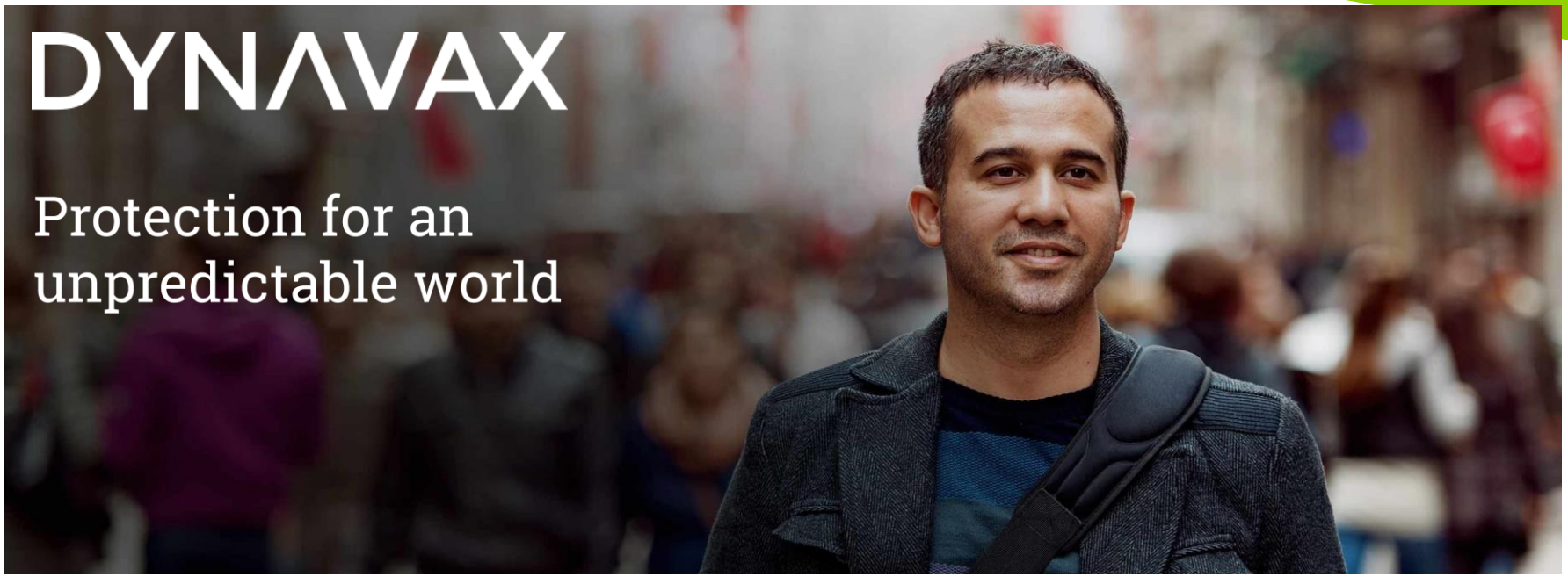


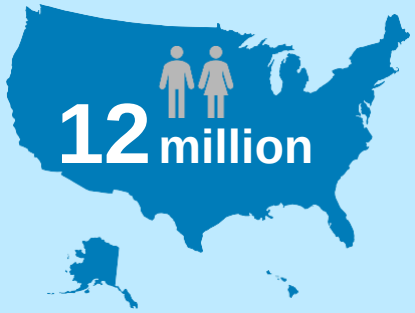
Considerations for Incorporating Heplisav-B into the Texas HIV Medication Program

Brian Faulconer, PharmD

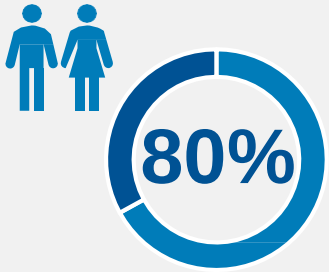
Regional Director of Medical Affairs at Dynavax Technologies

July 31, 2020

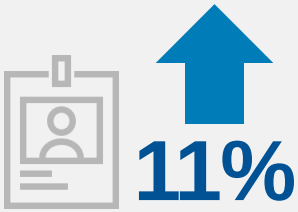
Hepatitis B Is on the Rise



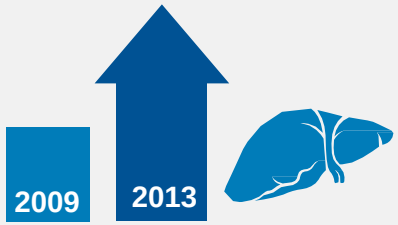
12 million Americans have been infected with HBV and **850,000 to 2.2 million are living with chronic infection**[1]



More than 80% of infected people **are unaware** they have HBV[2]



Estimated **new cases** of HBV in the United States have **risen 11%** over a 5-year period[3]

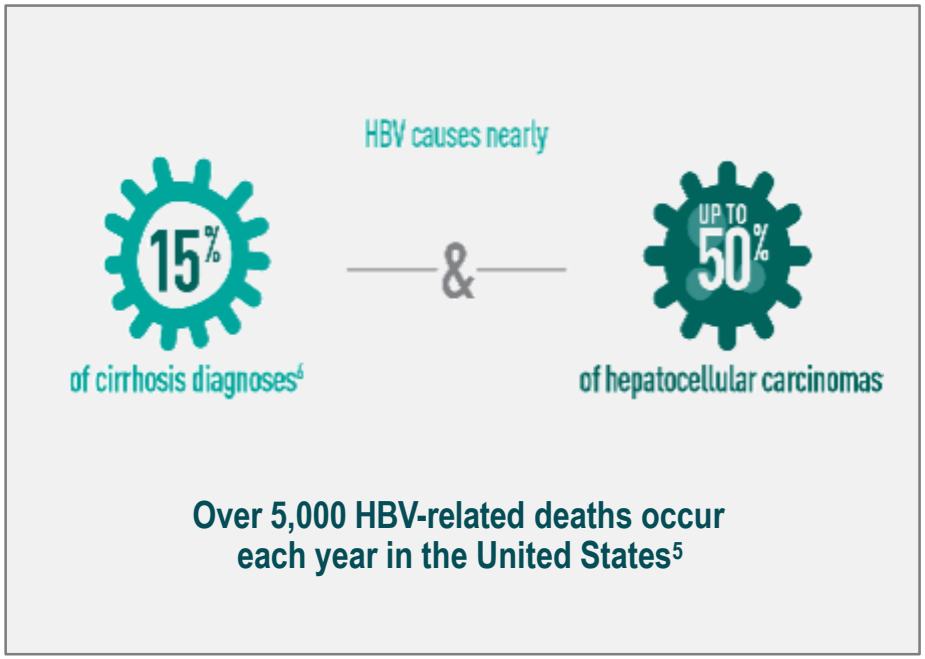


Hepatitis B infections have increased up to **114%** from 2009 to 2013 in some states affected by the opioid and heroin epidemics[4]

Sources: 1. Hepatitis B Foundation. What is hepatitis B? http://www.hepb.org/what-is-hepatitis-b/what-is-hepb/facts-and-figures. Accessed March 12, 2020.
2. Ogawa E, et al. JAMA Netw Open. 2020;3(4):e201844 3. Centers for Disease Control and Prevention. Viral hepatitis statistics and surveillance. https://www.cdc.gov/hepatitis/statistics. Accessed March 12, 2020.
4. Harris SA, Nicolai LA. Occupational exposures in emergency medical service providers and knowledge of and compliance with universal precautions. *Am J Infect Control.* 2010;38(2):86-94.

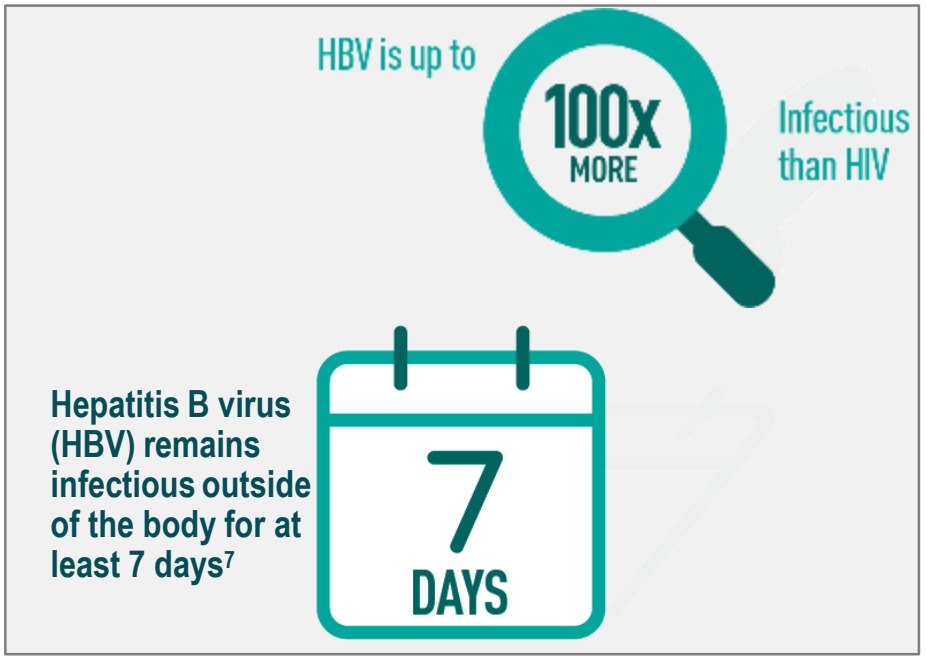
Hepatitis B Is an Important Public Health Concern[1]

Chronic HBV infection can lead to serious complications and death[3,4]



Over 5,000 HBV-related deaths occur each year in the United States[5]

HBV is highly infectious, resilient, and environmentally stable[2]



THERE IS NO CURE FOR HEPATITIS B,[8] BUT IT IS PREVENTABLE

Sources: 1. 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. 2. Centers for Disease Control and Prevention. *MMWR Morb Mortal Wkly Rep*. 2011;60(50):1709-1711. 3. Than TT, et al. *J Infect Dis*. 2019;219(7):1044-1048. 4. Centers for Disease Control and Prevention. Hamborsky J, et al, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 13th ed. Washington, DC: Public Health Foundation; 2015:149-174. 5. Finding a cure for hepatitis B: more NIH research is needed. http://hepbunited.org/wp-content/uploads/2017/08/HBU-2017-NIH-Overview.pdf. Accessed February 13, 2018. 6. Starr SP, et al. *Am Fam Physician*. 2011;84(12):1353-1359. 7. Keeffe EB. *Trans Am Clin Climatol Assoc*. 2006;117:227-238. 8. Finding a cure for hepatitis B: more NIH research is needed. http://hepbunited.org/wp-content/uploads/2017/08/HBU-2017-NIH-Overview.pdf. Accessed February 13, 2018

CDC Guidelines on Risk Groups Indicated for PrEP and HBV Vaccination Overlap

Medical Diagnoses

- Diabetes, aged 19 to 59 years
- Chronic liver disease
- **HIV infection**
- End-stage renal disease, including predialysis, hemodialysis, and home dialysis patients

Sexual Exposure

- **Sexually active patients who are not in a long-term, mutually monogamous relationship**
- **Patients seeking testing or treatment for a sexually transmitted disease**
- **Men who have sex with men**
- **Sexual partners of HBV-positive persons**

Occupational Risk

- Persons who have occupational risk of infection, including healthcare and public safety workers
- International travelers
- Employers must offer HBV immunization at no cost to healthcare and public safety workers[2]

Other Risk Factors

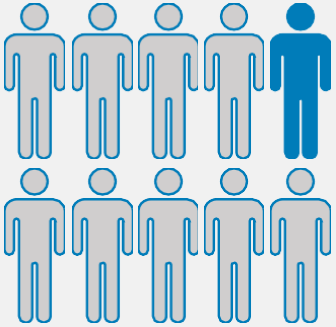
- **Current or recent injection drug users**
- Household contacts of HBV-positive persons
- All patients seeking protection from HBV infection

DESPITE GUIDELINES, <25% OF ADULTS HAVE RECEIVED A FULL HBV VACCINATION SERIES[3]

Source: 1. Mast EE, et al. *MMWR Recomm Rep*. 2006;55(RR-16):1-33. 2. Occupational Safety and Health Administration. Hepatitis B vaccination protection. https://www.osha.gov/OshDoc/data_BloodborneFacts/bbfact05.pdf. Accessed January 25, 2018. . 3. https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/pubs-resources/NHIS-2016.html#hepB.

Co-infection with HIV and HBV is common

Both viruses share the same routes of transmission



According to the CDC

~1 in 10

people living with HIV are **coinfected** with hepatitis B virus (HBV) and 1 in 10 HIV diagnoses occur among people who inject drugs[1]

Up to **2/3** of all HIV-infected people have a blood marker of past or present HBV infection[1]

For people living with HIV…

- HBV **progresses faster ,** is less likely to spontaneously cure, and has **increased rates of cirrhosis (10–20%), hepatocarcinoma and liver-related death**.[1-3]
- Hepatotoxic **side effects of (HAART)** are increased with HBV coinfection[1-3]
- HIV infection results **lower response rates to classic HBV vaccination** schedules than in the general population, and could be as low as 17.5%[1-3]

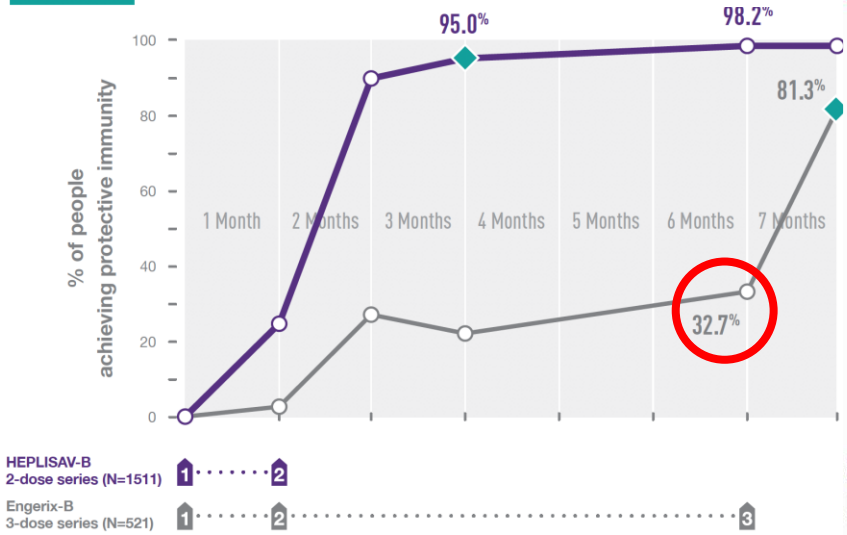
PROTECTION FROM HBV IS CRITICAL FOR ANYONE AT RISK OF HIV INFECTION

Source: 1. Piroth, Hepatitis B virus vaccination in HIV-infected people: A review; HUMAN VACCINES & IMMUNOTHERAPEUTICS 2017, VOL. 13, NO. 6, 1304–1313 https://doi.org/10.1080/21645515.2016.1277844. 2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5489285/. 3. Mena et al., Hepatitis B and A vaccination in HIV-infected adults: A review, Human Vaccines & Immunotherapeutics 11:11, 2582--2598; November 2015; Published with license by Taylor & Francis Group, LLC

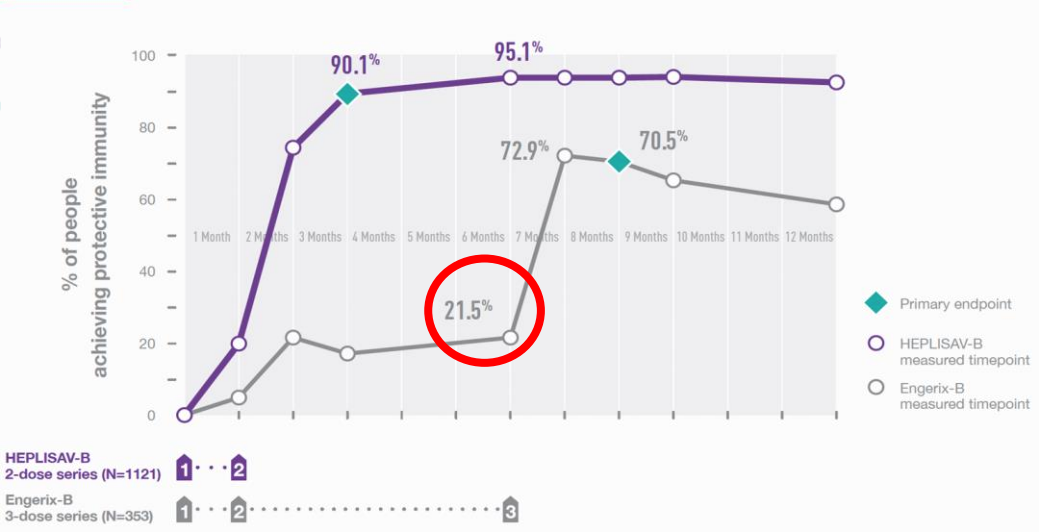
HEPLISAV-B Trial 1 and 2: Higher and Faster Rates of Protection[1,2]

SERIES COMPLETION AND TIME TO PROTECTION ARE IMPORTANT, PARTICULARLY FOR HIGH-RISK SEGMENTS

TRIAL 1 Patients aged 18-55



TRIAL 2 Patients aged 40-70



SELECT IMPORTANT SAFETY INFORMATION

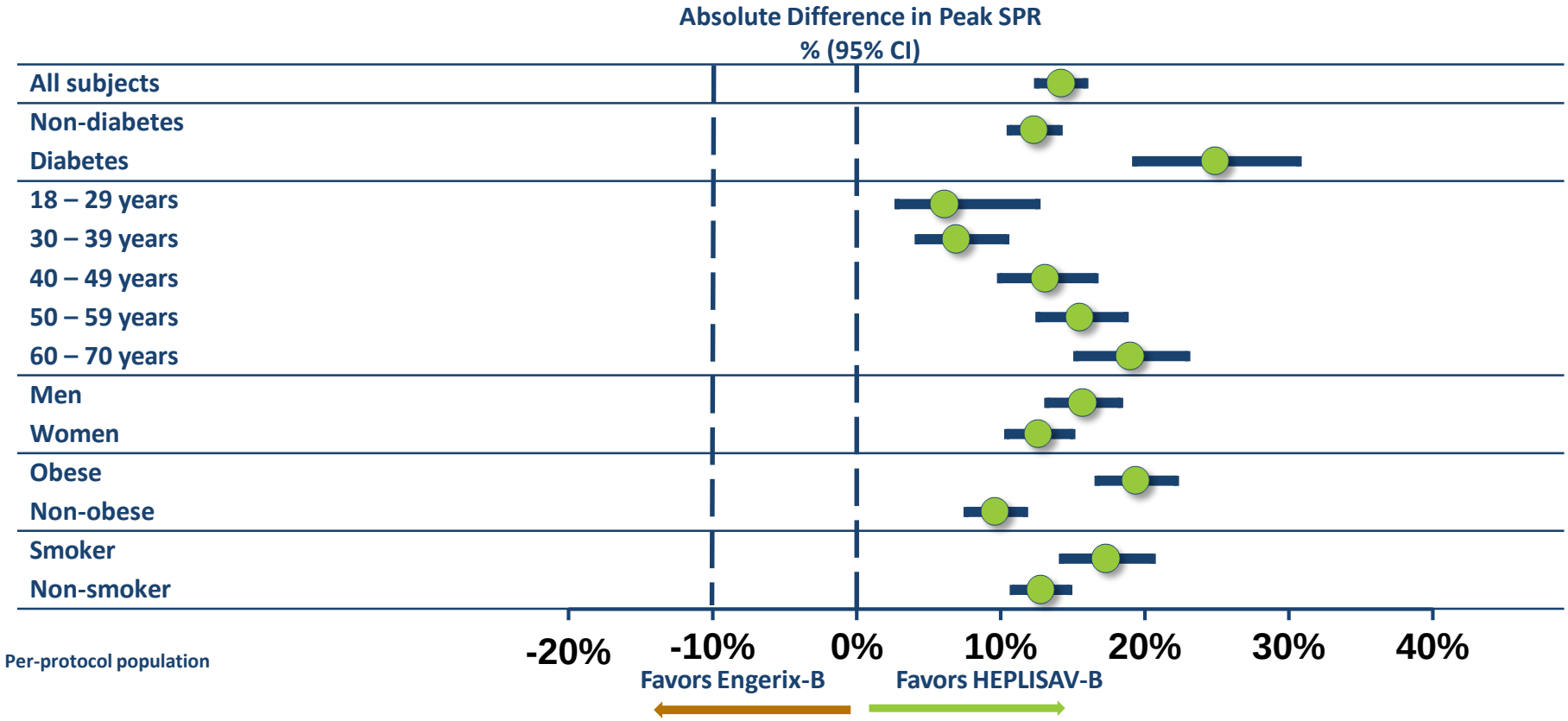
Hepatitis B has a long incubation period. HEPLISAV-B may not prevent hepatitis B infection in individuals who have an unrecognized hepatitis B infection at the time of vaccine administration.

Please see Select Important Safety Information throughout this presentation and accompanying full Prescribing Information.

Sources: **1.** HEPLISAV-B [package insert]. Berkeley, CA: Dynavax Technologies Corporation; 2018. **2.** Halperin S, et al. *Vaccine*. 2012;30:2556-2563. **3.** 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.

HEPLISAV-B Hepatitis B Vaccine (Recombinant), Adjuvanted Trial 3: Hyporesponsive Populations

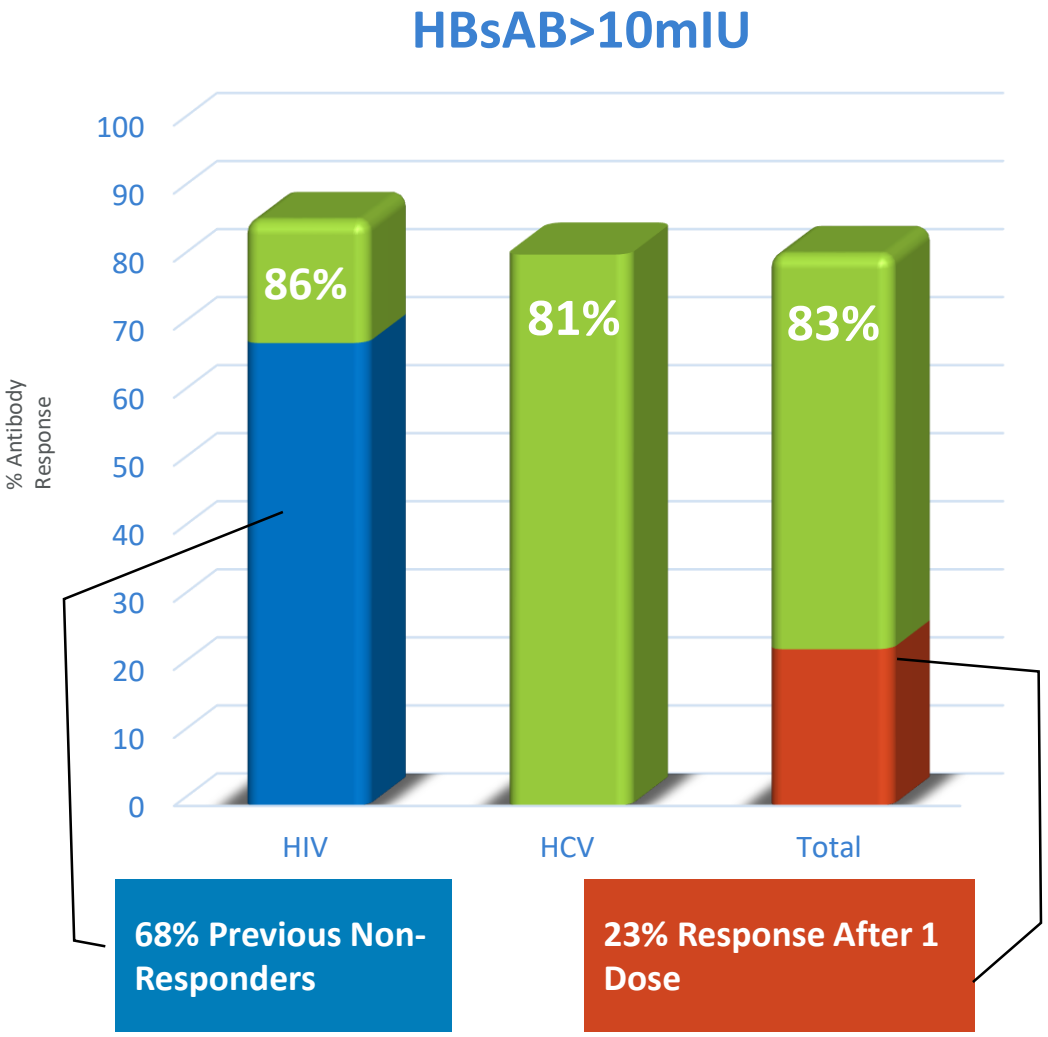
HEPLISAV-B provided statistically significantly higher rates of protection in diabetics and other known hyporesponsive populations[1-3]



Trial 3 (HBV 23) study design: A clinical trial in adults aged 18 to 70 years who receive HEPLISAV-B (N=4537) or Engerix-B (N=2289). The primary analysis evaluated the noninferiority of the rate of protective immunity at week 28 induced by HEPLISAV-B (n=640) to Engerix-B (n=321) in patients with type 2 diabetes melltitus. A secondary immunogenicity objective was to demonstrate the noninferiority of the rate of protective immunity with HEPLISAV-B at week 24 compared to Engerix-B at week 28 in all subjects and in subgroups designed by age, sex, body mass index (BMI), and smoking status among adults.

Sources: **1.** HEPLISAV-B [package insert]. Berkeley, CA: Dynavax Technologies Corporation; 2018. **2.** Halperin S, et al. *Vaccine*. 2012;30:2556-2563. **3.** 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.

Heplisav B Demonstrates an Improved Immune Response in HIV and Hepatitis C Patients



- Retrospective analysis of 137 patients of which 71 patients were assessed for immunity
- 86% (25/29) of HIV patients were found to be immune
- 68% (17/25) immune HIV patients were non-responders to a full prior HBV vaccination series
- 81% (34/42) of HCV patients were found to be immune
- Of the total cohort tested – 23% were protected after the first dose with a total response of 83%

Brooke Kimball. Katie Garrett. Abstract (605) from the 2020 Conference on Retroviruses and Opportunistic Infections.Top Antiv Med 2020. 28(1).483

Adult Hepatitis B Vaccine Selection Considerations

Key Factors

- Time until minimum protective titer levels are achieved
- Compliance profile for completing the series
- Rates of protection for those with weaker immune systems
- Best use of existing funds towards effective seroprotection

Effective HBV vaccination is critical to achieving the CDC's goal of eliminating HBV by 2030, by protecting those with highest-risk and saving public health resources

Please see Select Important Safety Information throughout this presentation and accompanying full Prescribing Information.

*Based on calculations comparing number of protected patients using HEPLISAV-B and Engerix-B using compliance and CPPP rates from Bruxvoort K, et al. IDSA October 2019, Comparing 2-dose and 3-dose Vaccines in KPSC Post-Marketing Study. CPPP of $287.24 for Engerix-B and $247.42 for HEPLISAV-B based on pooled SPR rates from Dynavax Clinical Trials, and price of $46.44 for Engerix-B plus $0.75 Federal Excise Tax per dose and price of $101.20 for HEPLISAV-B plus $0.75 Federal Excise Tax per dose; Results showed that using a 1 million budget would protect 560 more patients on HEPLISAV-B.

Sources: **1.** Halperin SA, Ward B, Cooper C, et al. Comparison of safety and immunogenicity of two doses of investigational hepatitis B virus surface antigen co-administered with an immunostimulatory phosphorothioate oligodeoxyribonucleotide and three doses of a licensed hepatitis B vaccine in healthy adults 18-55 years of age. Vaccine. 2012;30(15):2556-63. **2.** Heyward WL, Kyle M, Blumenau J, et al. Immunogenicity and safety of an investigational hepatitis B vaccine with a Toll-like receptor 9 agonist adjuvant (HBsAg-1018) compared to a licensed hepatitis B vaccine in healthy adults 40-70 years of age. Vaccine. 2013;31(46):5300-5. **3.** Jackson S, Lentino J, Kopp J, et al. Immunogenicity of a two-dose investigational hepatitis B vaccine, HBsAg-1018, using a toll-like receptor 9 agonist adjuvant compared with a licensed hepatitis B vaccine in adults. Vaccine. 2018;36(5):668-674.

DYNAVAX

Additional Slides

HEPLISAV-B®
[Hepatitis B Vaccine (Recombinant), Adjuvanted]

- **Indication**
  - HEPLISAV-B is indicated for prevention of infection caused by all known subtypes of hepatitis B virus in adults 18 years of age and older.
- **Dosing & Administration**
  - Administer 2 doses (0.5 mL each) intramuscularly 1 month apart
- **Important Safety Information**
  - Do not administer HEPLISAV-B to individuals with a history of severe allergic reaction (e.g., anaphylaxis) after a previous dose of any hepatitis B vaccine or to any component of HEPLISAV-B, including yeast.
  - Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of HEPLISAV-B.
  - Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to HEPLISAV-B.
  - Hepatitis B has a long incubation period. HEPLISAV-B may not prevent hepatitis B infection in individuals who have an unrecognized hepatitis B infection at the time of vaccine administration.
  - The most common patient-reported adverse reactions reported within 7 days of vaccination were injection site pain (23%–39%), fatigue (11%–17%), and headache (8%–17%).

HEPLISAV-B [Hepatitis B Vaccine (Recombinant), Adjuvanted]—Clinical Trial Safety Database (N=14,238)[17,29,30-32]

In Trial 1, the most common (>10%) local reaction was injection site pain (39%), and the most common systemic reactions were fatigue (17%) and headache (17%)[29]

PERCENTAGE WITH LOCAL OR SYSTEMIC REACTIONS WITHIN 7 DAYS OF VACCINATION[29]

	HEPLISAV-B		Engerix-B		
	Post Dose		Post Dose		
Reaction	**1**	**2**	**1**	**2**	**3**
Local	N=1810	N=1798	N=605	N=603	N=598
Injection site pain	38.5%	34.8%	33.6%	24.7%	20.2%
Injection site redness*	4.1%	2.9%	0.5%	1.0%	0.7%
Injection site swelling*	2.3%	1.5%	0.7%	0.5%	0.5%
Systemic					
Fatigue	17.4%	13.8%	16.7%	11.9%	10.0%
Headache	16.9%	12.8%	19.2%	12.3%	9.5%
Malaise	9.2%	7.6%	8.9%	6.5%	6.4%
	N=1784	N=1764	N=596	N=590	N=561
Fever†	1.1%	1.5%	1.8%	1.7%	1.8%

*Redness and swelling ≥2.5 cm.
†Oral temperature ≥100°F (38.0°C).

Please see additional Important Safety Information throughout this presentation and accompanying full Prescribing Information.

HEPLISAV-B [Hepatitis B Vaccine (Recombinant), Adjuvanted]—Clinical Trial Safety Database (N=14,238)[17,29,30-32] *(cont'd)*

In Trial 2, the most common (>10%) local reaction was injection site pain (23%), and the most common systemic reactions were fatigue (11%) and headache (8%)[29]

PERCENTAGE WITH LOCAL OR SYSTEMIC REACTIONS WITHIN 7 DAYS OF VACCINATION[29]

	HEPLISAV-B		Engerix-B		
	Post Dose		Post Dose		
Reaction	**1**	**2**	**1**	**2**	**3**
Local	N=1952	N=1905	N=477	N=464	N=448
Injection site pain	23.7%	22.8%	18.4%	15.9%	13.8%
Injection site redness*	0.9%	0.7%	0.6%	0.2%	0.2%
Injection site swelling*	0.9%	0.6%	0.6%	0.6%	0.2%
Systemic					
Fatigue	12.6%	12.8%	12.8%	12.1%	9.4%
Headache	11.8%	8.1%	11.9%	9.5%	8.5%
Malaise	7.7%	7.0%	8.6%	7.1%	5.1%
Myalgia	8.5%	6.4%	9.6%	8.0%	4.5%
	N=1923	N=472	N=472	N=459	N=438
Fever†	0.6%	0.6%	0.6%	0.9%	0.7%

*Redness and swelling ≥2.5 cm.
†Oral temperature ≥100°F (38.0°C).

Please see additional Important Safety Information throughout this presentation and accompanying full Prescribing Information.

HEPLISAV-B [Hepatitis B Vaccine (Recombinant), Adjuvanted]— Clinical Trial Safety Database (N=14,238)[17,29,30-32] *(cont'd)*

In Trial 3, the most common (≥1%) treatment-emergent, medically attended adverse events were upper respiratory tract infections, bronchitis, sinusitis, hypertension, urinary tract infection, and back pain[29]

	HEPLISAV-B (N=5587)[29] % (n)	Engerix-B (N=2781)[29] % (n)
Subjects with ≥1 qualify MAE	46.0 (2569)	46.2 (1286)
Upper respiratory tract infection	3.4 (192)	3.3 (92)
Bronchitis	3.2 (176)	3.7 (102)
Sinusitis	2.7 (149)	3.0 (84)
Hypertension	2.4 (133)	2.1 (59)
Urinary tract infection	2.4 (132)	2.3 (64)
Back pain	2.1 (116)	1.9 (54)
Arthralgia	1.8 (98)	1.9 (54)
Osteoarthritis	1.4 (77)	1.2 (32)
Pain in extremity	1.3 (72)	1.0 (28)
Type 2 diabetes mellitus	1.2 (67)	1.3 (37)
Cough	1.1 (62)	1.3 (37)
Acute sinusitis	1.1 (59)	1.3 (37)
Laceration	1.0 (54)	0.7 (19)
Musculoskeletal pain	0.8 (45)	1.1 (30)

MAE=medically attended event.

Please see additional Important Safety Information throughout this presentation and accompanying full Prescribing Information.

Some of the Highest at Risk Groups Have the Lowest Series Completion Rates

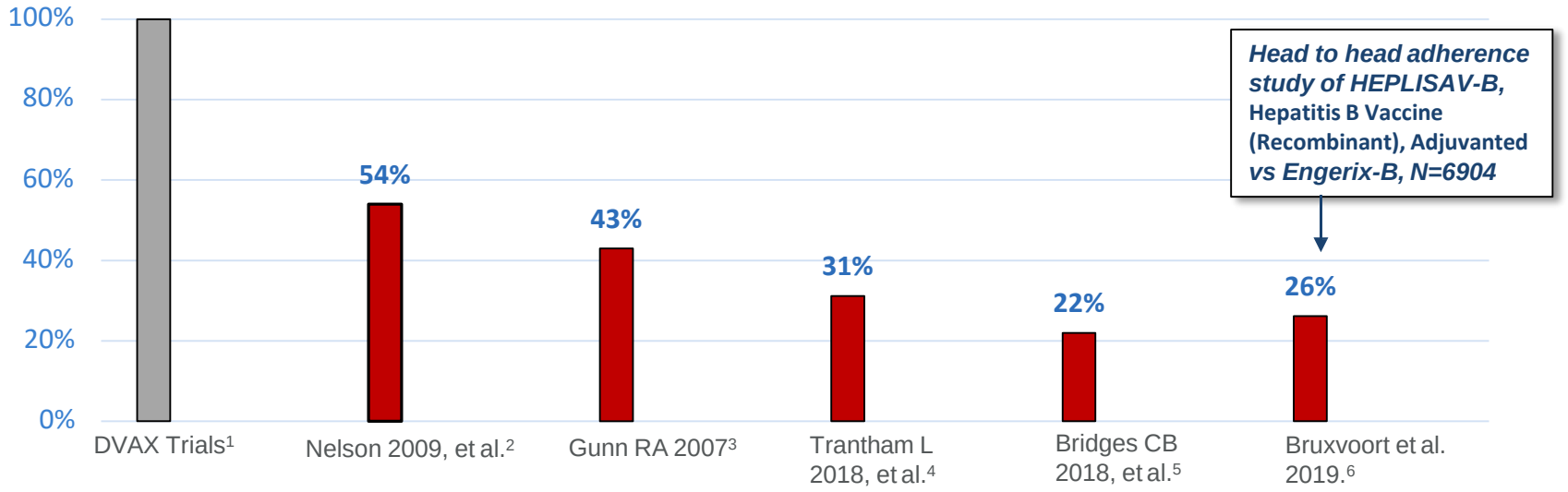
CDC sponsored study of nearly 30,000 adult hepatitis B vaccine recipients between 2012-2015[1]

Setting Type	Number or persons who received dose 1	Number (%) of dose 1 recipients who received dose 2	Number (%) of dose 1 recipients who received dose 3
STD Clinics	11,245	4,000 (35.6)	1,928 (17.1)
Department of Corrections	5,150	2,058 (40.0)	908 (17.6)
Other	3,447	1,552 (45.0)	1,079 (31.3)
Federally Qualified Health Center	2,432	1,359 (55.9)	923 (38.0)
Drug Treatment	2,564	791 (30.9)	349 (13.6)
Healthcare Facility Targeting IDU	2,008	674 (33.6)	325 (16.2)
HIV Clinics	1,278	551 (43.1)	379 (29.7)
Local Health Department Clinic	876	585 (66.8)	531 (60.6)
Healthcare Setting Targeting MSM	457	327 (71.6)	135 (29.5)
Total	**29,457**	**11,897 (40.4)**	**6,557 (22.3)**

Sources: 1. 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

Multiple Studies Indicate Suboptimal Series Completion Rates for 3-Dose Adult HBV Vaccines

Three-Dose Hepatitis B Vaccine Series Completion Rates



TRADITIONAL 3-DOSE HEPATITIS B VACCINES MAY CREATE A FALSE SENSE OF SECURITY THAT PUTS PATIENTS, HEALTHCARE PROVIDERS, AND INSTITUTIONS AT RISK [7,8]

Please see Select Important Safety Information throughout this presentation and accompanying full Prescribing Information.

Sources: **1.** Data on file. Dynavax Technologies Corporation,2019; **2.** Nelson J, et al. Am J Public Health. 2009;99:S389-S397; **3.** Gunn RA, et al. Sex Transm Dis. 2007;34(9):663-668; **4.** Trantham L, et al. Adherence with and completion of recommended hepatitis vaccination schedules among adults in the United States, Vaccine June 19, 2018, https://doi.org/10.1016/j.vaccine.2018.05.111; **5.** 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. **6.** 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; 7. . Mast EE, Weinbaum CM, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. *MMWR Recomm Rep. 2006; 55 (RR-16): 1-33* ; 8. Louther J, Feldman J, Rivera P, et al. Hepatitis B vaccination program at a New York City Hospital: Seroprevalence, seroconversion, and declination. *Am J Infect Control.* 1998;26(4):423-427.