CHILDREN'S HOSPITAL BOSTON
Meeting of Boston Children's Hospital Institutional Biosafety Committee
AGENDA
9/18/2025 11:30 AM to 1:00 PM
KARP 4th Floor, Conference Room

Members Present: MM, IJ, SG, DF, SVH, EG, KK, CH, DC, EC, JM, SD, BS, PW, HD, AR, TW, CH, SL

Members Absent: LW

Guests: None

RLSO: LA, JF, DW

SD chaired the meeting.

1. IBC Meeting Minutes

Boston Children's Hospital Institutional Biosafety Committee meeting (07/17/2025)

Boston Children's Hospital Institutional Biosafety Committee meeting (08/21/2025)

IBC Meeting Minutes were unanimously approved by the committee.

Committee Decision:

Motion: Approved

Majority (Approved): 18

Minority (Against): 0

2. Administrative Updates

- **Annual Research Fair:** October 23rd, 1:00 pm - 3:00 pm at KARP Boardroom

- **U.S. Poliovirus Containment Survey – Update**
  - **Committee Discussion:** The polio vaccine questionnaire has been reinstated, and the team is drafting a questionnaire to distribute to all PIs to verify possession of any poliovirus materials.

- **NIH Modernize and Strengthen Biosafety Oversight**: NIH Launches Initiative to Modernize and Strengthen Biosafety Oversight | National Institutes of Health (NIH):
  - **Committee Discussion:** NIH is launching a new initiative to expand biosafety oversight beyond recombinant and synthetic nucleic acids. The initiative will also evaluate low-risk recombinant work, including Risk Group 1 agents, which may be subject to reduced oversight. The first phase will be implemented this fall to build community awareness and encourage public feedback.

- **Herpes Simplex Virus (HSV-1) Training**

  - **Committee Discussion - Minor Modifications Requested:**
    1. Training content should be broadened beyond oncolytic HSV to include HSVs used as vector carriers (e.g., for CDA).
    2. Incident reporting language should be updated to direct reports to supervisors and managers rather than only the lead pharmacist.
    3. In the event of a needlestick, a risk assessment will be conducted to determine the need for antivirals.

    Committee Decision:

    Motion: Approved with minor modifications

    Majority (Approved): 18

    Minority (Against): 0

- **Research Laboratory Blood Sampling by Unlicensed Study Staff via Venipuncture Policy/Procedure and The Phlebotomy Space Criteria in Basic Research Buildings & Laboratories**

  - **Committee Discussion:**

1. A request was made for a list of individuals who may perform blood draws to support risk assessment and confirm hepatitis B protection.

2. The committee confirmed that either running water or alcohol-based sanitizer is acceptable for hygiene stations.
3. A suggestion was made to establish a common, designated phlebotomy area to simplify inspections and allow staff to schedule blood draws without using individual lab spaces.
4. The committee discussed whether the six-month evaluation is necessary after 20 venipunctures, noting that state certification is typically achieved at that point.
5. Clarification was requested on the policy requiring 20 initial venipunctures followed by a competency evaluation with an additional 10 venipunctures.
6. The committee noted that the training is intended to ensure safe practices for personnel without formal state certification, particularly when blood draws are performed outside the hospital setting.

Committee Decision: Approved

Motion: Approved with pending clarifications

Majority (Approved): 17

Minority (Against): 1

- Advancing Laboratory Safety: The Impact of Community Outreach and Training Initiatives at Boston Children's Hospital - ABSA Presentation

  ABSA poster submission was presented to the committee during the meeting.

3 Laboratory Events

1. **Puncture with a needle**

- **Incident summary:** A researcher sustained a puncture from an unguarded butterfly needle while changing a syringe on the 3-way connector of the perfusion setup.
- **Root Cause:**
  - Not paying attention to details.
  - The needle was unguarded.

- **Corrective Actions:**
    - The lab will place the needle in the tip box used during setup to secure it between syringe changes.

2. Cut/Laceration by a scalpel

- **Incident summary:** A researcher sustained a cut to their thumb while attempting to remove a frozen, unidentified human sample from a cryovial using a disposable scalpel.
- **Root Cause:**
    - Not evaluating safer sharp alternatives when removing the sample.
    - The Researcher was rushed due to time.
- **Corrective Actions:**
    - Use safety sharps such as plastic spatulas and ceramic blades, which reduce cutting hazards.
    - Allow adequate time to complete the procedures and avoid rushing.
    - Evaluate lockable clamps or pliers to securely hold the cryovial during sample extraction.

4	**New submission – Clinical**	
IBC-P00002132	VALOR	
	PI:	**LH**
	Motion:	Modifications Required for Approval – Return to IBC Analyst
	Discussion:	**IBC Discussion:** This is a Phase 1/2 multicenter, open-label, dose-escalation and expansion study of ASP2957, a non-replicating rAAV gene therapy vector, in patients with X-linked myotubular myopathy (XLMTM). XLMTM is a rare congenital myopathy caused by mutations in the MTM1 gene, which encodes myotubularin, a protein essential for the development and maintenance of skeletal muscle cells. ASP2957 is a non-replicating rAAV gene therapy vector with an engineered capsid (MyoAAV3.8) derived from wild-type AAV9, carrying a DNA sequence of the human MTM1

gene under the control of a muscle-specific promoter. The investigational product will be prepared and stored in the BCH Pharmacy and then transported to the participant's room for intravenous administration. Blood, stool, urine, saliva, and muscle biopsy will all be collected and transported to the lab for processing.

Regulations Applicable to this Protocol: The NIH Guidelines III-C and OSHA Bloodborne Pathogen Standards.

Motion: Modifications Required for Approval

- Majority (Approved): 18
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Provide a 2–3 sentence summary (in lay terms) that can be easily understood by non-scientific members of the committee. Note that the first paragraph is a text import from the IRB.
- Provide additional details regarding the timing of the two doses. Specify whether subjects will remain in-house for both doses and under what circumstances the second dose would be cancelled.
- Update the statement to specify that residual liquid will be inactivated with fresh 10% bleach for 30 minutes in the pharmacy before disposal.
- Clarify the statement: "Occupational exposure requires reporting to sponsor." Specify what information must be reported to the sponsor in the event of an exposure. Additionally, indicate what signs and symptoms research personnel (e.g., pharmacy, nursing, and other staff) should monitor for following potential exposure, noting that the previous generation vector was associated with fatal hepatitis.
- Specify the tests/techniques used for the testing of anti-capsid antibodies described in the protocol. Are these tests investigational or correlative? Would exposures be subject to testing?
- Describe what is meant by 'novel' in the statement "novel engineered capsid, MyoAAV3.8." The protocol also states: "To mitigate these risks, participants who

test positive for MyoAAV3.8 TAb are excluded from study participation." If the capsid is novel and engineered, clarify how participants could test positive for it prior to the study.

- Note that additional PPE is not required for post administration of study drug.

5	Laboratory Amendments

IBC-A04-253-8 Amendment 8 : Characterization of Mutant Mouse Strains and Human Genetic Diseases

PI:	**MF**
Motion:	Modifications Required for Approval – Return to IBC Analyst
Discussion:	**IBC Discussion:** The laboratory is focused on understanding the basis of red blood cell development using genetic tools such as CRISPR/Cas9, viral vectors, cell culture systems, and transgenic mouse models. The amendment adds experiments to overexpress ACVR1b, ACVRL1 (genes involved in blood vessel development), and their fusion using a GFP-FLAG-Lenti_BE583 vector under puromycin selection in established human cell lines (293T, Hep3b, Huh7, and Hepg2). Work with lentiviral particles and human cell lines will be done following BSL-2 practices and procedures and mouse injections with HSC CD34+ cells will be conducted at ABSL-2 followed by ABSL-1 housing. **Regulations Applicable to this Protocol:** The NIH Guidelines III-D and OSHA Bloodborne Pathogen Standard. **Motion: Modifications Required for Approval** • Majority (Approved): 18 • Minority (Against): 0 • Abstention: 0

Modifications Requested:

- The protocol states: "Unfixed tissue, generally skin, will be employed to generate fibroblast lines from patients." Provide additional details on the process by which

patient fibroblasts are obtained and clarify whether patient skin samples will be handled in the laboratory. If so, describe the related procedures.

- List and describe the GFP-FLAG-Lenti_ BE583.
- Include the newly added genes ACVR1b, ACVRL1 and the ACVR1B–ACVRL1 fusion construct.
- Remove the GFP-FLAG-Lenti_BE583 construct and instead include it under lentivirus human immunodeficiency virus 1 (HIV 1) entry.
- Include 'work with unfixed human tissues' if fibroblast primary cell lines will be generated from unfixed patient tissues in the lab.

IBC-A00001438-6 Amendment 6 : Immune Studies in Human and Murine Samples

PI:	**PN**
Motion:	Modifications Required for Approval – Return to IBC Analyst
Discussion:	**IBC Discussion:** The lab is studying the genetic and immunological factors that mediate rheumatologic diseases by using human samples to study the mechanisms of these autoimmune disorders, followed by testing their hypotheses in mouse models of disease. The amendment includes the intranasally or intratracheally administration of mycolic acid, lyophilized dermatophagoides pteronyssinus (house dust mites) extracts, or mycobacterium avium into mice. Mycobacterium avium is an opportunistic pathogen whose main route of infection is through inhalation of aerosols. Mice infected with mycobacterium avium are euthanized after 5-8 weeks via CO2 post infection then lungs and spleen are collected for analysis. Work conducted with mycobacterium avium is performed at BSL-2 and ABSL-2. **Motion: Modifications Required for Approval** • Majority (Approved): 18

- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Will the Mycobacterial strains be cultured and propagated in the laboratory? If yes, provide detailed description of the procedures that will involve culture and propagation of these strains.
- Detail the downstream analyses performed post mouse inoculation with LPS, Pam3CSK4, PolyI:C, IL-1β, fungal glucan particles, mycolic acid or lyophilized Dermatophagoides pteronyssinus (House dust mite, sterile) extract.
- Clarify the statement, "Experiments will employ intraarticular injection of ASO (1-10ng/joint) to inhibit gene expression to induce gene expression."
- In the Mycobacterial infection, it is mentioned "Lungs and spleen will be collected for downstream analyses". Specify whether these are the only tissues harvested from the inoculated mice. Will the tissues be fixed and/or unfixed. Detail the downstream analyses performed with these tissues.
- Clarify whether work with house dust mite extracts will be done on an open benchtop or in a BSC.
- Include biosafety risk for Mycobacterium and house dust mite extracts.
- Clarify the transport process for bacterial cultures from the lab to the animal facility. Specify whether infected tissues will be fixed before leaving the animal facility.
- Update the protocol to state that transport of unfixed tissues from infected animals (Influenza, CFA, *S. aureus*, *Pseudomonas*, and Mycobacterial strains) will use a primary leak-proof container placed inside a secondary rigid, self-sealing container.
- Update ABSL-2 entry to include animal inoculation with Mycobacterium avium.
- Update ABSL-1 extract to include work with mycolic acid and house dust mite extracts.
- Update the BSL-2 entry to include the strains of Mycobacterium avium.

IBC-A11-052-22 Amendment 22 : Molecular regulation of retinal angiogenesis and retinopathy

PI:	**LS**
Motion:	Modifications Required for Approval – Return to IBC Analyst
Discussion:	**IBC Discussion:** The lab is studying the molecular mechanism of retinal angiogenesis during development and

in retinopathy. The amendment includes a new target gene, GDF15 (growth/differentiation factor 15) that will be used in currently approved AAV studies. Procedures are performed at BSL-1 and ABSL-1.

Regulations Applicable to this Protocol: The NIH Guidelines III-E.

Motion: Modifications Required for Approval

- Majority (Approved): 18
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Clarify that the statement also applies to lentiviral constructs of oncogenes: "All work with AAV or lentivirus constructs expressing oncogenes and tumor suppressor genes will be conducted at BSL-2."
- For Adeno-associated virus (AAV), add GDF15 gene insert.
- In the human materials, include the use of IPSC- derived organoids.
- The animal section for AAV vectors notes that lentivirus is administered via subcutaneous and tail vein injections; however, the lentivirus section only mentions intravitreal delivery. Update the lentivirus section to include subcutaneous and tail vein administration.
- Include tail vein injections in the laboratory procedures.
- Clarify whether samples intended for sectioning will be fixed prior to processing.

IBC-A00000064-6 Amendment 6 : Recombinant DNA for Wu lab.

PI: **HW**

Motion: Modifications Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion:** This lab studies immune receptor signaling pathways that regulate inflammation, cytokine production, and cell death. This amendment involves the use of a genetically engineered TLR9-immortalized mouse dendritic cell line expressing recombinant transgenes, including the IL-1 receptor and human TLR4/MD-2/CD14, along with NF-κB/AP-1–regulated reporter systems. It also includes the use of synthetic HSV-derived oligonucleotides to transfect cells for activation of TLR9-dependent immune responses. All procedures involving synthetic HSV-derived oligonucleotides and the transfection of mouse cells will be conducted following BSL-1 work practices.

Motion: Modifications Required for Approval

- Majority (Approved): 18
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Clarify and describe what 'other molecular assays' will be conducted on the cells.
- Clarify if viruses will be used to infect TLR9 cells or only free oligonucleotides.
- As HSV-1 oligos are not infectious, they may be handled using BSL-1 work practices. Update this information.

6	**Administrative Reviews**
IBC-A00002024-1	Amendment 1 : A Phase 1/2 Study to Assess the Safety and Efficacy of OCU410ST for Stargardt Disease

PI: **AF**

Motion: Approved

Discussion: The amendment updates the protocol name from Phase 1/2 to Phase 2/3. Study visit frequency has been reduced and long term follow ups have been added one year after surgery. The control group also has the opportunity to crossover to the treatment arm after the study database is locked.

IBC-RN00001091-2 Renewal 2 : Development of oculomotor circuits

PI: **MW**

Motion: Administrative Approval

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

IBC-RN00001104-2 Renewal 2 : Dirty mice and skin immunology

PI: **SD**

Motion: Administrative Approval

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

IBC-A00002127-2 Amendment 2 : Molecular regulation of neurovascular retina

PI: **ZF**

Motions: Administrative Approval

Discussion: This protocol studies how new blood vessels form in the eye during normal development and in eye disease. AAV and lentiviral vectors are packaged in Human 293 T cells, then purified. AAV and lentiviral vectors are used to transduce human and mouse cells and then injected subretinal or intravitreally in mouse models. Retinal tissues are collected and analyzed for vascular or neuronal phenotypes. The amendment adds N/TERT-1 human keratinocyte cells, obtained from a collaborator which are used for RNA and

protein extraction. All work with human cell lines is conducted under BSL-2 procedures. There is no increase in biosafety risk.

IBC-A00001874-2 Amendment 2 : Noninvasive imaging of immune responses

PI: **MR**

Motion: Administrative Approval

Discussion: This amendment adds new human cell lines that will be transduced to express the Luc2 luciferase gene and the GFP gene under already approved procedures. This additional does not change the risk assessment.

IBC-A00001404-3 Amendment 3 : Control of tissue homeostasis and inflammation

PI: **XZ**

Motion: Administrative Approval

Agenda Notes: The lab is updating their shipping information. This change does not impact the risk assessment.

IBC-RN08-123-4 Renewal 4 : Signaling in oncogenic epithelial cell transformation

PI: **SH**

Motion: Administrative Approval

Discussion: Three- year renewal with no updates or changes to the risk assessment.

IBC-A00001315-8 Amendment 8 : Mechanisms of Platelet Production

PI: **JI**

Motion: Administrative Approval

Discussion: The amendment adds human iPSCs as a source of hematopoietic stem cells and megakaryocytes to support studies aimed at elucidating the molecular pathways that regulate platelet production.

IBC-A00000103-5 Amendment 5 : Wnt Signal Transduction in Vertebrates

PI: **AO**

Motion: Administrative Approval

Discussion: This amendment updates the PI ownership, removes all animal work, and updates the lab room location. This change does not impact the risk assessment.

IBC-RN00001033-2 Renewal 2 : Modeling cardiac arrhythmias

PI: **VB**

Motion: Administrative Approval

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

IBC-A00002130-1 Amendment 1 : Krystal Bio Phase 1

PI: **RP**

Motion: Administrative Approval

Discussion: The amendment specifies that contact precautions will be followed rather than airborne and contact precautions. This does not change the risk assessment.

IBC-A00002055-1 Amendment 1 : Arcturus Phase 2

PI: **GS**

	Motion:	Administrative Approval
	Discussion:	Protocol updated to indicate that airborne precautions are not required. This does not change the risk assessment.

7	**Laboratory Study Annual Reconfirmation**
11-078	Sensory Physiology of Normal and Genetically Engineered Organisms
	PI: **MTD**
IBC-P00001995	Characterization of Immune Cell Specificity and Function in Human and Murine Autoimmunity and Cancers
	PI: **AK**
IBC-P00000104	Reference Laboratory for Clinical Research Samples
	PI: **NR**
05-130	Inhibition of Angiogenesis using Adenoviral Semaphorins
	PI: **DB**
IBC-P00000420	Human cell responses to Staphylococcus aureus proteins
	PI: **YL**
IBC-P00000002	Cellular Signaling in the Primate Eye
	PI: **MTD**
IBC-P00001399	Endocardial Fibroelastosis
	PI: **IF**

IBC-P00000912 Performing functional assays using the MA900 Multi-Application Cell Sorter

PI: **LMC**

IBC-P00001942 Impact of Respiratory syncytial virus on early life immune and lung function

PI: **TC**

IBC-P00000323 The role of Staphylococcus aureus in atopic dermatitis model

PI: **RG**

11-052 Molecular regulation of retinal angiogenesis and retinopathy

PI: **LS**

IBC-P00001908 Exploiting Antigen Presentation Pathways for Precision Immune Engineering

PI: **NP**

10-105 Evaluation of vaccines against Staphylococcus aureus

PI: **RM**

IBC-P00001988 Mouse models of infectious diseases

PI: **BS**

IBC-P00001402 Genetic and Optic Dissection of Neural Circuits Controlling Metabolism

PI: **DK**

09-209 The Effect of Genetics and/or Angiogenic Modifiers on Angiogenesis in Mice

PI: **RD**

IBC-P00001315 Mechanisms of Platelet Production

PI: **JI**

IBC-P00000517 Molecular and Genetic Pathogenesis of Marrow Failure, MDS, and Cancer Predisposition

PI: **AS**

IBC-P00001949 Investigation of neural function using AAV in human brain slices

PI: **EO**

IBC-P00001907 Gene manipulation through AAV injection in brain

PI: **EO**

IBC-P00000840 In vitro and in vivo models for the study of capillary and arterio-venous-malformations

PI: **AG**