NIH Institutional Biosafety Committee Minutes
Location: Bethesda Main Campus
March 11, 2026
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:
*Provided comments *in absentia* for select reviews

Guests present (9)

Rebecca Anderson (RML)	Althea Treacy, RSBMB Chief	
Grace Markley (NBBTP)	Jocelyn Mendoza (NBBTP)	Theresa Bell (NCI Fred)
Madison Cahill (DS)		

Announcements & Call to Order

The meeting was called to order by Dr. Malech at 2:03PM.

Review of the Past IBC Meeting Minutes

04 February 2026 Minutes

a. Comments on minutes, as applicable
b. The minutes were unanimously approved with minor modifications and formatting corrections by 01/21/26.

New Committee Business

I. BSO preliminary registration approvals since the previous meeting

a. Pathogen registrations (8 total): 26-BMC-057, -060-063, -065-066, -069
b. rDNA and rDNA/pathogen registrations: 26-BMC-056 (Krashes), III-D-3-a/III-D-4-a- Rodent Work using Viral Vectors; registration updates and replaces registrations: 7312, RD-18-II-09, 7311, RD-18-II-08, 5951, RD-13-VI-07. This registration is an administrative replacement with no significant changes from previous IBC approvals. 26-BMC-058 (Hanover), III-E-1- Storage Only, potential for III-D-3-a (with work): Enzymes of O-GlcNAc cycling (plasmids); This registration is an administrative record of vectors, and recombinant adenoviral plasmids in storage not currently in use with no immediate plans for use. 26-BMC-059 (O'Shea), III-D-3-a/III-D-4-a- Viral vectors for DNA modifications in cells. This registration is an administrative update and replaces the previously approved registrations RD-14-IV-04, RD-22-II-06, 7004, and 8413. This registration is an administrative replacement with no significant changes from previous IBC approvals. 26-BMC-064 (Hu), III-D-3-a/ III-D-4-a- Role of pluripotency factors in development and disease; registration updates and replaces registrations: RD-09-XI-07 and 5068. This registration is an administrative replacement with no significant changes from previous IBC approvals. 26-BMC-067 (Zhu), III-D-3-a / III-D-4-a- Transcriptional Regulation of Immune Cell Development, Activation and Functions; registration updates and replaces registrations RD-12-IX-09, 5741 and

5753. This registration is an administrative replacement with no significant changes from previous IBC approvals. 26-BMC-068 (Alvarez), III-D-3-a - Role of striatal and midbrain structures in use disorders in non-human primates; registration updates and replaces registration 5029. Registration approved for working with established recombinant material, no new recombinant work is reviewed or approved in this registration. 26-BMC-070 (Bolduc), III-D-3-a / III-D-4-a-Neuromuscular Junction Platform Vector Gene Therapy; registration updates and replaces registration RD-19-XI-02. This registration is an administrative replacement with no significant changes from previous IBC approval. 26-BMC-071 (Robey), III-E-3- Generate of Cre-inducible Mab21l2-WT and Mab21l2-R51C mutant models (TG rodent creation protocol)

c. Registration amendments: **Approved RD amendments ('amend 260304') for the Minutes**: 26-BMC-001 (amend-Falgairolle), RD-25-BMC-082 (amend-Miyagishima), RD-22-IX-06 (amend-Greten), RD-20-X-10 (amend-Gulley), RD-20-X-09 (amend-Gulley), 24-BMC-204 (amend-Ng), 24-BMC-011 (amend-Kachar), RD-22-IX-01 (amend-Caspi), RD-22-VIII-08 (amend-Caspi)
Registration amendments: **Approved RD amendments ('amend 260311') for the Minutes:** RD-20-VII-05 (amend-Leopold), RD-22-VIII-10 (amend-Pierson), RD-21-X-02 (amend-Pierson), RD-18-III-11 (amend-Pierson), RD-23-X-08 (amend-Leopold), RD-17-II-06 (amend-Hoang), 24-BMC-065 (amend-Hassan), RD-17-VI-09 (amend-Gahl), 24-BMC-170 (amend-Koretsky), RD-22-II-08 (amend-Ruckwardt), RD-18-X-09 (amend-Gonzalez), RD-22-III-02 (amend-Ferre), RD-17-IV-11 (amend-Gahl), RD-14-V-06 (amend-Gahl), RD-23-X-08 (amend-Leopold), 26-BMC-014 (amend-Colbert), 24-BMC-043- (amend-Linehan) 26-BMC-001 (amend-Falgairolle), RD-20-V-25 (amend-Roper), 26-BMC-045 (amend-Katzelnick), RD-23-VIII-04 (amend-Kochenderfer), RD-14-XI-01 (amend-Lakhotia)

d. Committee discussion: No committee members voiced comments or concerns.
e. 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 with and formally approves the registrations and registration amendments.

II. Registrations and other submissions for Committee Review

a. Clinical trial reviews - None

b. Special reviews- None

c. Registrations for committee review

26-BMC-072, Bartley, Christopher

i. Reviewers: Craigie / Goff
ii. Review summary: The group plans to morphologically and functionally characterize iPSC-like microglia from individuals with Down Syndrome. Post-mortem studies of Downs Syndrome (DS) patients have identified altered microglial morphology and cytokine expression in adolescents and young adults with DS, with significant interindividual heterogeneity. Consistent with a possible immune basis for Downs Syndrome Regression Disorder (DSRD), immunotherapies have shown promise in clinical case series. Therefore, the laboratory proposes to test for intrinsic differences between iPSC-derived microglia from DSRD and DS patients without regression (DSWR). They plan to derive induced pluripotent stem cells (iPSC) from individuals with DSRD and DSWR, as well as karyotypically normal controls, and differentiate them to microglia-like cells (iMGL). Through differentiation, the cells will be characterized via flow cytometry and RNA-sequencing. At termination of differentiation, functional assays will be completed to measure cytokine production, phagocytic capacity, activation state, and motility. They plan to complete this with a minimum of 4 DSRD biospecimens, 4 DSWR biospecimens, and 4 karyotypically normal control biospecimens.

iii. Committee Discussion:

- This group proposes to look for differences in Downs Syndrome patients using iPSCs and differentiating them to microglial cells. Reprogramming will be carried out by a NINDS core service. iPSCs will be induced using the commercial kit, cells will be characterized with RNA sequencing and cytokine production and activation and motility will be assessed.
- All dual-use questions were appropriately answered 'no'. This is correct and part B is not applicable. Dr. Goff had no additional comments for the registration.

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 a protective lab coat, gloves and protective 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, eukaryotic work is approved under III-D-3-a.

x. The committee unanimously approved the registration.

xi. There were no conflicts of interest identified.

26-BMC-073, Lee, Kyung

i. Reviewers: Whitehead, Craigie

ii. Review summary: The group wishes to characterize centrosomal proteins associated with mosaic variegated aneuploidy syndrome (MVA). Related proteins of interest will be expressed using a lentiviral protein expression system. Respective endogenous proteins will be depleted when desired. MVA, which is caused by mutations in proteins critical for proper chromosome segregation, is a genetic disorder characterized by growth and developmental retardation and predisposition to cancer. While various mutations in the centrosomal scaffold, Cep57, have been linked to the development of MVA2 syndrome, its underlying mechanism remains poorly explored. By combining "MINFLUX nanoscopy" with physicochemical and structural approaches, the group plans to investigate the functions of various centrosomal proteins involved in centriole duplication.

iii. Committee Discussion:

- The committee is requesting more information from the investigators. The investigators will probe centrosomal proteins using lentiviral vectors to express scaffolding proteins. rDNA will be introduced into cultured cells such as U2OS cells, and replication deficient lentivirus will be used. The single sentence for eukaryotic work is not descriptive: "The vector (CMVΔR8.2) has been used safely in the laboratory for more than 20 years". The laboratory apparently has been working with this construct generating lentivirus for nearly 20 years (previous registration number was RD-05-IV-15, approved in 2005), but just a map is provided for the generic "8.2" plasmid vector. The committee was unclear on whether this represents first, second, or third generation packaging.
    - Since no prokaryotic work is proposed, the committee asked who is creating the vectors. The investigators do provide maps for the eukaryotic work. The envelope G protein is provided, but the investigators need to describe their workflow, which is not described in the document. The committee needs to know if they are generating the vector itself. They provide maps for a lentiviral vector (LV) packaging system and use a "first generation plasmid". The committee agrees the BSOs can determine the appropriate level, likely BSL-2/3, when the additional information is received.

- There were incomplete attachments. Whether the investigators are packaging LV particles needs to be addressed. All DURC questions are answered “no”. More information on what they will do with the transfected cells will be useful. More information on their workflow would be helpful. The secondary reviewer agreed with this assessment.

iv. Training and PPE requirements as established with BSL to be in line with a BSL-2 laboratory (using 3 level practices here), to include laboratory safety training and BBP training for individuals handling any human materials. PPE standards include protective lab coat (closed front), gloves and protective eyewear.
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, unless it can be approved at BSL-2 with more information.
ix. Relevant sections of the NIH Guidelines: III-D-3-a for eukaryotic work.
x. The committee unanimously approved the registration pending on complete information as discussed.
xi. No conflicts of interest were identified.

26-BMC-074, Hinnebusch, Alan

i. Reviewers: Goff, Lee
ii. Review summary: The goal of the laboratory is to elucidate molecular mechanisms of gene regulation at the levels of transcription, translation and mRNA degradation in the budding yeast Saccharomyces cerevisiae in response to changes in nutrient availability or cellular stresses. The laboratory studies molecular mechanisms underlying the assembly, function, and regulation of translation initiation using budding yeast as a model system to exploit its powerful combination of genetics and biochemistry. The translation initiation pathway was elegantly outlined and processes described. In these studies, the laboratory will construct recombinant DNA plasmid containing mutant or wild-type yeast genes using standard laboratory Escherichia coli bacterial strains to be introduced by transformation into mutant or wild-type strains of yeast Saccharomyces cerevisiae. The yeast strains are then subjected to a range of genetic, biochemical, genomics or cell biological assays to identify the consequences of the mutations on regulation of gene expression.

iii. Committee Discussion:
- The investigators will express numerous genes in different shuttle vectors in yeast (e.g. transcription factors (TFs), coactivators, etc.). Two different shuttle vectors will be used. Principal Investigator (PI) stated III-D work in E. coli and in yeast. Both reviewers agreed the eukaryotic work falls under section III-E of the NIH Guidelines.
- No significant discussion after protocol presentation, all Dual-use questions are correctly answered ‘no’ as there are no issues there.

iv. Training as is standard for the BSL level 2 laboratory, 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 answers were “no”.
vii. No additional public comments were given.
viii. Prokaryotic work under at III-D-2-a is approved at BSL-1. Eukaryotic work is approved at BSL-2.
ix. Relevant sections of the NIH Guidelines: III-E for eukaryotic work.
x. The committee unanimously approved this protocol as written.
xi. No conflicts of interest were identified.

26-BMC-075, Francini, Genoveffa

i. Reviewers: Denny, Goff

ii. Review summary: In this study Dr. Franchini and her team aim to increase the breadth of immune responses by testing a multiclade nucleic acid immunogen vaccine-based analysis on messenger RNAs + proteins vaccine delivering ΔV1 envelope immunogens of clade AE (A244), B (MN) and clade C (ZM96 and NP841). This study will allow them to assess the efficacy and evaluate the immune responses elicited by multi-clade ΔV1-env immunogens. To test this hypothesis, they will immunize 11 macaques with HIV-1 clade AE (A244), clade B (MN) and C (ZM96 and NP841) V1-deleted envelope immunogens (messenger RNAs and proteins). At the end of the immunization, different immune responses will be analyzed, both in blood and mucosa, to assess the ability of the immunogens to elicit immune responses. Following last immunization, vaccinated animals, together with 10 naïve controls, will be delivered mucosally to SHIV to assess the efficacy of the vaccine. This work builds on a long history of work as the laboratory has developed a non-human primate model of SIV mac251 infection that has successfully anticipated and mirrored the outcomes of several HIV vaccine clinical trials. Leveraging this model, her team has generated engineered immunogens that showed increased efficacy (ΔV1 envelope immunogens). Additionally, they have developed a nucleic acid immunogen based on messenger RNA vaccine that expresses engineered immunogen of env of the clade AE of HIV. When administered in macaques, this vaccine reduced the risk of SHIV infection in macaques.

iii. Committee Discussion:

- The team will aim to evaluate immune responses to multiple HIV proteins and develop multiple clade expression vectors. After immunization, the responses will be monitored in the blood, to determine the efficacy of the vaccine. Nine plasmids are listed and the maps are attached, four are NA immunogen based, and four are of the gp120 nucleic acid expression type. These immunogens will be delivered to NHP. Second type recombinant work is based on pcDNA3, with gp120 genes inserted. Plasmids express the protein to be administered to NHP as described. Recombinant vectors and their sources were listed and described well. All plasmids were for transient transformation.
- No prokaryotic work is proposed. Immunogens will be transferred to both cells in vitro and in vivo. Immuno-precipitation followed by Western blotting will be performed. Eukaryotic work with SHIV is III-D-3-a at BSL-2/3. All DURC questions are ‘no’ as appropriate. Pretty clearly written. NHP tissues and blood will be worked with and analyzed.
- Secondary reviewer had no additional 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 NHPs. Can 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 given.

viii. Work is approved at: No prokaryotic work is being proposed. Eukaryotic work at BSL-2/3 for in vitro work. Animal work is approved at ABSL-2.

ix. Relevant sections of the NIH Guidelines: Eukaryotic work at III-D-3-a for eukaryotic work and analysis of the NHP tissues. Animal work is approved under III-D-4-a at ABSL-2. Subsequent work with animal tissues at BSL-2. All SHIV work is approved at ABSL-2.

x. The committee unanimously approved as written.

xi. No conflicts of interest were identified.

26-BMC-076, Whitehead, Stephen (First)

i. Reviewers: Goff, Billioux

ii. Review summary: The investigators wish to re-register the longstanding project on WNV and SLEV. This proposal supports neurovirulent flavivirus research by characterizing West Nile virus

(WNV) and St. Louis encephalitis virus (SLEV) isolates. The primary focus of the laboratory's research is to create vaccine candidates against several flaviviruses, including WNV and SLEV. The preclinical vaccine research flow is: isolation of virus, sequencing, construction of attenuated antigenic chimeric viruses with rDENV-4 (C-prM-E or prM-E of rDENV4 replaced with those of WNV or SLEV), preclinical testing of candidate vaccine viruses. Importantly, this registration is a consolidation of PRD 8436 and legacy HPRD 3815, 3817, and RD-00-IV-04

WNV / SLEV isolates will be used for the following: (1) Isolate virus from infected serum, spinal fluid, or mosquitoes, (2) to make working stocks of infectious WNV and SLEV in tissue culture - Vero, LLC-MK2, C6/36, BHK, (3) Study tissue culture phenotypes and kinetics of growth, (4) Sequence structural gene coding regions or full-genome for comparative phylogenetic analysis, (5) Construct attenuated antigenic chimeric viruses by replacing C-prM-E or prM-E regions of rDEN4 with those from WNV or SLEV, (6) Use as control viruses in tissue culture plaque titration assays, (7) Use as target virus in plaque reduction neutralization assays, (8) Use as antigen in ELISA, and (9) Study replication, immunogenicity, and pathogenicity of WNV and SLEV in mice and NHPs

iii. Committee Discussion.
- The structural genes of the viruses and capsid membrane proteins and full length DENV have been generated- very good description and diagram have been given, particularly on p.3.
- The goal was to reduce neuroinvasiveness here for the generation of the therapeutics. All maps and protocols were attached as necessary.
- No other comments from the secondary reviewer. The chair explains the registration can be used as a model for anyone else submitting registration.

iv. Training and PPE requirements as established for BSL-2 laboratories, including LST and BBP training. Animal training for ABSL-2 work as outlined by Office of Animal Care and Use (OACU).

v. Animal studies proposed: Yes, both mice and NHP work as described.

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 received.

viii. Work is approved at: Prokaryotic work in E. coli is proposed at BSL-2, eukaryotic work is approved at BSL-2, Animal work in old world monkeys and in mice is approved at ABSL-2, followed by ABSL-2 for practices and containment, NIH MC 3044-2 for working with NHP.

ix. Relevant sections of the NIH Guidelines: Prokaryotic work is approved under section III-D-2-a. Eukaryotic work under section III-D-3-a. Animal work is approved under section III-D-4-a

x. The committee unanimously approved as written.

xi. Dr. Whitehead recuses himself from voting on this review.

26-BMC-077, Leonard, Warren

i. Reviewers: Lee, Goff

ii. Review summary: The title of this proposal is “Design and engineer of novel CAR-T formats with different T cell signaling molecules for immuno-therapy development”.

Novel CAR constructs targeting CD19 were designed and cloned into a gamma-retrovirus vector MSGV by a collaborator (Dr. James Yang’s lab, NCI). CAR encoding virus is generated by transient transfection of modified 293T cells with CAR containing transfer plasmids together with packaging plasmid (Addgene protocol). In this proposal, human PBMCs from healthy donors will be activated in vitro (anti-CD3 and anti-CD28 antibody) then transduced with CAR encoding virus (viral vector) by spin infection. The virus containing media is removed, and CAR-T cells will be further expanded in vitro for 5-14 days. CAR-T expression and activity will be assayed *in vitro* and *in vivo* after expansion. The CAR-T *in vivo* anti-tumor activity will be tested in an established Nalm6 ALL leukemia model (H-0087R6). The Nalm6-GL cells (from collaborator Dr. Naomi

Taylor's lab, NCI), will be injected (0.5-2 million) into NSG mice (i.v.). 3 days later, CD19 CAR-T cells (0-20 million) will be injected into mice by i.v. and tumor growth will be monitored by bioluminescence (NIH Mouse Imaging Facility) twice per week for 2-3 weeks, body weight will be measured at the same frequency right after imaging. Mice will be euthanized at predetermined time points or following the development of severe morbidity, such as the inability to walk or difficulty in eating or drinking or >20% body weight loss).

iii. Committee Discussion:
- Novel CAR constructs have already been created by Dr. James Yang's laboratory. BSL-2 into standard human cell lines. Gamma retrovirus vector has been used extensively since the 1990s.
- The description is pretty complete, but it is hard to tell if they are doing their own cloning since most constructs may have already been made. No prokaryotic work is really described. They have been provided the "close to clinical grade" CAR construct. If they are making novel CAR constructs, the title and description do not match (possibly the historical title just being carried over). It can be approved as is, but the safety team needs to clarify with Dr. Leonard if they will modify this in some way and if so, details should be provided. Most experiments will be approved at the same levels. Sounds like they will modify some aspects of the vectors.
- In the clinical work the envelope used is possibly the same.

iv. Training and PPE requirements for working in the BSL-2 environment 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. Work is approved at: Eukaryotic work will be approved at BSL-2 into eukaryotic cells. Animal practices at 2→ABSL-1 containment after delivery. Any subsequent work with animal samples potentially containing human cells must be handled at BSL-2.

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

x. The committee unanimously approved the proposal as written, if there are any changes this must be described by the PI.

xi. There were no conflicts of interest identified

26-BMC-078, Andrews, Sarah

i. Reviewers: Billioux, Whitehead

ii. Review summary: Under this protocol, the proposal is to study epitope-specific T-cells following vaccination. The laboratory plans to identify epitope-specific T-cells, express their T-cell receptors into a T cell line (Jurkat cells) and perform activation assays to characterize the epitope, and determine cross-reactivity and measure avidity. One vital component for these assays is the need for antigen-presenting cells that express the correct HLA molecules. For antigen presenting cells, they will use long-lived transformed B cells. By utilizing a retroviral vector to express Bcl-6 and Bcl-xL in primary B cells, they can induce long-term survival of primary B cells in vitro, where they continue express surface immunoglobulin, HLA molecules and maintain the ability to secrete antibodies. This method can also be used for B cell and antibody analysis where they hope to identify rare antibodies of interest and generate long-lived antigen-specific B cells.

iii. Committee Discussion:
- The investigators will use retroviral vectors to express proteins that were previously created in another lab, and a new registration is needed. These retroviral vectors are amphotropic (able to infect human, rat, and mouse cell types) and replication incompetent. Possibility of integration and oncogenesis are concerns. A mammalian packaging cell line will be used as described. Eukaryotic work is approved at BSL-2 with 3 practices as proposed.

- In these analyses they will perform *in vitro* studies with T cell lines to measure activation. Transformed B cells will serve as HLA-expressing antigen-presenting cells in these assays. One reviewer was not sure if the 'Yes' on the DURC questions was necessary. Question B on the DURC form is a YES, as it has the potential to transform other cell types. It is amphotropic and can transform, so it can remain a yes. This is a safety issue in exposure situations, but not a DURC concern so it does not require further DURC review. The committee agreed.

iv. Training and PPE requirements for working in a BSL-2 environment 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. Prokaryotic work is approved at BSL-1. Eukaryotic work is approved at BSL-2/3 as proposed.
ix. Relevant sections of the NIH Guidelines: III-D-2-a for prokaryotic work, III-D-3-a for eukaryotic work.
x. The committee unanimously approved with minor modifications.
xi. There were no conflicts of interest identified.

26-BMC-079, Appella, Ettore

i. Reviewers: Denny, Goff* (provided comments *in absentia*)
ii. Review summary: This laboratory studies colorectal cancer and their research focus is on understanding how two key cellular control proteins, SETD8 and JUND, work together to help cancer stem cells switch between active growth and dormant survival modes. When SETD8 protein levels drop, it appears to activate JUND, which drives the cancer cells into a protective dormant state that resists treatment. However, it is believed that if they block both pathways simultaneously, the cancer stem cells will become metabolically exhausted and die. A key innovation to the laboratory's approach is testing whether tumor growth resumes when they cease blocking the SETD8-JUND pathways (by removing doxycycline). This models the clinical scenario where patients might stop treatment due to side effects or drug resistance. Such reversibility studies require the temporal dynamics and tissue architecture only possible in living organisms as cancer stem cells exist within complex tissue environments where immune cells, blood vessels, and supporting cells profoundly influence their behavior. Therefore, they are proposing studies in animals.

iii. Committee Discussion:
- Registration includes studying pathways to oncogenesis, working with CT26 murine colon cancer cells, and will use two sets of lentiviral particles. RNA is only expressed on the presence of doxycycline. Due to risk of insertional mutagenesis, the lab will follow BSL-2 and work inside a BSC. rLV vectors are all third generation, however not all maps are present. Three groups of vectors are described: tet protein, KMT5A/SETD8 transcripts, and JunD shRNA under the tet promoter. Expression products are administered to animal, human (CT26 cell line), and mouse cell lines to generate the knockdowns and manipulate them at BSL-2. Standard chemical decontaminants are used.
- Limited plasmid maps were provided; these were looked up and stated as proprietary and could not be fully verified as third-generation vectors, but they were described that way.
- No prokaryotic work at all. No other significant comments, but the insert here is a 'transforming' insert so BSL-2/3 is appropriate. Tumor growth monitored and harvested in animals for analysis. Committee members and chair agreed with the assessment.
- All DURC questions are answered 'no' as appropriate.

iv. Training and PPE requirements for work in BSL-2 environments to include laboratory safety training and BBP training for individuals working with human cell lines.

v. Animal studies proposed: Yes, mice will be injected with transfected cells. (LCB-035)
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 approved at ABSL-2.
ix. Relevant sections of the NIH Guidelines: III-D-3-a and BSL-2 with 3 practices with containment centrifuge being used for any centrifugation. 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.

26-BMC-080, Sereti, Irini

i. Reviewers: Denny, Craigie
ii. Review summary: Under this protocol, the laboratory plans to study T-cell responses to microbial and environmental antigens. Specifically, the interrogation of T cell responses to microbial and environmental antigens requires the use of dendritic cells (DCs). DCs that develop *in vivo* present with relevant physiological properties such as antigen processing capability, presentation of relevant endogenous antigens including endogenous retroviruses at physiological levels, among others. To generate large amounts of DCs *in vivo*, the laboratory will induce expression of recombinant FLT3 ligand, which boosts the development of dendritic cells. They propose to do this using a plasmid encoding the cytokine FLT3L. To generate large amounts of dendritic cells (DCs) *in vivo*, mice will be inoculated IV via hydrodynamic tail vein injection with the recombinant plasmid expressing cytokine FLT3L. Mice will be euthanized up to 14 days after injection to isolate DCs that will be used to re-stimulate T cells *in vitro* for subsequent T-cell studies.

iii. Committee Discussion:
- Experiments entail producing dendritic cells and using a commercial lentiviral plasmid as a specialized plasmid (but not in combination with the other plasmids) to express ligand and promote expansion of dendritic cells. No prokaryotic or eukaryotic work to be done other than the re-stimulation of T-cells in vitro. Vector map is attached.
- Commercial preparation of recombinant plasmid to express the murine ligand gene, once injected into mice it will be transiently expressed. No prokaryotic or eukaryotic work is proposed with the plasmid. MMuLV construct will be used to express the ECD of the FLT3 ligand without envelope; that work can be at BSL-1. It is not infectious to humans and no prokaryotic or eukaryotic work is proposed. This plasmid will also be used analogously. Section K must be updated to include the recombinants and Dr. Sereti needs to be identified on the ASP as PI or co-PI. Recommend ABSL-1 containment per guidelines III-D-4-a. All DURC questions are answered ”no” appropriately. The chair questioned why they indicated “lentivirus” and the thought is its only for the MMuLV which is the backbone being used as a plasmid to express FLT3. Not an infectious virus. Should be listed as a “lentiviral (retroviral) plasmid”.

iv. Training and PPE requirements to include laboratory safety training and BBP training not required if individuals are not working with human cell lines.
v. Animal studies proposed: Yes, mice for hydrodynamic tail vain injection with dendritic cells.
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 is approved at ABSL-1.
ix. Relevant sections of the NIH Guidelines: No prokaryotic work, eukaryotic work restimulating murine T-cells does not apply. Animal work at III-D-4-a for animal work at ABSL-1 practices and containment.

x. The committee unanimously approved with minor modifications.
xi. There were no conflicts of interest identified.

26-BMC-081, Williamson, Peter (First review)

i. Reviewers: Whitehead, Lee
ii. Review summary: This registration updates and replaces the following registrations: RD-09-X-15, RD-12-I-10, and 5056. The proposal is entitled Pathogenesis of Cryptococcus complex. The laboratory will be studying how the fungal pathogens in the Cryptococcus complex cause disease in humans by modeling these infections in mice and by testing the role of fungal genes by knocking them out and seeing how their ability to cause disease is reduced both in wild-type mice and in previously generated recombinant mice. Cryptococcus complex (C. neoformans and C. gattii species) cause an estimated 180,000 deaths annually, but little is known about genetic susceptibility in humans or which genes in the fungus determine virulence. These studies seek to address these concerns. They will use synthetic nucleic acids to delete virulence genes in cryptococcus and to then complement the gene back into the deletion to restore function. Genes expressed will not increase virulence over the that of the laboratory parental strain H99. The lab will use gene fragments (in plasmids) to generate gene constructs to transform cryptococcal species to make them less virulent or to restore their original virulence.

iii. Committee Discussion:
- This is a pretty straightforward, well-written protocol; it needs to include a list of some of the genes they are targeting or “classes of genes”. They plan to use PCR amplification to amplify fungal genes as well as marker genes such as hygromycin resistant gene (HgR). These are linked together using restriction endonucleases in the E. coli, harvested and purified and then introduced into cryptococcus. Hygromycin is not an anti-fungal that is ever used clinically so this will not introduce any resistance of concern.
- Will inoculate primary mouse cells with these plasmids. BSL-2 is appropriate. Animal work is well described and is appropriate at ABSL-2 under section III-D-4-a.

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 lab coat, gloves and eyewear.
v. Animal studies proposed: Yes, mice by IV, or TVI and oro-pharyngeal inoculation.
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, animal work at ABSL-2.
ix. Relevant sections of the NIH Guidelines: Prokaryotic work is at III-D-2-a, eukaryotic work is approved under III-D-3-a. III-D-4-a for animal work.
x. The committee unanimously approved the registration.
xi. There were no conflicts of interest identified.

26-BMC-082, Peter Williamson (Second review)

i. Reviewers: Lee, Whitehead
ii. Review summary: This registration updates and replaces the following registrations: RD-09-X-16 and 5057 and is entitled ”Pathogenesis of Candida species”. These studies aim to identify mammalian genes involved in candida pathogenesis. These are the major causes of blood stream infections. The laboratory will express mammalian proteins (such as sea urchin domain (SEA) of MUC16 involved in binding of candida to the walls of blood vessels) in prokaryote expression vectors. They will then use it to block binding of candida fungus cells to purified endothelial cells harvested from euthanized mice as well as test binding of the protein to Candida

as well as other recombinant proteins such as Als3p or N-cadherin furnished from outside laboratories or commercial sources. They plan to express mammalian proteins in the prokaryote expression vector, pMAL, that allows expression in E. coli (DH10B) and convenient purification on amylose columns due to fusion of maltose binding protein at one end of the protein.

iii. Committee Discussion:
- The investigators want to study Candida and understand infection. They will block binding of the fungal cells to epithelial cells in this study. Protein will be expressed via the attached plasmid vector. BSL-2 for prokaryotic work, BSL-2 for eukaryotic work. They have a plan for any unintended exposed with oral antifungals. Aniaml work will be carried out at ABSL-2.
- All DURC questions are ”no” as appropriate. All trainings and programs appear appropriate.
- There are isolating epithelial cells in mice. The secondary reviewer had no additional comments.

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: Yes, in mice.

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: Prokaryotic work is approved at BSL-1. Eukaryotic work at BSL-2, animal work is approved at ABSL-2.

ix. Relevant sections of the NIH Guidelines: eukaryotic work under III-D-2-a, animal work is approved under III-D-4-a.

x. The committee unanimously approved as written.

xi. No conflicts of interest were identified.

26-BMC-083, Whitehead, Stephen (Second review)

i. Reviewers: Billioux / Craigie

ii. Review summary: The purpose of the proposal is to produce flavivirus reporter particles (RVPs). They are replication incompetent. RVPs can be used to interrogate the antibody response following viral infection. Using these RVPs the laboratory plans to define the characteristics of neutralizing antibodies using a flow-based reporter virus particle neutralization assay (RVPNA) system to supplement other antibody assays such as the standard plaque reduction neutralization titration (PRNT) assay and the ELISA. The flavivirus genome is single-stranded RNA (ssRNA) that expresses a polyprotein that is cleaved into 3 structural proteins (Capsid (C), Membrane (prM), Envelope (E)) and at least 7 non-structural proteins (NS1-NS5) required for viral replication.

RVPs contain a self-replicating RNA replicon sequence coding for the viral non-structural proteins (approximately 78% of the full viral genome) along with sequence for the expression of a reporter protein. This replicon is produced in cells from a transfected plasmid (pWNRep). The structural proteins that form the viral particle are provided in trans from a separate plasmid (pC & pME, pCME or pWME). Flavivirus replicons will be packaged into virus-like particles by complementation with the structural proteins of the virus in trans, resulting in the production of RVPs. Because the viral replicon and structural proteins are expressed from separate plasmids, RVPs are “pseudoinfectious” meaning they are replication incompetent and only capable of a single round of infection. Because the surface of the RVP mimics that of a virus particle, reaction with antibodies, including antibody-mediated neutralization, serves as a proxy for antibody binding to natural virus particles. Because pseudoinfectious, non-neutralized RVPs express a reporter protein (fluorescent or luciferase) after cell entry, the relative level of RVP neutralization can be determined by measuring the reporter response after RVP/antibody binding and subsequent infection of cells. Using the RVP system, the laboratory can safely determine the

quantity of virus-reactive antibodies produced in animals and humans and this serves as a clinical measure for our flavivirus vaccine development trials.

iii. Committee Discussion:
- Flavivirus RNA is a ssRNA. RVPs contain a single replicon, replicon is produced in cells from a plasmid, with certain proteins provided in trans using another vector. This was previously described in a paper attached. Human cell lines will be used.
- There was a paper by Mukerjee et al. describing this system. Cassettes will be greater than 60% of the viral genome. RVPs of Dengue, SLEV, YFV etc. expressed. Registration is very thorough and well described with listing of percent of each.
- Integration risks into the hosts genome are not expected. DURCs are all “no” as appropriate and there are no concerns there. Very thorough registration.
- The secondary reviewer has no additional comments.

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 lab coat, 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 in E. coli at BSL-1, eukaryotic work to generate RVPs is approved under III-D-3-a.

x. The committee unanimously approved the registration.

xi. Dr. Whitehead recuses himself from this review.

26-BMC-084, Cunningham

i. Reviewers: Whitehead, Billioux

ii. Review summary: The protocol is titled “Mechanisms of HSP-mediated protection of sensory hair cells”

The goal of this project is to determine how supporting cells mediate the death and survival of sensory hair cells. The laboratory uses an *in vitro* adult mouse utricle preparation to study hearing and balance disorders caused by ototoxic drugs, specifically aminoglycoside antibiotics and cisplatin. These drugs cause permanent sensory impairment in 12–20% of patients by triggering apoptotic hair cell death. They previously demonstrated that Hsp70 inhibits this cell death *both in vitro* (using Hsp70-overexpressing mice) and *in vivo* (mice showed resistance to aminoglycoside-induced loss). However, because the inner ear contains both hair cells and glia-like supporting cells, the specific site of Hsp70 action is unclear. Emerging evidence suggests supporting cells are critical regulators of hair cell viability. Since replication-deficient adenoviruses selectively infect supporting cells in our model, they plan to use adenovirus-mediated gene expression to isolate their role in hair cell survival under stress. All recombinant adenoviruses are sourced directly from a commercial vendor expressing markers like GFP, RFP, HSP70 and mutant, also mouse MEK1 and mutants at titers of approximately $1x10^{10}$ PFU/ml; no viral construction or propagation will occur in our laboratory.

iii. Committee Discussion:
- The investigators will study HSP70 action and roles in hair cell survival, and plan to develop therapeutic intervention to drug-induced hearing loss. The research investigates hearing loss resulting from exposure to ototoxic therapeutic drugs. These agents cause permanent

impairment by inducing sensory hair cell death within the inner ear. They have previously shown Heat Shock Proteins (HSPs) provide a protective effect against this damage. Interestingly, the findings indicate HSPs function within the adjacent supporting cells rather than the hair cells themselves.

- Current studies focus on the mechanisms by which supporting cells prevent hair cell apoptosis, with the ultimate goal of developing therapeutic interventions to prevent drug-induced hearing loss. An adenoviral genome map was attached. All rAd vectors come from a commercial source as described. All are replication incompetent.
- They propose BSL-2 for infections. No live animal work is proposed. DURC questions are all ”no” as appropriate. Eukaryotic work involves tissue culture explants (utricles) from adult mice are transferred to plates where Adenovirus is added. BSL-2 is proposed which is appropriate.

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.
ix. Relevant sections of the NIH Guidelines: III-D-3-a for eukaryotic work. No animal work is described.
x. The committee unanimously approved as written.
xi. No conflicts of interest were identified.

d. Registration amendments for committee review

24-BMC-013 amend 260311, Sowalsky, Adam

i. Reviewers: Denny, Billioux
ii. Review Summary: The title of the established protocol is “Mechanisms of Prostate Cancer Development”. They wish to modify their ASP to add recombinant AAVs. (previously approved for 2nd generation lentiviral vectors) They are studying prostate cancer development. Their rAAV will help to delete a ‘Gulo’ gene in the liver of receiving mice. They are using a recombinant AAV) to target L-gulonolactone oxidase ("GULO") using CRISPR, for the purpose of depleting the expression of GULO in the liver of recipient mice. This is a critical enzyme in the synthesis of vitaminC in mice. They will also use a control, non-targeting vector. The guide RNA is mouse-specific.

iii. Committee Discussion.

- Plasmid maps are attached. Recombinant vectors will be used to perform CRISPR. Additional cancer cell lines will also be used from NIH and work to be done at BSL-2 also human cancer cell lines will be used as listed. Cell lines will include prostate cancer lines (LNCaP and derivatives, PC3, VCaP and derivatives, and RWPE and derivatives). Cell lines will also include those acquired from other institutions and NCI that are of patient-origin (patient-derived cell lines), including lines that are

  maintained in mice as patient-derived xenografts and then cultured in the lab. They plan to use virus packaging lines such as 293/293T/293FT. Submission components are also attached. ABSL-2 standards will be used for inoculating mice.
- The secondary reviewer agreed and thought it was a well-written registration but a little confusing as there were two mouse sections, but it was fine.

iv. Training and PPE requirements consistent with the BSL-2 laboratory as already been established using standard precautions and BBP training for individuals handling human materials and cell lines.
v. Animal studies proposed: Yes, mice, at ABLS-2. No prokaryotic work is proposed.

vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that felt were 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 additional public comments were received.
viii. Eukaryotic work is established and approved at BSL-2. Previous eukaryotic work is performed using BSL-2. Animal work approved at ABSL-2 laboratory and practices.
ix. Relevant sections of the NIH Guidelines: Eukaryotic work at III-D-3-a. Animal work under III-D-4-a for work in mice.
x. The committee unanimously approved as written.
xi. No conflicts of interest were identified.

RD-23-III-14 amend 260311, Cohen, Jeffrey

i. Reviewers: Whitehead, Craigie
ii. Review Summary: The title of the established registration is “Create and study herpesvirus glycoprotein-SpyVLP nanoparticles as vaccine candidates”. The laboratory is previously approved for vaccine study work expressing Epstein Barr virus proteins on nanoparticles and performing work in mice and guinea pigs. They now wish to add additional animal protocols using NHP models (both Old World Rhesus macaques, and New World Cebus apella, but without challenge studies). They are displaying herpes simplex virus (HSV) or Epstein-Barr virus (EBV) glycoproteins onto nanoparticles to produce vaccines to protect against HSV and EBV infection.

iii. Committee Discussion.
- III-D-4 -a with ABSL-1 with NHP language added. (no challenge in the NHP work)
- Dr. Denny agrees.

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 there were no dual-use or ePPP concerns with the proposal.
vii. No public comments were given.
viii. Animal work is approved at the established level of ABSL-1 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.

26-BMC-026 amend 260311, Fujii

i. Reviewers: Billioux, Denny
ii. Review Summary: The title of the established protocol is “Preventing cancer metastasis by understanding the role of inflammation”. They were previously approved at ABSL-2 for containment and practices and request a downgrade in this request. Putting in an EGFP tag into cancer cells then transforming mice with these. The current ABSL-2 assignment was based on the use of a second-generation lentiviral vector system and the PI requests reconsideration of the animal containment level based on a revised risk assessment demonstrating that the overall risk to personnel and the environment is low and consistent with lower ABSL containment. The lentiviral vectors used in this study are replication-incompetent and produced by separating essential viral genes across multiple plasmids. The transfer vector lacks all HIV-1 accessory genes, and no genes required for viral replication are present in the integrated provirus. Viral particles are pseudotyped with VSV-G solely to facilitate entry during initial transduction and do not confer replication competence *in vivo*. There is no potential for the generation of replication-

competent lentivirus under the described experimental conditions. The encoded transgene (eGFP) does not confer pathogenicity, oncogenic potential, or enhanced survival or transmissibility. It is not secreted and does not alter host immune function or increase risk to personnel. All viral vector production and handling are conducted under BSL-2. Animals are immunocompetent, and there is no expectation of viral shedding, horizontal transmission, or environmental persistence following transduction. The route of administration does not involve aerosol generation. Based on the replication-incompetent nature of the vector system, the low-risk transgene, the animal model used, and the existing procedural safeguards, we believe that the current ABSL-2 designation exceeds what is necessary to mitigate risk.

iii. Committee Discussion.
- Committee did not have a major issue with the request. Dr. Denny had some questions about the vector maps. Safety should get clarification about the types of cells to be used in animals. The injection of human cells into animals should still be performed using ABSL-2 practices, but containment may be at ABSL-1 after that. If only mouse cells are being injected, ABSL-1 is fine. If human cells are used, any subsequent work with injected human cells must still be handled at BSL-2.
- It was questioned whether mouse or human cells were being used and this will be clarified. It appears that cancer cells (4T1-BR5, E0771-BR5) tagged with EGFP will be used.

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. The committee agreed that there were 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 additional public comments were received.
viii. Work is approved at: Animal work is approved at ABSL-2 practices for injection, followed by ABSL-1 containment.
ix. Relevant sections of the NIH Guidelines: Eukaryotic work at III-D-3-a, animal work at III-D-4-a.
x. The committee unanimously approved as written.
xi. No conflicts of interest were identified.

RD-23-XII-08 amend 260311, Seder, Robert

i. Reviewers: Whitehead, Craigie
ii. Review Summary: The established protocol is entitled “Enhancing cancer immunotherapy by adoptive transfer of tumor neoantigen-specific CD8+ T cells”. The amendment is to associate a new ASP with the original ASP. They are associating a new ASP (VRC-26-1114, entitled "Rapid Discovery and Screening of Tumor-Specific TCR-Engineered T cells in Mice") with the registration. In this ASP, they will be transferring retrovirally transduced primary murine T cells into mice. Previous studies transferred T cells isolated from spleens of transgenic mice; here they will identify anti-tumor TCRs, generate plasmids that encode these TCRs, transduce primary T cells, and transfer these cells into mice. (no prokaryotic work) In addition to vectors encoding TCR, they propose to add a retroviral vector encoding FITC-CAR for the universal vaccine boosting of transferred T cells

iii. Committee Discussion.
- No additional comments. Eukaryotic work in cells, and RV particle production in 293 cells to be done at BSL-2 under section III-D-3-a. Animal work under section III-D-4-a.
- Secondary reviewer had no additional comments.

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 there were no dual-use or ePPP concerns with the proposal.
vii. No public comments were given.
viii. No prokaryotic work here. Animal work is approved at the established level of ABSL-2 practices and containment; eukaryotic work is also established at BSL-2.
ix. Relevant sections of the NIH Guidelines: Eukaryotic work under section III-D-3-a. Animal work at III-D-4-a
x. The committee unanimously approved as written.
xi. No conflicts of interest were identified.

26-BMC-014 amend 260311, Colbert, Robert

i. Reviewers: Whitehead, Craigie
ii. Review Summary: The title of the established registration is “Spondyloarthritis pathogenesis”. In this amendment they are requesting to lower to BSL-2 with mammalian plasmids only being used as described in the previous amendment. This lab was originally approved for work with second generation lentiviruses at BSL-2/3 by the IBC, and they did not separate out mammalian vs lentiviral work. Now the lab no longer uses the second-generation lentiviral vectors for research work. This amendment is requesting a drop to BSL-2 for the work with mammalian vectors. The vectors will be expressed in HEK-293 cells, and the resulting expressed protein will be analyzed.

iii. Committee Discussion.
- Removing the lentivirus portion of the work. Also use heat-inactivated MTb. They are still storing the previous vectors. Downgrade seems reasonable. Ethanol (Alcohol) will be used as the inactivating agent, and it is recommended to suggest they also use (chlorine) bleach for work with their cell lines.
- Previously second-generation lentiviral vectors were used. Now, the laboratory is only using third generation vectors.
- Using expression plasmids and removing the use of lentivirus. Only list ethanol as an inactivation agent, and the recommendation here may be to include the use of bleach.
- They list other plasmids by map- but don’t describe use of the Topo vector as well as the Mir target vector and they should be asked to clarify these items. Will they also be keeping previously developed lentiviral particle plasmids and particles- that is also not clear. They list lentiviral work and at times will use them to transduce mammalian cells in cell culture in mammalian cells. Is the ‘stable transfection’ work with lentiviral vecotors still being performed? Is this leftover or still work where they are packaging lentiviral vectors? It is being clarified that they are actually NOT doing the lentiviral work that is described. Should the old work’ description be kept and included with the registration is the question. It is clear that if they wish to perform the LV work in the future, they will have to resubmit. Reviewers thought this language should be removed from the registration.

iv. Training and PPE requirements as established.
v. Animal studies proposed: Yes, TG rats as an animal model.
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 public comments were given.
viii. Animal work is approved at the established level of ABSL-1 practices and containment
ix. Relevant sections of the NIH Guidelines: Animal work at III-D-4-a
x. The committee unanimously approved as written after the minor changes are made.
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: In January, 2026 there were 21 research-related incidents. 1 involving rDNA, 13 sharps related incidents, 06 NHP related incidents- of these 5 were from old-world NHP and 1 was new world, 6 incidents were involving work with 'other animals' (4 of those mouse bites), 0 apparent HBBF exposures, and none involving other potential 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.

The BSO also mentioned that an NIH-IBC-wide document for guidance related to SARS-CoV-2 work has been developed and will be shared with committee members for their awareness and any additional input.

Other reports: None

Around the Room/Committee Discussion

- The April meeting will take place April 1st as typically scheduled.
- As required now by the OSP, all IBC minutes will be publicly posted on our electronic records website. Please review the minutes in our 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 by Dr. Craigie (as acting Chair as Dr. Malech excused himself at 3:00pm) at 3:41 PM.

Next meeting: April 1st, 2026