# Community Conversation

## Patients Leading the Way: How PEDDLE is Shaping the Future of MASH Trials

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# Community Conversation Agenda

- Overview of the Liver Forum
  - Sehyr Khan, Forum for Collaborative Research
- Overview of Patient Engagement
  - Michael Betel, Fatty Liver Alliance
- MASH POWER Council
  - Rosemarie Sellati, Regeneron
- Patient Engagement at Madrigal
  - Chris Frates, Madrigal Pharmaceuticals
- Patient Engagement in the Regulatory Context
  - Henry Chang, Fatty Liver Foundation
- What is PEDDLE Doing?
  - Michael Betel, Fatty Liver Alliance

# Overview of the Liver Forum



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# Overview of the Forum for Collaborative Research

The Forum for Collaborative Research, a public/private partnership and part of the UC Berkeley School of Public Health, has addressed cutting-edge regulatory science and policy issues for over 20 years through a process of stakeholder engagement and deliberation.

POSITION PAPER

## Twenty-five years of addressing cutting-edge scientific, policy, and regulatory issues through collaboration: The Forum for Collaborative Research

Robin Schaefer | Alessi Ayvaz | Christopher R. Hoffman | Margot Yann | Zachary Rooney | Mitchell Leus | Shilpa Mitra | Veronica Miller | for the Forum for Collaborative Research

JOURNAL ARTICLE

## Consensus Definitions of Cytomegalovirus (CMV) Infection and Disease in Transplant Patients Including Resistant and Refractory CMV for Use in Clinical Trials: 2024 Update From the Transplant Associated Virus Infections Forum

Per Ljungman, Roy F Chemaly, Fareed Khawaya, Sophie Alain, Robin Avery, Cyrus Badshah, Michael Boeckh, Martha Fournier, Aimee Hodowanec, Takashi Komatsu, Ajit P Limaye, Oriol Manuel, Yoichiro Natori, David Navarro, Andreas Pikis, Raymund R Razonable, Gabriel Westman, Veronica Miller, Paul D Griffiths, Camille N Kotton, for the CMV Definitions Working Group of the Transplant Associated Virus Infections Forum

JOURNAL ARTICLE

## Chronic Hepatitis B Finite Treatment: Similar and Different Concerns With New Drug Classes

Marion G Peters, Man-Fung Yuen, Norah Terrault, John Fry, Pietro Lampertico, Ed Gane, Carey Hwang, Luisa M Stamm, Mitchell Leus, Mala K Maini, Patricia Mendez, Isabelle Lonjon-Domanec, Thomas Berg, Su Wang, Poonam Mishra, Eric Donaldson, Stephanie Buchholz, Veronica Miller, Oliver Lenz on behalf of the HBV Forum Stopping Finite Therapy Working Group
Author Notes

*Clinical Infectious Diseases*, Volume 78, Issue 4, 15 April 2024, Pages 983–990, https://doi.org/10.1093/cid/ciad506
**Published:** 26 August 2023 **Article history**

SPECIAL ARTICLE

## Case definitions for inclusion and analysis of endpoints in clinical trials for nonalcoholic steatohepatitis through the lens of regulatory science

Siddiqui, Mohammad Shadab[1,†]; Harrison, Stephen A.[2,†]; Abdelmalek, Manal F.[3]; Anstee, Quentin M.[4]; Bedossa, Pierre[5]; Castera, Laurent[6]; Dimick-Santos, Lara[7]; Friedman, Scott L.[8]; Greene, Katherine[14]; Kleiner, David E.[9]; Megnien, Sophie[10]; Neuschwander-Tetri, Brent A.[11]; Ratziu, Vlad[12]; Schabel, Elmer[13]; Miller, Veronica[*14]; Sanyal, Arun J.[1]; on behalf of the Liver Forum Case Definitions Working Group
Author Information

*Hepatology* 67(5):p 2001-2012, May 2018. | **DOI:** 10.1002/hep.29607

OPEN

Review

## A proposal from the liver forum for the management of comorbidities in non-alcoholic steatohepatitis therapeutic trials

Raluca Pais[1,2], Bertrand Cariou[3], Mazen Noureddin[4], Sven Francque[5,6], Jörn M. Schattenberg[7], Manal F. Abdelmalek[8], Gadi Lalazar[9], Sharat Varma[10], Julie Dietrich[11], Veronica Miller[12], Arun Sanyal[13], Vlad Ratziu[1,14,*], on behalf of the Liver Forum NAFLD-Associated Comorbidities Working Group



Berkeley Public Health

THE FORUM For Collaborative Research™

**Ocular Diseases Forum 2**

Saturday, September 28, 2024
University of California, Washington Center
1608 Rhode Island Avenue NW, Washington DC 20036
**AGENDA**

OPINION

## Promising results of HIV prevention trials highlight the benefits of collaboration in global health: The perspective of the Forum HIV Recency Assay Working Group

**Robin Schaefer[1*], Logan Donaldson[1], Mitchell Leus[1], Chukwunomso E. Osakwe[1], Benjamin Chimukangara[2], Shona Dalal[3], Ann Duerr[4], Fei Gao[4], David V. Glidden[5], Beatriz Grinsztejn[6], Jessica Justman[7], Grace Kumwenda[8], Oliver Laeyendecker[9], Ha Youn Lee[10], Frank Maldarelli[11], Kenneth H. Mayer[12,13], Jeffrey Murray[14], Bharat S. Parekh[15], Brian Rice[16], Michael N. Robertson[17], Suzue Saito[7], Vani Vannappagari[18], Mitchell Warren[19], Diana Zeballos[20], Jörg Zinserling[21], Veronica Miller[1]**

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# Overview of the Liver Forum

- **What:** a platform for ongoing multi-stakeholder dialogue to identify barriers, prioritize research and identify solutions to accelerate therapeutic development for MASLD/MASH
- **How:** provide a neutral, independent, safe space for discussion and deliberation across stakeholder groups
  - Focus on developing consensus, increasing synergy and collaboration, and reducing duplication and uncertainty
  - Ongoing working group activity throughout the year anchored by larger project events twice yearly
  - Active & engaged participation


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# Liver Forum Steering Committee

**Co-Chairs**
- Veronica Miller, *Forum for Collaborative Research*
- Arun Sanyal, *Virginia Commonwealth University*
- Michelle Long, *Novo Nordisk*

**Regulatory**
- Ruby Mehta, *FDA/ CDER/ DHN*
- Joachim Musaus, *European Medicines Agency*
- Charmaine Stewart, *FDA/CDER/DHN*

**Patient Advocates**
- Donna Cryer, *Global Liver Institute*
- Wayne Eskridge, *Fatty Liver Foundation*
- Lorraine Stiehl, *American Liver Foundation*

**Consortia**
- Quentin Anstee, *LITMUS*
- Sudha Shankar, *NIMBLE*

**Society**
- Naga Chalasani, *AASLD*
- Annalisa Berzigotti, *EASL*

**Academia**
- Manal Abdelmalek, *Mayo Clinic*
- Mazen Noureddin, *Houston Research Institute*
- Jörn Schattenberg, *Universitätsklinikum des Saarlandes*
- Stavra Xanthakos, *Cincinnati Children's Hospital Medical Center*

**Industry**
- Judith Ertle, *Boehringer Ingelheim*
- Margery Connelly, *LabCorp – Monogram Biosciences*
- Céline Fournier, *Echosens*
- Melissa Palmer, *Liver Consulting LLC*
- David Shapiro, *Industry Consultant*



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# Liver Forum Sponsors

# The Forum Team

**Veronica Miller – Director & Faculty Lead**

**Program Leads and Project Managers**

- Robin Schaefer – Postdoctoral Scholar
- Logan Donaldson – Research Associate
- Sehyr Khan – Research Associate
- Mitchell Leus – Research Associate
- Shilpa Mitra – Research Associate
- Ekene Osakwe – Research Associate
- Edyth Dwyer – Research Associate

**Data & Analysis Center**

- Chris Hoffman – IT and Operational Director
- Margot Yann – Lead Data Scientist
- Mengxi Bai – Research Data Analyst
- Zachary Rooney – Technical & Infrastructure Lead

**Administration**

- Donna Dahrouge – Assist. Director, Administration
- Christopher Berry – Sr Events and Operations Manager
- Donnice Butler – Sr Admin Assistant
- Alicia Jellinek – Program Financial Analyst
- Jordan Cathey – Development Consultant

**Program Advisors**

- Claire M. Gelfman – Program Advisor
- Richard Haubrich – Program Advisor
- Jeffrey S. Murray – Program Advisor
- Mike Robertson – Program Advisor
- John Sninsky – Program Advisor

**Student Assistants**

- Roma Ranade – Graduate Student Assistant
- Kathy An – Undergraduate Student Assistant
- Alessi Ayvaz – Undergraduate Student Assistant
- Allison Li – Undergraduate Student Assistant



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# Ongoing Working Group Efforts

- Combination Therapy
  - Dr. Alina Allen, Mayo Clinic & Dr. Michelle Long, Novo Nordisk
- Patient Engagement in Drug Development: Leading Through Example (PEDDLE)
  - Mr. Michael Betel, Fatty Liver Alliance & Mr. Henry Chang, Fatty Liver Foundation & Mrs. Rosemarie Sellati, Regeneron
- Pediatric MASH
  - Dr. Stavra Xanthakos, Cincinnati Children's Hospital Medical Center & Dr. Miriam Vos, Emory University
- Pooling of Endpoints
  - Dr. Jasmohan Bajaj, VCU & Dr. Michelle Long, Novo Nordisk
- MetALD/ALD
  - Dr. Maja Thiele, Odense University & Dr. Nikhil Vergis, GSK
- NITs for RLSE
  - Dr. Richard Haubrich, Forum for Collaborative Research & UC San Diego

# What is PEDDLE?

- Launched at Liver Forum 17 on September 4, 2024
- Aims to put patients at the core of MASH clinical development
- Assess the current landscape of patient engagement
- Discuss common hurdles with industry and patient engagement
- Establish touchpoints with regulators


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# Patient Engagement

# Patient Engagement

What is it?

“Patient engagement is the meaningful involvement of patients, caregivers, and the healthcare community at large throughout the research process, from planning and design to implementation and dissemination of results. This engagement ensures that the perspectives and experiences of patients drive research priorities, study design, and outcomes.”



pcori®
Patient-Centered Outcomes Research Institute

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# Patient Engagement Examples

1. Real-World Symptom Tracking and Lifestyle Integration

2. Including Mental Health and Behavioral Support Metrics

3. Reducing the Burden of Invasive Procedures

4. Diverse Representation in MASH Trials

# Patient Engagement Examples

1. Real-World Symptom Tracking and Lifestyle Integration

- MASH patients often report symptoms like fatigue and brain fog that may not be captured. Engaging patients in trial design helps ensure these symptoms are considered.
  - help add symptom-tracking measures and patient-reported outcomes
  - make trials more relevant to patient experiences and provide a fuller picture of therapeutic impact.

# Patient Engagement Examples

## 2. Including Mental Health and Behavioral Support Metrics

- Many MASH patients experience stress, anxiety, and lifestyle challenges related to diet and exercise regimens. Patients have advocated for the inclusion of mental health assessments and behavioral support metrics as part of the trial.
  - patient input has led to the inclusion of mental health evaluations and support components (access to nutritional or psychological counseling)
  - helps evaluate the full impact of the treatment

# Patient Engagement Examples

## 3. Reducing the Burden of Invasive Procedures

- Engaging patients in trial design has led to the reduction of certain invasive procedures, such as liver biopsies, and the inclusion of non-invasive liver assessments like FibroScan
  - MASH trials include imaging technologies like MRI-PDFF or FibroScan, allowing more comfortable and accessible liver assessments
  - shift may have been largely driven by patient feedback on reducing procedure-related stress and enhancing convenience

# Patient Engagement Examples

## 4. Diverse Representation in MASH Trials

- Given the prevalence of MASH among those with type-2 diabetes and obesity, patient engagement has highlighted the need for trials to include a more diverse population representing varying metabolic profiles, ethnic backgrounds, and lifestyle factors.
  - trials in the MASH space increasingly incorporate input from diverse patient groups
  - study populations better reflect the broad demographics of those affected by MASH
  - provides more generalizable and equitable data

# Patient Engagement Practical Strategies

1. Forming Patient Steering Committees and Advisory Boards
2. Patient Friendly Trial Materials and Processes
3. Incorporating Tool and Technology
4. Recognizing and Addressing Health Literacy Levels
5. Sharing Trial Results with Participants

# MASH POWER Council



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# Value of Early Patient Engagement

## "New standard" led by regulators, legislatures, advocacy groups

"The informed, empowered patient is becoming the norm." - Drug Information Association (DIA)

- Transformational approach to identifying and responding to the unmet needs of patients worldwide
- Global movement building since early 2010s
- Benefits to **patients**, **sponsors** and **society**
- More meaningful clinical trials with **increased feasibility**, **enhanced recruitment / retention**, and real-world **outcomes**
- **FDA Guidance** provides new details on **Diversity Action Plans** required for certain clinical studies


- Food and Drug Administration
- European Medicines Agency
- DIA Patient Engagement
- National Institute for Health Research
- National Health Council
- Patient-Centered Outcomes Research Institute
- European Patients' Academy on Therapeutic Innovation

# Value of Early Patient Engagement

## Not just the “right thing” to do

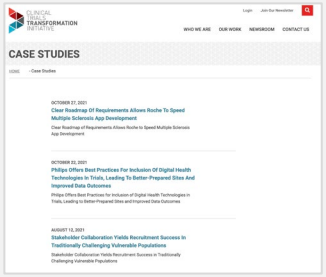
Patient engagement impacts the bottom line

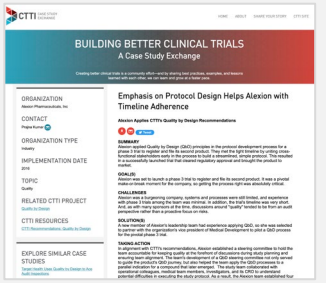
### Financial Value of Patient Engagement
**Study Results[1]**

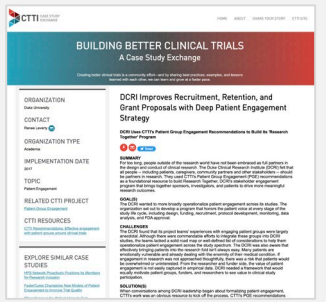
| | |
|---|---|
| **3 Months** | **Earlier launch** |
| **25%** | **Reduction in enrollment time** |
| **$65M** | **Calculated median financial impact** |

Dozens of case studies show:

- Quantifiable impact on **revenue**, **cost**, **time**
- Powerful expression of **good corporate citizenship**
- Improvement in **trial design/execution**
- Reduction in study **risks/mitigation** of conflicts of interest




50 percent of confirmatory Phase III trials fail. (Applied Clinical Trials, April 2016)

Estimates vary on the cost of a failed clinical trial, but figures range anywhere from $800 million to $1.4 billion (FDA)

TOTAL MEDIAN DIRECT COST FOR A SUBSTANTIAL AMENDMENT: Phase II and Phase III protocols

**$141,000 & $535,000**

1. Impact of a patient engagement activity in Phase 2 Trial that avoids one protocol amendment and improves enrollment, adherence, and retention Bennett Levitan, MD, PhD,1 Kenneth Getz, MBA,2 Eric L. Eisenstein, DBA,3 Michelle Goldberg, MBA,4 Matthew Harker, MPH, MBA,5 Sharon Hesterlee, PhD,6 Bray Patrick-Lake, MFS,7 Jamie N. Roberts, MPH, MA,7 and Joseph DiMasi, PhD2 *Assessing the Financial Value of Patient Engagement, 2017*

# Case Study-MASH POWER Council

POWER=Patient Organizations Who Empower Results

## Overall Goals

- Establish a **Patient Advocate Council** with members representing different perspectives
- Provide **ongoing patient expertise and insights** to inform Regeneron MASH Program strategy
- Disseminate findings to **advance the field of study**

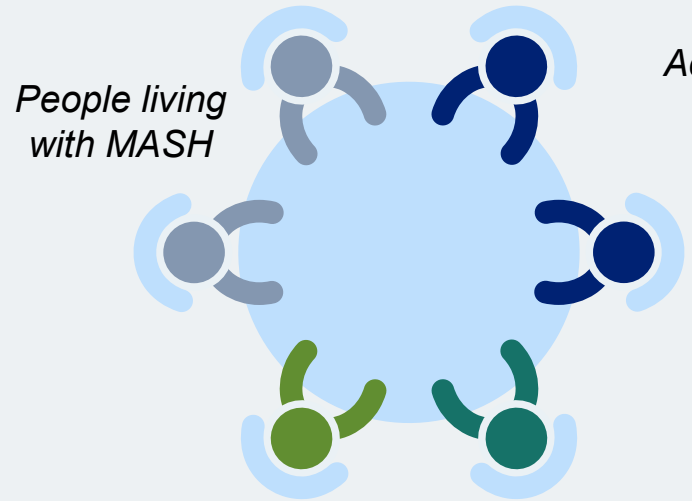
## Key Objectives

- Map the **patient journey**, from symptomology through disease management, to define the patient experience from a humanistic perspective
- Identify **barriers to clinical trial participation**, including differences for subpopulations
- Understand **community engagement** models in rural and underserved regions
- Identify high impact opportunities to publish and **share Council insights**
- Build **meaningful collaborations** with patients, caregivers, and community members

## Output

- Deliverables include a **patient journey map**, an **educational infographic**, **video testimonials**, and a planned **publication**

**Council members providing specific expertise**



# Case Study-MASH POWER Council

## The Council provided insights into awareness and motivation challenges, informing opportunities for meaningful engagement with Hispanic and Latino communities

### Lack of Urgency

- HCPs often do not **effectively communicate the severity** of the disease, so patients may not understand the urgency to seek treatment or enroll in clinical trials
- Patients prioritize **managing their comorbid conditions** (e.g., diabetes, obesity, kidney disease, cardiovascular disease) as a more imminent need

### Unawareness

- Patients are often not diagnosed until they are late stage and **ineligible for trials** due to a lack of HCP awareness
- There are **few channels** for patients to become aware of clinical trials; notable ones include **HCPs and Patient Groups**

### Mistrust

- Marginalized populations may experience a deep mistrust of the healthcare system and clinical trials due to a **history of exploitation and mistreatment**
- The COVID-19 pandemic and anti-vaccination movement reinforced the fear, suspicion, and mistrust of the healthcare system

### Cultural Challenges

- Patients may be motivated to enroll in a clinical trial, but receive push-back from their community, because pharma and HCPs are viewed as **"outsiders"**
- In some cultures, the use of **traditional medicine** or **healing** is encouraged over "Western medicine"

*"Not putting the unmet medical needs of patients first, early in the development process, can lead to wrong priorities, wrong decisions on research design, and potentially costly late-stage failure." – Clinical Trials Transformation Initiative (CTTI)*

# THANK YOU

**Regeneron plans to continue engaging with the MASH POWER Council and sharing insights with the broader community**



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# Patient Engagement at Madrigal

# Christopher Frates

## Vice President, Corporate Communications and Patient Advocacy, Madrigal Pharmaceuticals

Disclosure: Madrigal employee

# Patient Engagement at Madrigal

**Madrigal is a biopharmaceutical company focused on delivering novel therapeutics for MASH**

- Madrigal developed the first medication for MASH with moderate to advanced fibrosis to receive accelerated approval from the FDA
- Madrigal has worked closely with the MASH patient advocacy community to gather insights about the burden of MASH and support disease education

*Photos from an August 2024 Patient Advocacy Summit hosted by Madrigal*

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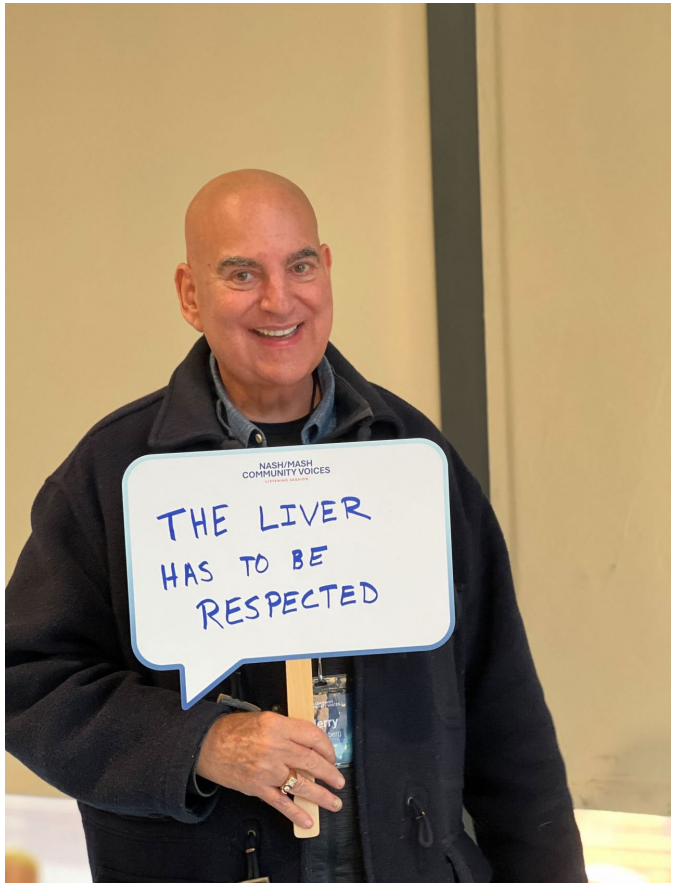
# Madrigal Organized a Listening Session that Explored Research Priorities for the Patient Community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# Madrigal Organized a Listening Session that Explored Research Priorities for the MASH Patient Community

**What we heard from patient advocates:**

- Seek patient input early
- Move away from biopsy
- Improve diversity in clinical trials
  - Extend reach into underserved communities, both rural and urban
- Accelerate research in the pediatric MASH population




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# Patient Engagement Challenges and Opportunities: Industry Perspective

| Challenges | Opportunities |
| --- | --- |
| Patient input is valued, but process for collecting isn't always standardized | Toolkit to define how and when to collect patient input on a development program |
| Patient advocacy function may not exist at smaller companies; may be 'siloed' in larger ones | Build a more expansive understanding of patient advocacy's role in biopharma |
| Hard for many patients to attend conferences like The Liver Meeting due to cost of travel | Establish grants/scholarships to support larger patient presence at medical meetings |

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# Patient Engagement in the Regulatory Context

# Patient Engagement in the Regulatory Context

**Henry E. Chang**
**Co-Chair, PEDDLE Working Group, Liver Forum**
**Executive Director, Fatty Liver Foundation**
***henry@fattyliverfoundation.org***



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# Co-Creation of Patient-Centric Trial Protocols and Informed Consent Forms

## ENGAGEMENT ROLE

Patients and patient advocates collaborate with study sponsors during the protocol development phase (e.g. Phase IIb and III) to ensure trial designs reflect patient priorities and minimize burdens.

## IMPACT

For MASH trials, this might include advocating for the use of non-invasive diagnostic tools (e.g., imaging or biomarkers) instead of liver biopsies. Patients can also provide feedback on visit frequency, transportation needs, and other logistical barriers that affect enrollment and retention.

## REGULATORY RELEVANCE

The U.S. FDA encourages trial designs that reduce barriers and promote patient-focused outcomes, aligning with patient-centric drug development principles.

# Collaborating on Diversity Action Plans (DAPs) → Ensuring Inclusive Study Design

## ENGAGEMENT ROLE

Patients and patient advocates collaborate with sponsors to co-develop DAPs, addressing barriers to participation for underrepresented populations disproportionately affected by MASLD/MASH, including Hispanic/Latino, Native Americans, Asian Americans, African Americans, and low-income populations facing systemic healthcare disparities.

## IMPACT

Improves the inclusivity of recruitment strategies, ensuring diverse populations are adequately represented in MASH clinical trials.

## REGULATORY RELEVANCE

Aligns with the Food and Drug Omnibus Reform Act (FDORA) of 2022 requirements for DAPs, enhancing FDA compliance and promoting equitable representation in MASH drug development.

# Collaborating on Diversity Action Plans (DAPs) → Community Outreach and Education

## ENGAGEMENT ROLE

Advocacy groups engage with underrepresented communities to build trust, address misconceptions about clinical trials, and highlight the importance of diverse participation in MASH research.

## IMPACT

Increases awareness, enrollment, and retention in clinical trials while fostering a sense of ownership and inclusion among diverse patient populations.

## REGULATORY RELEVANCE

Supports FDA goals for diversity and inclusivity in clinical trials, contributing to the robustness of trial data for regulatory review.

# Collaborating on Diversity Action Plans (DAPs) → Feedback on Enrollment Goals

## ENGAGEMENT ROLE

Patients and patient advocates review and provide input on DAP enrollment targets to ensure they are realistic, culturally appropriate, and address real-world barriers like language, transportation, and childcare.

## IMPACT

Ensures that recruitment plans are practical and tailored to patient needs, improving the likelihood of meeting diversity goals.

## REGULATORY RELEVANCE

Helps sponsors create actionable, FDA-compliant DAPs that strengthen the credibility and applicability of trial outcomes.



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# PEDDLE Next Steps

# What does PEDDLE want to accomplish?

1. Establish Regular Working Group Meetings
   - collaborative sessions with deliverables

2. Develop and Promote Consensus on the Value of Patient Engagement
   - create a unified stance

3. Link Patient Engagement to Scientific and Economic Outcomes
   - build evidence

4. Create Tangible Deliverables for Stakeholders
   - whitepapers, guidelines

# Thank You!



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