and autoimmune disease, and on developing improved diagnostic and therapeutic approaches. This amendment introduces an in vivo CAR-T model designed to evaluate the efficacy of the lab's CAR-Enhancer strategy. In this study, immunodeficient mice will first be humanized with human PBMCs, followed by systemic delivery of a non-replicating lentiviral vector encoding the CAR construct. Subsequently, the CAR-Enhancer protein will be administered to assess its ability to selectively expand and activate CAR-T cells within a functional human immune system. The inoculations of PMBC cells in mice will occur at ABSL-2 inoculations, ABSL-1 housing work practices, and procedures. The inoculation of lentivirus will occur at ABSL-2 (72 hours) work practices and procedures.

Regulations Applicable to this Protocol: NIH Guideline section III-D and OSHA Bloodborne Pathogens Standard.

Motion: Modifications Required for Approval

- Majority (Approved): 13
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Provide details of the plasmid components, including the CAR-T fragment, promoter, and any additional genetic elements.
- Include information on potential off-target expression, and any anticipated toxicities (e.g., hepatic effects).
- The protocol references radiation and radioactive mice; as these activities fall outside the IBC's scope, the committee recommends removing all radiation-related language from the submission.
- Confirm the viral vector used and update to HIV-1, not HIV-2.
- Update to include additional planned routes such as subcutaneous, mammary fat pad, and footpad injections.
- Confirm whether safety needles are available for all listed injection routes.
- Clarify whether animal injections will be done in a biosafety cabinet or on bench top. The committee strongly recommends performing procedures in the BSC rather than on a bench top given that these mice are immune suppressed.
- Update to include sharps used for necropsy.
- Update to include Freund's adjuvant to materials transported.

IBC-A00001586-6 Amendment 6 : Human Neuron Core

PI: MS

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: The lab generates human neurons from patient samples to model various neurological disorders to identify therapeutic approaches. The lab is amending its protocol to add a new human cell line BT869, derived from a diffuse midline glioma, and expresses an eGFP construct via lentiviral transduction. The lab is also employing CDKL5 lentiviral vector to overexpress CDKL5 in iPSCs from patients with CDKL5 deficiency. iPSCS will be differentiated into neurons to see if overexpressing CDKL5 reverts patient neuron phenotypes to be more similar to

control neurons. The proposed work involving the human cell line, its lentiviral transduction, and the use of the CDKL5 lentiviral vector will be conducted under BSL-2 work practices.

Regulations Applicable to this Protocol: NIH Guidelines section III-D and the OSHA Bloodborne Pathogens Standard.

Motion: Modifications Required for Approval

- Majority (Approved): 13
- Minority (Against): 0
- Abstention: 0

Modification Requested:

- Add culture of the human cell line BT869 (derived from a diffuse midline glioma) to the BSL-2 work description.

IBC-A00000064-7 Amendment 7 : Recombinant DNA for Wu lab.

PI: HW

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: The lab studies immune receptor signaling pathways that regulate inflammation, cytokine production, and cell death. This amendment proposes the addition of new recombinant DNA work involving THP1-KO-NIRC4 and THP1 MYD88 K2E cells, lentiviral transduction for expression of tagged proteins, and CRISPR/Cas9-mediated MyD88 knockout in RAW264.7 cells. The modified cells will be stimulated with synthetic DNA ligands such as Poly(dA:dT) and HSV-1 DNA fragments to study inflammasome activation and DNA-sensing pathways. All work will be performed under BSL-2 practices and procedures.

Regulations Applicable to this Protocol: NIH Guidelines section III-D and OSHA Bloodborne Pathogens Standard.

Motion: Modifications Required for Approval

- Majority (Approved): 13
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Rewrite this section in plain language so nonscientific members of the committee can understand the main goals of the research.
- Shorten the description of procedures. Listing the procedures is sufficient; details such as buffer pH or NaCl concentrations in wash buffers are not needed.
- The description of cell line work is overly detailed. Plate size, specific media formulations, and timing of splits are not required.
- The section states that cells are disposed of in 10% bleach. Instead, reference that all biological liquid waste will be disposed of by "adding bleach to a final concentration of 10%".
- The general waste statement currently includes both liquid and solid waste being decontaminated with 1:10 bleach. Remove "solid" and revise to indicate that liquid waste is treated by adding bleach to a final concentration of 10%.
- The committee suggests for future amendments and to simplify submissions, the PI should list the cell line followed by the phrase "with mutations as well" to cover potential knockouts and knock-ins.
- Clarify if the lab is transporting infectious materials off-site or to another location. If so, specify the destination and update the Transporting/Shipping section to reflect where the materials are being transported.
- Clarify if HSV-1 is being amplified in the lab. If yes, provide a brief description of the virus propagation process, including the cell lines used and the storage location of the viral stocks.
- Add a description of the specific risks associated with sharps use, such as the increased risk of percutaneous exposure to infectious, recombinant, or toxic materials through punctures, cuts, or lacerations.
- Include the antibiotic resistance genes that you are using for bacterial transformations.
- Remove the storage of HSV from the Select agent or Toxin section.
- Confirm and reconcile whether a second- or a third-generation plasmid system is used for lentivirus. Update the plasmid information to reflect the system.
- Clarify whether sharps will be used.

7 3 year Lab Study Renewals

IBC-RN00000334-4 Renewal 4 : Global regulators converge to orchestrate metabolism, biofilm, and pathogenesis

PI: PW

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: The goal of the lab is to understand how to manipulate carbohydrate signals to shift V. cholarae to a state of low infectivity and virulence. This renewal expands the lab's prior work on Vibrio cholerae by introducing recombinant constructs to study small RNAs (sRNA) regulated by acetylation of the transcription factor CRP. The lab will generate a CRP K52Q acetylation mimic mutant and a VSVG-tagged Hfq construct through double homologous recombination to identify sRNAs specifically activated by CRP acetylation. Affinity purification and RIL-seq will be performed to isolate and sequence sRNA–mRNA pairs in both wild-type and mutant backgrounds. Downstream analyses will include qRT-PCR and Western blotting and RNA sequencing to evaluate effects on mRNA stability, translation, and biofilm regulation. Vibrio cholerae cloning, fractionation experiments, growth experiments, RNA preparation experiments, and chromatin immunoprecipitation will be done at BSL-2.

Regulations Applicable to this Protocol: NIH Guidelines section III-D.

Motion: Modifications Required for Approval

- Majority (Approved): 13
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Indicate which experiments will utilize pBAD-TOPO and pFLAG-CTC plasmids.
- Include the description of Vibrio cholerae infectious dose in the scientific description.
- Update the E.coli entry to include Hfq.
- Reconcile whether mutations will be generated in ArcAB or in PepA.
- Clarify if VC0176 will be mutated and specify all the genes proposed for mutation.

- Include Hfg in the Vibrio cholerae entry.
- Select Section III-E and III-E-1 since cloning studies are proposed.
- Select III-F and III-F-1 if any of the cloning will involve DNA fragments generated by PCR.
- Update pBAD-Topo to indicate which genes gene family are present in these plasmids.
- Remove references to only having one BSC.

8	**Human Study Annual Reconfirmation**
IBC-P00002000	ALD-107: An Expanded Access Protocol for Patients with Early Cerebral Adrenoleukodystrophy (CALD) to Receive Elivaldogene Autotemcel Non-conforming Drug Product PI: **CD** Motion: Approved Discussion: This study is active and open to enrollment.
IBC-P00001775	A phase II trial to evaluate the safety and efficacy of oral encapsulated Microbiota Transplantation Therapy in peanut allergic patients. PI: **RR** Motion: Approved Discussion: The study is active and open to enrollment. There have been 17 study participants that have completed the study. There are no reported SAE's.

9 Administrative Reviews

IBC-RN00001730-1 Renewal 1 : Measles and Vaccinia: Self vs Non-self RNA Discrimination by the Innate Immune System

PI: **SH**

Motion: Administrative Approval

Discussion: This is a three-year renewal with no updates or changes to the risk assessment.

IBC-RN09-131-5 Renewal 5 : Injection of cardiotoxin in live mice to induce muscle degeneration

PI: **EG**

Motion: Administrative Approval

Discussion: The renewal adds an additional mouse strain (KDM6A) to support their ongoing studies on muscle regeneration. This update does not change the risk assessment.

IBC-RN99-179-5 Renewal 5 : Functional Imaging of Disease

PI: **AP**

Motion: Administrative Approval

Discussion: This is a three-year renewal with no changes or updates to the risk assessment.

IBC-A10-275-6 Amendment 6 : Molecular Basis of Cancer

PI: **SP**

Motion: Administrative Approval

Discussion: The lab examines signal transduction pathways in tumor cells to identify the pathways or molecules that promote angiogenesis. The amendment includes the addition of two oncogenic cell lines G-402 and A-204 for cell proliferation and cell survival assays following treatments with pharmacological inhibitors. Work will be conducted at BSL-2 work practices. There is no change in the risk assessment.

IBC-A00002033-2 Amendment 2 : Taysha REVEAL 101 Study

PI: **DL**

Motion: Administrative Approval

Discussion: The pharmacy manual was updated. This update does not change the biosafety risk of the study product.

IBC-RN05-057-5 Renewal 5 : Molecular Genetics of Neuromuscular Disorders, Autism and Interstitial Cystitis

PI: **LK**

Motion: Administrative Approval

Discussion: This is a three-year renewal with no changes to the risk assessment.

IBC-A00000709-6 Amendment 6 : Human Immune Function Studies and The Genes Involved

PI: **TC**

Motion: Administrative Approval

Discussion: This amendment changes the PI and updates lab locations for sample storage.

IBC-RN00000986-2 Renewal 2 : Zinc nutritional status in preterm infants

PI: **ZH**

	Motion:	Administrative Approval
	Discussion:	This is a three-year renewal with no changes or updates to the risk assessment.

IBC-RN00001654-1 Renewal 1 : Cell adhesion assay using centrifugal force

	PI:	**WW**
	Motion:	Administrative Approval
	Discussion:	This is a three-year renewal with no changes to the risk assessment.

IBC-RN00000183-4 Renewal 4 : Biomarker Discovery

	PI:	**RL**
	Motion:	Administrative Approval
	Discussion:	This lab's renewal has been updated to reflect a change in one collaborator, the addition of the human cell line HEK293, and revised language pertaining to blood draws. These updates do not impact the risk assessment.

IBC-A00002039-1 Amendment 1 : Cabaletta 201-001

	PI:	**SP**
	Motion:	Administrative Approval
	Discussion:	The lab added new team members to the protocol. This does not change the risk assessment.

10	**Laboratory Study Annual Reconfirmation**

99-179 Functional Imaging of Disease

	PI:	**AP**

IBC-P00000301 Regulation of protease and protease inhibitors in a mouse model of inflammation.

PI: **KY**

IBC-P00001598 Immune and intestinal investigations in neonates

PI: **AO**

IBC-P00000328 Mouse and human cancer cells

PI: **GD**

IBC-P00001194 Characterizing the immune response to respiratory virus infection in the nasal mucosa

PI: **BH**

IBC-P00001785 Investigating Mechanisms of Attention and Attention Dysfunction

PI: **BF**

IBC-P00000191 Gastrointestinal Organoid Culture and Implantation into Mice

PI: **DB**

IBC-P00000639 Human T cell proliferation and BH4

PI: **CW**

IBC-P00000242 Studying autism and rare neurodegenerative disorders in neurobiological systems

PI: **TY**

IBC-P00000719 Signal transduction in neutrophils-part 1

PI: **HL**

IBC-P00001257 Control of gene expression in Acinetobacter baumannii

PI: **SD**

11-246 Toggling cell expression and states of choroid plexus cells and neurons in rat, mouse, and cell culture models

PI: **ML**

04-112 Gene Transfer in Mammalian Central Nervous System Neurons Mediated by Adeno-Associated Virus

PI: **CC**

IBC-P00002025 Investigations on the Role of S1PRs In Bacterial Meningitis

PI: **TH**

IBC-P00001963 Investigations of S1P Signaling as a Therapeutic Target in Congenital Heart Disease

PI: **TH**

IBC-P00000973 Axon repair and regeneration

PI: **JQ**

IBC-P00002019 Immune Studies of Rheumatologic Diseases

PI: **MC**

IBC-P00001873 Developing a Swine Model of Repetitive Mild Traumatic Brain Injury

PI: **RM**

IBC-P00001868 Direct activation of pain-sensing neurons by bacteria and their ligands

PI: **CW**

11-016 Effect of Systemic Metabolic Status on Cancer Incidence and Progression

PI: **NK**

IBC-P00002045 Micro/nanoparticle for melanoma treatement

PI: **DK**

08-075 The roles of the Thyroid receptor interacting protein-11 (Trip 11) in adipocytes

PI: **PS**

04-237 Molecular Mechanisms of Tumor Progression and Angiogenesis

PI: **RW**

IBC-P00000726 Role of insulin resistance in the development of metabolic syndrome

PI: **JM**

IBC-P00001287 CRISPR screen in ALL mouse model

PI: **NK**

08-031 Plasticity in the Adult Somatosensory System after Peripheral Nerve Injury or Inflammation Mice

PI: **CW**

IBC-P00000384 Gene regulation in hematopoiesis

PI: **DB**

IBC-P00000834 Stem Cell Regulators in Zebrafish

PI: **TN**

IBC-P00000904 Vaccine development against Salmonella and Shigella

PI: **YL**

10-145 Evaluation of vaccines against Salmonella Typhi

	PI:	**RM**
IBC-P00000373	Generation of genetically modified mice	
	PI:	**GD**
IBC-P00000955	Combined effects of VEGF isoforms and anticoagulants on lung regeneration	
	PI:	**MP**
IBC-P00001987	Modeling Down Syndrome Neurogenesis	
	PI:	**BK**
IBC-P00001772	Mechanisms of host immunity	
	PI:	**JC**

11	**Completions**
IBC-P00000268	The effect of silencing sensory neuron on chronic allergic airway inflammation
	PI: **CW**