HEPATITIS D GLOBAL COMMUNITY ADVISORY BOARD (HDV-CAB)

CHARTER

I. **Mission:** The mission of the HDV-CAB is to integrate community perspectives and expertise into hepatitis D drug development and clinical research to ensure that the voices of those living with and affected by hepatitis D are represented, and to drive progress toward effective hepatitis D therapeutics.

II. **Scope:** The HDV-CAB advises exclusively on hepatitis D drug development and clinical research.

III. **Goals/Objectives**

A. Provide training and education to facilitate increased community engagement in hepatitis D drug development and clinical trials.
B. Establish and maintain opportunities for community members to interact with researchers and provide their input/recommendations on drug development and clinical trials.
C. Promote diverse and inclusive representation of communities highly affected by hepatitis D in drug development and clinical trials.

IV. **Values Statement:** The HDV-CAB values the demonstration of highest respect for each of its members, and the diversity of knowledge, experiences, backgrounds, and perspectives they have to share. It serves as a safe and inclusive space in which all ideas are welcomed and trust is high enough to foster open dialogue and thought expression, free from fear of judgment or aspersion. Perfection and expertise are not expected; risk-taking is encouraged and will be supported by the group. Leadership and responsibility are jointly shared among members and no one is stretched beyond their capacity. Above all, the HDV-CAB is a community, every member of which is valued for who they are and what they bring.

V. **Diversity and Inclusion:** The HDV-CAB strives for its membership to reflect the demographics of the hepatitis D epidemic globally, emphasizing the inclusion of traditionally underserved or underrepresented communities. Membership is open to persons living with and affected by hepatitis D, including family members and caregivers.

VI. **Membership and Term Limit:** The HDV-CAB is an all-volunteer group composed of 8-12 people living with and affected by chronic hepatitis D, who provide individual expertise to inform hepatitis D drug and clinical trial development.

A. The HDV-CAB will include members representing each WHO region as follows: two to three members from Africa, two to three members from the Americas, one member from

South-East Asia, two members from Europe, two members from the Eastern Mediterranean, and one member from the Western Pacific.

B. HDV-CAB members serve 24-month terms.

VII. **Application and Selection Process:** Interested individuals are invited to submit their application to the HDV-CAB. Applications are reviewed and voted on by the HDV-CAB. Two-thirds of our membership must approve new members. (For the first year, applications will be reviewed and voted on by Hepatitis B Foundation staff and key partners.) Members are selected based on their interest, availability, and expertise in hepatitis D drug development and research, in addition to their personal experience living with or caring for someone with hepatitis D.

VIII. **Member Roles and Responsibilities**

A. Training and Education: All HDV-CAB members will be required to complete scientific and leadership training. Training will be completed virtually. Training completion demonstrates commitment to developing an understanding of issues where members may have little expertise.

B. CAB Meetings: Members are expected to attend and actively participate in all HDV-CAB meetings, which will be held virtually (by conference call or online video conference) three to four times per year. Each meeting will last one to two hours and provide time for members to:

1. Discuss HDV-CAB strategies, activities and progress, as well as challenges.
2. Provide insights and meaningful feedback on HDV-related issues and concerns from their perspective, and that of their community.
3. Discuss content from training/education modules in further detail and ask follow-up questions about the material.
4. Prepare for external meetings with industry, nonprofit and governmental partners.
5. Provide updates and feedback on external meetings, as well as other HDV-CAB activities.
6. Participate in team-building activities.

C. Meetings with Drug and Clinical Trial Developers: Members will serve as liaisons to schedule and participate in meetings and strategy sessions with drug and clinical trial developers.

D. Other Activities: As needed, HDV-CAB members may be periodically asked to:

1. Represent the hepatitis D community at public events and conferences.
2. Provide input into design of patient-focused clinical trials, strategies for study recruitment and retention, and development of informed consent forms and other study related documents.
3. Assist in community outreach and education focused on clinical trials, including providing feedback on outreach strategies and educational materials.
4. Disseminate clinical trial information to their local community.
5. Recruit and orient new HDV-CAB members.

IX. **Hepatitis B Foundation Roles and Responsibilities**

A. Serve as administrator for the CAB.
B. Establish and maintain opportunities for community members to interact with researchers and provide their input/recommendations on drug development and clinical trials.
C. Schedule and provide logistical support for CAB meetings.
D. Provide and facilitate all required trainings.
E. Create a secure communications channel for CAB members.
F. Serve as a mediator if any challenges arise between CAB members and/or industry, nonprofit, or governmental partners.
G. Support leadership development of CAB members.

X. **Compensation:** CAB members will be compensated for their time and expertise. Details of this arrangement can be found in a separate memorandum of understanding.

XI. **Background:** Chronic hepatitis D (CHD) infection is a liver infection caused by the hepatitis delta virus (HDV) that results in the most severe form of viral hepatitis known to humans. HDV is dependent upon the hepatitis B virus (HBV) for reproduction and survival, so only those already living with hepatitis B can acquire hepatitis delta (unless both viruses are acquired simultaneously, which is less common).

Due to low screening levels and a historical lack of viable and accessible treatments, the exact global prevalence of hepatitis D remains unknown. Estimates range from around 15 million people globally to as many as 70 million affected people around the world. HDV does seem to be more prevalent in certain areas of the world, and is found most commonly in Mongolia, Romania, Russia, India, Pakistan, the Middle East, Georgia, Turkey, West and Central Africa, and the Amazonian river basin. Many areas in which HDV seems to occur most frequently are also those with more limited access to healthcare and financial resources, thus further unduly burdening these populations and deepening existing health disparities. Additionally, fewer than 10% of those living with chronic hepatitis B alone currently access sustainable care and treatment and, given the significantly lower rates of diagnosis for hepatitis D, the respective linkage to care statistic for hepatitis B and D coinfection is estimated to be even lower.

Due to under-diagnosis and lack of surveillance, it is unclear how many deaths are the direct result of HDV globally each year. It is known, however, that the risk of progression to liver cirrhosis (or scarring) for those living with both chronic hepatitis B and D viruses is as high as 70%, compared to 15-30% for those living with chronic hepatitis B alone. Cancer of the liver, which is the world's second deadliest cancer (with a 5-year survival rate of only 18%), is also a greater risk for those living with chronic hepatitis B and D coinfection. Although there has been limited research conducted to understand the effect of hepatitis delta itself on quality of life for those living with this disease, extrapolation from data collected from people living with HBV alone suggests that, in addition to physical symptoms, infected individuals often suffer reduced quality of life and significant mental health concerns, including depression, anxiety, fear of disease progression, and reduced ability to participate in work and social aspects of life. Perceived and actual stigma, discrimination, and marginalization also pose significant challenges to affected individuals.

Antiviral treatments that are effective in controlling hepatitis B have no effect on hepatitis delta, but are often recommended as part of a patient's treatment plan to control their hepatitis B. Until very recently, the treatment landscape for hepatitis delta specifically was very sparse. For 40 years, beginning in 1980, the primary treatment used for hepatitis delta was unapproved pegylated interferon alpha, which was found to be effective in fewer than 25% of patients, and generally caused severe side effects and significant declines in quality of life. The first approved treatment for hepatitis delta, Hepcludex (generic bulevirtide), was approved in July of 2020 for prescription in the European Union. In 2021, the American pharmaceutical company Gilead Sciences, Inc. acquired MYR Pharma, the small German company responsible for the development of the drug, and has since submitted a Biologics License Agreement to the US FDA with hopes of getting the drug approved for prescription in the United States and then elsewhere in the world. Two other promising drugs in the hepatitis delta pipeline are Lonafarnib and PEG-interferon Lambda, both manufactured by Eiger BioPharmaceuticals in the United States.

While the development of all of these new treatments gives cause for hope, questions remain about treatment access and affordability, particularly in the areas of the world most affected by hepatitis delta, as well as length of treatment and impact on both risk of progression to cirrhosis and liver cancer, and on quality of life. Additionally, we have only a limited understanding of the broad impact of chronic hepatitis D on affected individuals. Many aspects of the disease, including the experiences of living with and being treated for CHD, have not been formally captured in clinical trials or public health studies.