Protocol for Hepatitis B Containing Vaccines
(ENGERIX-B®, HEPLISAV-B®, PREHEVBRIO®, RECOMBIVAX HB®, TWINRIX®)

1. What's New

A. N/A

2. Immunization Protocol

A. Administer an IM dose of Hepatitis B vaccine appropriate for the person's age, risk group, and the formulation being used.

B. May be given with all ACIP-recommended child and adult vaccinations.

3. Vaccine Schedule

Pediatric Hepatitis B Vaccine[1,3,4] (Engerix-B®, Recombivax-HB®) Dose and Route – 0.5-mL, IM		
Dose	**Acceptable Age Range**	**Minimum Acceptable Spacing**
1	7-19 years	
2		4 weeks
3		8 weeks after dose 2 **and** 16 weeks after dose 1

Adult Hepatitis B Vaccine[2,3] (HEPLISAV-B®) Dose and Route – 0.5-mL, IM		
Dose	**Acceptable Age Range**	**Minimum Acceptable Spacing**
1	≥18 years	
2		4 weeks
Adult Hepatitis B Vaccine[3] (PREHEVBRIO®) Dose and Route – 1.0-mL, IM		
Dose	**Acceptable Age Range**	**Minimum Acceptable Spacing**
1	≥18 years	
2		4 weeks
3		8 weeks after dose 2 **and** 16 weeks after dose 1
Adult Hepatitis A – Hepatitis B Combination Vaccine[3] (TWINRIX®) Dose and Route – 1.0-mL, IM		
Dose	**Acceptable Age Range**	**Minimum Acceptable Spacing**
1	≥18 years	
2		4 weeks
3		5 months after dose 2 **and** 6 months after dose 1
Adult Hepatitis B Vaccine[1,3,4] (Engerix-B®, Recombivax-HB®) Dose and Route – 1.0-mL, IM		
Dose	**Acceptable Age Range**	**Minimum Acceptable Spacing**
1	≥20 years	
2		4 weeks
3		8 weeks after dose 2 **and** 16 weeks after dose 1

4. Licensed Vaccines

Product Name	**Vaccine Components**	**Presentation**	**FDA Approved Age Range**	**Thimerosal**
Engerix-B®[1], pediatric formulation	Hepatitis B	0.5-mL single-dose vials and prefilled syringes	Birth-19 years	None
Recombivax HB®[4], pediatric formulation		0.5-mL single-dose vials and prefilled syringes	Birth-19 years	
HEPLISAV-B®[2]		0.5-mL prefilled syringes	≥18 years	
PREHEVBRIO®[3]		1.0-mL single-dose vials	≥18 years	

ENGERIX-B®, adult formulation[1]		1.0-mL single-dose vials and prefilled syringes	≥20 years	
RECOMBIVAX HB®[4], adult formulation		1.0-mL single-dose vials and prefilled syringes	≥20 years	
RECOMBIVAX HB®[4] Dialysis		1.0-mL single-dose vials	≥20 years	
TWINRIX®[5]	Hepatitis A Hepatitis B	1.0-mL prefilled syringes	≥18 years	None

5. Recommendations for Use

A. Additional schedules:

Catch-up Pediatric Hepatitis B Vaccine Schedule		
Dose	**Preferred Spacing**	**Minimum Spacing After Previous Dose**
1		
2	8 weeks after dose 1	4 weeks
3	4 months after dose 2 **and** 6 months after dose 1	8 weeks after dose 2 **and** 16 weeks after dose 1

Alternative Pediatric Hepatitis B Vaccine Schedules[1, 2]							
Vaccine and Formulation	**Dose Volume**	**Number of Doses in Series**	**Age at First Dose**	**Interval from 1 to 2**	**Interval from 2 to 3**	**Interval from 1 to 3**	**Interval from 1 to 4**
Engerix-B® (20 mcg/mL)	0.5 mL	4	1–10 years	4 weeks	4 weeks	8 weeks	12 months
		3	5-16 years	12 months	12 months	24 months	
	1.0 mL*	4	11-18 years	4 weeks	4 weeks	8 weeks	12 months
		3		4 weeks	8 weeks	6 months	
Recombivax HB® (10 mcg/mL)	1.0 mL	2	11-15 years◊	4 to 6 months			

* 1.0-mL dose recommended for persons who travel to endemic areas, sexual exposure, and children born to Hepatitis B surface antigen positive (HBsAg+) mothers.

◊ Both doses must be 1.0 mL of Recombivax HB®. Series must be completed prior to 16th birthday or an additional dose is required.

TWINRIX® Accelerated Schedule[5]		
Dose	**Acceptable Age Range**	**Minimum Acceptable Spacing**
1	≥18 years	
2		7 days after dose 1
3		14 days after dose 2
4		11 months after dose 3 **and** 12 months from dose 1
ENGERIX-B® Accelerated Schedule[1]		
Dose	**Acceptable Age Range**	**Minimum Acceptable Spacing**
1	≥20 years	
2		4 weeks after dose 1

3		4 weeks after dose 2
4		10 months after dose 3 **and** 12 months from dose 1

ENGERIX-B® Dialysis Schedule[1]			
Dose	**Acceptable Age Range**	**Dose Volume**	**Minimum Acceptable Spacing**
1	≥20 years	One 2.0-mL dose or Two 1.0-mL doses	
2			4 weeks after dose 1
3			4 weeks after dose 2
4			4 months after dose 3
RECOMBIVAX HB® Dialysis Schedule[4]			
Dose	**Acceptable Age Range**	**Dose Volume**	**Minimum Acceptable Spacing**
1	≥20 years	1.0 mL (40-mcg formulation)	
2			4 weeks after dose 1
3			8 weeks after dose 2 **and** 16 weeks from dose 1

B. Hepatitis B vaccination is recommended for all adults 19–59 years of age.
C. Adults ≥60 years of age with risk factors for hepatitis B infection.
D. Persons at risk for infection through sexual exposure:
   a. Sexual partners of hepatitis B positive persons
   b. Persons seeking evaluation or treatment for a sexually transmitted infection
   c. Sexually active persons not in a long-term, mutually monogamous relationship
   d. Men who have sex with men (MSM)
E. Persons at risk for infection by percutaneous or mucosal exposure to blood[7]:
   a. Recent or current injection-drug use
   b. Household contacts of Hepatitis B surface antigen (HBsAg) positive persons
   c. Residents and staff of facilities for developmentally disabled persons
   d. Healthcare and public-safety personnel with reasonably anticipated risk for exposure to blood or blood-contaminated body fluids
   e. Hemodialysis patients and pre-dialysis, peritoneal dialysis, and home dialysis patients
   f. Persons with diabetes mellitus aged <60 years; and persons with diabetes mellitus aged ≥60 years at the discretion of the treating clinician
F. Persons with[7]:
   a. Hepatitis C virus infection
   b. Human immunodeficiency virus
   c. Chronic liver disease (including, but not limited to, those with cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and an alanine aminotransferase (ALT) or aspartate aminotransferase (AST) level greater than twice the upper limit of normal)
G. Others[7]:
   a. Travelers to countries with high or intermediate levels of endemic hepatitis B virus (HBV) infection (HBsAg prevalence ≥2%)
   b. Incarcerated persons
   c. Immigrants, refugees, or adoptees from countries where HBV infection is endemic and their household members
   d. Other persons seeking protection from hepatitis B virus infection even without acknowledgment of a specific risk factor

6. Contraindications[5]

A. Severe allergic reaction (e.g., anaphylaxis) to a previous dose or to any vaccine component.
B. Engerix-B®, Heplisav-B®, Recombivax HB®, Twinrix®: Hypersensitivity to yeast
C. Heplisav-B®: Pregnancy
D. Recombivax HB®: Hypersensitivity to soy peptones
E. Twinrix®: Hypersensitivity to neomycin, polysorbate 80, polymyxin B

Vaccine	Contains[8]
ENGERIX-B®	aluminum hydroxide, yeast protein, sodium chloride, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate
HEPLISAV- B®	yeast protein, yeast DNA, deoxycholate, phosphorothioate-linked oligodeoxynucleotide, sodium phosphate, dibasic dodecahydrate, sodium chloride monobasic dehydrate, polysorbate 80
PREHEVBRIO®	sodium chloride, potassium chloride, disodium hydrogen phosphate dodecahydrate, potassium dihydrogen phosphate anhydrous. Each dose may contain residual amounts of Chinese hamster ovary (CHO) cell proteins, CHO cell DNA, bovine serum albumin and formaldehyde.
RECOMBIVAX HB®	formaldehyde, potassium aluminum sulfate, amorphous aluminum hydroxyphosphate sulfate, yeast protein
TWINRIX®	MRC-5 cellular proteins, formalin, aluminum phosphate, aluminum hydroxide, amino acids, sodium chloride, phosphate buffer, polysorbate 20, neomycin sulfate, yeast protein

7. Warnings and Precautions

A. Engerix-B®[1], Recombivax HB®[4] - dry natural rubber latex is used in the vial stopper, the syringe plunger stopper and tip cap.

8. Other Considerations [1-3]

A. Vaccine Interchangeability:
   a. Heplisav-B®[2]: A 2-dose series only applies when both doses in the series consist of Heplisav-B®. Series consisting of a combination of 1 dose of Heplisav-B® and a different vaccine should consist of a total of 3 vaccine doses and should adhere to the 3-dose schedule minimum intervals. A series containing 2 doses of Heplisav-B® administered at least 4 weeks apart is valid, even if the patient received a single earlier dose from another manufacturer.
   b. Twinrix®[5]: Recommended for persons at risk for hepatitis A or hepatitis B. The hepatitis B component of Twinrix® is equivalent to a standard adult dose of hepatitis B vaccine, the hepatitis A component has 50% of the adult standard dose. A total of 3 Twinrix® doses are required to complete the series. If Twinrix® is unavailable or not used to complete the Twinrix® series, administer single-antigen vaccine as follows:
      i. If 1 dose of Twinrix® was given, complete the series with 2 adult doses of hepatitis B vaccine and 2 adult doses of hepatitis A vaccine
      ii. If 2 doses of Twinrix® were given, complete the schedule with 1 adult dose of hepatitis A vaccine and 1 adult dose of hepatitis B vaccine
B. Booster Doses

a. Hemodialysis patients: Post vaccination serology testing is recommended annually. Booster doses should be provided when anti-HBs levels decline to <10 milli-international units/mL.[7] Anti-HBs testing 1–2 months following the booster dose to assess response is not recommended.
b. Other immunocompromised persons: In HIV-infected persons, hematopoietic stem-cell transplant recipients, and persons receiving chemotherapy, the need for booster doses has not been determined. Annual anti-HBs testing and booster doses should be considered for persons with an ongoing risk for exposure.

C. Lactation and Pregnancy[7]
   a. Pregnant women who are identified as being at risk for HBV infection during pregnancy (e.g., having more than one sex partner during the previous 6 months, been evaluated or treated for an STI, recent or current injection-drug use, or having had an HBsAg-positive sex partner) should be vaccinated with Recombivax HB® or Engerix-B®. Do not use Heplisav-B®[2] or Prehevbrio®[3].
   b. Lactation: Breast feeding is not a contraindication to vaccination for mother or infant.
D. Adoptees born in Asia, the Pacific Islands, Africa, and other regions of high or intermediate hepatitis B endemicity should undergo serologic testing for HBsAg regardless of vaccination status. Adoptees born in countries other than those mentioned above whose records indicate receipt of ≥3 doses of vaccine can be considered protected if ≥1 dose was administered at age ≥6 months.
E. Pre-vaccination serological testing* is recommended for[7]:
   a. Persons born in countries of high and intermediate hepatitis B virus endemicity (HBsAg prevalence ≥2%)
   b. HIV positive persons
   c. Household, sex, and needle-sharing contacts of HBsAg-positive persons
   d. Men who have sex with men (MSM)
   e. Past or current injection drug users

*Hepatitis B vaccine should be administered immediately after collection of blood for testing. Serologic testing comprises testing for HBsAg, antibody to HBsAg (anti-HBs), and antibody to hepatitis B core antigen (anti-HBc).

F. Postvaccination serologic testing[7]
   a. Postvaccination serologic testing 1–2 months after the final dose of the complete vaccine series is recommended for:
      i. Hemodialysis patients and others who might require outpatient hemodialysis (e.g., pre-dialysis, peritoneal dialysis, and home dialysis)
      ii. HIV-infected and other immunocompromised persons
      iii. Other immunocompromised persons (e.g., hematopoietic stem-cell transplant recipients or persons receiving chemotherapy)
      iv. Health-care personnel and public-safety workers
      v. Sex partners of HBsAg-positive persons
   b. Postvaccination serologic testing should be performed using a method that allows determination of the protective level of anti-HBs (≥10 milli-international units/mL).
G. Revaccination for non-responders[7]:
   a. Persons with anti-HBs <10 milli-international units/mL following receipt of 2 doses of Heplisav-B® (HepB-CpG) should be revaccinated with a second complete Heplisav-B® series or any 3-dose hepatitis B series, followed by anti-HBs testing 1–2 months after the final dose.

b. Alternatively, revaccination may consist of administration of an additional single hepatitis B vaccine dose (challenge dose) followed by anti-HBs testing 1–2 months later.
c. If anti-HBs remains <10 milli-international units/mL, completion of a second hepatitis B vaccine series followed again by anti-HBs testing 1–2 months after the final dose.
d. Administration of more than two complete hepatitis B vaccine series is generally not recommended, except for hemodialysis, and potentially immunocompromised patients.
e. Heplisav-B® (HepB-CpG) may be used for revaccination following an initial hepatitis B vaccine series that consisted of doses of HepB-CpG or doses from a different manufacturer.
f. Healthcare personnel who do not respond to a challenge dose should complete revaccination and retesting for anti-HBs.

9. Side Effects and Adverse Reactions[1-5]

Adverse Events Adults	**Frequency**
Pain at the injection site	Up to 52%
Mild systemic complaints (fatigue, headache)	Up to 25%
Temperature up to 37.7 C (≤99.9°F)	Less than 2%
Any severe reaction	Rare
Adverse Events Children	**Frequency**
Pain at the injection site	Uncommon, up to 9%
Fatigue, headache, other mild systemic symptoms	Common, up to 20%
Temperature up to 37.7 °C (≤99.9°F)	Uncommon, up to 6%
Any severe reaction	Rare

10. Storage and Handling

A. Upon storage, a fine white deposit with a clear colorless layer above may be present. Shake well before use to obtain a slightly opaque, white suspension.
B. Store medications according to OAR 855-041-1036.
C. All clinics and pharmacies enrolled with the Vaccines for Children (VFC) Program must immediately report any storage and handling deviations to the Oregon Immunization Program at 971-673-4VFC (4823).

Vaccine	**Temp**	**Storage Issues**
Engerix-B®, Heplisav-B®, Prehevbrio®, Recombivax HB®, Twinrix®	Store at 2°to 8°C (36° to 46° F)	Do not use if vaccine has been frozen.

11. References

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3. Prehevbrio®. [Package insert]. November 2021. Available at: https://www.prehevbrio.com/wp-content/uploads/2021/11/PreHevbrio-Full-Prescribing-Information.pdf. Accessed 14 July 2023.
4. Recombivax® HB. [Package insert]. April 2023. Available at: https://www.merck.com/product/usa/pi_circulars/r/recombivax_hb/recombivax_pi.pdf. Accessed 14 July 2023.
5. Twinrix®. [Package insert]. April 2023. Available at: www.fda.gov/media/119351/download. Accessed 14 July 2023.
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8. Centers for Disease Control and Prevention. Vaccine Excipient Summary. Available at: https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/appdx-full-b.pdf. Accessed 14 July 2023.

12. Appendix

A. N/A