AAMC Standardized Immunization Form 2025

Hepatitis B Vaccine – Frequently Asked Questions

(Information from the CDC)

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1. What are the hepatitis B vaccines licensed for use in the United States?

Four hepatitis B vaccines and two combination hepatitis B vaccines are currently licensed in the U.S.

Hepatitis B vaccines:

Trade Name – Licensure Date	Abbreviation	Number of Doses	Minimum Age
RECOMBIVAX HB® (1986)	1A-HepB	3 doses	Birth through adult
ENGERIX-B® (1989)	1A-HepB	3 doses	Birth through adult
HEPLISAV-B® (2017)	HepB-CpG	2 doses	Adult ≥18 years
PREHEVBRIO® (2022)	3A-HepB	3 doses	Adult ≥18 years

Hepatitis B combination vaccines:

- PEDIARIX®: Combined hepatitis B, diphtheria, tetanus, acellular pertussis (DTaP) and inactivated poliovirus (IPV) vaccine. Cannot be administered before 6 weeks of age or after 7 years of age.
- TWINRIX® and TWINRIX® Junior: Combined hepatitis A and hepatitis B vaccine. Recommended for use in persons 1 year of age and older who are at increased risk for both HAV and HBV infections.

2. What are the recommended schedules for hepatitis B vaccination?

The vaccination schedule most often used for children and adults is three doses given at 0, 1, and 6 months. Alternate schedules have been approved for certain vaccines and/or populations. A new formulation, Heplisav-B (HepB-CpG), is approved to be given as two doses one month apart.

3. If there is an interruption between doses of hepatitis B vaccine, does the vaccine series need to be restarted?

No. The series does not need to be restarted but the following should be considered:

- If the vaccine series was interrupted after the first dose, the second dose should be administered as soon as possible.
- The second and third doses should be separated by an interval of at least 8 weeks.
- If only the third dose is delayed, it should be administered as soon as possible.

4. Is it harmful to administer an extra dose of hepatitis B vaccine or to repeat the entire vaccine series if documentation of the vaccination history is unavailable or the serology test is negative?

No, administering extra doses of single-antigen hepatitis B vaccine is not harmful.

5. Can Heplisav-B or PreHevbrio be used to complete a vaccination series started with Engerix-B or Recombivax HB?

Doses of Engerix-B or Recombivax-HB single antigen hepatitis B (1A-HepB) vaccines are considered interchangeable. However, there are limited data on the safety and immunogenicity effects when doses of Heplisav-B (HepB-CpG) or PreHevbrio (3A-HepB) vaccine are interchanged with HepB products from other manufacturers. When feasible, the same manufacturer's vaccines should be used to complete the series. However, vaccination should not be deferred when the manufacturer of the previously administered vaccine is unknown or when the vaccine from the same manufacturer is unavailable.

6. When Heplisav-B (HepB-CpG) vaccine is used to complete a hepatitis B vaccine series started with Engerix- B or Recombivax HB, are there changes in the dosing schedule?

- The 2-dose HepB vaccine series only applies when both doses consist of HepB-CpG administered at least 4 weeks apart.
- If one dose of HepB-CpG is used in a vaccine series in combination with two doses of Engerix-B or Recombivax HB, adhere to the 3-dose schedule minimum intervals of 4 weeks between doses #1 and #2, 8 weeks between doses #2 and #3, and 16 weeks between doses #1 and #3.
- However, if HepB-CpG is used as dose #2 of a vaccine series beginning with Engerix-B or Recombivax HB as dose #1, a provider has the option of administering the next dose of HepB-CpG a minimum of 4 weeks from the previous dose to complete the 3-dose series.

7. Who should receive post-vaccination testing?

Testing for vaccine-induced immunity is advised for certain persons whose subsequent clinical management depends on knowledge of their immune status. This includes health care workers (and health care students/trainees) and public safety workers at high risk for continued percutaneous or mucosal exposure to blood or body fluids. This also includes persons who are immunocompromised.

8. When should post-vaccination testing be done?

Post-vaccination testing for anti-HBs levels (i.e., quantitative serum titers of antibodies [HBsAb] against Hepatitis B Surface Antigen [HBsAg]) should be performed 4-8 weeks after completion of the vaccine series.

- **An anti-HBsAg titer ≥10 mIU/mL is considered a correlate of vaccine-induced protection for people who have completed an approved vaccination series.**
- If testing is performed more than 2 months after the last dose of vaccine, any negative anti-HBs serum titers are uninterpretable. In these situations, the individual should consult with their health care provider regarding boosting or completing a second hepatitis B vaccine series before rechecking the serum titers.

9. If a recently vaccinated HCP has an antibody (HBsAb) titer <10 mIU/mL, what are the next steps?

CDC guidance states that HCP with anti-HBs <10 mIU/mL after receipt of the primary series should be revaccinated. For these HCP, administration of a second complete series on an appropriate schedule, followed by anti-HBs testing 1– 2 months after the final dose, is usually more practical than conducting serologic testing after each additional dose of vaccine. In order to document the HCP's vaccine response for future exposures, anti-HBs testing should be performed 1–2 months after the final vaccine dose. (3,4)

- Limited studies showed that administration of a single-dose vaccine booster and testing the HBsAB titer 1-2 months after the dose improved the vaccine response rate in approximately 50 percent of the non-responders to the primary 3-dose HBV vaccine series. When 2 additional doses of HBV vaccine were given to persons who did not respond to the first revaccination dose and they were tested 1-2 months after the last of the 3 revaccination doses, the cumulative seroconversion rate approached 70 percent. (3)
- A more recent analysis of published evidence-based studies on persons with a non-response to the primary 3-dose HBV vaccine series showed that repeating the complete vaccine series increased immunologic seroconversion to a level approaching 90 percent in several populations of non-responders, although there was notable variation in response rates among the risk groups.(5)
- Many employee health and occupational health clinics find that completing a second HBV vaccine series followed by serologic testing is the most practical approach for management of HCP that do not have an adequate immunologic response to the primary HBV vaccine series.
- Another option to keep in mind is Heplisav (HepB-CpG) vaccine (there are some data that suggest that Heplisav vaccine results in greater immunogenicity compared to the vaccines with the alum adjuvants). Heplisav is administered as 2 doses separated by 4 weeks, so that would result in protection sooner than the typical 6 months to complete the primary or secondary series with the other HBV vaccines. (6)

10. What is the definition of a "non-responder"?

The CDC considers a HBV vaccine "non-responder" as a vaccinee whose anti-HBs remains less than 10 mIU/mL after 2 complete series of HBV vaccine have been received.

11. Can anti-HBs levels following vaccination decline over time?

Yes. Following vaccination, anti-HBs levels decline over time. Immunocompetent people who achieve an anti-HBs level ≥10 mIU/mL 1–2 months after completing the hepatitis B vaccine series remain protected (presumably because of persistent cellular immunity), even if anti-HBs levels decline to <10 mIU/mL beyond that time.

12. What is a challenge dose of vaccine for assessment of immunologic status in a remotely vaccinated HCP?

The CDC guidance cites data from a few published studies that show that a "challenge dose" of HBV vaccine can be used to determine the presence of vaccine-induced immunologic memory through generation of an anamnestic response. The challenge dose (booster dose) is a single dose of HBV vaccine given to remotely vaccinated HCP (receipt of primary HBV vaccine series years ago) who lack a written dated record of their anti-HBs level following completion of the vaccine series. HCP with an anti-HBs response of ≥10 mIU/mL 1-2 months after a challenge dose are considered protected regardless of future declines in anti-HBs.(3)

13. How long does protection from hepatitis B vaccine last?

Studies indicate that immunologic memory remains intact for at least 30 years among healthy people who initiated hepatitis B vaccination at >6 months of age. The vaccine confers long-term protection against clinical illness and chronic hepatitis B virus infection. Cellular immunity appears to persist even though antibody levels might become low or decline below detectable levels. Booster doses of vaccine are not recommended once the health care worker (or health care student/trainee) has developed protective antibodies (an anti-HBs level ≥10 mIU/mL 1–2 months after completing the hepatitis B vaccine series).

14. If a nonimmune person had a high-risk exposure to hepatitis B virus and became infected, how long does it take to test HBsAg-positive after exposure?

HBsAg will be detected in an infected person's blood an average of four weeks (range: 1-9 weeks) after exposure to the virus. About half of patients will no longer be infectious by seven weeks after onset of hepatitis symptoms, and all patients who do not remain chronically infected will be HBsAg negative by 15 weeks after onset of symptoms.

15. Can Hepatitis B vaccine be given during pregnancy or lactation?

Yes, Hepatitis B vaccine contains no live virus, so neither pregnancy nor lactation should be considered a contraindication to vaccination of women. Until additional safety data are available for Heplisav-B (HepB-CpG) and PreHevbrio (3A-HepB) vaccines, providers should use Engerix-B or Recombivax HB single antigen (1A-HepB) vaccines to vaccinate pregnant women needing hepatitis B vaccination.

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