NIH Institutional Biosafety Committee Minutes
Location: Bethesda Main Campus
December 03, 2025
2:00 PM – 5:00 PM
Virtual via Microsoft Teams

Members present: (12)
Quorum met: Yes

Harry Malech, Chair, clinician	Stephen Denny, animal research expert	Alicia Alexion, unaffiliated member
Richard Baumann, BSO	Clevetta Drew, unaffiliated member	Michael Kujawa, ABSO
Emily Lee, recombinant and molecular techniques	Steve Whitehead recombinant and molecular techniques, virology	Stephanie Goff, Clinician*
Jeanne Billioux*, Clinician		

- absent members: Robert Craigie*
*Provided comments *in absentia* for select reviews

Guests present (9)

Rebecca Anderson (RML)	Clint Allen	Scott Norberg
Grace Markley (NBBTP)	Jocelyn Mendoza (NBBTP)	Theresa Bell (NCI Fred)
Ravi Madan	Megan Hausler	Melissa Abel (NCI)
Madison Cahill (DS)	Althea Treacy, Biorisk Chief	

Announcements & Call to Order

The meeting was called to order by Dr. Malech at 2:04 PM.

Review of the Past IBC Meeting Minutes

03 September 2025 Minutes

a. Comments on minutes, as applicable
b. The minutes were unanimously approved with minor modifications and formatting corrections by 12/10/25.

New Committee Business

I. BSO preliminary registration approvals since the previous meeting

a. Pathogen registrations (23 total): 25-BMC-172-175, -178-180 // 185-188, -190, 192-195, 197-202, -204

rDNA and rDNA/pathogen registrations: 25-BMC-171 (Kindt) -III-D-2-a/III-D-4-a - Transgenesis and mutagenesis of zebrafish. This registration updates and replaces registrations RD-13-IX-12 and 6008, previously approved by the IBC; 25-BMC-176 (Platt) -III-E-3- Large Artery damage in sickle cell disease; 25-BMC-177 (Lazarevic) -III-D-2-a/III-D-III-a- Role of Th1 and Th17 specific gene products in induction and regulation of experimental autoimmune encephalomyelitis (EAE). This registration updates and replaces registration RD-11-XI-10 with no significant changes from prior approval; 25-BMC-189 (Tanner) -III-D-3-a/III-D-4-a - Elucidating the role of tissue biophysics in organ colonization. This registration administratively updates and replaces registrations: RD-12-VIII-16 and 5718 with no significant changes from prior approval; 25-BMC-191 (Gonzalez) -III-D-3-a/III-D-4-a- Use of AAV vectors to deliver gene products to liver in mice; 25-BMC-196 (Burgess) -III-E-1/ III-D-4- Transgenic analysis of neuronal circuits in zebrafish. This registration administratively updates and replaces registration RD-12-X-02 with no significant changes from prior approval; 25-BMC-203 (McGuire) -III-D-3-a/III-D-4-a- Infection and immunity in mitochondrial disease: Animal models and cell work. This registration administratively updates and replaces registrations 5413, 5414, and RD-11-III-10. Also replaces 5546 and RD-11-XII-16 with no significant changes from prior approval.

b. Registration amendments: **Approved RD amendments ('amend 251001') for the Minutes**: RD-23-VIII-16 (amend-Seder), RD-23-VII-03 (amend-Pierson), RD-23-III-06 (amend-Morcillo), RD-22-IX-17 (amend-Ng), RD-23-VI-18 (amend-Ng), RD-14-III-01 (amend-Biesecker), 24-BMC-245 (amend-Kovacs), 24-BMC-174 (amend-Silbert), RD-15-VIII-31 (amend-Ruckwardt), RD-23-II-03 (amend-Plenz), RD-22-VI-05 (amend-Bowers), 24-BMC-241 (amend-Brownell), RD-22-V-07 (amend-Seder), RD-19-X-13 (amend-Zhao), RD-22-XI-16 (amend-Weyemi)24-BMC-251 (amend-Adoro) RD-22-XI-07 (amend-Luo)

Approved RD amendments ("amend 251105") for the Minutes: 24-BMC-177 (amend-Hanchard), RD-22-XI-16 (amend-Weyemi)

Approved RD amendments ("amend 251203") for the Minutes: 25-BMC-077 (amend-Schuck), RD-19-VI-01 (amend-Kanekiyo), RD-15-VIII-20 (amend-Lovinger), 24-BMC-028 (amend-Chudasama), RD-19-X-12 (amend-Connors), 24-BMC-066 (amend-Lifson), RD-21-IX-05 (amend-Allen), RD-22-IX-21 (amend-Zhou), RD-20-XI-06 (amend-Caspi)

c. Committee discussion: The reporting of activity spans more than 1 month due to the government shutdown in October and November. No committee members voiced comments or concerns.

d. After providing descriptions, the BSO asked if there were any questions or concerns with the preliminary approvals. Hearing none and following the formal review and discussion at the meeting, the IBC concurs unanimously and formally approves the registrations and registration amendments.

II. Registrations and other submissions for Committee Review

a. Clinical trial reviews

25-BMC-181, Ravi Madan (Presented by Ravi Madan)

i. Reviewers: Malech, Goff, Billioux, All

ii. Review summary: CT-01 Madan: This trial seeks to understand the potential for effective immunotherapy in participants who have had previous SBRT which has become a de facto standard of care in the biochemically recurrent disease state despite limited data. Furthermore, a majority of patients will experience PSA progression after a short-lived PSA response. This study will estimate the efficacy of N-803 alone or with ETBX-071 vaccine, each administered for 6 months, in participants with biochemically recurrent prostate cancer following PSA progression after Stereotactic Body Radiation Therapy (SBRT). Previous data from therapeutic cancer vaccines in biochemically recurrent prostate cancer informs expectations of vaccine alone in this setting along with a current study of 2 vaccines at the NCI (NCT03315871). The proposed study of N-803 is supported clinically by the efficacy seen when added to the QuEST1 regimen, increasing PSA responses from 8 to 44%. Preclinical data suggests the efficacy of the combination of vaccine and N803 providing a rationale to explore the combination which has produced no safety signals in prior studies including QuEST1. To increase the chance of positive impact, participants will be enrolled who have 3 or greater lesions given higher likelihood of PSA progression. The low toxicity of the individual immunotherapy components and previous clinical experience suggests a favorable combination. This is an important consideration for BCR prostate cancer, which is asymptomatic and can take years to progress to metastatic disease, including in participants who have visible disease on PET imaging.

Background information was provided in slides with chief principal investigator presentation.

iii. Committee discussion:

- This is a Phase II trial of IL-15 Superagonist with or without Vaccine in Biochemically Recurrent Prostate Cancer after Previous Stereotactic Body Radiation Therapy. The study examines N-803 with or without the PSA ETBX-071 vaccine in biochemically recurrent prostate cancer. Both N-803 and PSA ETBX-071 have been used in clinical trials that have been reviewed. While N-803 has not been used with this vaccine specifically before, it has

been used with other vaccines without major concerns. The vaccine has been used in a clinical trial as a combination of three vaccines without major safety concerns. The ETBX-071 vaccine will be commercially manufactured and supplied. ETBX-071 is an adenoviral-based vaccine against PSA. ETBX-071 vaccine will be delivered directly to the Clinical Center Pharmacy. N-803 is manufactured and supplied commercially. There is plan for 5-year follow-up. No specific questions or concerns from an IBC standpoint.

- The protocol is well described, and this is a drug/ agent the CC is very familiar with so the handling of this is no issue at the clinical center. All biosafety precautions have been handled appropriately.

iv. Bloodborne pathogen training (BBP) for anyone handling clinical samples, and PPE as appropriate for standard precautions and as determined by risk assessment including gloves, gown, and face protection, which will mitigate risks of inadvertent exposure during preparation and administration especially when working outside of primary containment such as a Biological Safety Cabinet (see protocol details in registration).

v. Animal studies proposed: N/A

vi. The committee discussed the dual-use and ePPP potential of these experiments and agreed that there were no dual-use or ePPP concerns with this clinical protocol.

vii. There were no additional public comments.

viii. The clinical protocol is approved with standard precautions as described in place for handling therapeutic agent including gown gloves and surgical mask.

ix. Relevant sections of the NIH Guidelines: III-C-1.

x. The committee unanimously approved as written.

xi. There were no conflicts of interest indicated.

25-BMC-205, Harry Malech (Presented by Harry Malech)

i. Reviewers: Goff, Billioux, All (review occurred at end of meeting)

ii. Review summary: This is a company-sponsored, multicenter vector dose escalation clinical trial of EN-374 Drug Product in vivo gene therapy targeting hematopoietic stem cells (HSC) for treatment of X-linked chronic granulomatous disease (X-CGD). EN-374 administered by intravenous injection, is a mixture of two gutless Adenovirus (Ad) 5/35 capsid packaged recombinant DNA cargos. Though produced and packaged in a helper mediated manufacture system, the final Ad 5/35 vectors contain no adenovirus gene sequence. The Ad35 capsid knobs of the Ad 5/35 capsids have been mutated to specifically bind human CD46 preferentially expressed on human HSC. The first of the two Ad 5/35 vectors in the EN-374 mixture contains two mini-gene elements situated inversely back to back on a single DNA strand that include the therapeutic X-CGD human CYBB gene cDNA driven by the Cathepsin G/cFes hybrid myeloid specific promoter plus the O6-benzyguanine (O6-BG) resistant P140K mutant human methyl guanine methyl transferase (MGMT P140K) selection gene cDNA driven by the EF1-alpha short constitutive promoter. These genetic elements in this first Ad capsid are flanked by Sleeping Beauty (SB) 100x transposase recognition site inverted repeats and FRT sites recognized by Flp recombinase. The second of the two Ad 5/35 vectors in the EN-374 mixture similarly contains two mini-gene elements situated inversely back to back on a single DNA strand that include the Flp recombinase cDNA driven by the EF1-alpha short promoter that excises and circularizes a plasmid derived from the therapeutic elements of the first Ad vector, and the SB100X transposase cDNA driven by the CatG/cfes myeloid specific promoter that mediates integration of the resultant therapeutic element circular plasmid into the target HSC genome. Adults will be treated first in a 3 × 3 dose escalation in Part 1 of the study assessing EN-374 at 3.0 × 10e12 gene copies (gc)/kg first and then, as tolerated, 6.25 × 10e12 gc/kg second (Cohorts 1 and 2, respectively). The highest tolerated dose in adults will then be used in Part 2 of the study of pediatric participants at decreasing aged groups in Cohorts 3 (12 to < 18 yrs), 4 (2 to < 12 yrs), and 5 (3 mo to < 2 yrs). There will be 3 - 6 participants recruited to each of the five Cohorts. The NIH study site will not enroll into Cohort 5. The primary objective is to evaluate safety of EN-374 administration and the associated treatment regimen components. The secondary objective is to evaluate the effect of the EN-374 treatment regimen on the production of functional oxidase positive neutrophils in the peripheral blood. Exploratory objectives include but are not limited to measuring pace and time of clearance of EN-374, immunogenicity of EN-374, sites of integration

in the genome of EN-374, and incidence and severity of CGD related infections and autoimmune problems

Following informed consent, patients with X-CGD satisfying the entry criteria for the protocol will be treated with 5 daily injections of granulocyte colony stimulating factor (G-CSF) plus a single injection of plerixafor on the day of EN-374 gene therapy injection to synergistically mobilize HSC from the bone marrow to the peripheral blood. Mobilization of HSC to the peripheral blood enhances the
frequency of encounters in the peripheral blood between EN-374 and the CD46 on surface of the mobilized HSC. Patients are also pretreated with dexamethasone, tocilizumab and anakinra on the day of gene therapy to reduce the potential of immune reactions to the Ad 5/35 capsid. If any detectable level of gene marking is achieved, then three cycles of selection conditioning treatment will be administered to progressively increase the level of gene corrected HSC and resultant oxidase positive circulating neutrophils with a final goal of at least 10% or greater oxidase positive corrected circulating neutrophils. Successive selection cycles will be initiated as tolerated on Day 29, Day 57 and Day 85 post-gene therapy, respectively. A selection cycle consists of treatment with O6-BG 120 mg/m2 administered by IV bolus injection followed by O6-BG 1.25 mg/m2/hour administered by IV infusion for 48 hours plus temozolomide 472 mg/m2 PO administered < 2 hours after completing the O6-BG IV bolus injection. Gene marking and oxidase activity in peripheral blood neutrophils will be monitored before and at intervals after each cycle of selection treatment. Incidence and severity of blood cytopenia will be monitored. Final assessments will occur at one year post gene therapy, though patients will be monitored long term to at least 15 years post gene therapy.

iii. Committee Discussion:
- *In vivo* use of the gene therapy vector. Patients have an issue fighting infections. The study focuses on the X-linked form of this disease. Carriers with less than 10% oxidase normal neutrophils are at some risk of CGD infections, but those above 10% are not at a statistically significant greater risk of infection than healthy controls. The risk of autoimmune disease in carriers is less than patients with CGD, but they are at some risk even with higher than 10% oxidase normal neutrophils.
- Patients with partial function mutations (making a small amount of superoxide) have better survival outcomes. Increasing any amount of superoxide will help with survival.

iv. Bloodborne pathogen training (BBP) for anyone handling clinical samples, and PPE as appropriate for standard precautions and as determined by risk assessment including gloves, gown, and face protection, which will mitigate risks of inadvertent exposure during preparation and administration especially when working outside of primary containment such as a Biological Safety Cabinet (see protocol details in registration).

v. Animal studies proposed: N/A

vi. The committee discussed the dual-use and ePPP potential of these experiments and agreed that there were no dual-use or ePPP concerns with this clinical protocol.

vii. There were no additional public comments.

viii. The clinical protocol is approved with standard precautions as described in place for handling therapeutic agent including gown gloves and surgical mask.

ix. The relevant sections of the NIH Guidelines: III-C-1.

x. The committee unanimously approved as written.

xi. The chair Dr. Harry Malech recused himself as chair (Dr. Denny acting as chair for this review), and from voting as this is from his laboratory.

25-BMC-206, Scott Norberg (Presented by Dr. Scott Norberg)

i. Reviewers: Malech, Billioux, All

ii. Review summary: This is PRGN-2012, an FDA-approved HPV-specific immunotherapy that utilizes a gorilla adenoviral DNA vector encoding fusion proteins of HPV 6 and 11 early antigens capable of eliciting a potent HPV-specific T cell response in patients. The NIH Clinical Center conducted the first-in-human clinical study of PRGN-2012 and found the drug to be safe and effective.

Recurrent respiratory papillomatosis (RRP) is a rare papillomatous disease of the respiratory tract caused by Human Papilloma Virus (HPV) types 6 or 11. RRP can progress to cause severe voice disturbance, airway compromise, fatal pulmonary lesions, and, rarely, invasive cancers. The group conducted the pivotal phase 1/2 clinical study of PRGN-2012 (NCT04724980), a gorilla adenovirus vector-based gene therapy capable of eliciting HPV6/11-specific T cell immunity. The study was found to be positive, and a Biologics License Application (BLA) submission for this agent was accepted by the US Food and Drug Administration (FDA). On August 15th, 2025, the FDA granted full approval of PRGN-2012, making it the first FDA-approved medical therapy for adult patients with RRP. Unfortunately, 50% of study participants did not achieve a complete response in the pivotal study, indicating that additional research into therapeutic strategies is still needed. The team is currently conducting a phase 2 clinical trial of bevacizumab (NCT00803062) to assess the safety and clinical benefit of this agent in adults with RRP. Bevacizumab has demonstrated an acceptable safety profile with consistent and rapid clinical benefit by significantly reducing papillomatous disease burden and eliminating the need for clinical interventions in 20 consecutively treated patients. Unfortunately, disease regrowth occurs following cessation of bevacizumab therapy, and prolonged treatment can lead to systemic toxicity. Community physicians will soon be using both PRGN-2012 and systemic bevacizumab in clinical practice, but the combined safety and appropriate sequencing of these agents has yet to be studied. The aim is to combine this therapy with another FDA-approved medication, bevacizumab, that has also demonstrated clinical activity in RRP.

iii. Committee Discussion:
- Specifically, this consists of a non-replicating non-integrating gorilla adenoviral vector that transfects specifically APCs into the patient's cells.
- One reviewer asked if there is a standard when people use bevacizumab-bvzr alone. The investigator responded there is no true standard, but the disease will return without it. Patients have received it every 6-12 weeks depending on how they can tolerate it.
- A reviewer asked how far out in the protocol patients will be followed to give them a second round. The response was that they follow them for an entire year then keep communicating for another 2 years. If they relapse, then they go through the cycle again.

iv. Training is BBP for anyone handling clinical samples, and PPE as appropriate for standard precautions and as determined by risk assessment including gloves, gown or labcoat, and eye protection and as described (see in registration).
v. Animal studies proposed: N/A
vi. The committee discussed the dual-use and ePPP potential of these experiments and agreed that there were no dual-use or ePPP concerns with this clinical protocol.
vii. There were no additional public comments.
viii. The clinical protocol is approved with standard precautions as described in place for handling therapeutic agent.
ix. Relevant sections of the NIH Guidelines: III-C-1(for HGT work in humans)
x. The committee unanimously approved the clinical trial as written with precautions described.
xi. There were no conflicts of interest indicated.

b. Special reviews- None

c. Registrations for committee review

25-BMC-182, Doria Rose

i. Reviewers: Denny, Whitehead
ii. Review summary:

The group plans to use viral vectors to express B cell receptors on the surface of a cell line. This will

allow them to mix potential B cell activating antigens with these cells and measure B cell activation

via flow cytometry using several methods. These include fixing cells after activation and measuring phosphorylation of a signaling protein or taking measurement of signal-induced calcium release in the cells that can be measured by a fluorescent dye loaded in the cell suspension. This model can be used to identify promising vaccine candidates and validate fluorescently labeled proteins that can be used in B cell isolation and monoclonal antibody discovery.

iii. Committee Discussion:

- This group will use lentiviral vectors as described using a 4th generation packaging system and vectors. Vector maps are provided. Custom LV (lentiviral vector) plasmids generated commercially. Prokaryotic work is not proposed, eukaryotic work is proposed for cell assays, and HEK293 cells will be used. Statements made about exposure to animal cells, but no other information was provided. III-D-3-a at BSL-2 practices. Pretty straightforward, well-written protocol. No further review comments were provided.
- There was a question as to whether prokaryotic work was proposed here, this would seem to make sense but was not indicated on the registration. If they are, the stated levels are appropriate. There are no DURC related issues.

iv. Training and PPE requirements as established with BSL to be in line with a BSL-2 laboratory, to include laboratory safety training and BBP training for individuals handling any human materials. PPE standards include protective labcoat, gloves and eyewear.

v. Animal studies proposed: Not described here.

vi. The committee discussed the dual-use and ePPP potential of these experiments. All answers were ”no”. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

vii. There were no additional public comments.

viii. Work is approved at: Prokaryotic work is not described, but if performed may be approved at BSL-1, eukaryotic work is approved at BSL-2. No animal work is proposed by this investigator.

ix. Relevant sections of the NIH Guidelines: Prokaryotic work is at III-D-2-a (if performed), eukaryotic work is approved under III-D-3-a.

x. The committee unanimously approved the registration.

xi. There were no conflicts of interest identified.

25-BMC-183, Doria-Rose

i. Reviewers: Whitehead, Denny

ii. Review summary: The use of B cells transduced with second generation lentiviral vectors. The investigators plan to use cell lines that express antibodies of interest on the cell surface to measure the ability of antigens to activate B cells as a model to identify promising vaccine candidates and validate fluorescently labeled proteins that can be used in B cell isolation and monoclonal antibody discovery.

iii. Committee Discussion:

- The investigators will use second generation lentiviral vectors as described. No prokaryotic work. Eukaryotic work performs some cell-based assays by flow cytometry and will use BSL-2/3 as is appropriate. Section III-D.
- There were six attachments, one was from “No additional discussion after review”. Safety to check on the unusual attachment.

iv. Training and PPE requirements as established with the ABSL-2 with level 3 practices and BBP training for those working with human materials.

v. Animal studies proposed: No.

vi. There were no dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

vii. There were no additional public comments.
viii. Work is approved at: Eukaryotic work at BSL-2 with 3 practices.
ix. Relevant sections of the NIH Guidelines: III-D-3-a for eukaryotic work.
x. The committee unanimously approved as written.
xi. No conflicts of interest were identified.

25-BMC-184, Aladjem

i. Reviewers: Goff, Craigie
ii. Review summary: The goal of the project is to know if the TAU protein interferes with DNA replication. Tau is a protein that is very abundant in the central nervous system, with the highest abundance in the cerebral cortex. Tau primarily role in neurons is to increase the stability of microtubules in axons. Tau is associated with pathologies of the nervous system such as Alzheimer and Parkinson diseases. However, TAU is also expressed in actively dividing cells like cancer cells and can be internalized by microglia in the brain. Because a fraction of TAU can be localized in cell nuclei, the investigators seek to find out if TAU could interfere with DNA replication.

iii. Committee Discussion:
- The NCI investigators plan to investigate role of TAU protein in DNA replication by investigating the WT form and a mutant form in a LV expression system. The LV plasmids will be used directly into the cells of interest without an intermediate. III-D-2-a. Prokaryotic work in E. coli to propagate is BSL-1. Then into human cells at BSL-2. They use the word 'transduction' which would make it III-D-3-a.
- No significant discussion after protocol presentation.

iv. Training as is standard, including Laboratory Safety Training and BBP training for individuals working with human materials (as applicable).
v. Animal studies proposed: None
vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal. All responses were "no".
vii. No additional public comments were made.
viii. Prokaryotic work under III-D-2-a is approved at BSL-1. Eukaryotic work is approved at BSL-2.
ix. Relevant sections of the NIH Guidelines: III-D-2-a and III-D-3-a
x. The committee unanimously approved this protocol as written.
xi. No conflicts of interest were identified.

25-BMC-207, Muallem

i. Reviewers: Lee, Craigie
ii. Review summary: Ca2+ signaling and HCO3- secretion in exocrine glands. The investigators plan to identify the role and causes of impaired Ca2+ signaling mechanisms and HCO3- secretion by duct cells in the function of salivary glands and pancreas. Multiple preliminary data suggest that Ca2+ signaling by acinar cells in these exocrine glands is over activated, most likely the function of Ca2+ influx channels, that cause cell death and tissue damage. The initiator of this altered function is impaired HCO3- secretion by the duct related to altered CFTR function. Different ion channels, lipid transfer proteins, kinases and phosphatases. Currently, they plan to use siRNA and cDNA delivery for the three extended synaptotagmins and for the lipid scramblase anoctamin 6 (TMEM16F). The team may decide to manipulate other genes as the study progresses. The investigators are using recombinant adenovirus as described. HEK and HeLa cells will be transfected to express to previously described proteins. Cells are used exclusively for testing in tissue culture and NOT administered to animals.

Animal work statement: Deletion of the tree-extended synaptotagmins (chronic) had no apparent phenotypes, while deletion of extended synaptotagmin 3 by siRNA (acute) markedly affected salivary and pancreatic function. Therefore, the laboratory will need to use acute manipulation of the tree-extended synaptotagmins to understand their physiology. In the case of ANO6, deletion

in mice resulted in inhibition of regulated exocytosis. ANO6 functions as both phosphatidylserine (PtdSer) scramblase and as a Cl- channel. It is not clear which activity is required for exocytosis. To determine if the wild-type and mutant ANO6 restore exocytosis to the salivary glands, the team will deliver to the salivary glands of mice depleted of ANO6 cDNA of wild-type ANO6 and of mutant ANO6 that retains Cl- channel activity but not PtdSer scrambling.

iii. Committee Discussion:
- Knock-out mice will be generated by the NICHD mouse core and commercial vendor. Manipulated and handled at ABSL-2, according to III-D-4-a.
- The secondary reviewer had no other comments.

iv. Training and PPE requirements as established with BSL-2, to include laboratory safety training, and minimal PPE requirements including protective lab coat and eyewear.

v. Animal studies proposed: Yes, in mice, to be approved at ABSL-2.

vi. The committee discussed and agreed that there were no dual-use or ePPP concerns with the proposal.

vii. No additional public comments were made.

viii. Work is approved at: No prokaryotic work is being proposed. Eukaryotic work at BSL-2.

ix. Relevant sections of the NIH Guidelines: Eukaryotic work at III-D-3-a using in house established system with 293T cells. Animal work is approved under III-D-4a.

x. The committee unanimously approved as written.

xi. No conflicts of interest were identified.

25-BMC-208, Michael Ombrello

i. Reviewers: Goff, Lee

ii. Review summary: Investigation of innate immune cell signal transduction and inflammation via viral transduction. The Ombrello lab studies the genetic underpinnings of human inflammatory syndromes, including Still's disease (sJIA or systemic juvenile idiopathic arthritis in children and Adult-onset Still's disease in adults). Through various genetic analyses, including genome and whole exome sequencing of individuals and family trios, data mining genetic databases, and targeted resequencing of genes in pathways of interest, the lab has identified several candidate genetic variants that may contribute to disease progression. In order to study the mechanisms of how these gene variants contribute to the inflammatory states observed in patients, the team plans to introduce these variants into primary human immune cells. Utilizing viral transduction will allow the lab to analyze these introduced genes in immune cells contributing to the inflammatory state and better understand how these genetic variants contribute to sJIA.

One problem is that they state in the protocol, “A lentiviral system will be used to exogenously express genes of interest,” which is rather general. However, the investigators later go on to explain they will introduce genetic variants of TNF Receptor 1 (TNFR1, TNFRSF1A) into immune cells to study their mechanism of function via lentiviral vector transduction. They will use both monocyte-like cell lines, such as THP-1, as well as primary human immune cells derived from healthy volunteers. The replication-defective lentivirus vectors will be produced via commercial vendor. By introducing genetic variants of endogenous genes, they hope to explore the molecular mechanisms underlying the inflammatory phenotype of Still's Disease in children.

iii. Committee Discussion.
- One reviewer questioned if the WT and three variants are in a group of both constitutively expressed models as well as conditionally expressed. This was briefly discussed. Most work is III-D-3-a. Eukaryotic work in 293T cells is at BSL-2 for the fourth generation LV system and is proposing no animal work.
- Dr. Lee had no additional comments.

iv. Training and PPE requirements as established, including LST and BBP training. Using proper PPE and safety protocols minimizes exposure risk, replication-defective lentiviral vectors do not replicate.

v. Animal studies proposed: No animal work.
vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
vii. No additional public comments were made.
viii. Work is approved at: Prokaryotic work is proposed at BSL-1, eukaryotic work is approved at BSL-2.
ix. Relevant sections of the NIH Guidelines: Eukaryotic work is approved under section III-D-3-a.
x. The committee unanimously approved as written.
xi. No conflicts of interest were identified.

25-BMC-209, Ian Fraser

i. Reviewers: Whitehead, Craigie
ii. Review summary: Lentiviral Mediated Stable Cell Line Production. The goal of this study is to create lentiviral vectors for making stable cell lines where gene expression is modified through either CRISPR/Cas9 gene editing, shRNA-based RNA interference or over-expression of cDNA for the study of gene function in mammalian cells. The investigators will use lentiviral vectors expressing either sgRNA (for CRISPR) or shRNA (for RNAi) designed against various genes of interest to their research program. Similarly, cDNAs of certain genes will be cloned into lentiviral plasmids for over expression. They will transfect these plasmids into HEK 293T cells along with lentiviral packaging plasmids to produce replication-deficient lentivirus. These viral vectors will be used to transduce mammalian cells (such as THP1, RAW264.9, HEK 293T cells, HeLa cells, A549 cells) and selected with antibiotics to produce stable gene knockdown or cDNA over expressed cell line. They will target a broad range of genes which have functions relevant to the innate immune response, and full details of each gene are provided in an attachment.
iii. Committee Discussion:
- The investigators provide a list of over 120 genes as an appendix. They will target genes in the categories of TLR, Initial signaling, NFkB module, MAPK module, TRIF module, some signaling genes, transcription factors, cytokine/chemokine regulation, and negative regulators.
- There are many LV vectors (pTRIX (Viral Expression Vector), including lentiviral packaging plasmids psPAX2, pMD.G, pRSV-Rev. Maps of these plasmids were provided and they are third generation. BSL-1 for prokaryotic work. Transfection of 293T cells in eukaryotic work is approved at BSL-2, appropriate for this system. No significant discussion after this review.

iv. Training and PPE requirements to include laboratory safety training and BBP training for individuals working with human cell lines.
v. Animal studies proposed: No
vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.
vii. There were no additional public comments.
viii. Work is approved at: Eukaryotic work will be approved at BSL-2.
ix. Relevant sections of the NIH Guidelines: Eukaryotic work at III-D-3-a.
x. The committee unanimously approved the proposal as written.
xi. There were no conflicts of interest identified

25-BMC-210, Lusso

i. Reviewers: Denny, Goff
ii. Review summary: The investigators previously developed an mRNA vaccine for HIV-1 that induced protective antibodies and reduced the risk of infection in rhesus macaques. However, CD8 responses were not optimal. Now they plan to combine mRNA with VSV vectors expressing the same HIV-1 immunogens in order to potentiate CD8 responses in pre-clinical studies in macaques. In previous studies by a collaborator (and registered in 25-BMC-164/ Dr. Mark Connors) 3 DNA immunizations followed by replication-competent VSV did drive CD8+ T cells

that had avidity equivalent to the high levels detected in elite HIV controllers. They now plan to associate VSV with mRNA in prime-boost studies to potentiate specific antiviral CD8 responses.

iii. Committee Discussion:
- Dr. Goff remarked there is no description of eukaryotic work above, and the registration states that a few times. The reason for that is this RD is only for animal work. Dr Lusso is apparently performing none of the rDNA work before its use in animals.
- Under this protocol, replication incompetent LV vectors. Using VSV-Indiana to produce VSV-gag or envelope protein in position 3 or 4. This is a non-integrative virus. No prokaryotic or eukaryotic work is proposed. AAV plasmids will be used to boost some proteins. AAV2 vectors and AAV.44.9 for in vivo experiments will come from a commercial vendor. All III-D-3-a at BSL-1 for AAV work. NHP specimens to be looked at in the laboratory. Samples will be centrifuged in a Class II BSC.

iv. Training and PPE requirements include laboratory safety training and BBP training for individuals working with human cell lines. OACU training for working with NHP and NHP BBF.

v. Animal studies proposed: Yes, NHPs

vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal. DU questions were all answered no and there were no issues in that regard.

vii. There were no additional public comments.

viii. Eukaryotic work is approved at BSL-2 for VSV, animal work at ABSL-2.

ix. Relevant sections of the NIH Guidelines: III-D-3-a for possible eukaryotic work being performed or as previously registered. Animal work at III-D-4-a for animal work at ABSL-2 practices and containment and following the standard practices for working with NHP as established by NIH Manual Chapter 3044-2.

x. The committee unanimously approved the registration as written.

xi. There were no conflicts of interest identified.

25-BMC-211, Suresh Ambudkar

i. Reviewers: Lee, Craigie

ii. Review summary: The investigators aim to elucidate the role of ABC drug transporters in the development of multidrug-resistant cancer and to aid the discovery of new therapeutic strategies to increase the efficiency of chemotherapy for cancer patients. They are using multidisciplinary approaches including biochemical, *in silico* molecular modeling, and molecular dynamics simulations to understand the molecular basis of polyspecificity and the mechanism of P-gp-mediated drug transport.

Clinical resistance to multiple chemically and functionally dissimilar drugs is multifaceted. P-glycoprotein (P-gp, ABCB1) and ABCG2 appear to contribute to this problem due to their broad and overlapping substrate specificities. Both transporters also play an important role in drug-drug interactions as well as in the bioavailability and pharmacokinetics of several drugs. The team designed a coordinated strategy using multidisciplinary approaches in order to understand the molecular basis of the mechanism of drug transport. They focused on identifying residues on the homologous TMHs 6 and 12 that modulate the direction of transport from efflux to uptake. They also

characterized second-site suppressor mutations in the ICH4 and the Q-loop of NBD1 that rescue the function of a non-functional mutant. The studies focus on human P-gp and use Bac-Mam baculovirus HeLa cells for characterization of transport properties and the High Five insect cell-baculovirus expression system for biochemical and structural studies. In addition, they use *in silico* molecular docking and MD simulations to supplement the experimental data.

Baculovirus is used for transient expression of P-glycoprotein and ABCG2 in HeLa and insect cells. The team is working with multidrug resistance-linked P-glycoprotein (ABCB1) and ABCG2. These transporters pump out anticancer drugs from cultured cells resulting in the development of multidrug resistance. Bac-Mam baculovirus is used for transient expression of P-glycoprotein or

ABCG2 wild type and variants in HeLa cells for functional characterization. In addition, baculovirus encoding ABCB1 or ABCG2 is used for large-scale expression in High-Five or Sf9 insect cells.

iii. Committee Discussion: No significant discussion after review presentation.

iv. Training and PPE requirements to include laboratory safety training and BBP training for individuals working with human cell lines.

v. Animal studies proposed: No.

vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

vii. There were no additional public comments.

viii. Eukaryotic work is approved at BSL-2, animal work at ABSL-2.

ix. Relevant sections of the NIH Guidelines: III-D-2-a, possibly III-F for baculovirus work.

x. The committee unanimously approved with minor modifications.

xi. There were no conflicts of interest identified.

25-BMC-212, Tongqing Zhou

i. Reviewers: Goff, Denny

ii. Review summary: Studies of Stabilizing of Pre-Fusion Respiratory Virus Glycoprotein. The goal of this proposal is to apply structure-based protein engineering to stabilize the prefusion conformation of HMPV and HPIV fusion proteins, thereby enabling immunogen designs that induce potent and broadly neutralizing antibody responses. Respiratory viruses including Respiratory Syncytial Virus (RSV), Human Metapneumo-virus (HMPV), and Human Parainfluenza Viruses (HPIVs) cause substantial disease in infants and the elderly, yet there are no licensed vaccines for HMPV or HPIV. These viruses, all members of the Paramyxoviridae family, share a type I fusion (F) glycoprotein that mediates viral entry by transitioning from a metastable prefusion trimer to a highly stable “post-fusion” state. Stabilizing the prefusion conformation of F is a promising vaccine strategy, as demonstrated for RSV, where engineered prefusion F proteins elicit high titers of neutralizing antibodies. Therefore, they are constructing recombinants for expression of HMPV and HPIV fusion glycoprotein to be synthesized and cloned into VRC8400 vectors for expression and analysis.

iii. Committee Discussion:

- Under this protocol, the investigators are studying the process on how to create a more stable pre-fusion state in HPIV and HMPV. Work is being done by a contractor external to his laboratory. Eukaryotic work is at BSL-2. The laboratory has an aim to mutate all of the F glycoproteins. Animal work in mice under III-D-4-a at ABSL-2. Three ASPs are mentioned. HPIV alterations, NPV alterations or to study antibody responses. All DU questions are negative. They are hoping to introduce mutations, which seems appropriate, it is unclear if any would impact virulence but that is unlikely.
- No additional discussion after review, Dr. Denny had no additional comments.

iv. Training and PPE requirements to include laboratory safety training and BBP training for individuals working with human cell lines.

v. Animal studies proposed: Yes, mice

vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

vii. There were no additional public comments.

viii. Eukaryotic work is approved at BSL-2, animal work at ABSL-2.

ix. Relevant sections of the NIH Guidelines: III-D-3-a and BSL-2 with containment centrifuge. Animal work at III-D-4-a for animal work at ABSL-2 practices and containment.

x. The committee unanimously approved with minor modifications.

xi. There were no conflicts of interest identified.

25-BMC-213, James Kochenderfer

i. Reviewers: Whitehead, Lee

ii. Review summary: Development of new chimeric antigen receptors (CARs) and T-cell receptors (TCRs) encoded by gamma-retroviruses or lentiviruses. The investigators perform standard recombinant DNA methods such as restriction enzymes, ligation, and DNA fragment synthesis to construct new chimeric antigen receptors (CARs) and T-cell receptors (TCRs). The CARs and TCRs all target antigens on cancer cells, and the goal is to develop new cancer therapies. The CAR and TCR sequences will be cloned into a commonly used replication-incompetent gammaretroviral vector backbone (MSGV1) or a common 3rd generation replication incompetent lentiviral vector designated LSIN.

CAR T cells have been shown to be highly effective to treat many hematologic malignancies, and this laboratory has generated hundreds of new CAR sequences over the past 15 years. T cells can also be genetically modified to express TCRs that recognize antigens expressed by cancer cells. CARs and TCRs are expressed with either a gamma-retroviral vector called MSGV1 or a lentiviral vector called LSIN. This registration updates and replaces previous registrations held: 6518 and RD-15-VIII-13 for "Use of gammaretroviral vectors". Also it covers work previously registered in RD-11-III-20 (Development of Novel CARs). New work is described with lentiviral vectors (3rd generation), and the PI has been asked for additional information.

iii. Committee Discussion:

- This is established work that is being updated in the new system, and the group has been registered for this work for many years. Two vectors will be used; both are expression plasmids designed to express proteins on the surface of T cells. One is a replication incompetent gamma-retroviral vector, MSGV1 (mouse stem cell virus-based splice-gag vector), and the other is a replication incompetent 3rd generation lentivirus, LSIN (lentivirus self-inactivating). CAR and TCR sequences will be ligated into these gamma-retroviral or lentiviral backbones. These vectors will be used to genetically modify primary human T cells and human cell lines. The lentiviral vector system (LSIN) is a 3rd generation lentiviral system that requires 3 packaging plasmids (pRSV-Rev, pMDLgpRRE, and pMD2.G) in order to make the self-inactivating vector.
- The Biorisk group is contacting the PI to get an updated ASP amendment describing the use of LV vectors in animals.
- No significant discussion after review, Dr. Lee had no additional comments.

iv. Training and PPE requirements to include laboratory safety training and BBP training for individuals working with human cell lines.

v. Animal studies proposed: Yes, mice

vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

vii. There were no additional public comments.

viii. Prokaryotic work is approved at BSL-1. Eukaryotic work is approved at BSL-2, animal work at ABSL-2 at injection followed by level 1 housing.

ix. Relevant sections of the NIH Guidelines: III-D-2-a for prokaryotic work. III-D-3-a and BSL-2. Animal work at III-D-4-a for animal work at ABSL-2 practices for injection.

x. The committee unanimously approved with minor modifications.

xi. There were no conflicts of interest identified.

25-BMC-214, Genoveffa Franchini

i. Reviewers: Lee, Craigie

ii. Review summary: "mRNA preventive strategy with or without protein and SAMT-247". In this study the investigators will be (1) testing the immunogenicity and efficacy of the SIV-based mRNA + protein preventive strategy and simplify the immunization regimen by eliminating the protein boost while maintaining only the mRNA immunizations, and (2) include the use of intravaginal

rings releasing SAMT-247 microbicide (SAMT-247 IVRs) prior, during, and following the challenge phase, to increase vaccine efficacy and extend its durability.

The lab has developed a non-human primate model of SIVmac251 infection that has successfully anticipated and mirrored the outcomes of several HIV vaccine clinical trials (RV144, HVTN702 and HVTN705). Leveraging this model, the team has optimized an anti-HIV preventive strategy set to be tested in the HIV vaccine Phase I trial, designated as Combined Long-term Efferocytosis and ADCC Responses (CLEAR), in collaboration between the NCI and the WRAIR. However, the complexity of this regime (four components plus an adjuvant) raises concerns about its feasibility in resource-limited, remote areas of HIV endemicity. To address this, the NCI investigators have established a collaboration with professors Weissman (Penn University) and Cardozo (NYU). In an exploratory study, they tested a simple and flexible mRNA platform to deliver Dr. Franchini's V1-deleted (ΔV1) engineered envelope immunogens. The clade AE ΔV1 env immunogen, delivered as an HIV-based mRNA preventive strategy with a protein boost adjuvanted in alum, reduced the risk of infection in macaques. This study demonstrated that the mRNA platform could synergize with Dr. Franchini's V1 immunogens to mediate protective immune responses. Additionally, in another exploratory study, Dr Franchini's team tested the use of mucosal adjuvant/microbicide SAMT-247 delivered as intravaginal rings prior, during, and following the challenge phase. This study demonstrated high vaccine efficacy, ameliorated immunogenicity and prolonged reduced risk of SIVmac251 acquisition when administered with the SIV-based V1 DNA/ALVAC/gp120 vaccine.

iii. Committee Discussion:
- The overview was thoroughly given and little discussion followed, no prokaryotic descriptions given. Total of 48 macaques used to receive different combinations of antigens and then receive (III-D-3, RG-3) SIVmac251 challenge. Culture will be at BSL-2/3. Animal work in 14D will be ABSL-2/3. Linked their ASP and included ASP amendment. All dual use answers are "no".
- mRNAs expressing p55 gag of HIV-1 clade IIIB LAI and gp160 env of SIVmac251 as immunogens for preventive strategies.

iv. Training and PPE requirements to include laboratory safety training and BBP training for individuals working with human cell lines.

v. Animal studies proposed: Yes, NHP.

vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

vii. There were no additional public comments.

viii. Eukaryotic work is approved at BSL-2 with 3 level practices, animal work at ABSL-2/3 as well.

ix. Relevant sections of the NIH Guidelines: III-D-3-a and BSL-2 for eukaryotic work. Animal work at III-D-4-a for animal work at ABSL-2 with 3 level practices. Personnel to follow NIH MC 3044-2 for the safe handling of NHPs.

x. The committee unanimously approved with minor modifications.

xi. There were no conflicts of interest identified.

25-BMC-215, David Young

i. Reviewers: Denny, Lee

ii. Review summary: Manipulation of human and rhesus macaque iPSC, blood and tissues. The investigators aim to develop gene and cell therapies for the treatment of human inborn and acquired diseases, and to use genetic modification techniques to study the biology of blood cell production and stem cell transplantation in vitro and in predictive animal models.

The laboratory plans to use replication incompetent second and third generation or higher safety-modified lentiviral vectors based on HIV and SIV backbones to transfer genes and genetic sequences with high efficiency and low toxicity into human, non-human primate (rhesus

macaque) and murine cell lines and primary cells. Replication-incompetent lentiviruses allow high efficiency transfer of genes into many susceptible cell types, including primary hematopoietic stem and progenitor cells which are very difficult to genetically-modify using nonviral methods such as electroporation. Lentiviruses are more efficient at transduction of quiescent target cells, such as hematopoietic stem and progenitor cells, and have a better safety profile regarding insertional mutagenesis, since they do not target transcription start sites of genes, and have deleted enhancer regions in their long terminal repeats (LTRs).

Replication-incompetent minimal viral backbones derived from HIV or SIV consist of a U3-deleted 5' LTR, a psi packaging signal, a rev-responsive element (RRE), an internal promoter to drive a transgene or transgenes, a WPRE element to increase vector titer and stability, and a U3 self-inactivating 3' LTR. All endogenous viral genes are removed from the vector, making the vector replication-incompetent, and the gag/pol/env/rev genes are provided in trans to package the vector viral RNA into a vector particle able to transduce target cells. In second-generation vectors, a tat responsive element is retained, requiring tat provided in trans for transcription. In third-generation vectors, the tat responsive element is removed, and an internal promoter is responsible for driving all gene expression.

Vector particles are produced by transfecting three (2nd generation) or four (3rd generation) plasmids into 293T producer cells: the vector plasmid, an env plasmid (VSV-G envelope gene), a gag/pol plasmid, and a rev plasmid for 3rd generation, or a gag/pol/rev/tat plasmid for 2nd generation. The packaging plasmids have no viral sequences besides the genes themselves and a rev responsive element in the gag/pol plasmid. They do not contain packaging signals, which is only included in the vector plasmid. After transfection into 293T cells, culture supernatant is collected for 24-96 hours, and vector-containing media is used to transduce target cells following concentration and titering. Vector can be frozen and thawed as required. They work with a number of basic HIV and SIV backbones and packaging plasmids, all with the same general structure and maps are provided.

iii. Committee Discussion:
- Under this protocol numerous classes of genes will be studied including some drug resistance genes (for selection, not ‘front-line), suicide genes, marker genes, potential therapeutic genes and other CAR constructs. Replication incompetent LV vectors will be used in 293T producer cells. Third generation vectors and also the homologous SIV based vector. Eukaryotic work is proposed to be done. Animals will be followed long-term and imaging will be done *ex vivo*. Prokaryotic work in E. coli is approved at BSL-1 (III-D-2-a). Eukaryotic work is approved at BSL-III-D-3-a some can be at BSL-2. Lentiviral work in HEK293T cells per III-D-3-a at BSL-2 and animal work at ABSL-2. All primate tissues, blood and urine should be handled at BSL-2.
- No additional discussion after review, Dr. lee had no additional comments.

iv. Training and PPE requirements to include laboratory safety training and BBP training for individuals working with human cell lines.

v. Animal studies proposed: Yes, mice and NHP.

vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that there were no dual-use or ePPP concerns with the proposal.

vii. There were no additional public comments.

viii. Prokaryotic work is approved at BSL-1. Eukaryotic work is approved at BSL-2 with 3 level practices. Animal work at ABSL-2 at injection followed by level 1 housing, assuming no weeping. To follow NIH MC 3044-2 for NHP studies.

ix. Relevant sections of the NIH Guidelines: III-D-3-a and BSL-2 with containment centrifuge. Animal work at III-D-4-a for animal work at ABSL-2 practices and containment.

x. The committee unanimously approved with minor modifications.

xi. There were no conflicts of interest identified.

d. Registration amendments for committee review

24-BMC-042 amend 251203, Zayd Khaliq

i. Reviewers: Whitehead, Denny

ii. Review Summary: The investigators would like to add the use of rabies virus as well as a helper virus in the experiments in order retrogradely label inputs to the nucleus of the solitary tract (NTS). The main rabies virus is called EnvA G-Deleted Rabies-Cre-EGFP and the helper virus is called AAV8-hSyn-FLEX-TVA-P2A-eGFP-2A-oG. These two viruses will be injected at different time periods via intracranial injections. Both will need to be expressed in order to produce rabies that can label neuronal inputs to NTS neurons. This virus cannot replicate and is not pathogenic.

iii. Committee Discussion.

- The group proposes to study neuronal circuitry in mice and now wants to use AAV and G-deleted rabies virus. The RV infects one cell due to provision of the right receptor protein via AAV, and it is a one cell transmission. No eukaryotic work. Mouse work involved stereotactic injection of AAV and then electrophysiological recordings. Section K (Biological Agents) needs to include rabies virus, also ASP mentions 'retroviruses' and this might be a mistake. ABSL-2 to ABSL-1 72 hours after infection.
- Approved. The ASP states "retrovirus" when they meant rabies virus.
- Dr. Denny provided no additional comments after this brief discussion.

iv. Training and PPE requirements as already been established using standard precautions.

v. Animal studies proposed: Yes, mice

vi. The committee discussed the dual-use and ePPP potential of these experiments.

vii. No additional public comments were received.

viii. Work is approved at: Eukaryotic work is already established at BSL-2. Animal work is approved at ABSL-2 at injection and for 72 hours, followed by level 1 housing.

ix. Relevant sections of the NIH Guidelines: Eukaryotic work at III-D-3-a, III-D-4-a for animal work.

x. The committee unanimously approved as written.

xi. No conflicts of interest were identified.

RD-23-IV-10 amend 251203, Tijana Ivanovic

i. Reviewers: Whitehead, Craigie

ii. Review Summary: For IBC review this amendment features several mutations that will confer resistance to monoclonal antibodies and the drugs Baloxavir and Oseltamivir. All mutations are either lethal or do not create increases in pathogenicity.

iii. Committee Discussion.

- They provide a list of 8 mutations and references are provided for all of them and indicate they are involved in acquisition of drug resistance in some of them, but nothing novel that has not been identified before and resistances will not occur at the same time. Aggregated clusters containing two virus strains will study how viruses persist or dominate in infection. They postulate how some sequences may persist or be kept. To address what viruses will be paired with the PR8 strains, only wild type PR8 will be paired. Also, a single mutation is only what they are doing here. However, double mutations may give more concern. They responded "Yes" to the dual-use question related to drug resistance. All mutations have been previously published and described. They are making recombinant viruses, but state it is well-established that PR8 strain is not a novel pathogen.
- Out of an abundance of caution, the IBC will send to the ICDUR with a statement that the IBC has found it to not fall under dual use; none of the virus backbones are new and resistances will not occur at the same time.

iv. Training and PPE requirements as established.

v. Animal studies proposed: Yes, NHPs.

vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that they believe there are no dual-use or ePPP concerns with the proposal, but to be cautious they will advance the proposal on for consideration by the NIH ICDUR for determination as to whether the DURC-IRE will need to review.
vii. No public comments were made.
viii. Animal work is approved at the established level of ABSL-2 practices and containment and following the standard procedures for working with NHP as established in NIH MC 3044-2.
ix. Relevant sections of the NIH Guidelines: Animal work at III-D-4-a.
x. The committee unanimously approved as written.
xi. No conflicts of interest were identified.

III. Committee Review of Inactivation Procedures

IV. Standard Operating Procedures/Plans: None

V. Serious Adverse Events in Clinical Trials reviewed by the Committee: None

Reports

I. Biosafety Officer Report will be electronically sent for committee review. In June and July 2025, there were 28 research-related incidents. none apparently involved work with rDNA, 10 sharps-related incidents, 11 related to work with NHPs (6-direct and 5 associated with work with NHP), 13 involving research with other animals (mostly rodent bites), 2 related to potential exposures to HBBF for research related incidents (not related to patient care), and 1 involved potential exposure to "other" human pathogens.

The BSO reminded everyone he has reviewed the preliminarily approved registrations and registration amendments and asked again if there were any other concerns or questions about those approvals. In the absence of any further comments, these registrations and registration amendments are formally approved.

Other reports: None

Around the Room/Committee Discussion

- The January meeting will take place in the second week of January as typically scheduled (January 14th)
- A reminder that OSP mandated all IBC minutes will be publicly posted in a streamlined format. Please review the minutes in the new template and it is expected that IBC members must recuse themselves from discussions where they have conflicts of interest (as they have always done).
- The BSOs are always available prior to the meeting for any questions or concerns on reviews.

Adjournment

The meeting was adjourned at 4:45 PM.

Next meeting: January 14, 2026