

Houston Methodist Research Institute IBC Meeting Minutes
Houston, Texas
8/6/2026

Meeting Time Records

Meeting start time: 10:00 am

Meeting end time: 11:29 am

VOTING MEMBER ATTENDANCE				
Name of Member	Status (member or alternate)	IBC role	If Voting Alternate, Member Substitution	Present in Person or Virtually (TEAMS)?
Biana Godin, PhD, M.Sc. Pharm	Chair	Scientific, Affiliated		Yes, virtually
Vicente Zuno, BS, RBP	Member	Biosafety Officer, Affiliated		Yes, virtually
Joan E. Nichols, PhD	Member	Scientific, Affiliated		Yes, virtually
Chas Gray, RPh	Member	Scientific, Affiliated		Yes, virtually
Tanya Herzog, DVM	Member	Animal Expert, Affiliated		Yes, virtually
Edward Graviss, PhD	Member	Scientific, Affiliated		Yes, virtually
Wenhao Chen, PhD	Member	Scientific, Affiliated		Yes, virtually
Daniel Kiss, PhD	Member	Scientific, Affiliated		Yes, virtually
Tamara Steele, BS	Member	Community member, Non-affiliated		Yes, virtually
Jillian Chahal, MPH, CSP	Member	Community member, Non-affiliated		Yes, virtually
Francesca Taraballi, PhD	Member	Scientific, Affiliated		No
Jiangyong Shao, MS	Member	Scientific, Affiliated		Yes, virtually
Nagendran Tharmalingam, PhD	Member	Laboratory representative, Affiliated		Yes, virtually
Anjana Tiwari, PhD	Member	Laboratory representative, Affiliated		Yes, virtually
Dimitrios Wagner, MD PhD	Member	Human gene transfer expert, Non-affiliated		Yes, virtually

Gretchen Gotlieb, MS	Member	Safety representative, Affiliated		Yes, virtually
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NON-VOTING MEMBER ATTENDANCE

Name of Member	IBC Role	Present in Person or Virtually (Teams)?
Brenda Hartman, BA	Ex officio, Director, Central Laboratory Operations	Yes, virtually
Enid Burns	Ex officio, Central Laboratory Operations Safety Representative	Yes, virtually
Michael Smith	Ex officio, Legal Counsel	Yes, virtually
Michael Metcalf	Ex officio, Environmental Safety	No
Tiffany Gunter	Ex officio, Employee Health Representative	No
Astrid Marcela Quiroga	Ex officio, Employee Health Representative	Yes, virtually
Leon Brown, MS	Ex officio, HMRI Radiation safety officer	Yes, virtually
Wanda Quezada, CIP	Ex officio, Director Regulatory Oversight	Yes, virtually
Don Sibley, PhD	Consultant, Expert Reviewer	Yes, virtually

QUORUM INFORMATION

Number of IBC members on the roster: 16

Number required for quorum: 9

All members attending via Microsoft Teams received all pertinent materials before the meeting and were able to actively and equally participate in all discussions

ORP STAFF

Malissa Mayer-Diaz, Safety Committees Manager
Perla J. Rodriguez, Sr. Analyst
Shane Wilson, Analyst
Prince Agyapong, Analyst
Rebecca Corrigan, IACUC Manager
Joylise Mitchell, IACUC Analyst
Joanna Espinosa, Analyst QI & Education

ATTENDANCE STATUS AND VOTING KEY

ABSTAIN:	Present for the vote and not voting "For" or "Against."
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ABSENT:	Absent for discussion and voting for reasons other than a conflicting interest.
RECUSED:	Absent from the meeting during discussion and voting because of a conflicting interest.
SUBSTITUTION:	When regular members and their alternate(s) are listed in the ATTENDANCE table above and an alternate member substitutes for the regular member, this identifies the name of the alternate to indicate which individual is serving as the voting member for this vote. May be deleted if there are no substitutions.

CALL TO ORDER

The Institutional Biosafety Committee convened a virtual meeting via Microsoft Teams on August 6, 2026. The meeting was called to order at 10:00 a.m., with 15 members participating, exceeding the quorum requirement of 9 members.

REPORTS

BSO Report: Non compliance Incident

The Biosafety Officer reported that, on July 16, 2026, a requisition for plasmids intended for use in a research laboratory was placed on hold pending submission of an associated IBC protocol. The materials ordered included:

- A suicide vector designed for generation of gene knockouts in *Streptococcus pyogenes*.
- An expression backbone plasmid.

During follow-up discussions, it was determined that the investigator believed IBC review was not required for the proposed work based on prior guidance received. The Office of Research Protections (ORP) was consulted and clarified that plasmid work involving gene knockouts and Risk Group 2 agents requires IBC review and approval.

The investigator subsequently submitted a new IBC protocol for review. The submission was received in time for full committee review and was included on the current meeting agenda.

Committee

Discussion

Committee members discussed the importance of ensuring investigators and laboratory personnel understand current IBC submission and review requirements. Discussion indicated that the misunderstanding may have stemmed from information communicated at the laboratory management or supervisory level. Members agreed that additional education and communication regarding IBC review requirements for recombinant DNA/plasmid work involving RG2 organisms would be beneficial. The committee acknowledged that corrective action had been taken through submission of the appropriate IBC protocol. The committee recommended continued outreach and education to investigators and laboratory leadership regarding current IBC review requirements to prevent similar occurrences in the future.

ORP Report: NIH Policy Update

ORP informed the committee of a new NIH policy, released July 20, 2026, establishing a federal oversight framework for certain high-risk life sciences research, including dangerous gain-of-function research, international research activities, and enhanced institutional compliance requirements. ORP noted that the policy is not expected to significantly impact the institution's current research portfolio, as existing review processes already align with applicable federal requirements. ORP will conduct a detailed assessment of the policy and evaluate whether updates to committee applications, guidance documents, screening questions, or review procedures are needed.

Committee Discussion

The committee discussed the importance of broadly communicating the new policy to investigators and research personnel to promote awareness and demonstrate institutional due diligence. Members also reviewed the policy's focus on international collaborations and noted that current IBC processes do not consistently capture this information for all research activities. The committee agreed that further evaluation is needed to determine whether revisions to applications, review processes, or continuing review requirements are necessary and emphasized the importance of coordinating with existing institutional mechanisms to avoid duplicative reporting.

The committee supported continued evaluation of the NIH policy by ORP, broad communication of the policy to investigators, and assessment of potential enhancements to committee processes related to international collaborations and compliance oversight. Any proposed procedural changes will be presented to the committee for review and discussion before implementation.

EDUCATION

None provided

CONFLICT OF INTEREST

Committee members were reminded by the IBC Chair to recuse themselves in the event of any conflicts of interest.

OLD BUSINESS

- A list of approved protocols was shown to Committee members prior to and during the meeting.

NEW BUSINESS

- A list of approved amendments via designated member review was distributed to the Committee members one week prior to the meeting and shown during the meeting.

- A list of approved administrative amendments was distributed to the Committee members one week prior to the meeting and shown during the meeting.
- A list of approved continuing reviews via designated member review was distributed to the Committee members one week prior to the meeting and shown to the Committee members during the meeting.

MINUTES REVIEW

The meeting minutes from July 9, 2026 were reviewed. A motion to approve was made and seconded, and the minutes were approved.

Motion: Approved

- Yes votes: 15
- No votes: 0
- Abstained: 0

AGENDA ITEMS

IBC NEW APPLICATIONS

IBC00002775

Title: Research using recombinant mRNA, plasmids & viral vectors to express/deliver therapeutic genes or antibody in tumor, autoimmune disease & neuron degeneration system in both cell line & mouse models to study therapeutic outcomes

Principal Investigator: Shu-Hsia Chen

Study Overview: The committee reviewed a resubmission involving the use of recombinant mRNA, plasmids, and viral vectors to deliver and express therapeutic genes or antibodies in cell lines and mouse models. The research aims to evaluate therapeutic strategies for cancer, autoimmune diseases, and neurodegenerative diseases, with a focus on immune regulation, myeloid cell biology, inflammation, tumor progression, and cancer stemness. The protocol includes the use of adenoviral, lentiviral, retroviral, and adeno-associated viral (AAV) vectors, as well as CAR T-cell and other gene therapy approaches to modulate target gene expression in vitro and in animal models. The study team reported ongoing work involving several molecular targets relevant to cancer therapy and has demonstrated continued productivity through peer-reviewed publications.

Gene targets siRNA knockdown: CMTM4, CMTM6, PTPN6/PTPN11 and CAMK2b/CAMK4

Gene expression targets via AAV, retroviral and lentiviral vectors: CMTM4, CMTM6, anti-LILRB2, anti-LILRB2-CD40L and anti-LILRB2-41BBL as well as shRNA target on PTPN6/PTPN11 and CAMK2b/CAMK4

- **Training:** All staff members have completed training.
- **Applicable NIH Guidelines:** Section III-D-1, 3 & 4

- **Containment Conditions to be implemented:** BSL-2
- **Risk Assessment & Discussion:** The protocol involves the use of recombinant mRNA, plasmids, replication-defective adenoviral, lentiviral, retroviral, and adeno-associated viral (AAV) vectors, as well as CAR T-cell and other gene therapy approaches in established cell lines and mouse models. Research activities include the use of lentiviral-, adenoviral-, and retroviral-transduced cell lines. The recombinant viral vectors used in the study are replication-defective and will be handled under established institutional biosafety procedures. Potential occupational exposures include accidental sharps injuries, contact with non-intact skin, mucous membrane exposure, and aerosols generated during cell culture manipulations. Exposure could result in unintended cellular transduction and expression of recombinant gene products. Transduced cell lines may remain viable under laboratory conditions; however, any residual viral particles are expected to be readily inactivated through standard decontamination procedures, including approved disinfectants and autoclaving.
- Containment measures include implementation of BSL-2 practices for lentiviral- and adenoviral-transduced cell lines, including use of biological safety cabinets, appropriate personal protective equipment, sharps precautions, and routine decontamination. Retroviral-transduced cell lines will be handled under appropriate containment procedures consistent with their replication-defective nature and low potential for environmental persistence. Although lentiviral vectors theoretically possess a very low potential for recombination with endogenous retroelements, the vectors have been verified as replication-defective, minimizing this risk.
- Both reviewers found the protocol to be well written and determined that the proposed biosafety measures appropriately mitigate the identified risks. No additional concerns, questions, or comments were raised during committee discussion.
- **Comments sent to the PI for clarification:** none
- **The motion to approve the study as is was seconded and passed.**

Motion: Approved

- Yes votes: 15
- No votes: 0
- Abstained: 0
- Recused: 0
- Absent: 0

IBC00002854

Title: Molecular Mechanisms of Endothelial Activation and Senescence in Cell and Mouse Models of Atherosclerosis

Principal Investigator: Nhat-Tu Le

Study Overview: The committee reviewed a resubmission that involves the use of

recombinant constructs to investigate genes associated with cellular signaling, metabolism, apoptosis, vascular function, extracellular matrix regulation, and telomere-related processes. The research includes the use of adeno-associated virus serotype 8 (AAV8) vectors, plasmids, and replication deficient recombinant adenoviral vectors to evaluate the biological effects of specific gene variants in mouse models, including studies of molecular pathways involved in hypercholesterolemia and atherosclerosis. Reviewers found the application to be well written and determined that the overall study objectives, experimental design, and animal procedures were clearly described.

Gene expression AAV8: PCSK9 D377Y

Plasmid transient gene expression: ERK5, DDIAS, ACLY, MMRN2, and TERF2IP

- **Training:** All staff members have completed training.
- **Applicable NIH Guidelines:** Section III-D-1 & 4
- **Containment Conditions to be implemented:** BSL2
- **Risk Assessment & Discussion:** The reviewers agreed that the proposed research does not present biosafety risks beyond those addressed through the protocol's BSL-2 containment practices, engineering controls, and personal protective equipment requirements. The study involves recombinant plasmids, AAV vectors, and replication-deficient adenoviral vectors. Potential occupational exposures include accidental inoculation, contact with non-intact skin or mucous membranes, and aerosol generation during laboratory procedures. While recombinant plasmids are noninfectious, viral vectors may transduce exposed cells and express the encoded transgene. The potential biological effects of an exposure are dependent on the specific transgene being utilized. The committee determined that the containment measures and decontamination procedures described in the protocol are appropriate to mitigate both occupational and environmental risks associated with the proposed work.

The primary issue identified during review involved the use of the term "gain of function" in the hazard identification section. Committee members noted that this terminology is commonly associated with research involving increased virulence, pathogenicity, or transmissibility and could be misleading in this context. The committee recommended replacing the phrase with more specific language describing the biological activity of the construct. For example, reviewers suggested describing the agent as an AAV8 vector encoding the mouse PCSK9 D377Y mutant, a variant with increased PCSK9 activity used to study molecular signaling pathways involved in atherosclerosis, rather than characterizing the work as gain-of-function research.

- **Comments sent to the PI for clarification:**
 - **Hazard Identification** - To avoid potential confusion, please replace the phrase "gain of function" with more precise terminology describing the experimental objective. The term is frequently associated with research that increases virulence, pathogenicity, or transmissibility, and may not accurately represent the activities proposed in this study. A brief description of the specific functional change being evaluated would be

preferred.

For example: "Adeno-associated virus serotype 8 (AAV8) encoding the mouse PCSK9 D377Y mutant, a variant with increased PCSK9 activity. This agent will be used to study molecular signaling pathways that regulate atherosclerosis in mice. Previous studies have shown that injection of recombinant AAV8 encoding the PCSK9 D377Y mutant induces hypercholesterolemia and promotes atherosclerosis in mice."

- **The motion to approve the study via administrative review after modifications was seconded and passed.**

Motion: Approval after Administrative Review

- Yes Votes: 15
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 0

IBC00002876

Title: IBC for isogenic gene deletion in Group A and Group C *Streptococcus* for molecular pathogenesis research

Principal Investigator: Randall Olsen

Study Overview: The committee reviewed a new internally funded study investigating the molecular pathogenesis of Group A and Group C *Streptococcus*. The research aims to better understand how differences in gene content contribute to infection at distinct anatomical sites and to support the development of improved diagnostics, therapeutic approaches, and future vaccine strategies. The proposed work includes the use of *Streptococcus pyogenes* and *Streptococcus dysgalactiae* parental strains, as well as genetically modified derivatives generated through targeted gene deletion approaches. Molecular biology techniques will be used to evaluate the contribution of virulence-associated genes, including the use of the pKOSPY-sagB suicide vector and a commercially available Addgene vector backbone. The committee noted that deletion of the *sagB* gene affects production of streptolysin S but is not anticipated to increase organism virulence.

- **Training:** All staff members have completed training.
- **Applicable NIH Guidelines:** Section III-D-1 & 4
- **Containment Conditions to be implemented:** BSL-2
- **Risk Assessment & Discussion:** The committee reviewed the risks associated with the proposed genetic modification of *Streptococcus pyogenes* and *Streptococcus dysgalactiae* strains, including the generation of mutant derivatives through targeted gene deletion. Members requested clarification regarding the full scope of the planned genetic modifications and asked that all target genes proposed for deletion be clearly identified in the protocol to ensure an accurate assessment of the

recombinant organisms being generated.

- The committee discussed the risk profile of the MGCS36044-*sagB* deletion mutant. While deletion of *sagB* is expected to reduce virulence through loss of streptolysin S production, reviewers noted that the strain remains a live genetically modified derivative of a pathogenic *Streptococcus* organism. The committee emphasized that the attenuated phenotype does not eliminate the potential for occupational exposure or opportunistic infection and agreed that standard BSL-2 containment practices, engineering controls, and personal protective equipment remain appropriate for laboratory and animal work involving the strain.
- The committee also reviewed procedures involving transport of the recombinant organisms between laboratory and animal facilities. Members requested clarification of transportation procedures to ensure that packaging, containment, and movement of biological materials are conducted in a manner that minimizes the risk of accidental release or exposure during transit. Additionally, the committee confirmed that the animal facility utilizes negative-pressure containment and agreed that ABSL-2 housing and handling practices are appropriate for the proposed animal studies.
- Following discussion, the committee concluded that the proposed work could be conducted safely under the described BSL-2 and ABSL-2 containment conditions, provided the requested clarifications and protocol revisions are addressed.
- **Comments sent to the PI for clarification:**
 - **Summary of Proposed Research** - If genes other than *sagB* are planned for deletion, please list all target genes in the application. The current description identifies only *sagB*; all genes proposed for deletion must be clearly specified so that the full scope of the genetic modifications is accurately documented. If *sagB* is the only gene currently targeted for deletion, please confirm.
 - **Hazard Identification** - Please remove the wild-type streptococcal strains MGCS-36044 and MGAS-2221 from the Hazard Table. As these are non-recombinant wild-type strains, they do not fall under the IBC's review scope, which is limited to research involving recombinant or synthetic nucleic acids. Only agents relevant to the recombinant/synthetic nucleic acid work should be included in the Hazard Table. Under #5 *"Please check below all that will be involved in your research"*: Deselect "plasmids" for agents that are not plasmids. Only pSWITCH & pKOSpy-*sagB* should be listed in the plasmid section.
 - **Exposure Management – Laboratory** - For each agent being transported, under #5, Transportation: *"Describe how you will transport the agent through public areas (this should include packaging and transport routes),"* a Transport SOP containing the required details was provided as an attachment in the Summary of Proposed Research section. Please reference this SOP within the transportation description by revising the current statement: *"Transported to the RIB3 ABSL2 small animal vivarium in a closed screw-cap 2 mL tube placed in a sealed specimen bag."* to:

"Transported to the RIB3 ABSL2 small animal vivarium in a closed screw-cap 2 mL tube placed in a sealed specimen bag. Please refer to the Transport SOP attached in the Summary of Proposed Research for additional transportation procedures, packaging requirements, and transport route details." Additionally, please remove the attachment under Section 5.1, as the attached document does not contain sufficient transport-specific details and should instead be referenced from the Summary of Proposed Research section. Agent: MGCS360044-SagB_deleted Please revise the response to more accurately describe the potential hazards to laboratory personnel and the environment. While the MGCS360044-SagB_deleted strain has reduced virulence due to deletion of the sagB gene and the resulting loss of streptolysin S production, it remains a live genetically modified derivative of a pathogenic Streptococcus strain. As such, it still presents a biological hazard and requires standard BSL-2 containment and handling practices. The response should acknowledge that, although the risk is attenuated compared with the parental strain, the organism retains other bacterial components and characteristics that could pose a risk of exposure or opportunistic infection. Please update the hazard description to reflect these considerations and explain how the required PPE and BSL-2 practices mitigate these risks.

- **Exposure Management - Animal Facility:** Pressure in the animal facility is negative. Please update neutral to "negative".
- **Exposure Management - Animal Areas:** Agent: MGCS360044-SagB_deleted - Please revise the response to more accurately describe the potential hazards to Animal Care Personnel and the environment. While the MGCS360044-SagB_deleted strain has reduced virulence due to deletion of the sagB gene and the resulting loss of streptolysin S production, it remains a live genetically modified derivative of a pathogenic Streptococcus strain. As such, it still presents a biological hazard and requires standard BSL-2 containment and handling practices. The response should acknowledge that, although the risk is attenuated compared with the parental strain, the organism retains other bacterial components and characteristics that could pose a risk of exposure or opportunistic infection. Please update the hazard description to reflect these considerations and explain how the required PPE and BSL-2 practices mitigate these risks.

- **The motion to approve the study via designated member review after modifications was seconded and passed.**

Motion: Approval after Designated Member Review

- Yes Votes: 15
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 0

IBC00002865

Title: Phase 1_ P-BCMA-ALLO1_Multiple Myeloma_CAR-T

Principal Investigator: Siddhartha Ganguly

Study Overview: The committee reviewed a Phase 1 clinical trial evaluating P-BCMA-ALLO1, an investigational allogeneic CAR-T cell therapy for the treatment of multiple myeloma. P-BCMA-ALLO1 consists of genetically modified donor-derived CD4+ and CD8+ T cells engineered to express a chimeric antigen receptor (CAR) targeting B-cell maturation antigen (BCMA), a cell surface antigen selectively expressed on multiple myeloma cells. The product is manufactured by electroporation of healthy donor T cells with mRNAs encoding gene-editing and cell engineering components, including Cas-CLOVER, Super PiggyBac transposase, CD2z Booster, guide RNAs targeting B2M and the T-cell receptor beta chain, and a transposon carrying the BCMA-targeting CAR transgene. Following genetic modification, the cells are expanded, purified to remove TCR-positive cells, and cryopreserved for clinical use.

The study includes a dose-escalation Phase 1 component designed to evaluate the safety and tolerability of P-BCMA-ALLO1 across seven planned dose levels ranging from 0.0625×10^6 to 15×10^6 CAR-T cells/kg. During the previous three years, nine subjects were enrolled at dose levels 2 and 3. The committee noted that a protocol-defined dose-limiting toxicity resulting in a participant death occurred at another study site within the P-BCMA-ALLO1 plus methotrexate cohort of the Phase 1 study. The sponsor has placed the study on hold while the event is under investigation. The IRB was notified of the event and acknowledged the report.

- **Training:** All staff members have completed training.
- **Applicable NIH Guidelines:** Section III-C-1
- **Containment Conditions to be implemented:** BSL-2
- **Risk Assessment & Discussion:**
- **Comments sent to the PI for clarification:**
 - **Staff Identification:** Alice Quach's IBC CITI Credentialing training expired on July 31, 2026. Please ensure that she completes the required re-credentialing before protocol approval. If re-credentialing has not yet been assigned, please contact HMRI Credentialing to request assignment of the training. If the training has already been completed, please ask HMRI Credentialing to update her profile to reflect the current credentialing status.
 - **Study Progress:** In the summary, please mention what level is MP1.5 which potentially caused the death of a patient at another site. From the investigational brochure (see below) it is unclear what dose of the agent was used.

"Arm MP1.5 (Enhanced LD with Methotrexate Administration)
- LD: cyclophosphamide (750 mg/m²) and fludarabine (30 mg/m²) administered IV daily for 3 consecutive days (from Day -5 to Day - 3)

- P-BCMA-ALLO1: A single cell dose will be administered IV after LD on D0. The starting cell dose will be $\leq$ the maximum cleared dose level in Arm P 1.5.
- Methotrexate (MTX): MTX 7.5 mg (oral) will be administered on Days 1, 4, 7, 10, Week 2, and thereafter once weekly at 15 mg from Week 3 until 3 months post P BCMA-ALLO1 infusion." For consistency and reviewer clarity, please use the same dosing nomenclature in this section as is used in the Hazard Identification section.

- **The motion to approve the study via designated member review after modifications was seconded and passed.**

Motion: Approval after Designated Member Review

- Yes Votes: 15
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 0

IBC00002780

Title: CD7.CAR T cells, H-57819: NEO-CRIMSON phase I clinical trial for patients with relapsed/refractory T-cell leukemia and lymphoma

Principal Investigator: LaQuisa Hill

Study Overview: The committee reviewed a Phase I dose-escalation clinical trial evaluating the safety of allogeneic CD7.CAR/28 ζ T cells for the treatment of relapsed or refractory T-cell malignancies, including T-cell acute lymphoblastic leukemia and T-cell lymphomas. The investigational product consists of donor-derived T cells genetically modified using a gammaretroviral vector to express a CAR directed against CD7, a surface antigen commonly expressed on malignant T cells. The CAR construct incorporates an anti-CD7 single-chain variable fragment linked to CD28 and CD3 ζ signaling domains to enhance T-cell activation and antitumor activity.

The cell therapy product is manufactured under current Good Manufacturing Practice (cGMP) conditions at the Center for Cell and Gene Therapy using a clinical-grade replication-incompetent gammaretroviral vector. Following genetic modification and expansion, the cells are cryopreserved and transported for patient administration. The study will evaluate four dose levels ranging from 1×10^7 to 1×10^8 transduced CAR T cells/m² administered as a single intravenous infusion following lymphodepleting chemotherapy. The primary objective is to assess safety and determine the maximum tolerated dose with participants monitored for dose-limiting toxicities and other adverse events following infusion.

- **Training:** All staff members have completed training.

- **Applicable NIH Guidelines:** Section III-C-1
- **Containment Conditions to be implemented:** BSL-2
- **Risk Assessment & Discussion:** The committee reviewed the risks associated with the use of genetically modified allogeneic CD7 CAR T cells produced with a replication-incompetent gammaretroviral vector. Members noted that the investigational product consists of ex vivo engineered human T cells expressing an anti-CD7 chimeric antigen receptor and that patient administration will occur in a controlled clinical environment following standard cell therapy procedures. The committee agreed that the primary biosafety considerations relate to the handling, storage, transport, and administration of the genetically modified cellular product, as well as management of patient materials following infusion.
- The committee determined that the proposed containment measures, transport procedures, and clinical handling practices are appropriate for the investigational product. The use of cGMP-manufactured, replication-incompetent retroviral vector technology and cryopreserved cell products was considered consistent with the proposed risk level. Based on the nature of the genetically modified cellular therapy and the clinical activities described, the committee agreed that the proposed biosafety procedures provide adequate protection for personnel, patients, and the environment. The committee found the risk assessment acceptable as presented.
- **Comments sent to the PI for clarification:**
 - **Viral Studies:** Under "are the viral vectors replication competent" Please change to "no" as the retroviral vector is indicated to be replication incompetent.
 - **Recombinant & Synthetic Nucleic Acids:** Please move the transport SOP to the appropriate section: Exposure Management Clinic/Hospital, #7 Transportation.
- **The motion to approve the study via administrative review after modifications was seconded and passed.**

Motion: Approval after Administrative Review

- Yes Votes: 15
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 0

IBC00002869

Title: AURORA Study: Acute Upper Respiratory Outcomes and Responses Across the Lifespan Involving Influenza Virus Specimens

Principal Investigator: Heather Smallwood

Study Overview: The protocol investigates the molecular mechanisms that regulate respiratory virus infection and host immune responses. The research combines studies of human clinical specimens, primary cell cultures, organoid models, viral infection systems, and systems biology approaches to identify host-directed therapeutic and preventive strategies that improve outcomes following respiratory virus infection while preserving protective immunity. The study utilizes Influenza A virus strain PR8NS1M, genetically modified nasal epithelial organoids and human bronchial epithelial cells, and siRNA oligonucleotide duplexes targeting PI3K δ , p70S6K, and PDK3. In vivo viral infection studies will be conducted with PI3K knockout mice. These mice will be generated by breeding Sftpc-CERT2 mice with Pik3cdflox/flox mice on a C57BL/6J background.

The proposed work includes the culture, expansion, storage, and functional analysis of primary human cells and organoids, including nasal epithelial and lymphoid-derived models. Experimental activities include respiratory virus propagation and infection studies, assessment of host-pathogen interactions, and gene-silencing experiments using siRNA delivered by electroporation to evaluate the role of specific host factors in antiviral responses. Human source materials, including blood and respiratory specimens, will be collected and analyzed to support translational studies and correlate laboratory findings with clinically relevant immune responses. Biological materials will be handled under appropriate containment conditions, and specimens, cell cultures, organoids, viral stocks, and human-derived samples will be transported between approved research locations using established containment and transport procedures. The overall objective is to advance understanding of respiratory viral pathogenesis and host immunity to support development of novel therapeutic and preventive interventions.

- **Training:** All staff members have completed training.
- **Applicable NIH Guidelines:** Section III-D-4 & 7, Section III-E-3
- **Containment Conditions to be implemented:** BSL-2
- **Risk Assessment & Discussion:** The committee reviewed the proposed research involving recombinant and modified influenza virus materials, human-derived organoid models, and associated human source materials. Members requested clarification regarding the specific biological agents included in the study to ensure that each material is accurately characterized and assessed according to its individual biosafety profile. The committee noted that PR8NS1M and IAV-BPL represent distinct agents with different risk characteristics and should be described separately within the protocol. Similarly, nasal epithelial organoids and lymphoid organoids should be identified as separate biological constructs to accurately reflect the materials used in the research.
- Particular attention was given to the recombinant influenza strain PR8NS1M. The committee requested additional information regarding the NS1 amino acid substitutions and their impact on viral replication, virulence, pathogenicity, and overall risk. While the modifications may attenuate the virus through disruption of specific host signaling pathways, members noted that PR8NS1M remains a replication-competent influenza virus with the potential for laboratory-acquired exposure and therefore requires a clear justification of the proposed containment

practices. The committee also requested confirmation that PR8NS1M is the only mutant influenza strain that will be used under the protocol, noting that any additional recombinant influenza strains would require prior IBC review through amendment.

- The committee further discussed the inclusion of β -propiolactone-inactivated influenza virus (IAV-BPL) and requested clarification regarding the parent viral strain and whether the material contains any recombinant or synthetic nucleic acid modifications. In addition, members requested clarification regarding the proposed use of respiratory syncytial virus (RSV), including whether recombinant or genetically modified RSV strains will be used as part of the study.
- Reviewers also requested clarification regarding animal studies, specifically identifying which agents, if any, will be administered to mice and the locations where animals will be housed. The committee noted that appropriate risk assessments and containment measures must be aligned with the specific agents used in vivo. Human source materials, including peripheral blood mononuclear cells, blood, nasal rinse samples, and tonsillar tissue, were also discussed, and the committee emphasized the importance of ensuring these materials are reviewed under the appropriate oversight mechanisms.
- Additional discussion focused on transport and containment practices. The committee requested revisions to transportation procedures to clearly identify specimen origins, destinations, routes, and containment measures used during movement of materials. Reviewers also identified facility-specific containment information requiring correction to accurately reflect laboratory operating conditions. Overall, the committee agreed that the proposed work could be conducted safely provided the requested clarifications and revisions are incorporated into the protocol and supporting documentation.
- **Comments sent to the PI for clarification:**
 - **Study Identification:** Although the primary study contact, will not be handling the biological hazards associated with this study, Institutional Biosafety Credentialing is scheduled to expire on October 31, 2026. Please ensure the completion of the required recredentialing before the expiration date to maintain compliance with institutional training requirements.
 - **Hazard Identification Agent:** Please list PR8NS1M and IAV-BPL as separate agents rather than grouping them together under mutant influenza virus strains, as they represent distinct materials with different biosafety considerations. PR8NS1M: Please revise the agent description to clearly summarize the biosafety implications of the NS1 amino acid substitutions (residues 164-167) and provide supporting references, if available. Although disruption of NS1-p85 binding and reduced PI3K/Akt signaling may attenuate the virus compared to wild-type influenza A virus, PR8NS1M remains a replication-competent influenza virus with aerosol transmission potential. Please describe how these mutations affect viral replication, virulence, and pathogenicity, and explain how these characteristics support the proposed containment level and handling procedures. If available, include experimental data or literature references

supporting the attenuated phenotype. Additionally, please confirm whether PR8NS1M is the only mutant influenza virus strain that will be used under this protocol. Any additional mutant strains must be submitted to the IBC for review and approval through an amendment prior to use. Please identify the parent influenza strain that was inactivated using β -propiolactone (BPL) (e.g., A/Puerto Rico/8/34 [PR8] or another strain) and update the agent description accordingly. In addition, please clarify whether this agent contains any recombinant or synthetic nucleic acid modifications. If IAV-BPL is solely a chemically inactivated wild-type virus and does not contain recombinant or synthetic nucleic acid modifications, it may not fall within the scope of IBC oversight and should instead be described in the corresponding HSC protocol, as appropriate. List the nasal epithelial organoids and lymphoid organoids as separate agents/constructs. Although they may originate from the same donor source, they are distinct biological constructs and should be described separately to accurately reflect the materials used in the study. Please clarify whether RSV will be used as part of this research. If genetically modified RSV strains (e.g., mutant or recombinant strains) will be used, please add them to the protocol and provide a description of the genetic modifications. If only wild-type RSV strains will be utilized, please indicate whether they are covered under the associated HSC protocol. This information is needed to ensure that all agents are reviewed under the appropriate oversight mechanism. It is currently unclear whether any of the agents listed in this application will be administered to mice. Please identify which agents, if any, will be used in animal studies and specify the animal housing location(s). If any registered agents will be administered to animals, please select "Animals" under #5, Hazard Identification ("*Please check all that will be involved in your research*") and update the hazard assessment accordingly. Please ensure that PBMCs, blood, nasal rinse fluid, and tonsil tissues are included in the associated HSC protocol for appropriate review and oversight.

- **Risk Assessment:** Question #11: *Does your proposed project involve influenza viruses containing the H2 hemagglutinin (HA) segment? Does this protocol involve the H2 HA gene in cold-adapted, live attenuated vaccine strains (e.g., A/Ann Arbor/6/60 H2N2) ?* (Sec.III.D.7.a) Please revise your response to Item 11 to "No." The influenza virus strain described in this protocol is not an H2 hemagglutinin (HA) subtype contained within a cold-adapted or live attenuated influenza virus strain (e.g., A/Ann Arbor/6/60 H2N2). Based on the virus information provided, this criterion does not apply to the agents proposed for use in this study. Question #12: *Does this protocol involve work with Risk Group 2 influenza viruses containing genes from human H2N2 other than the HA gene?* Please revise your response to Item 12 to "No." This protocol does not involve the reconstruction, generation, or use of H2N2 influenza virus genes. Based on the agents and genetic modifications described in the application, the activities proposed do not meet the criteria addressed in Item 12.
- **Summary of Proposed Research:** Please expand this section to provide a

more complete description of the study activities. The current response is primarily a list and does not adequately describe the research objectives, methods, and use of biological materials. The submitted Master Protocol contains sufficient information that can be used to develop a more detailed summary of the proposed research. The transport SOP is incomplete and should be updated to include the location(s), date, and appropriate signature(s). The transport procedures also do not clearly identify the origin and destination of the specimens. Please revise the SOP to specify where specimens will be collected, where they will be transported, and the route and locations involved in the transport process.

- **Viral Studies:** This section is meant to capture viral vectors. Please deselect "viruses" in the hazard identification section under #5 *Please check below all that will be involved in your research.*
 - **Funding Information:** Please provide the grant title and information. If a grant has not yet been obtained, please expand the response in part 3 and provide grant application titles that have been submitted and are undergoing review.
 - **Other Agents:** Please provide the associated HSC protocol number. If radioactive materials are involved, please link the relevant RSC protocol or update the answer to "no"
 - **Exposure Management - Animal Facilities:** It is unclear which agents will be administered to mice and where mice will be housed. If any of the agents registered in this application are to be administered to mice, please select "animals" under #5 *Please check below all that will be involved in your research* in the Hazard Identification section.
 - **Exposure Management - Laboratory Facility:** Pressure in R7-317 should be negative, not neutral.
- **The motion to approve the study via designated member review after modifications was seconded and passed.**

Motion: Approval after Designated Member Review

- Yes Votes: 15
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 0

Title: Phase 2_Rapcabtagene Autoleucel (CYTB323K12201) for Refractory Diffuse Cutaneous Systemic Sclerosis

Principal Investigator: Sarah Kazzaz

Study Overview: This Phase 2 study evaluates the safety and efficacy of rapcabtagene autoleucel (YTB323), an investigational autologous CD19-directed CAR-T cell therapy, compared with rituximab in patients with severe refractory diffuse cutaneous systemic sclerosis.

The study involves the ex vivo genetic modification of autologous human T cells using the CTL019 HIV-1–based lentiviral vector, a replication-incompetent third-generation lentiviral vector. Patient T cells are collected via leukapheresis and shipped to the sponsor's manufacturing facility, where they are transduced to express an anti-CD19 CAR. The genetically modified cells are then expanded and formulated as rapcabtagene autoleucel (YTB323) prior to release testing and shipment back to the clinical site.

Following lymphodepletion, participants receive a single intravenous infusion of 12.5×10^6 CAR-positive viable T cells. The genetically modified T cells are designed to recognize and eliminate CD19-expressing B cells. No genetic modification procedures are performed at Houston Methodist Hospital; all genetic engineering activities occur at the sponsor's manufacturing facility.

The investigational cellular product will be received and handled by the Ann Kimball & John W. Johnson Center for Cellular Therapeutics. Upon receipt, the product will be stored, prepared, transported, and administered according to institutional cellular therapy procedures. The final product is transported to the bedside in a labeled biohazard container and administered via intravenous infusion, preferably through a central venous catheter.

Training: All staff members have completed training.

- **Applicable NIH Guidelines:** Section III-C-1
- **Containment Conditions to be implemented:** BSL-2
- **Risk Assessment & Discussion:** (YTB323) consists of autologous T cells genetically modified ex vivo using the CTL019 (murine) HIV-1–based lentiviral vector to express a CD19-directed CAR. The clinical site will not handle the lentiviral vector, as all transduction, manufacturing, and quality control activities are performed at the Novartis manufacturing facility prior to product release. Site activities are limited to receipt, storage, thawing, transport, and intravenous administration of the final YTB323 product. No intentional environmental release is anticipated other than administration to enrolled study participants. A theoretical risk of occupational exposure exists during product handling, such as from a leaking infusion bag or accidental spill. In such events, cleanup should follow institutional biosafety procedures for human blood and other potentially infectious materials. Standard PPE and spill-response procedures are considered sufficient. YTB323 is not an infectious agent, and the genetically modified T cells are not expected to survive or persist outside the human body. Because the lentiviral vector is used only

during off-site manufacturing and no vector manipulation occurs at the clinical site, the risk of environmental release or transmission to healthcare personnel, the public, or the environment is considered minimal. No additional product-specific containment measures are required beyond standard precautions for handling human cellular therapy products.

- **Comments sent to the PI for clarification:**
 - **Staff Identification:** Title: There is a typo in the title. It should be “refractory” and not “refactory” – please change this
 - **Summary of Proposed Research:** Please complete this sentence: "*The administration dose is a*"
 - **Viral Studies:** Under host range, the response provided does not provide a host range for the vector. Please update with the host range. For the question “*Are the viral vectors replication competent?*” Update this to "no", replication-defective, recombinant third-generation self-inactivating (SIN) lentiviral vectors are not replication competent.
- **The motion to approval via administrative review after modifications was seconded and passed.**

Motion: Approval after Administrative Review

- Yes Votes: 15
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 0

IBC AMENDMENTS

IBCA00001632

Title: Hazard Amendment 2 for Phase 1/2 First-in-Human Study of NVC-001 (AAV9 Vector Expressing Dominant Negative SUN1) to Assess Safety, Tolerability & Preliminary Efficacy in LMNA-Related Dilated Cardiomyopathy

Principal Investigator: Barry Trachtenburg

Amendment Summary: This amendment requests the addition of Protocol Amendment 4 documents, including the updated Protocol, Investigator’s Brochure (IB), and Informed Consent Form (ICF), which are currently under IRB review. NVC-001 (AAV9-dnSUN1) is a recombinant, non-replicating single-stranded adeno-associated virus serotype 9 (AAV9) vector. NVC-001 expresses a dominant-negative form of the naturally occurring human SUN1 protein (dnSUN1) under the control of a cardiac-specific cis-regulatory module 4 (CS-CRM4) enhancer and cardiac-specific synthetic hTNNT2 (Syn-hTNNT2) promoter to restrict expression specifically to cardiomyocytes.

Key updates included in Amendment 4 are as follows:

- Added Cohort 3, which will receive the highest dose level of 9.0×10^{13} vg/kg.
- Following completion of Cohort 3, the Data Safety Monitoring Board (DSMB) will review the available safety and efficacy data and determine whether progression to Phase 2 is warranted.
- No changes are proposed to the overall study objectives or the investigational product; the amendment primarily updates study design, dose escalation, participant monitoring, and related protocol procedures.

Training: All staff members have completed training.

- **Applicable NIH Guidelines:** Section III-C-1
- **Containment Conditions to be implemented:** BSL-2
- **Risk Assessment & Discussion:** The amendment includes changes to participant enrollment, dose cohorts, and other study design elements; however, these modifications do not alter the nature of the investigational AAV9 vector or the overall biosafety profile of the study. Reviewers noted several administrative corrections, including clarification of the term "SAD cohort," and correction of protocol language describing the AAV vector as replication competent. These issues were determined to be documentation-related and did not raise new biosafety concerns. Based on the information provided, the committee concluded that the amendment does not introduce additional risks to study personnel, participants, or the environment, and that existing containment, handling, and safety procedures remain appropriate.
- **Comments sent to the PI for clarification:**
 - **Hazard Identification:** Please define "SAD" for reviewer clarity
 - **Viral Studies:** Update replication competence to "no" - this is a non-replicating, single-stranded AAV9 vector and it is not replication competent.
- **The motion to approve the study via administrative review after modifications was seconded and passed.**

Motion: Approval after Administrative Review

- Yes Votes: 15
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 0

IBCA00001641

Title: Hazard Amendment 5 for IBC for CPRIT-RNAcore for mRNA manufacturing and assessment

Principal Investigator: John Cooke

Amendment Overview: This amendment broadens the scope of the RNA Core manufacturing activities covered under the protocol to include the production of self-amplifying RNA (saRNA) constructs in addition to existing mRNA and circular RNA (circRNA) manufacturing services. The RNA Core provides custom in vitro transcription, synthesis, purification, and quality control of RNA constructs for academic and biotechnology clients, supporting non-clinical research and process development.

The amendment expands protocol language to encompass the manufacture of a wider range of client-requested RNA constructs, including saRNA constructs derived from various source organisms and representing the appropriate associated risk groups, as applicable. The plasmids encode a self-replicating Venezuelan equine encephalitis (VEE) virus RNA, T7-VEE-GFP. No changes are proposed to the core manufacturing processes, facilities, or containment practices.

- **Training:** All staff members have completed training.
- **Applicable NIH Guidelines:** Section III-D-2
- **Containment Conditions to be implemented:** BSL-2
- **Risk Assessment & Discussion:** The committee determined that the risks associated with the manufacture and handling of these non-infectious RNA constructs remain appropriately managed under existing containment and operational procedures. No new hazards to personnel, the public, or the environment were identified, and the amendment does not require additional biosafety controls beyond those already in place. The committee further discussed that an amendment must be submitted and approved prior to the addition of any new constructs to the study. These amendments will be reviewed by designated member reviewers of the IBC and only escalated to full committee review if deemed necessary by the reviewers. All newly added constructs must be documented in the Hazard Identification section, specifically within the Agent "Description" column corresponding to the appropriate hazard.
- **Comments sent to PI for clarification:**
 - **15.0 Exposure Management – Laboratory:** The application references saRNA constructs containing VEE replicon elements (e.g., T7-VEE-GFP in the hazard identification section) and discusses EEEV-derived sequences in the exposure management section. Please clarify which alphavirus replicon backbones will be permitted under this protocol (VEEV, EEEV, or others)
- **The motion to approve the amendment via designated member review after modifications was seconded and passed.**

Motion: Approve after Designated Member Review

- Yes Votes: 15
- No Votes: 0
- Abstained: 0

- Recused: 0
- Absent:0

ADJOURNMENT

The meeting adjourned at 11:29 am.
