NIH Institutional Biosafety Committee Minutes
Location: Bethesda Main Campus
July 09, 2025
2:00 PM – 5:00 PM
Virtual via Microsoft Teams

Members present
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
Bridgette Billioux, clinician, virology	Emily Lee, Virology, recombinant and mol. tech.	Steve Whitehead* recombinant and molecular techniques, virology
Robert Craigie, recombinant and molecular techniques		

- absent members Stephanie Goff, Althea Treacy, Steve Whitehead, Luz Angela Rosas
*Provided comments *in absentia*

Guests present

Rebecca Anderson	Avijeet Chopra	Andrew Martin
Grace Markley	Jocelyn Mendoza	Raluca Semeniuc

Announcements & Call to Order

The meeting was called to order by Dr. Malech at 1:05 PM.

Review of the Past IBC Meeting Minutes

06 June 2025 Minutes

a. Comments on minutes, as applicable
b. The minutes were unanimously approved with minor modifications.

New Committee Business

I. BSO preliminary registration approvals since the previous meeting

a. Pathogen registrations (9): 25-BMC-110-112, 116, 118, 119, 121-123
b. rDNA and rDNA/pathogen registrations: 25-BMC-109 (Harvey)- III-E-1 / III-R-4-a - Identification of afferents to different cell types of the brain reward system. Registration updates or replaces registrations RD-12-X-08, RD-12-X-21, RD-13-V-17, RD-15-III-10, RD-18-XII-12, and 6426 (previously registered by Dr. Flor Morales). 25-BMC-113 (Hodge)- III-D-4-a- TROP2 directed antibody drug conjugate to treat TROP2-expressing murine cancer (Use of commercially available murine cells expressing TROP2 in animals). 25-BMC-114 (Andrews)- III-E-1- Profiling of human and non-human primate blood, tissues and mucosal fluids. 25-BMC-115 (Henderson)- III-E-1- Development of anti-microbials targeting bacterial elongation factor EF-Tu. 25-BMC-117 (Biesecker)- III-E-1- Recombinant DNA Studies. 25-BMC-120 (Chandrasekharappa)- III-E-1- Fanconi anemia:genotype-phenotype correlations. 25-BMC-124 (Histed) - III-D-4-a- Neurophysiological Recording and Microstimulation in Behaving Mice; This registration was re-registered by Dr. Husted after his reinstatement to administratively replace IBC approved registrations RD-16-II-08 and PRD #6692.

c. Registration amendments: Approved RD amendments ('amend 250709') for the Minutes: RD-23-V-03 (amend-Akira), RD-20-XII-08 (amend-Dekker), RD-13-XI-02 (amend-Forrest), RD-24-BMC-043 (amend-Echtenkamp), RD-19-XII-04 (amend-Robey), RD-20-III-07 (amend-Liu), RD-22-IV-09 (ConRev-Hassan), RD-17-VI-12 (ConRev-Yang), RD-22-II-08 (amend-Ruckwardt), RD-22-VI-11 (amend-Sheppard), RD-22-IX-06 (amend-Greten), RD-21-I-06 (amend-Misteli), RD-22-V-05 (amend-Douek), 24-BMC-115 (amend-Liang), RD-24-II-26 (amend-Terabe), 25-BMC-012 (amend-Katzelnick)

d. Committee discussion: None

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

25-BMC-125, Anupama Khare

i. Reviewers: Billioux, Lee

ii. Review summary: The NCI investigators aim to understand how the co-infecting pathogens Pseudomonas aeruginosa, Staphylococcus aureus, and Stenotrophomonas maltophilia interact with each other. (Replacing legacy registration #6593). Stenotrophomonas maltophilia is an emerging opportunistic pathogen that is increasingly isolated in infections especially in the context of cystic fibrosis. Pseudomonas aeruginosa, Staphylococcus aureus, and Stenotrophomonas maltophilia are frequently found in coinfections in cystic fibrosis patients and it is likely that they interact in these conditions. Studies suggest that the presence of P. aeruginosa can inhibit the growth and survival of S. aureus as well as other species. They propose to identify novel interactions that occur in a multi-species system and characterize the molecules and mechanisms that underlie this interaction. Currently, they have identified that S. maltophilia aggregates upon exposure to P. aeruginosa cell-free supernatant, specifically the quorum sensing molecule PQS, and are characterizing this interaction further. To do this they will generate mutants and promoter reporters, label strains in Pseudomonas aeruginosa and Stenotrophomonas maltophilia. (GFP, MKO, dsRed, etc). They will generate mutations in any genes we identify from genetic screens that are putatively involved in the interaction between these species. (Haven't really defined which). In S. maltophilia, these include genes like smf-1 and SMLT_RS03370, that are involved in the formation of fimbriae. They will also test genes involved in motility and signaling pathways. In P. aeruginosa, they will test genes that are involved in the production of small secreted factors like PQS. Plasmids will be inserted into the appropriate bacterial strains, the strains will be selected on the appropriate selective plates, and mutants generated will be verified by PCR and sequencing. The vector maps were provided (pSEK109, and pDONRPEX18Gm - used to make markerless mutations, pUC18-mini-Tn7 plasmids for fluorescent labeling of strains. Will use different nutritional standards and test interfering molecules. Work is also done in S. Aureus with different vectors. Some strains noted with Ab resistance, but none of concern and still susceptible to different classes of antibiotics.

iii. Committee Discussion: Multiple agents can be listed in registrations so many may have different sections. Different recombinant parts are discussed here- regarding the different pathogens. There is co-culturing being done in S. Aureus but that is all it is. They should state they are not changing the Ab resistance, and that they are not performing GOF. If all they are doing is knocking out genes- that is fine. The BSOs will clarify these matters. The organisms being studied come as they are with some Ab resistance, and so long as they are not adding

new Ab resistances, that is okay. It is important working with these strains and caution must be used due to this and it all must be clarified.

iv. Training and PPE requirements as established with BSL to be in line with BSL-2, to include laboratory safety training. PPE standards include protective lab coat, gloves and eyewear.

v. Animal studies proposed: No.

vi. The committee discussed the dual-use and ePPP potential of these experiments. All answers were 'no' and investigators will be asked to confirm with the BSOs. The committee agreed that there were no dual-use or ePPP concerns with the proposal so long as no GOF experiments were being performed.

vii. There were no additional public comments.

viii. Work is approved at: Prokaryotic work is approved at BSL-2, No eukaryotic work or animal work is proposed.

ix. Relevant sections of the NIH Guidelines: Prokaryotic work is at III-D-1-a.

x. The committee unanimously approved with minor modifications and clarifications as discussed.

xi. There were no conflicts of interest identified.

25-BMC-126, Barbara Felber

i. Reviewers: Denny, Whithead

ii. Review summary: The NCI investigators have identified a novel vaccine platform comprising DNA formulated with a cationic Lipid inorganic nanoparticle emulsion (LION) that is administered by IM injection and is highly immunogenic in macaques. We reported induction of robust, long-lasting (>2 years) cellular and humoral immunity, including increased neutralization breadth to SARS CoV-2 Spike. T-cell responses were predominantly CD8+, differing from other DNA vaccines (Karaliota, S., et al: Highly immunogenic DNA/LION nanoparticle vaccine potently activates lymph nodes inducing long-lasting immunity in macaques (iScience. 2025, 28:112232; PMID: 40230522). Their aim is to expand this vaccine regimen to HIV Env and gag and test for development of antibody and T cell responses. They are testing novel HIV Env DNA/LION vaccines with the aim to induce high titer, durable tier-2 neutralizing antibodies, a feature that is difficult to achieve in NHP and humans. They are comparing DNA/LION to self-amplifying RNA/LION vaccine expressing the same immunogen and testing their clinical grade HIV Conserved Element (CE) DNA/LION vaccine towards development of a next generation clinical trial. For HIV and SIV envelope gags and other expressed genes, there are listed plasmids for these envelopes, including maps of most. The proposed studies include collection of samples for in-depth "multi-omics" approaches to understand innate and adaptive immune responses and to dissect the mechanism(s) of function of the nucleic acid DNA vaccine that resulted in the strong activation of lymph nodes and the activation of myeloid, T cells and B cells. Recombinant known risks they consider negligible (no reports of such) and have no prokaryotic or eukaryotic work proposed. Animal work is proposed in rhesus monkeys to induce immune responses with intramuscular administration. ASP is complete in Section K and for rDNA they list all apparent constructs, including the envelope replicon containing IL15 and IL17 segments.

iii. Committee Discussion: Sources of some of the DNAs could be identified. No additional discussion after review.

iv. Training and PPE requirements as established with the ABSL-2 level, to include laboratory safety training and animal training requirements per OACU.

v. Animal studies proposed: Yes. Rhesus monkeys

vi. There were no apparent 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: Animal work at ABSL-2 practices and containment
ix. Relevant sections of the NIH Guidelines: Animal work at III-D-4-a, also with NIH OACU BSSC guidelines, AEP, and including NIH MC 3044-2 for working with NHP.
x. The committee unanimously approved as written.
xi. No conflicts of interest were identified.

25-BMC-127, Andre Nussenzweig

i. Reviewers: Lee, Billioux
ii. Review summary: The NCI investigators plan to generate human iPSC lines mutant in DNA repair genes using CRISPR interference (CRISPRi), CRISPR knockout (CRISPR-KO), and a degron system to study the role of single-strand DNA breaks (SSBs) and repair pathways in iPSCs. The cell lines and CRISPRi vs. CRISPR-KO Strategy will use human iPSCs engineered to express mouse neurogenin-2 (NGN2) under a doxycycline-inducible promoter at the AAVS1 safe harbor locus (WTC11 background). Differentiation of iPSCs into post-mitotic neurons relies on the doxycycline-inducible expression of the Ngn2 transgene. Human iPSC lines used in these studies differ by whether they do or do not express CAG-dCas9-BFP-KRAB at the Clybl promoter. KRAB is a potent repressor domain that is used to silence gene expression. 2 different lentifvial systems- a 2nd generation system and a 3rd generation system.

For CRISPRi knockdown: Performed in iPSCs that stably express dCas9-KRAB. For CRISPR knockouts- these are performed in the same iPSCs without the dCas9-KRAB cassette. For lentivirus production for CRISPR, lentiviral vectors carrying sgRNAs for CRISPRi will be produced in HEK293T cells. Cells will be plated in 10-cm dishes (10–15 million cells/dish) in DMEM + 10% FBS and cultured overnight to 75–80% confluency. Transfection will use X-tremeGENE 9 in Opti-MEM, with the following plasmid mix: Lenti-Guide-NLS–GFP + sgRNA, pRSV-Rev, pMDLg-pRRE, pCMV-VSV-G. Supernatant will be collected at 48 and 72 hours post-transfection, filtered, and concentrated by centrifugation (19,400 × g, 2 hours). The viral pellet will be resuspended in 300 µL of DMEM/F12.

For lentivirus production for CRISPR-KO, (this is 2nd generation- gag, pol rev and tat all in the same vector) CRISPR-KO lentivirus will be generated in Lenti-X 293T cells. Cells will be plated at 7.5 million cells/dish in DMEM + 10% FBS and cultured overnight to 90% confluency. Transfection will use Lipofectamine 3000 and a mix containing: psPAX2, pMD2.G, pAdVantage, lentiviral sgRNA vector. Medium will be changed the next day to fresh DMEM + 10% FBS + viral boost reagent. Virus-containing supernatant will be collected after 3 days, centrifuged to remove debris, and concentrated using Lenti-X concentrator. Final virus will be resuspended in PBS (1:10 or 1:100 dilution). For lentivirus transduction of iPSCs: 0.5 million iPSCs will be infected in suspension with 150 µL of concentrated virus mixed with 150 µL E8 medium + ROCK inhibitor. Cells will incubate for 1 hour at 37°C, centrifuged at 300 × g, and plated into fresh medium with ROCK inhibitor. Clonal lines will be expanded after cell selection with antibiotic. Knockout or knockdown efficiency will be validated by Western blotting.

Third system- Degron tag system- cell lines of DNA repair genes. To study regulated degradation, they use CRISPR-mediated knock-in of a degron tag at the N-terminus of genes using two gene-specific guides. The donor DNA will include: eGFP–P2A–FKBP-V degron cassette, flanked by gene-specific homology arms, cloned into vector BPK3082 via isothermal assembly. Cas9 protein will be complexed with sgRNAs and co-electroporated into iPSCs with the donor DNA using the Lonza 4D-Nucleofector system. GFP-positive cells will be sorted, expanded as single clones, and screened for correct integration by PCR. Protein degradation will be induced using 0.5 µM dTAG-13 overnight and validated by Western blotting.

Some corrections are needed for the proposal. The lab will need to implement BSL-2 with 3 practices for the 2nd generation systems and correct their description. They are knocking out genes involved in DNA repair, there is a concern for personnel working on this and therefore BSL-2/3 is warranted.

iii. Committee Discussion. The proposal was very thoroughly reviewed. On inspection of the plasmids there are two different sets of vectors. One of the sets of vectors includes the rev gene on the packaging vectors making in 2nd generation. They may wish to change this but at current it will remain at this level. It's also a concern for the wt Cas9 to be produced together here- and BSL-2 with 3 practices are warranted.

iv. Training to include an exposure control plan training and PPE requirements as established with BSL 2 with 3 calls for additional measures as will be noted. Training to include laboratory safety training, and BBP training for individuals working with human materials.

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. No additional public comments were given.

viii. Work is approved at: Prokaryotic work at BSL-1, eukaryotic work at BSL-2 with 3 level practices implements including working in a BSC only, wearing a closed front grown, gloves, protective eyewear as standard, and using containment centrifuge cups that are gasketed for centrifugations taking place outside of the BSC.

ix. Relevant sections of the NIH Guidelines: Prokaryotic work at III-D-2-a, eukaryotic work at III-D-3-a.

x. The committee unanimously approved this protocol only after additional information is given as described.

xi. No conflicts of interest were identified.

25-BMC-128, Masaki Terabe

i. Reviewers: Denny, Whitehead

ii. Review summary: Creating a tumor cell line with modified genes. The NCI investigators will investigate the effects of gene disruption on the behavior of murine tumor cells (glioma cells) whose genes have been disrupted using CRISPR-Cas9 technology. The tumor cells with the modified gene will be used for *in-vitro* assays and/or inoculated into mice for further investigation. Targeting mlxip under hypoxic conditions, a transcription factor that migrates to the nucleus and upregulated targets that ware involved in glycolysis. Genetic alterations have been shown to influence tumor cell biology, and they will create murine tumor cells disrupted for a specific gene using CRISPR-Cas9 technology and use them for multiple assays to gain an understanding of the gene's function. Cancer cell line is SB28, resembles the human glioblastoma cell line. Recombinant is px459v2. Multiple cell lines will be created and used to understand gene function. Expression will be in eukaryotic work and animal cells. Administration in animals will subcutaneous or intra-cerebral and is described in ASP, attached. Negligible tumor oncogenic risk for humans. DURC question 6 (enhanced susceptibility to the host population) is erroneously answered yes, not appropriate because they are only knocking out a gene. Maps are provided.

iii. Committee Discussion: Was this an amendment or a change to an existing registration- it wasn't clear. The updated registration can be approved as written.

iv. Training and PPE requirements as established with BSL-1, to include laboratory safety training, and minimal PPE requirements including protective lab coat and eyewear.

v. Animal studies proposed: Yes. Mice

vi. The committee discussed the dual-use and ePPP potential of these experiments and agreed question 6 does not come into play here since they are not changing the mouse population. The committee 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-1 as all work is performed in mice cells. Animal work at ABSL-1 practices and containment.
ix. Relevant sections of the NIH Guidelines: Eukaryotic work at III-D-2-a, animal work at III-D-4-a
x. The committee unanimously approved as written.
xi. No conflicts of interest were identified.

25-BMC-129, Farran Briggs

i. Reviewers: Craigie, Denny
ii. Review summary: Goal is to understand the function of neuro-circuits. The NEI investigators plan to understand the function of specific neuronal circuits in the brain. One of the circuits, called the corticogeniculate circuit, connects the visual cortex with the visual thalamus in the feedback direction. Other critical feedback circuits in the visual system, termed corticocortical circuits, connect visual areas. They want to understand how these particular feedback circuits contribute to visual perception. To selectively manipulate the activity of neurons in these circuits (i.e. without changing the activity of any other neurons in the brain), they need a vehicle to deliver genetic material to feedback neurons. That vehicle is a modified virus (e.g. modified rabies virus, rabies-pseudotyped lentivirus, or retro-AAV). They will inject the virus into the visual thalamus and/ or visual cortex and, due to the properties of virus, it will infect only feedback projection neurons and not other neurons in the brain. These viruses have all been modified to contain genes that encode proteins that we can then use to manipulate the activity of feedback neurons with light of specific wavelengths (e.g. LEDs). Using a virus as a vehicle, we can therefore express light-sensitive proteins selectively in feedback neurons. This enables them to test the function of corticogeniculate and corticocortical circuits in visual perception. Using ferrets or non-human primates (macaques), procedures involving virus occur in the following order to each animal (each experimental session uses one animal). 1) In sterile surgery, virus is injected into the visual thalamus and/or visual cortex. 2) Some animals may undergo behavioral and/or neurophysiological study in which light is used to control neuronal activity during behavior. 3) Some animals may also undergo a terminal, non-recovery neurophysiological recording session in which electrodes are placed in the brain and recordings are made from neurons while light is used to drive the activity of virus-infected feedback neurons. 4) Following euthanasia and perfusion with PBS followed by 4% paraformaldehyde in phosphate buffer, the brain and sometimes eyes are removed and the tissue prepared for histological processing, including using antibody staining against the proteins expressed selectively in virus-infected neurons. ASP is attached and is pending ACUC approval. Animals will survive 5 days to years. Some experiments involve injection of multiple viruses.
iii. Committee Discussion. Dr. Denny had questions about some of the agents and the appropriate biosafety level for the animal experiments. The agents are administered through intra-cerebral injection, which could be performed using ABSL-2 for injection and then ABSL-1 for housing. With primates it may stay at ABSL-2 or could be considered ABSL-1 with NIH 3044-2; ferrets can be housed down to ABSL-1 after intra-cerebral injection.
iv. Training and PPE requirements as established for ABSL-2 at injection, to include laboratory safety training and working with
v. Animal studies proposed: Yes, NHPs and ferrets
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: There is no prokaryotic or eukaryotic cell work. Animal work is approved at ABSL-2 at injection, followed by ABSL-1 housing with NIH MC 3044-2 for working with NHP.
ix. Relevant sections of the NIH Guidelines: Animal work is approved under section III-D-4-a
x. The committee unanimously approved as written.
xi. No conflicts of interest were identified.

25-BMC-130, Joseph Ziegelbauer

i. Reviewers: Billioux, Whitehead
ii. Review summary: The NCI investigators aim to study HHV8/KSHV-infected cell lines to understand virus-host interactions. They are planning to grow infected primary effusion lymphoma cells harboring the virus, stimulate viral replication with sodium valproate, spin down cells, filter the supernatant, pellet virions in the filter supernatant using centrifugation, resuspend the pelleted virions, and freeze the resuspend virions. The resuspended virions will be used to infect human cell lines (293, SLK) and primary endothelial cells (HUVEC, LEC). They do not plan to make any mutant viruses, and some of this work includes purifying RNA from human tissue samples from NCI clinical trials. Another goal is to study RNA expression in these samples to then test how these genes are responding to HHV8 infections in cell culture systems. They will use siRNAs and lentivirus vectors to manipulate specific genes of interest to study infection consequences. Their goal is to develop new biomarkers for newly developed cancers. They are targeting the human genes STC1 and FLT4 genes, but additional genes will be studied in the future (to be amended). With transfect siRNAs into human cells and study effects and use lentivirus to overexpress a HHV8 non-coding RNA (circK12). Vector Builder is making the lentivectors. The registration did not include all lentiviral plasmids so it's unclear what generation, but that may be proprietary. BCL and BAC16 strains for HHV-8. DURCS are all answered 'no'. Must provide maps but have not been able to obtain.
iii. Committee Discussion: No additional discussion after review.
iv. Training and PPE requirements to include laboratory safety training and BBT 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 with level 3 practices as standard.
ix. Relevant sections of the NIH Guidelines: Animal work at III-D-III-a for eukaryotic work in established human cell lines.
x. The committee unanimously approved with minor modifications.
xi. There were no conflicts of interest identified.

d. Registration amendments for committee review

RD-23-VIII-12 amend 250709, Ted Pierson

i. Reviewers: Lee, Craigie
ii. Review Summary: The NIAID (VRC) investigators previously described the use of single cycle/replication-incompetent VSV-pseudotyped with orthobunyavirus Gn/Gc glycoproteins. We would now like to add the use of replication-competent VSV + GnGc pseudovirus. Many different bunyaviruses as listed. Previous purposes are the same, both used for neutralization assays and experiments. Newly generated chimeras will be amplified in permissive human cells for use in neutralization studies. Previously VSV chimeric and replication-incompetent viruses have been studied, so in general this seems low-risk. SARS-CoV-2, Chickungunya, Lassa

glycoprotein expressing VSV have been made before (risk group 3 and risk group 4 viral glycoproteins). Dual-use question 5: Not sure if this is truly a 'no', since it may impact the degree by which these bind cells. While this seems low-risk, it's worth mentioning to the committee.

iii. Committee Discussion. Observation that there may be a change in the binding characteristics of the virus is going to be addressed. Dr. Pierson is currently adding justification for the 'no' response here. VSV is already broad as far as infecting cells, so what is more likely is lowering the virus's ability to broadly infect. Perhaps Q5 should read 'increase' the host range rather than 'alter' to make this question more clear. Per Executive Order, the proposal does not seem to involve any 'serous societal consequences' here, and we can get clarification from the ICDUR. Analogous registrations using VSV have gone to the DURC-IRE for review and do not involve such consequences. The committee agrees it doesn't need to go the DURC-IRE, but they will pass it on for consideration by the ICDUR for the DURC-IRE.

iv. Training and PPE requirements as already established.

v. Animal studies proposed: No.

vi. The committee discussed the dual-use and ePPP potential of these experiments. The committee agreed that they 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. Work is approved at: Eukaryotic work is established at BSL-2.

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

x. The committee unanimously approved as written pending and dependent on the review of the proposal by the NIH ICDUR and if determined, the NIH DURC-IRE.

xi. No conflicts of interest were identified.

RD-23-VIII-07 amend 250709, Ted Pierson

i. Reviewers: Craigie, Lee

ii. Review Summary: The NIAID (VRC) investigators are studying bunyavirus vaccines using non-infectious subviral particles and developing plasmids for expression. They are adding a new amendment (#6) to ASP VRC-23-1018 associated with this registration. The laboratory was previously approved to test several vaccine platforms for the orthobunyaviruses LACV and OROV (DNA-, mRNA-, and VLP- based vaccines) in mice. In this amendment they would like to extend this animal work to include DNA, mRNA, and VLP vaccines for other orthobunyaviruses related to LACV: California encephalitis virus (CEV), Snowshoe hare virus (SSHV), Chatanga virus (CHATV), Tahyna virus (TAHV), Jamestown Canyon virus (JCV), Inkoo virus (INKV), Keystone virus (KEYV), and Trivittatus virus (TVTV). This additional work will use the equivalent gene products previously described in this registration that they used for LACV and OROV (M polyprotein expression constructs) as DNA/mRNA vaccines and to produce the VLPs (following transfection of cells in vitro) for these additional viruses. They were previously approved to work with M polyprotein expression constructs for these additional viruses, so the new work described here is putting them *in vivo*. (mice) Previously approved at ABSL-2. ASP has been amended and there is no indicated change in biosafety.

iii. Committee Discussion. No additional comments and Dr. Lee agreed it was straightforward.

iv. Training and PPE requirements as established.

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. No public comments were given.

viii. Work is approved at: Animal work is established at ABSL-2 practices and containment

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.

RD-14-III-01 amend 250709, Leslie Biesecker

i. Reviewers: Billioux, Whitehead
ii. Review Summary: The NHGRI investigators will be adding adeno associated virus (AAV) and lipid nano particles (LNPs) to treat the mice. The past work in the lab has shown that Proteus Syndrome (PS) is caused by a mutation in the AKT1 gene. (mosaicism). AKT1 is part of a pathway that transmits signals from the environment to the machinery responsible for many cellular functions including growth and proliferation. The mutation causes the AKT1 protein to remain active in PS patients at times when it would normally be inactive in unaffected individuals. To study this disorder, they will use an animal model in order to better understand how PS lesions develop and progress and to investigate therapeutic options for treating patients with this disease. AAV virus carrying the CRE gene and lipid nanoparticles carrying Cas9. rAAV vector cannot replicate without the cap and rep genes. Mice will be very useful because their development is similar to humans. They believe the results of these studies will be useful not only to understand PS but also to understand mosaic overgrowth disorders that result from mutations in other genes in the same signaling pathway. Pilot studies in eukaryotic cells will occur in primary human fibroblasts. Recombinant molecules will deliver the appropriate mutations. Animal work will have tissue specific expression to deliver the Cas9 nickase specifically. In mice that contain an Akt1 variant as a CRE conditional mutation. Adeno-associated viruses (AAVs) carrying Cre recombinase under tissue-specific promoters will be used to activate expression of the conditional AKT1E17K allele in vivo. Following activation, we will administer lipid nanoparticles (LNPs) formulated to deliver a Cas9 nickase–reverse transcriptase fusion along with the pegRNA(s). This dual-delivery approach allows activating the mutant allele using AAV-Cre vectors first, and then selectively inactivating it with programmable prime editing via LNPs. LNPs will be used in primary human cells to inactivate the variant. Amended ASP is attached, all DURC questions are answered no.
iii. Committee Discussion. The review performed here by the secondary reviewer was good and is completely suffice, despite the absence of the other indicated reviewer. This is an unusual case but the review was very straightforward. This is also why we are also reviewing together as a committee with the chair displaying the protocol as we go through it. It should also be noted that the orange indications on the amended registration documents indicate what is changed over the previously approved registration, making it very easy to review, and where the system doesn't automatically indicate this, the BSOs will highlight the new information for committee review as was done here.
iv. PPE and training requirements as established and to include BBP training for individuals handling human materials.
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. No public comments were given.
viii. Work is approved at: Eukaryotic work at BSL-2, animal work is approved at ABSL-1 containment and practices
ix. Relevant sections of the NIH Guidelines: Animal work at III-D-4-a
x. The committee unanimously approved the registration as written.
xi. No conflicts of interest were identified.

25-BMC-018 amend 250709, Daniel Douek

i. Reviewers: Denny, Craigie
ii. Review Summary: The NIAID investigators are amending this registration for the isolation of antibodies specific to the Hepatitis D virus. Original registration approved for mammalian plasmids. Immunizing mice with two doses of the small delta antigen (SDA) protein, as described in the original protocol, failed to stimulate a robust antibody response sufficient for identifying high-affinity antibodies. Therefore, they propose amending the current protocol to include two modifications aimed at enhancing the immune response to SDA and facilitating the generation of high-affinity antibodies for diagnostic purposes. First, to increase the number of immunizations from two to three and schedule terminal bleeds two weeks after the third dose. Second, they will employ mRNA–Lipid Nanoparticles (LNPs) due to the highly immunogenic nature of the mRNA platform in producing antibodies. Prokaryotic work in their laboratory. ASP for animal work is attached. Delivery is IM and it is explained well. No DURC concerns. ABSL-2 because the small delta fragment of hepatitis D is a RG2 agent.
iii. Committee Discussion:
iv. PPE and training requirements as established.
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. No public comments were given.
viii. Work is approved at: Prokaryotic work at BSL-1, no additional eukaryotic work over what is already approved, animal work at ABSL-2 containment and practices.
ix. Relevant sections of the NIH Guidelines: Prokaryotic work at III-D-2-a, animal work at III-D-4-a
x. The committee unanimously approved with minor modifications.
xi. No conflicts of interest were identified.

III. Committee Review of Inactivation Procedures: None.

IV. Standard Operating Procedures/Plans: None

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

Reports

I. Biosafety Officer Report: In May 2025, there were 23 research-related incidents. Three were three initially indicated as involving rDNA but this was incorrect- we are investigating and resolving all (a recombinant mouse bite, other 2 falsely misidentified material-, or exposure-wise), therefore none apparently involved work with rDNA, 10 sharps-related incidents, 6 related to work with NHPs, 9 involving research with other animals (rodent bites), 1 related to potential exposures to HBBF for research related incidents (not related to patient care), and 2 involved potential exposure to "other" human pathogens.

The BSO re-iterated the report includes research-related incidents in all labs (even Clinical Center) but excludes routine patient-care events, which are managed separately. The committee was asked for further input, and no additional comments were made.

Other reports: None

Around the Room/Committee Discussion

- As of June 2025, all IBC minutes will be publicly posted in a streamlined, uniform format across the four NIH IBCs; members have reviewed the new template and must recuse themselves from discussions where they have conflicts of interest (as they have always done).

- A new campus-wide sharps-injury committee has been formed and is chaired by the Biosafety Officer, to review research-related sharps incidents quarterly. Committee members were encouraged to volunteer and as business proceeds with this committee the IBC will be informed of activities.
- There will be no meeting in August as per our usual business activity.
- Dr. Emily Lee announced she will be on medical leave and will miss the September meeting.

Adjournment

The meeting was adjourned by Dr. Malech at 3:17 PM.

Next meeting: September 03, 2025