

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

*Board on Health Sciences Policy
Forum on Regenerative Medicine*

**Exploring Novel Clinical Trial Designs for Gene-Based Therapies –
A Workshop**

November 13, 2019

National Academy of Sciences Building
Lecture Room
2101 Constitution Avenue NW
Washington, DC 20418

Statement of Task:

Designing clinical trials to test the safety and efficacy of regenerative medicine therapies, such as gene- and gene-editing- based therapies, can be complex for several reasons including challenges with determining an optimal dosage, delivering the product effectively, and successfully recruiting patients to what may be “single chance” trials, to name a few. To explore the design complexities and ethical issues associated with clinical trials for these types of therapies, an ad hoc planning committee will hold a one-day public workshop in Washington, DC. Speakers at the workshop may be asked to discuss patient recruitment and selection for gene-based clinical trials, assessing the safety of new therapies, dose escalation, and ethical issues such as informed consent and the role of clinicians in recommending trials as options to their patients. The concept of repeat dosing and sensitization treatments may also be explored. A broad array of stakeholders may take part in the workshop, including academic and industry researchers, regulatory officials, clinicians, bioethicists, and individuals/patients and patient advocacy groups. The planning committee will develop the workshop agenda, select and invite speakers and discussants, and may moderate the discussions. A proceedings of the workshop will be prepared by a designated rapporteur in accordance with institutional policy and procedures.

Forum on
REGENERATIVE MEDICINE



BACKGROUND

As a way to define the scope of this workshop, the planning committee used the following definition of *gene therapy* from the FDA, which is “the administration of genetic material to modify or manipulate the expression of a gene product or to alter the biological properties of living cells for therapeutic use.” Similarly to the FDA the committee also considered any use of gene editing (techniques including CRISPR/Cas9 that allow for precise changes in the nucleic acids of a person, animal, or other living organism) to be a gene-based therapy. The workshop scope may also include discussions of topics related to gene therapies in the context of other available and potentially curative treatments (e.g. bone marrow transplantation for hemoglobinopathies) and the decision-making process faced by patients and clinicians.

AGENDA

8:30 a.m. **Opening Remarks**

KATHY TSOKAS, *Forum Co-Chair*
Regulatory Head of Regenerative Medicine & Advanced Therapy
Johnson & Johnson

8:35 a.m. **Charge to Workshop Speakers and Participants**

KRISHANU SAHA, *Workshop Co-Chair*
Associate Professor
Retina Research Foundation Kathryn and Latimer Murfee Chair, Department of
Biomedical Engineering
University of Wisconsin-Madison

8:45 a.m. **Trial by “First”: Lessons from the Frontlines of Clinical Trials in Gene Therapy**

KATHERINE HIGH
President and Head of R&D
Spark Therapeutics

9:05 a.m. **Clarifying Questions from Workshop Participants**

SESSION I: DEVELOPING FIRST IN HUMAN GENE THERAPY CLINICAL TRIALS

Session Objective:

- Explore the issues arising in the design of early stage clinical gene therapy trials, including choice of endpoints, relevance and requirements for preclinical data, and identifying and using appropriate controls or natural history datasets.

Session Moderator: Cindy Dunbar, NHLBI, NIH

9:15 a.m. JONATHAN KIMMELMAN
Director of Biomedical Ethics Unit

McGill University

- 9:30 a.m. RICHARD FINKEL
Division Chief, Neurology
Department of Pediatrics
Nemours Children's Health System
- 9:45 a.m. PETRA KAUFMANN
Vice President, R&D Translational Medicine
AveXis
- 10:00 a.m. **Panel Discussion with Speakers and Workshop Participants**
- 10:30 a.m. **Break**

SESSION II: UNDERSTANDING THE COMPLEXITIES OF PATIENT SELECTION, ENROLLMENT, AND THE CONSENT PROCESS

Session Objectives:

- Understand ethical issues surrounding patient selection, enrollment, and consent for gene-based therapies and how they differ from conventional clinical trials.
- Identify what resources are available to help patients and providers accurately understand the potential risks and benefits of participating in a gene-based clinical trial.
- Explore communication strategies aimed at helping patients make informed decisions about participating in trials for gene-based therapies.

Session Moderator: Mildred Cho, Stanford University

- 10:45 a.m. COURTNEY FITZHUGH
Lasker Clinical Research Scholar
Laboratory of Early Sickle Mortality Prevention
National Heart, Lung, and Blood Institute
National Institutes of Health
- 11:00 a.m. JOHN TISDALE
Senior Investigator and Director, Cellular and Molecular Therapeutics Laboratory
National Heart, Lung, and Blood Institute
National Institutes of Health
- 11:15 a.m. JENNIFER PUCK
Professor, Department of Pediatrics
UCSF
- 11:30 a.m. PAT FURLONG
Founding President and CEO
Parent Project Muscular Dystrophy

Patient and Family Perspectives

11:45 a.m. RON BARTEK

11:50 a.m. MARIA JOSE CONTRERAS

11:55 a.m. TESHA SAMUELS

12:00 p.m. **Panel Discussion with Speakers and Workshop Participants**

12:30 p.m. **Working Lunch**

SESSION III: CONSIDERING THE CHALLENGES WITH DEVELOPING ENDPOINTS FOR GENE THERAPY CLINICAL TRIALS

Session Objective:

- Learn about successes and challenges in accurately measuring clinical endpoints and outcomes for gene-based therapies and moving products through the translational pathway.

Session Moderator: Larissa Lapteva, FDA

1:30 p.m. LARISSA LAPTEVA
Associate Director for Clinical and Nonclinical Regulation, Division of Clinical
Evaluation, Pharmacology, and Toxicology
Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research
(CBER)
Food and Drug Administration (FDA)

1:45 p.m. DWIGHT KOEBERL
Professor, Department of Pediatrics/Division of Medical Genetics, and Department of
Molecular Genetics and Metabolism
Medical Director, Biochemical Genetics Laboratory
Duke University

2:00 p.m. ALBERT MAGUIRE
Professor of Ophthalmology
Hospital of the University of Pennsylvania
Presbyterian Medical Center of Philadelphia

2:15 p.m. JULIE KANTER
Associate Professor, Hematology & Oncology
University of Alabama at Birmingham (UAB) School of Medicine

2:30 p.m. **Panel Discussion with Speakers and Workshop Participants**

3:00 p.m. **Break**

SESSION IV: INTEGRATING A GENE-BASED THERAPY INTO CLINICAL PRACTICE: EXPLORING LONG-TERM PATIENT MANAGEMENT AND FOLLOW-UP ISSUES

Session Objectives:

- Explore the implications of long-term clinical management of patients who participate in gene-based clinical trials (e.g., side effects, immunological implications).
- Discuss how data from a limited number of patients can be effectively utilized to determine if a gene-based therapy is safe and/or effective.

Session Moderator: Michael DeBaun, Vanderbilt University

- 3:15 p.m. TEJASHRI PUROHIT-SHETH
Director, Division of Clinical Evaluation, Pharmacology, and Toxicology
Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research
U.S. Food and Drug Administration
- 3:30 p.m. LESLIE ROBISON
Chair, Department of Epidemiology and Cancer Control
Co-Leader, Cancer Control & Survivorship Program
St. Jude Children's Research Hospital
- 3:45 p.m. DAVID CHONZI
Vice President, Pharmacovigilance and Epidemiology
Allogene
- 4:00 p.m. BRUCE MARSHALL
Senior Vice President of Clinical Affairs
Cystic Fibrosis Foundation
- 4:15 p.m. **Patient Perspective**
BOB LEVIS
- 4:20 p.m. **Panel Discussion with Speakers and Workshop Participants**

SESSION V: NEXT STEPS & WRAP UP SESSION

Session Objectives:

- Discuss ways forward to support the clinical development of safe and effective gene-based therapies.
- Summarize the lessons learned and topics discussed throughout the workshop.

Session Moderator: Celia Witten, FDA

- 4:50 p.m. **Final Panel Discussion**
- RON BARTEK
MILDRED CHO

DAVID CHONZI
RICHARD FINKEL
PAT FURLONG
KATHERINE HIGH
JULIE KANTER

5:20 p.m. **Final Remarks from Workshop Co-chairs**

CELIA WITTEN, *Workshop Co-Chair*
Deputy Director, Center for Biologics Evaluation and Research
U.S. Food and Drug Administration

5:30 p.m. **Adjourn**
Evening Reception – East Court