SPEARHEAD 2.0 2025 RFP:

Screening imPlEmentation and linkage to cARe in HEpAtitis Delta

Chronic hepatitis delta virus (HDV) is the most severe form of viral hepatitis, occurring in some patients who are infected with hepatitis B virus (HBV). HDV leads to a rapid progression of liver disease, increasing the risk of cirrhosis, decompensated cirrhosis, liver transplant, HCC, and mortality compared to HBV alone. [1,2,3] The global prevalence of HDV is estimated to be between 5% to 13% in HBsAg-positive patients, accounting for 12 to 60 million infected individuals worldwide.[4,5] However, HDV is largely underdiagnosed due to due to the lack of universal testing of HBV-positive individuals for HDV.[6] Given the disease severity and general underdiagnosis of HDV, there is an unmet need for enhanced screening and linkage to care in those with HBV.

The European Association for the Study of the Liver (EASL) recommends HDV screening for all patients infected with HBV.[8] Even with this guideline recommendation in place, recent data from Europe have demonstrated that a large proportion of HBV patients remain untested for HDV.[9,10] Interventions such as the implementation of reflex testing have shown to be effective at significantly improving screening practice leading to the identification of previously undiagnosed patients.[11,12]

To understand and address barriers to HDV screening and linkage to care, Gilead launched the **SPEARHEAD** RFP program in 2022 in the US, extended the program to Europe in 2023, and globally in 2024. The program will be relaunched in 2025 with updated research objectives and will support individual projects up to 200,000 USD. Projects greater than 200,000 USD will require discussion with Gilead before submission.

Applications should include projects that can be completed within 18 months and demonstrate clear objectives, include defined timelines, offer a comprehensive operational plan, propose data that have relevance to the medical community and policymakers, and includes plans for the data to be submitted to relevant congresses and journals. The program is open to applications from all countries; however, special emphasis will be placed on geographies with high HDV burden and in countries where treatment for HDV is available*.

Gilead may provide research funds for screening & testing support only if it is an essential component of a valid study design to address the research needs outlined in the RFP. Gilead will not consider proposals that request HDV study drug and is not seeking studies that focus on treatment outcomes. Proposals should be treatment/drug agnostic.

Application Criteria

- Gilead will evaluate and support select programs that will aim to address one or both of the below scientific objectives:
    1. Generate data to assess current HDV linkage to care practice, identify barriers, develop, and implement novel approaches to enhance linkage to care
        - Examples include but are not limited to:
            - Implementation and streamlining the most sensitive assays across regions and/or countries
            - Novel approaches to engage and educate patients and caregivers, particularly among immigrant populations
            - Implementation of active and dedicated screening programs associated with new and effective models of diagnosis and linkage to care and cure among immigrants from high-risk countries

    2. Generate data to determine who should be tested or retested for anti-HDV antibody and/or HDV RNA and the optimal timing for retesting to ensure accurate diagnosis.
        - Examples include but are not limited to:
            - HDV RNA retesting in patients with abnormal AST/ALT levels despite NUC treatment
            - Retesting based on patient risk factors and baseline indicators (e.g., patients with high-risk behaviors, immigrants from regions with high HDV prevalence, rapid progression of liver fibrosis or cirrhosis)
            - Leveraging EMR and other digital platforms to identify patients for HDV RNA retesting
        - Studies should aim to evaluate HDV retesting practice before and after study implementation, including the proportion of HBsAg+ patients retested, number of HDV diagnoses, and HDV prevalence rates

Additional Key Criteria:

- Both investigator-sponsored research study proposals and collaborative research study proposals (developed in conjunction with Gilead) will be considered (link to additional information on ISR vs collaborative studies)
- The principal investigator is not currently receiving Gilead grants to conduct HDV screening
    - The same institution may receive multiple grants for HDV screening if they are mutually exclusive to the sponsoring department (i.e. Hepatology vs ED)
- Research proposals should include a comprehensive publication plan to present study results in scientific forums, and to publish results in peer reviewed journals
- Proposed budget is under 200,000 USD and should be proportional with the scope of the study; advance discussion with Gilead Medical Affairs is required prior to submission of proposal with a budget over 200,000 USD
    - The budget should include overhead costs and applicable taxes
    - Proposed overhead costs should not exceed 30% of the total budget
- The proposed study design should be feasibly executed within 18 months

- Proposals should include clearly written study objectives, as well as study endpoints (i.e. what will be measured to determine if the study objectives are met?)
- Proposals will be evaluated for scalability and sustainability of the program after funding completion (when applicable)
- Funding for screening & testing supplies may be provided as part of a valid study design to address the research needs outlined in the RFP
- Funding for or contribution of study drugs will not be provided
- There must be no more than one sponsor for contract negotiations and/or Institutional Review Board (IRB) review
- As the study sponsor, the principal investigator will be responsible for compliance with all laws and regulations applicable to research sponsors, including satisfying local requirements and obtaining all necessary regulatory and ethical approvals before beginning the study

Gilead Sciences, Inc. 333 Lakeside Drive Foster City, CA 94404 USA
www.gilead.com
phone 650 574 3000 *facsimile* 650 578 9264

Application Process
To apply for consideration for funding under the **SPEARHEAD 2.0 RFP 2025 Program**, you will need to submit an LOI that is no longer than two pages, containing a concise overview of the proposed project, including the total estimated budget. Applicants should submit the LOI application in the Gilead OPTICS (G. OPTICS) portal. Submitted LOIs can be investigator-sponsored research (ISRs) or collaborative studies.**

Gilead will evaluate all LOIs received on a rolling basis until funds are exhausted. After an initial LOI review, invitations will be issued for selected applicants to submit a full application with a detailed budget. **It is recommended to submit as soon as possible to increase the likelihood that funding is available for your proposal.**

- **Friday, March 14th, 2025 at 00:00 AM (in your time zone): Submission window opens**
- **Friday, May 23rd, 2025 at 23:59 PM (in your time zone): Submission window closes**

Questions about the RFP or the application process can be submitted to your local Gilead Medical Science Liaison. A review of the LOIs will result in invitations for selected LOI applicants to submit a full proposal with a detailed budget.

LOIs will be rigorously reviewed by a Gilead internal committee. Each complete LOI that meets program requirements will be assigned to multiple reviewers. Each reviewer will review the LOI and evaluate how well the proposal addresses the RFP, the potential impact of the study, the strength of the objectives/study design, sustainability/scalability of the proposal/intervention, and the site's and study team's ability to recruit the proposed study population and execute on study objectives. Investigators with the top submissions will be offered the opportunity to submit a full proposal, which should include a comprehensive publication plan to present study results at scientific forums and publish results in peer-reviewed journals as well as a detailed budget, adequate and proportional to the study's scope, which will be similarly reviewed.

How to Submit an LOI in G.OPTICS for the SPEARHEAD 2.0 RFP

1. Create an account or log into your account in G.OPTICS.
2. Select "New Letter of Intent (LOI)."
3. Select "HDV: SPEARHEAD 2.0 RFP" from the list of active RFPs.
4. Complete the required fields.
5. Submit the LOI.

No Guarantee of Funding
Gilead reserves the right to approve or decline any application at its sole discretion. Submission of an LOI or a full application does not guarantee funding. Awards shall be for research purposes only; routine medical care or other costs associated with routine medical care will not be considered for funding. Gilead discourages proposals that solely request study drug or funds for HDV screening costs.

No Inducement or Reward
Gilead approval of awards does not take into account the past, present, or future volume or value of any business or referrals between the parties. Awards are not being given, directly or indirectly, as an inducement or reward with respect to the past or potential future purchase, utilization, recommendation or formulary placement of any Gilead product. Furthermore, except for the use of

the Gilead product in an approved award/research, the awardee is not required to purchase, order, recommend or prescribe to any patients any products manufactured by or available through Gilead.

About Gilead Sciences

Gilead Sciences, Inc. is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients suffering from life-threatening diseases worldwide. Gilead has operations in more than 30 countries worldwide, with headquarters in Foster City, California.

Gilead Sciences, Inc. 333 Lakeside Drive Foster City, CA 94404 USA
www.gilead.com
phone 650 574 3000 *facsimile* 650 578 9264

References

1. Romeo R, Petruzziello A, Pecheur EI, et al. Hepatitis delta virus and hepatocellular carcinoma: an update. *Epidemiol Infect*. 2018;146(13):1612-1618. doi:10.1017/S0950268818001942.
2. Fattovich G, Giustina G, Christensen E, et al. Influence of hepatitis delta virus infection on morbidity and mortality in compensated cirrhosis type B. The European Concerted Action on Viral Hepatitis (Eurohep). Gut. 2000;46(3):420-426. doi:10.1136/gut.46.3.420.
3. Höner Zu Siederdissen C, Cornberg M. Management of HBV and HBV/HDV-Associated Liver Cirrhosis. Visc Med. 2016;32(2):86-94. doi:10.1159/000445518.
4. Miao Z, Zhang S, Ou X, et al. Estimating the Global Prevalence, Disease Progression, and Clinical Outcome of Hepatitis Delta Virus Infection. J Infect Dis. 2020;221(10):1677-1687. doi:10.1093/infdis/jiz633.
5. World Health Organization. Hepatitis D. July 28, 2020. Accessed June 30, 2021. https://www.who.int/news-room/fact-sheets/detail/hepatitis-d.
6. Rizzetto M, Hamid S, Negro F. The changing context of hepatitis D. J Hepatol. 2021;74(5):1200-1211. doi:10.1016/j.jhep.2021.01.014.
7. Terrault NA, Bzowej NH, Chang KM, et al. AASLD guidelines for treatment of chronic hepatitis B. Hepatology. 2016;63(1):261-283. doi:10.1002/hep.28156.
8. European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol. 2017;67(2):370-398. doi:10.1016/j.jhep.2017.03.021
9. Trimoulet P, Foucher J, Tumiotto C, Hermabessière P, Delamarre A , Irlès-Depé M, Lafon ME, De Ledinghen V. On the way to HDV elimination. A call for reflex testing in the large program "Bordeaux metropolis without viral hepatitis". AASLD 2021. Poster #720
10. Palom A, Rando-Segura A, Barciela MR, Barreira-Diaz A, Rodriguez-Frías F, Esteban-Mur R, Buti M. Low adherence to guidelines recommendation for testing hepatitis D in HBsAg positive patients leads to a high rate of undiagnosis. AASLD 2021. Oral #224
11. Palom A, Rando-Segura A, Vico J, et al. Implementation of anti-HDV reflex testing among HBsAg-positive individuals increases testing for hepatitis D. JHEP Rep. 2022;4(10):100547. Published 2022 Jul 21. doi:10.1016/j.jhepr.2022.100547
12. Brichler S, Roulot D, Dziri S, Gerber A, Le Gal F, Delagrèverie H, Alloui C, Gordien E. EASL 2022; Poster #THU355

*****_Bulevirtide 2mg is approved for use by the EC (Europe), MHRA (UK), Swissmedic (Switzerland), and TGA (Australia), as well as the Ministry of Health (Russia) through a separate marketing authorization holder (Hepatera)._

**LOIs are not binding documents for either party. The purpose of the LOI is a brief summary of the proposed study to enable Gilead to determine on a preliminary basis whether the proposed study and related budget are aligned with the criteria, timeline, and scope of this RFP.