Stanford University Administrative Panel on Biosafety

The APB is the Institutional Biosafety Committee for Stanford

Minutes of Meeting July 16, 2025

Present (voting)

M. Holodniy, MD (Chair)
Y. Maldonado, MD (Co-Chair)
A. Bhatt, MD, PhD
S. Feldman, PhD
R. Paulmurugan, PhD
P. Yang, PhD
C. Campos
S. Chen (Alternate)
S. Felt, DVM, MPH, DACLAM, DACVPM
S. Vleck, PhD, RBP/CBSP(ABSA)

Also Present (Not Voting)

D. Berdnik, PhD, RBP(ABSA)
D. Cunanan
A. Fausto, PhD
K. Lin, PhD
R. Moore (VA Palo Alto Health Care System)
K. Nobrega
S. Oliver, PhD
S. Rayate (Research Compliance Office)
L. Taylor, PhD
J. Yamada
Y. Zhang, PhD

Guests

M. Wheeler (3:38pm-3:56pm), APB 5694
F. Khan (3:38pm-3:56pm), APB 5694
J. Alexander (4:17pm-4:30pm) APB 5797

The meeting was called to order at 3:32PM by M. Holodniy, Chair. A quorum (five or more voting members) was present. The meeting was held virtually online.

Early Agenda Items

1. The first order of business was a reminder that the Panel proceedings are confidential, though the meeting minutes shall be made publicly available. All protocols reviewed and/or presented, including proprietary information, should not be discussed outside convened meetings.

2. The second order of business was a reminder that any person with a conflicting interest in a protocol must leave the room during discussions and voting on the protocol. "Conflicting interest" includes participating in or supervising the project, an outside interest, a personal or fiduciary relationship, or some other situation giving rise to a conflicting interest as defined in the Guidelines for APB members on Conflicting Interest. A member who leaves the room for any reason will not be counted in the quorum for any vote that takes place during their absence.

3. The third order of business was the reminder that all APB members have agreed in advance, in writing, to use Designated Member Review (DMR) subsequent to Full Committee Review when a modification is needed to secure approval of any of the protocols being discussed and voted on today. APB members will have the modified research protocol available to them, and any APB member may at any time request Full Committee Review of the protocol.

4. The fourth order of business was review and voting on the minutes of the May 21, 2025, meeting which were distributed electronically to all APB members prior to this meeting.

    - No concerns were raised.
    - Voting: A motion was made to approve the minutes and was seconded.
    - Total 10, For 10, Opposed 0, Abstain 0

5. The fifth order of business was APB Panel Business.

    - Reminder: NIH Implementation Update: Promoting Maximal Transparency Under the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, Notice Number: NOT-OD-25-082
        - Reminder: minutes will be published for any meetings taking place on or after June 1, 2025.
            - APB Meeting Minutes will be posted online following approval at subsequent APB meeting
        - APB Roster is now available on the NIH website
    - Request for feedback: Transition to hybrid meeting format
        - Panel Members expressed support, though some note they will still need an online option when they cannot be present in person.

Protocol Review

6. The sixth order of business was the presentation, discussion and voting on protocols.

Biosafety staff performed the reviews, including considering agent characteristics (e.g., virulence, pathogenicity, environmental stability), the types of manipulations planned, the sources of the nucleic sequences (e.g., species), the nature of the nucleic acid sequences (e.g., structural gene, oncogene), the hosts and vectors to be used, and whether an attempt will be made to obtain expression of a transgene, and if so, the function of the protein that will be produced, as appropriate. The protocols, reviewer comments and PI responses were made available through eProtocol to all APB members prior to the meeting. All reviewer and member concerns were sufficiently addressed, except as noted in discussions below. The Panel presented, discussed and voted on the following protocols:

Clinical Protocols

PI	Protocol
1. Wheeler, M.	[5694] A Phase 1/2, Open-Label, Multicenter, Dose Finding and Dose Expansion Study to Investigate the Safety, Tolerability, and Efficacy of ALXN2350 Gene Therapy in Adult Participants with BAG3 Mutation Associated Dilated Cardiomyopathy
Comments	**New Protocol** **Training:** Complete **Applicable Section of the NIH Guidelines:** Section III-C, III-D **Containment Conditions:** BSL1 **Special Provisions:** Hospital/Clinic Infection Control precautions **Summary:** ALXN2350 is an Adeno-associated virus (AAV) 9 gene therapy that confers expression of transgenic human BAG3 in the heart. ALXN2350 is being developed with the intent to be a one-time disease-modifying gene therapy for the treatment of patients with Dilated Cardiomyopathy (DCM) who have confirmed pathogenic or likely pathogenic BAG3 mutations. This study aims to explore safety, tolerability, and efficacy across several dose ranges starting with the anticipated minimally effective dose. **Discussion:** ● A Panel Member asked if animal models only received one dose as well. The Principal Investigator answered yes. ● A Panel Member asked if serial liver enzymes will be followed for safety. The Principal Investigator answered yes, follow up visits will include measurement of liver enzymes. ● A Panel Member noted that a watch is being used and asked what is being measured. The Principal Investigator answered activity; they noted the FDA requires assessment to see if people are doing more activities at home. ● A Panel Member asked, regarding the protocol information regarding pre-clinical work with animal models, how long did it take for noted liver abnormalities to resolve. The Principal Investigator didn't know and said they can ask the sponsor; they noted animals in the high dose group were resolved by the time of necropsy with the exception of immunosuppressed animals. The panel did not specifically request further follow-up with the Sponsor. ● A Panel Member asked about immunosuppression and whether it is common for intravenous administration or just for cardiac

	interventions. The Principal Investigator answered yes, many trials have had some degree of prednisone and sirolimus administration starting between 2-6 weeks and this protocol is on the longer side. They noted that there has been a lot of discussion in the cardio world about suppression regimens and noted that over-immunosuppression is also a risk. **Voting**: A motion was made to Approve the protocol and was seconded. Total 10, For 10, Opposed 0, Abstain 0
2. Dahiya, S.	[5804] CIT7022: A Phase 1 Open-label, Multiregional, Multicenter, Basket Study Evaluating the Safety and Efficacy of KITE-363, an Autologous Anti-CD19/CD20 CAR T Therapy in Participants with Refractory Autoimmune Diseases
Comments	**New Protocol** **Training:** Complete **Applicable Section of the NIH Guidelines:** Section III-C, III-D **Containment Conditions:** BSL1 **Special Provisions:** Hospital/Clinic Infection Control precautions **Summary:** The purpose of this study is to evaluate the safety and tolerability of KITE-363, made up of autologous peripheral-blood T cells that are transduced with 3rd generation replication-deficient lentiviral vector to introduce bicistronic anti-CD19 and anti-CD20 chimeric antigen receptors (CAR) gene, in participants with autoimmune disease, namely Systemic Lupus Erythematosus, Lupus Nephritis, Systemic Sclerosis, and Idiopathic Inflammatory Myopathies. This study has a dose-escalation phase called Phase 1a and a dose-expansion phase called Phase 1b. The results of Phase 1a will help determine the recommended dose for Phase 1b. **Discussion:** ● A Panel Member asked if previous use of this product was only for lymphomas and not autoimmune diseases. The Presenter answered yes, only lymphomas ● A Panel Member asked if subjects were allowed to have other immunosuppressant therapies. The Presenter noted this will need to be confirmed with the Sponsor. The Panel did not request further follow up with the Sponsor. ● A Panel Member asked if the study included lymphodepletion. The Presenter answered yes. ● A Panel Member noted the study is targeting B cells, and they

	thought it was interesting that the study would do lymphodepletion. The Panel Member further noted that the purpose of lymphodepletion is to kill B cells and reset the immune system following cancer; they wondered what was the depletion rate? The panel discussed this and concluded it did not raise the biosafety risk and may have some merit to reduce autoimmune effects. ● A Panel Member said corticosteroid treatment may not be necessary and shouldn't be used without a need for corticosteroids, but also noted there was a clause stating these weren't required. ● A Panel Member was concerned about toxicity from CAR itself. The panel discussed and concluded that the protocol had proper safety measures for addressing toxicity associated with CAR. ● A Panel Member wondered what constitutes refractory autoimmune disease, particularly where the sponsor is exposing patients to high risk and how to define that very high risk population seems important; the Panel Member asked if there was information on inclusion and exclusion requirements. The Presenter answered this was included. **Voting**: A motion was made to Approved with Contingency, and was seconded. Total 10, For 10, Opposed 0, Abstain 0 Conditions of Approval: 1. Update informed consent form to include risks of viral vector, including risk of replication competent virus, information that lentivirus vector is based on Human immunodeficiency virus (HIV), and the risk of false positive HIV testing. 2. Provide the rationale for lack of independent oversight for this study and attach the Charter of the oversight group. 3. Regarding manufacturing, provide information on where this occurs and the conditions for accepted release criteria.
3. Alexander, J.	[5797] A Phase 2, Multicenter, Open-Label Study Of CC-97540 (BMS-986353), CD19-Targeted NEXT CAR T Cells, in Participants with Active SLE (Including Lupus Nephritis) with Inadequate Response to Glucocorticoids and at Least 2 Immunosuppressants (Breakfree-SLE) [GENE TRANSFER]
Comments	**New Protocol** **Training:** complete **Applicable Section of the NIH Guidelines:** Section III-C, III-D

	Containment Conditions: BSL1 **Special Provisions:** Hospital/Clinic Infection Control precautions **Summary:** Lupus is an autoimmune disorder that causes inflammation and progressive organ damage. Current treatment options are limited, and do not stop disease progression for all patients. This trial will test whether CD19-CAR can prevent lupus disease progression and possibly allow patients to reduce other drugs needed to manage their disease. CD19 is being targeted because the CD19 marker is expressed on all B cells and plasmablasts, which make the autoantibodies that perpetuate the lupus disease pathway. BMS-986353 is a CD19-directed cellular immunotherapy that comprises patient-specific autologous CD4+ and CD8+ T-cell populations that have been transduced using a genetically-engineered replication-incompetent, third-generation, self-inactivating (SIN) lentiviral vector encoding a CD19-specific CAR. **Discussion:** ● A Panel Member asked if a related study used this specific product or a different CAR T. The Principal investigator answered it was slightly different CAR T but it had the same transgene. The Panel Member subsequently asked if the difference was a change in manufacturing the process and not the vector itself, and also asked about a truncated epidermal growth factor receptor (eGFR). The Principal Investigator answered there was a truncated eGFR. ● A Panel Member asked about the treatment timeline. The Principal Investigator answered that treatment will be administered over 3 days. **Voting**: A motion was made to Approve the protocol and was seconded. Total 10, For 10, Opposed 0, Abstain 0
4. Enns, G.	[5828] A Phase 1/2, Global, Open-Label, Extension Study to Evaluate the Long-Term Safety and Clinical Activity of mRNA-3927 in Participants Previously Enrolled in the mRNA-3927-P101 Study (mRNA-3927-P101-EXT)
Comments	**New Protocol** **Training:** complete **Applicable Section of the NIH Guidelines:** Section III-C **Containment Conditions:** BSL1 **Special Provisions:** Hospital/Clinic Infection Control precautions **Summary:** This is a Phase 1/2, in humans study designed to understand

	if mRNA-3927 is safe long-term in participants with Propionic acidemia (PA). mRNA-3927 is anticipated to restore endogenous production of enzymatically active propionyl-CoA carboxylase in the mitochondria of liver cells, therefore restoring flux through the propionate metabolism pathway in the liver and improving manifestations of the disease by addressing the primary metabolic defect. **Discussion:** ● A Panel Member asked if there is any safety data or noted toxicities. The Presenter answered that there were no major safety issues, DLTs, and no efficacy data. ● A Panel Member asked if they only have grade 1 and 2 adverse effects (AEs)? The Presenter answered yes and asked if the Panel Member wanted to see the list of grade 1 and 2's AEs, but the Panel Member answered no, they only wanted to confirm a lack of more severe AEs. **Voting**: A motion was made to Approve the protocol and was seconded. Total 10, For 10, Opposed 0, Abstain 0

Basic Protocol

PI	Protocol
1. Davis, M.	[5585] Testing BCG efficacy against Mtb infection in human organoids
Comments	**New Protocol** **Training:** Complete **Applicable Section of the NIH Guidelines:** Section III-D **Containment Conditions:** BSL2 **Special Provisions:** Medical surveillance required (baseline testing) **Facility Visit:** 6/23/2025 **Summary:** The goal of this project is to analyze the efficacy of the Bacillus Calmette-Guerin (BCG) vaccine against Mycobacterium tuberculosis (Mtb) infections in human organoids. The lab will co-culture healthy human spleen organoids pre-treated with BCG together with healthy human lung organoids infected with either the attenuated Mycobacterium tuberculosis strains mc² 7901 or mc² 7902 or their Green Fluorescent Protein (GFP) and tandem dimer Tomato derivatives via in vitro experiments. Immune profiling will be assessed by flow cytometry of fixed, infected lung cells and Enzyme-Linked Immunosorbent Assay

	(ELISA) assays of culture supernatants after 2 weeks of the co-culturing experiment. **Discussion:** ● A Panel Member asked whether any Mtb muti-drug resistant (MDR) strains would be used for the study. Biosafety confirmed no MDR strains will be used. ● A Panel Member asked about the mode of BCG administration into the spleen organoid. Biosafety answered that bacteria will be added into the medium on top of the organoid with a pipette; no sharps will be used for this project. ● A Panel Member asked if supplements are being added to the Mtb auxotroph strains while co-cultured with organoids. Biosafety confirmed that amino acid supplements will be added. ● A Panel Member asked about the way of disposing of the culture medium. Biosafety confirmed that all culture media will be bleached with fresh bleach at a 10% end concentration for 30 min before disposal outside the biosafety cabinet (BSC). ● A Panel Member asked whether the long term goal of this project is to repeat the experiment with wildtype risk group 3 (RG3) Mtb strains at BSL3. Biosafety informed the APB that the lab has approval for a similar BSL3 project but has decided to work first with attenuated Mtb strains at BSL2 and may later seek approval for the same experiments at BSL3 for proof of concept. ● A Panel Member expressed concern about ELISA assays being performed on the bench. Biosafety confirmed that all steps involving ELISA assay development will be done inside the BSC except the last step involving an ELISA plate reader in the same room but outside the BSC. Biosafety noted that during this step, plates will be sealed with parafilm and surface decontaminated before being transported and placed into the plate reader. ● A Panel Member raised concern about aerosolization of bacteria and decontamination of the plate washer before taking it out of the BSC. Biosafety confirmed with the lab that no plate washer will be used for this project. Instead, ELISA plates will be washed manually inside the BSC. This was noted in the precaution section of the protocol. ● A Panel Member raised concern about immunocompromised personnel working with BCG strains. Biosafety confirmed that all personnel are required to undergo consultation with the Occupational Health Center (OHC) before working on this project. ● A Panel Member asked if lab personnel and the OHC are informed about the symptoms of BCGosis in order for physicians

	to be able to distinguish these from general tuberculosis symptoms. Biosafety confirmed that the distinction of the symptoms is noted in the risk section of the protocol and personnel have been informed. In addition, it is the OHC's policy that all personnel working with BCG and/or attenuated Mtb strains undergo a medical consultation and a baseline Quantiferon test before the beginning of the project. ● A Panel Member asked if the OHC has access to APB protocol content and antibiograms of the bacterial strains used for the project. Biosafety confirmed that the medical director of the OHC and some selected staff have direct access to protocols but are also able to request information from Biosafety as needed. **Voting:** A motion was made to approve the protocol and was seconded. Total 10, For 10, Opposed 0, Abstain 0
2. Rosser, J.	[5809] Seroprevalence of vector and water borne infectious diseases
Comments	**New Protocol** **Training:** Complete **Applicable Section of the NIH Guidelines:** N/A **Containment Conditions:** BSL2 **Special Provisions:** none **Facility visit:** 7/2/2025 **Summary:** This lab's project will involve culturing and propagation of arboviruses, Chikunguya Virus and Ross River virus, to develop serological assays to study the exposure history of human participants using human serum samples. Serological assays to be developed are Enzyme-linked immunosorbent assays (ELISAs) and 50% Plaque Reduction Tests. These serological assays will also be developed for typhoid serology, examining anti-hemolysin E antibodies. Establishment of these serological assays will help determine rates of seroprevalence for pathogens of interest and help study pathogen-specific antibody responses. **Discussion:** ● A Panel Member asked how it is determined that the virus is actually inactivated using the proposed inactivation protocol. Biosafety noted that literature supports inactivation of enveloped RNA viruses at 56°C for 30 minutes, but researchers have agreed to perform work with all inactivated viruses within the Biosafety Cabinet (BSC) as an added precaution.

	• A Panel Member inquired about the standard protocol for confirming inactivation protocols and whether a plaque assay is required. The Biosafety Officer noted that if the method is well-documented in the literature, it has been the position of the panel in the past that additional validation may not be necessary, but the Biosafety group can request further evidence if the Panel requests it; it was not requested. The Panel agreed that if work continues to be conducted within the BSC, validation of viral inactivation protocol is not needed. However, if researchers wish to move inactivation steps to the bench, further validation may be required. • Panel Members discussed CDC recommendations and availability of Chikunguya Virus vaccines for researchers. Panel members with medical degrees determined it was not recommended. **Voting:** A motion was made to approve the protocol and was seconded. Total 10, For 10, Opposed 0, Abstain 0

The meeting was adjourned at 5:21 PM