

July 9, 2020

The Honorable Alex M. Azar II  
Secretary  
U.S. Department of Health and Human Services  
200 Independence Avenue SW  
Washington, DC 20201

Dear Secretary Azar:

We, the undersigned organizations, appreciate all the steps the U.S. Department of Health and Human Services has taken to work towards hepatitis B elimination, including ensuring that adults in the U.S. are protected from hepatitis B through vaccination. However, we are deeply concerned regarding the continuous rise in the number of adults contracting hepatitis B and the connection between the spread of this infectious disease and the low adult vaccination rates, including the lack of completion of the three-dose over six-month hepatitis B vaccine series.

As you know, the Food and Drug Administration (FDA) approved a two-dose in one-month vaccine for the prevention of hepatitis B in November 2017. The two-dose in one-month vaccine provides faster and higher rates of seroprotection than three-dose over six month options, and was subsequently recommended by the CDC Advisory Committee on Immunization Practices (ACIP) in February 2018. The two-dose hepatitis B vaccine offers a shorter dosing regimen and has exhibited higher immunogenicity among both the healthy and immunosuppressed populations<sup>1</sup>.

**As organizations dedicated to the elimination of hepatitis B, we encourage the Department, and in particular the Centers for Disease Control and Prevention (CDC), to prioritize its adult vaccination efforts and consider expediting the Advisory Committee on Immunization Practices (ACIP) preferential review of this two-dose in one-month vaccine.**

The two-dose vaccine presents a significant advancement in public health, particularly when vaccination is still the primary means for preventing hepatitis B infection and its severe, long-term consequences. Not only is this a more clinically and logistically effective solution, but it is also a more cost effective solution.

While we defer to the CDC ACIP and its scientific expertise, we note the two-dose vaccine has three critical advantages over the three-dose vaccine, including completion, efficacy and the cost per protected patient.

**Completion:** Dose completion is critical for any vaccine to work successfully. Multiple recent studies indicate suboptimal series completion rates for the three-dose adult hepatitis B vaccines. Alarming low rates of third-dose completion -- 31%, 22% and 26% -- leave approximately

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<sup>1</sup> HEPLISAV-B [package insert]. Berkeley, CA: Dynavax Technologies Corporation; 2018.; Halperin S, et al. *Vaccine*. 2012;30:2556-2563.; FDA Advisory Committee Briefing Document: HEPLISAV-B™ [Hepatitis B Vaccine (Recombinant), Adjuvanted]. Presented at: Meeting of the Vaccines and Related Biological Products Advisory Committee; Silver Spring, MD; July 28, 2017.

70%<sup>2</sup> of patients who have started the three-dose adult hepatitis B vaccine regimen unprotected, creating an illusion of successful vaccination for them, their providers and the public health infrastructure. Among our own community efforts reaching underserved populations including high-risk first and second generation Americans and persons who inject drugs, we have difficulty administering the third dose - in Philadelphia, we have seen less than 20% of those who start the vaccine series with us complete the third dose. The hepatitis B vaccine is particularly important for Asian Americans, Pacific Islanders, and African immigrants, who face a disproportionate burden from the virus. Asian Americans and Pacific Islanders account for approximately five percent of the U.S. population but account for over 50% of all chronic hepatitis B cases while African immigrant communities can have up to a 15% infection rate.<sup>3,4</sup>

**Efficacy:** Effective rates of seroprotection in adults who have received only two doses of the three-dose hepatitis B vaccine range in the area of 22%-32%<sup>5</sup>. In comparison, the two-dose vaccine has a seroprotection rate of 90%-95%<sup>6</sup> after one month and two doses. Statistically significantly higher rates with the 2-dose vs. the 3-dose were also observed in persons with diabetes and other known hyporesponsive populations.<sup>7</sup>

**Cost Per Protected Patient:** The cost of protecting adults from hepatitis B is critically important to our role as stewards of good fiscal responsibility. In 2019, the CDC Public Health Awardees

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<sup>2</sup> Compliance rates for third dose completion are from 1) Nelson J, et al. *Am J Public Health*. 2009;99:S389-S397; Gunn RA, et al. *Sex Transm Dis*. 2007;34(9):663-668; 2) Bruxvoort et al. *Hepatitis B Vaccine Adherence*.; and 3) Bridges CB, Watson TL, Nelson NP, et al. *Hepatitis B Vaccine 3-Dose Series Completion in Settings in which a High Proportion of Adults have Hepatitis B-Related Risk Factors — United States 2012-2015*. Poster presented at: 48th National Immunization Conference (NIC); May 15-17, 2018; Atlanta, Georgia.

<sup>3</sup>Centers for Disease Control and Prevention. (2020). *Asian Americans and Pacific Islanders and Chronic Hepatitis B*. Centers for Disease Control and Prevention Division of Viral Hepatitis. Retrieved 2 July 2020, from <https://www.cdc.gov/hepatitis/populations/api.htm>.

<sup>4</sup> Rossi, C.; Shrier, I.; Marshall, L.; Cnossen, S.; Schwartzman, K.; Klein, M.B.; Schwarzer, G.; Greenaway, C. Seroprevalence of Chronic Hepatitis B Virus Infection and Prior Immunity in Immigrants and Refugees: A Systematic Review and Meta-Analysis. *PLoS ONE* 2012, 7, e44611.

<sup>5</sup> Engerix-B second dose seroprotection rates data can be found in: HEPLISAV-B [package insert]. Berkeley, CA: Dynavax Technologies Corporation; 2018.; Halperin S, et al. *Vaccine*. 2012;30:2556-2563. ; FDA Advisory Committee Briefing Document: HEPLISAV-B® [Hepatitis B Vaccine (Recombinant), Adjuvanted]. Presented at: Meeting of the Vaccines and Related Biological Products Advisory Committee; Silver Spring, MD; July 28, 2017.; Second dose seroprotection (SPR) rates for Engerix-B in Dynavax clinical trials HBV-10 and HBV 16 were 33.7% (ages 18)and 21.5% (ages 40-70) respectively.

<sup>6</sup> Heplisav-B second dose seroprotection rates can be found in: HEPLISAV-B [package insert]. Berkeley, CA: Dynavax Technologies Corporation; 2018.; Halperin S, et al. *Vaccine*. 2012;30:2556-2563. ; FDA Advisory Committee Briefing Document: HEPLISAV-B® [Hepatitis B Vaccine (Recombinant), Adjuvanted]. Presented at: Meeting of the Vaccines and Related Biological Products Advisory Committee; Silver Spring, MD; July 28, 2017.; Second dose seroprotection (SPR) rates for Heplisav-B in Dynavax clinical trials HBV-10 and HBV 16 were 95% (ages 18)and 90.1% (ages 40-70) respectively.

<sup>7</sup> HEPLISAV-B [package insert]. Berkeley, CA: Dynavax Technologies Corporation; 2018.; Halperin S, et al. *Vaccine*. 2012;30:2556-2563; FDA Advisory Committee Briefing Document: HEPLISAV-B™ [Hepatitis B Vaccine (Recombinant), Adjuvanted]. Presented at: Meeting of the Vaccines and Related Biological Products Advisory Committee; Silver Spring, MD; July 28, 2017.

purchased 164,700<sup>8</sup> adult 3-dose hepatitis B vaccine doses, at a cost of \$5,435,100<sup>9</sup>. Given the low rates of third-dose completion stated above, approximately 75%<sup>10</sup> of the patients receiving those doses remain unprotected. This translates into a budget wastage of \$4,098,065 or 75.4% of public funds invested. Low compliance rates are not limited to the public health setting. There is equivalent low compliance for state Medicaid programs, Medicare and Managed Care Organizations, with associated budget wastage ranging from 50%-70% of adult hepatitis B dose spend for the three-dose vaccine in these payer segments.<sup>11</sup>

The CDC has been asked by Congress to come up with a plan for hepatitis B elimination and we encourage you to take the necessary steps to evaluate the utility of the two-dose vaccine as a stronger, more effective weapon in our fight to eliminate hepatitis B. An estimated 2.2 million people in the United States live with hepatitis B virus<sup>12</sup>, with more than half unaware they are living with the disease. Despite being a vaccine preventable disease, little to no progress has been made to reduce the number of chronic hepatitis B cases in the U.S. The number of reported acute hepatitis B cases across the country rose for the first time since 2006, increasing by 20.7% in 2015, largely due to low adult vaccination rates. Only about 30% of adults aged 19-49 years and 16% of adults over 50 years are vaccinated against hepatitis B<sup>13</sup>.

We are concerned that as a result of the opioid crisis, in particular, infections of viral hepatitis have spiked at alarming rates in parts of the nation most impacted by it: rates of acute hepatitis B increased ranging from 56% to 457% in states most heavily affected by the opioid epidemic,

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<sup>8</sup> CDC Awardee Program, 2019 reported doses from CDC

<sup>9</sup> Cost based on CDC price for Engerix-B, as listed on CDC Adult Vaccine Price List;

<https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html>

<sup>10</sup> Source, Dynavax Technologies. Poster presented at: 48th National Immunization Conference (NIC); May 15-17, 2018; Atlanta, Georgia.

<sup>11</sup> Compliance rates for Managed Care Organizations are sourced from 1) Nelson J, et al. Am J Public Health. 2009;99:S389-S397; Gunn RA, et al. Sex Transm Dis. 2007;34(9):663-668; and 2) Bruxvoort et al. Hepatitis B Vaccine Adherence. Comparing 2-dose and 3-dose Vaccines. Poster presented at: IDSA: 2019 October 2nd – 6th; Washington, D.C

<sup>12</sup> Kowdley KV, Wang CC, Welch S, Roberts H, Brosgart CL. (2012). Prevalence of chronic hepatitis B among foreign-born persons living in the United States by country of origin. *Hepatology*, 56(2), 422-433.

<sup>13</sup> TABLE 5. Estimated proportion of adults ≥19 years who received Hepatitis B vaccination\*, by age group, increased-risk status†, and race/ethnicity‡, National Health Interview Survey, United States, 2016; <https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/pubs-resources/NHIS-2016.html#hepB>. Accessed April 2020.

including in Kentucky, Tennessee, West Virginia, North Carolina, and Maine<sup>14,15,16,17</sup>. While the recent increase in hepatitis B cases has been attributed to homelessness and the opioid crisis, infections have also increased amongst many high-risk populations such as patients suffering from diabetes, end stage renal disease (ESRD) and HIV. These increases are evidence that our current vaccination efforts of those most vulnerable are not working. Effective, rapid vaccination is critical in the short-term to stem the tide of HBV infection.

In addition, hepatitis B vaccination saves millions of dollars of health care spending in the U.S. In fact, hepatitis B vaccination is the most cost-effective strategy towards eliminating hepatitis B and related liver cancers. Hepatitis B remains a leading cause of liver cancer; 50% of all liver cancers are caused by hepatitis B<sup>18</sup>-- one of the most lethal, most expensive to treat, and fastest growing cancers in America<sup>19</sup> -- with 5-year survival rates of only 15%. The hepatitis B vaccine was named the first “anti-cancer” vaccine by the U.S. Food and Drug Administration because it prevents chronic hepatitis B infections, thereby preventing liver cancer caused by the hepatitis B virus.

The United States is falling short on hepatitis B elimination goals with significant outbreaks of this disease across the U.S. The two-dose vaccine provides an essential option for protecting adults from hepatitis B. We know that this is a challenging time for our public health leaders and advisors, but especially now, it is imperative that we move forward efforts to improve adult vaccine rates for hepatitis. We ask that CDC and CDC’s ACIP continue to prioritize hepatitis B and consider a timely review and implementation of strategies to improve adult vaccine rates, including a review of preferential status for the two-dose vaccine.

Sincerely,

Hepatitis B Foundation  
Hep B United  
National Viral Hepatitis Roundtable  
The AIDS Institute

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<sup>14</sup>Centers for Disease Control and Prevention. [https://www.cdc.gov/hai/pdfs/bbp/exp\\_to\\_blood.pdf](https://www.cdc.gov/hai/pdfs/bbp/exp_to_blood.pdf). Updated July 2003. Accessed January 25, 2018. ; Centers for Disease Control and Prevention.

<https://www.cdc.gov/hepatitis/featuredtopics/youngpwid.htm>. Accessed March 25, 2019

<sup>15</sup> Harris AM, Iqbal K, Schillie S, et al. Increases in acute hepatitis B virus infections—Kentucky, Tennessee, and West Virginia, 2006-2013. *MMWR Morb Mortal Wkly Rep.* 2016;65(3):47-50. doi:10.15585/mmwr.mm6503a2. Centers for Disease Control and Prevention. [https://www.cdc.gov/hai/pdfs/bbp/exp\\_to\\_blood.pdf](https://www.cdc.gov/hai/pdfs/bbp/exp_to_blood.pdf). Updated July 2003.

<sup>16</sup> Maine Center for Disease Control and Prevention. Maine surveillance report 2018: acute hepatitis B. <https://www.maine.gov/dhhs/mecdc/infectious-disease/epi/publications/index.shtml#surveillance>.

<sup>17</sup> Hepatitis B, C on rise in N.C.; health officials encourage precautions, testing [press release]. Raleigh, NC: North Carolina Department of Health and Human Services; May 30, 2017. <https://www.ncdhhs.gov/news/press-releases/hepatitis-b-c-rise-nc-health-officials-encourage-precautions-testing>.

<sup>18</sup> Centers for Disease Control and Prevention. Hepatitis B. In: Hamborsky J, Kroger A, Wolfe S, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 13th ed. Washington, DC: Public Health Foundation;2015:149-174. <https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/hepb.pdf>. Accessed October 16, 2017

<sup>19</sup> <https://www.cancer.org/latest-news/death-rates-from-liver-cancer-are-increasing-especially-in-men-with-less-education.html>

ADAP Advocacy Association  
Alliance for Positive Change  
African Family Health Organization (AFAHO)  
American Association for the Study of Liver Diseases  
Any Positive Changes Inc.  
Asian Center - Southeast Michigan  
Asian Pacific Health Foundation  
Asian & Pacific Islander American Health Forum (APIAHF)  
Asian Pacific Liver Center  
Association of Asian Pacific Community Health Organizations (AAPCHO)  
Bay Clinic Pharmacy  
The Bonnie Morgan Foundation for HCV  
Caring Ambassadors Program, Inc.  
Coalition on Positive Health Empowerment  
Community Access National Network (CANN)  
Community Health Care Network  
Community Liver Alliance  
Community Welfare Services of Metro Detroit  
Desert AIDS Project  
Dynavax  
End Hep C San Francisco  
Georgia AIDS Coalition  
Global Liver Institute  
Hawaii Comprehensive Cancer Control Program  
Hawaii Health & Harm Reduction Center  
Hawai'i Immunization Coalition  
Hep B United Philadelphia  
Hep Free Hawaii  
Hepatitis B Initiative of Washington DC (HBI-DC)  
Hepatitis C Association  
Hepatitis C Mentor and Support Group (HCMSG)  
Hepatitis Education Project  
HIV Medicine Association  
Immunization Action Coalition  
Immunize Colorado  
Infectious Diseases Society of America  
Latino Commission on AIDS  
National Alliance of State & Territorial AIDS Directors (NASTAD)  
National Nurse-Led Care Consortium  
National Task Force on Hepatitis B Focus on Asian and Pacific Islander Americans  
Northeast Philadelphia Chinese Association (NEPCA) of Culture Trust Greater Philadelphia  
Robert G Gish Consultants LLC  
San Francisco Hep B Free - Bay Area  
Sidney Kimmel Cancer Center at Jefferson  
Treatment Action Group  
TruCare Internal Medicine & Infectious Diseases

Vietnamese American Cancer Foundation  
Vietlead

cc: Elinore F. McCance-Katz, M.D., Ph.D.  
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Robert R. Redfield, M.D.  
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Carolyn Wester, MD, MPH  
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Centers for Disease Control and Prevention