Call for Educational Grant Requests

Adult Hepatitis B Vaccination (Still) Matters

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VBI Vaccines Inc. (VBI) is a biopharmaceutical company driven by immunology in the pursuit of powerful prevention and treatment of disease. Aligned with our mission to target and overcome significant infectious diseases, we are committed to supporting the healthcare community's ability to improve patient outcomes related to the prevention of hepatitis B.

This document provides details regarding the rationale of this Call for Educational Grant Requests (CEGR), guidance for the organization and content of grant requests, and sets timelines for review and approval. Qualified organizations with vaccine experience are invited to submit a proposal addressing the components of this CEGR.

For all independent medical education grants, the grant recipient is responsible for the design, implementation, conduct, and assessment of the initiative supported by the grant. VBI will have no involvement in any aspect of activity planning, development, or execution. VBI will, however, request periodic status updates and outcomes reports during the active period and following expiration.

General information

Eligibility	The following organizations may apply: • Medical, nursing, pharmacy, and allied health professional schools • Healthcare institutions • Professional associations and medical societies • Medical education companies • Other entities related to healthcare professional education and/or healthcare improvement If the initiative involves multiple departments within an institution and/or different institutions / organizations / associations, all collaborators must have a relevant role and the requesting organization must have a key role in the initiative. The requesting organization must be fully accredited to provide continuing education for the proposed target audiences.
Geographic scope	The funded education is intended for Healthcare Providers (HCPs) in the US (see definition in Audience section below); HCPs in other countries may also have access to the

	educational activities.
Audience	Primary Care Providers, Pharmacists, advance practice practitioners such as NPs or PA, relevant physician specialties such as endocrinologists, transplant medicine, etc.

Rationale for this CEGR	**Hepatitis B (HBV) prevention is critical**
	• Addressing vaccine-preventable diseases in adults is a critical public health need, which has recently been underscored by the COVID-19 pandemic
	• Many vaccines are underutilized in adults, leaving large groups of people unprotected and at-risk of HBV infection
	• There are several barriers to an effective adult vaccination action plan, including low awareness of true disease burdens and incomplete adherence to full series of vaccination
	
	Current HBV Disease State and Disease Burden in the U.S.
	• An estimated 257 million people are living with chronic hepatitis B virus (HBV) infection worldwide,[1] and the World Health Organization estimates that prevalence of HBV infection ranges from 0.7% to 6.2% of the population, depending on the region[2]
	• The estimated incidence of reported new HBV infections in the US increased from 18,900 in 2011 to 21,600 in 2018[3]
	• As of 2016, only 10.5% of all people estimated to be living with HBV were aware of their infection status[2], increasing the likelihood of transmission
	
	Risks of failing to prevent HBV
	• If left undiagnosed and untreated, HBV infection can lead to chronic liver disease, including cirrhosis and hepatocellular carcinoma[5]
	  ○ Most liver cancer cases are attributable to chronic or persistent HBV infection, suggesting HBV infection remains a critical public health problem[5]
	  ○ Hepatitis B is associated with premature death and with elevated rates of death from all causes and from liver-related causes, including hepatocellular carcinoma[5]
	• The best way to prevent HBV infection and diseases caused by HBV is through seroprotection with HBV vaccines that have demonstrated efficacy in adult populations[6]
	• Serology – diagnosis and serology – importance of vaccine
	
	Current Standard-of-Care (SOC) and low rates of adherence to HBV guidelines
	• Chronic HBV currently has no cure and requires life-long monitoring and treatment with therapeutic interventions that have high toxicities and significant side effects[6]
	• All three currently-available HBV vaccines in the U.S are yeast-derived, monovalent, expressing only one of the three HBV surface antigens (S antigen), and with varying adjuvants
	• Vaccines are frequently administered in multiple doses for optimal immunogenicity and efficacy. Timely and complete vaccination with multiple scheduled doses is of public health importance, because an incomplete administration of vaccine can lead to suboptimal disease protection[7]
	• Clinicians should vaccinate all unvaccinated adults at risk for infection, including pregnant women, healthcare and public safety workers, adults with chronic liver

	disease, end-stage renal disease, HIV, and travelers to HBV-endemic regions, against HBV [7]
	• Low levels of adherence to HBV screening and management guidelines among health care providers leads to low rates of vaccination and missed opportunities for vaccination in adult populations[8-9]
	  ○ Recent data suggests that less than 30% of adults have been vaccinated against hepatitis B[9]
	Unmet need – Low response rates to current vaccines
	• Non-responsiveness to the most widely used HBV vaccines is attributed to factors such as age, chronic illness, obesity, and other health/immune-related issues[10-13]
	• Seroprotection following vaccination can vary greatly between different ethnic groups, which may reflect different environmental and genetic influencing factors.
	• Additionally, reduced seroprotection is observed in older adults, and in people who are obese, smoke, or have significant comorbidities such as diabetes, chronic kidney or liver failure[10-13]
	  ○ Individuals with dialysis-dependent renal failure, or those with immunosuppression, do not develop protective responses following HBV vaccination[11-12]
	  ○ After two standard doses for a single antigen HBV vaccine, seropositive rates at six months for healthy people over 40 only ranged from 21%-73%[13]
	
	Emerging vaccines
	• A 3-antigen HBV vaccine (3A-HBV) is commercially available in Israel and Hong Kong and recently completed the pivotal Phase 3 program in the U.S., Europe, and Canada
	  ○ 3A-HBV vaccine is alum-adjuvanted and manufactured in mammalian cells
	  ○ 3A-HBV's 3-antigen conformation contains pre-S1, pre-S2, and S HBV surface antigens (HBsAg), resembling naturally occurring HBV particles in terms of protein composition[12]
	• In Phase 3 studies, 3A-HBV elicited higher SPRs and achieved higher anti-HBs titers when compared to a single-antigen, yeast-derived HBV vaccine[12]
	• 3A-HBV has well-established safety profile, and was generally well-tolerated with no safety signals observed in Phase 3 trials[12]

Format of grant requests	There is a 15-page limit for the grant request, not including the cover letter and appendix (see below for more detail). The cover letter, grant request, and appendix should be submitted as a single document.
Funding	Requests for CME grants funding up to $100,000 per event will be considered.
Submission	Grant requests should be sent to grants@vbivaccines.com with the subject line "CEGR: Grant Request". Grant requests that do not conform to the requirements outlined in this CEGR will not be reviewed.
Timing	Grant requests are due before 11:59 pm EST on July 21, 2021. Applicants may be asked for additional clarification during the review period. We anticipate notifying applicants of award decisions via email by August 10, 2021. Grants will be distributed following a fully executed agreement (50% upon initiation and 50% upon launch of all activities).

	Activity planning should begin after contract execution. Activities should be launched starting in December 2021
Questions	Questions regarding this CEGR should be sent to grants@vbivaccines.com with the subject line "Hepatitis B Vaccine CEGR: Questions".
References	1. CDC. Hepatitis B Questions and Answers for the Public, <https://www.cdc.gov/hepatitis/hbv/bfaq.htm> (2020). 2. World Health Organization. Hepatitis B. (Geneva, Switzerland, 2020). 3. CDC. Viral Hepatitis Surveillance Report 2018 — Hepatitis B, <https://www.cdc.gov/hepatitis/statistics/2018surveillance/HepB.htm> (2018). 4. MacLachlan, J. H. & Cowie, B. C. Hepatitis B virus epidemiology. Cold Spring Harb Perspect Med 5, a021410-a021410, doi:10.1101/cshperspect.a021410 (2015). 5. Bixler D. et al, Mortality Among Patients With Chronic Hepatitis B Infection: The Chronic Hepatitis Cohort Study (CHeCS). Clin Infect Dis 68(6), 956-963 (2019). 6. Abara, W. E., Qaseem, A., Schillie, S., McMahon, B. J. & Harris, A. M. Hepatitis B Vaccination, Screening, and Linkage to Care: Best Practice Advice From the American College of Physicians and the Centers for Disease Control and Prevention. Annals of Internal Medicine 167, 794-804, doi:10.7326/M17-1106 (2017). 7. Nelson, J. C. et al. Compliance with multiple-dose vaccine schedules among older children, adolescents, and adults: results from a vaccine safety datalink study. American journal of public health 99 Suppl 2, S389-397, doi:10.2105/ajph.2008.151332 (2009). 8. Mukhtar, N. A. et al. Provider, Patient, and Practice Factors Shape Hepatitis B Prevention and Management by Primary Care Providers. J Clin Gastroenterol 51, 626-631, doi:10.1097/MCG.0000000000000738 (2017). 9. Vaccination coverage among adults in the United States, National Health Interview Survey, 2017. Centers for Disease Control and Prevention. Accessed November 17, 2020. <https://www.cdc.gov/vaccines/imzmanagers/coverage/adultvaxview/pubs-resources/NHIS-2017.html>. 10. Yang, S. et al. Factors influencing immunologic response to hepatitis B vaccine in adults. Sci Rep 6, 27251-27251, doi:10.1038/srep27251 (2016). 11. Van Den Ende, C., Marano, C., Van Ahee, A., Bunge, E. M. & De Moerlooze, L. The immunogenicity and safety of GSK's recombinant hepatitis B vaccine in adults: a systematic review of 30 years of experience. Expert review of vaccines 16, 811-832, doi:10.1080/14760584.2017.1338568 (2017). 12. Saco, T. V., Strauss, A. T. & Ledford, D. K. Hepatitis B vaccine nonresponders: Possible mechanisms and solutions. Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology 121, 320-327, doi:10.1016/j.anai.2018.03.017 (2018). 13. Vesikari, T. et al. Immunogenicity and safety of a tri-antigenic hepatitis B vaccine, Sci-B-Vac®, compared with a mono-antigenic Hepatitis B vaccine, Engerix-B®, in adults: the PROTECT randomized clinical trial. Lancet Infect Dis, 2021; (published online May 11.) https://doi.org/10.1016/S1473-3099(20)30780-5

Cover letter and content and organization of the grant request

Cover letter	Include a cover letter as the first page of the submission (it does not count in the page limit). The cover letter should briefly summarize the proposed education and its desired outcomes for the target audience, the expertise and role of the requestor and collaborators (if any), and include the amount of funding requested. It should be signed by the individual responsible for communication with VBI regarding this CEGR.
Organization and team overview	Provide a brief summary of the relevant expertise of the requesting organization (the accredited provider) and any collaborators, including key outcomes metrics for recent hepatitis- and vaccine-related activities (e.g., absolute and relative changes in learners' knowledge and competence, effect sizes). List the names and credentials (e.g., degrees and certifications) of key team members responsible for instructional design, content development and validation, project management, and assessment and reporting.
Needs assessment	Summarize your assessment of clinicians' practice gaps and underlying educational needs related to hepatitis B vaccination. A detailed literature review is not required nor desired, but the data should be fully referenced. Include the desired outcomes of the proposed education.
Learning objectives	List the objectives of each activity; include the targeted level on the Moore outcomes scale (Moore DE et al. *Med Teach*. 2018;40:904-913.)
Instructional design	Briefly describe the number and format of the proposed activities/events (e.g., virtual journal clubs, podcasts, webinars, social media-based education) and the rationale for their selection. Include an overview of the proposed content of each activity and where the activities will be hosted/disseminated
Accreditation and Compliance	List the requestor's accreditation status related to each profession among the target audience; briefly describe your commitment to and process for implementing the ACCME's updated Standards for Integrity and Independence in Accredited Continuing Education.
Audience engagement	Describe the learners to be targeted for the proposed education and how they will be recruited to participate in the activities. Include estimates of the number of clinicians who will engage with the content of each activity and who will complete them and request credit. Describe how you will target clinicians that are likely hepatitis B vaccinators (e.g., Primary CPs, Pharmacists, advance practice practitioners such as NPs or PA, relevant physician specialties such as endocrinologists, transplant medicine, etc.). Describe what methods you might construct to help engage potential learners by allowing them to identify, describe, and analyze the professional practice gap (PPG) related to knowledge of the disease burden from hepatitis B, vaccine options, immunization rates, and vaccine protocols.
Assessment plan	Describe how participants' achievement of the learning objectives will be assessed and reported; include key metrics. Quantify the amount of change expected from this initiative and describe how your organization will determine if the activities were successful.
Sharing of results	Describe how you will share learnings from the initiative with relevant clinical and educational communities. VBI prefers a brief slide deck at 3 months post activity launch and a final report within a month of activity expiration.

Content and organization of the appendix (these items are <u>not</u> included in the 15-page limit for the grant request)

Timeline	Provide timing for key milestones (e.g., faculty recruitment, content development, activity launch, learner engagement, outcomes reporting).
Budget	Provide a line-item budget. Describe contingency plans for less than full funding.
References	Provide references for the literature cited in the "Needs Assessment" and elsewhere throughout the proposal.