OREGON STATE PUBLIC HEALTH DIVISION, DHS
IMMUNIZATION PROGRAM

RECOMBINANT HEPATITIS B VACCINE

Revisions as of 01/08:

- New Hemodialysis and Immunocompromised schedule in Section IV, p.7.
- Updated Postexposure Prophylaxis Recommendations in Section V, p.8 (table 1 & 2).

I. ORDER

1. Screen for contraindications.
2. Provide a current Vaccine Information Statement (VIS), answering questions.
3. Obtain a signed Vaccine Administration Record (VAR).
4. Give hepatitis B vaccine to persons according to risk group, age, type of vaccine and vaccine status.
   a. May be given simultaneously with all other routine childhood and adult vaccines.

Note: Give hepatitis B vaccine by IM injection only in the deltoid for adults and children with adequate muscle mass, and in the anterolateral thigh for infants and toddlers.

Signature Health Officer or Medical Provider Date

II. A. LICENSED MONOVALENT HEPATITIS B VACCINES[1]			
Product Name	**Vaccine Components**	**Acceptable age range**	**Thimerosal**
Recombivax HB®	Hepatitis B	Birth – Adult	No
Engerix-B®	Hepatitis B	Birth - Adult	Trace (<1 mcg)
B. LICENSED COMBINATION HEPATITIS B VACCINES[1]			
Comvax®[2,3]	Hepatitis B,(as in Recombivax HB®) PRP-OMP (as in PedVaxHIB®)	6 weeks to age 5 years	No
Pediarix™ [2,3]	DTaP (Infanrix®) IPV Hepatitis B (Engerix-B®)	6 weeks to age 7 years	No
Twinrix®[4]	Hepatitis A (Havrix®) and Hepatitis B (Engerix-B®	18 years and older	Trace (<1 mcg)

[1] The immune response when doses of hepatitis B vaccine from one manufacturer are followed by subsequent doses from a different manufacturer has been shown to be comparable to the response after a full series using vaccine from a single manufacturer.

[2] Comvax® and Pediarix™ are approved by the Advisory Committee on Immunization Practices (ACIP) to complete the hepB series in children born to HBsAg+ and HBsAg unknown mothers

[3] Do not give combination hepatitis B vaccines to infants less than 6 weeks of age.

[4] Twinrix® is NOT approved for use in persons less than 18 years of age

III. RECOMMENDATIONS FOR USE

Pre-exposure

1. Hepatitis B vaccination is recommended for all infants, children and adolescents ages birth through 18 years regardless of whether the patient has known risk factors for contracting hepatitis B.
2. Optimally, all infants should be immunized at birth. Infants born to mothers who are HBsAg positive should receive hepatitis B vaccine and HBIG within 12 hours of birth.
3. Infants born to mothers whose HBsAg status is unknown should receive hepatitis B vaccine within 12 hours of birth. The mother should have blood drawn as soon as possible; if she is HBsAg positive, the infant should receive HBIG as soon as possible (no later than age 1 week).
4. All unvaccinated adults at risk for hepatitis B virus (HBV) infection and adults seeking protection from HBV infections (e.g., health and public safety workers). Acknowledgment of a specific risk factor is not a requirement for vaccination.
5. In the following settings where a high proportion of adults are likely to have risk factors for HBV infection all unvaccinated adults should receive Hepatitis B vaccine:
   - Sexually transmitted disease (STD) testing and treatment facilities,
   - Human immunodeficiency virus (HIV) testing and treatment facilities,
   - Facilities providing drug abuse treatment and prevention,
   - Correctional facilities,
   - College health services,
   - Chronic hemodialysis facilities and end-stage renal disease programs,
   - Institutions and nonresidential daycare facilities for developmentally disabled persons,
   - Health care settings targeting services to injection-drug users,
   - Health care settings targeting services to men who have sex with men
6. Hepatitis C-positive individuals
7. Immigrants, refugees, or adoptees from countries where HBV infection is endemic, and their household members.
8. International travelers spending 6 months or more in an area with high rates of HBV infection and who will have close contact with the local population.
9. Alaska Natives and Pacific Islanders.
10. Individuals engaged in commercial sex work.

IV. VACCINE SCHEDULES

A. Premature Infant Vaccine Schedule (weight < 2000 grams)

DOSE 0.5 ml	Born to HBsAg-POSITIVE or UNKNOWN Moms Minimum age	Minimum spacing[1]	Born to HBsAg-NEGATIVE Moms[3] Minimum age	Minimum spacing[1]
1	Birth (0-12 hrs.)[2]		4 weeks[3]	
2	4 weeks [4]	4 weeks after birth dose #1	8 weeks	4 weeks after dose #1
3[5]	8 weeks	4 weeks after dose #2	24 weeks[5]	8 weeks after dose #2[5]
4	24 weeks	8 weeks after dose #3 and 16 weeks after dose #1		

1 For retrospective checking, doses that violate the minimum spacing or age by 4 or fewer days do not need to be repeated. Doses administered 5 days or earlier than the minimum interval or age should be repeated as age appropriate.

2 Premature **infants born to HBsAg-Positive mothers and mothers with unknown HBsAg status** must receive immunoprophylaxis with hepatitis B vaccine and hepatitis B immunoglobulin (HBIG) within 12 hours after birth. This initial dose of vaccine should not be counted towards completion of the hepatitis B vaccine series. Three (3) additional doses of hepatitis B vaccine should be administered, beginning when the infant is ≥ 1 month of age.

3 The 1st dose of hepatitis B vaccine for premature infants (<2000 grams) **born to HBsAg-negative mothers** can be given at ≥ 1 month of age, including infants who remain in hospital. Preterm infants discharged from hospital before chronological age of 1 month can also be administered HepB vaccine at discharge, if medically stable and have gained weight consistently.

4 CHRONOLOGICAL age of 1 month (4 weeks since birth date).

5 A 3rd dose will complete the HepB series provided that the 3rd dose is given at ≥ 24 weeks of age, at least 8 weeks after the 2nd dose, and follows the 1st dose by at least 16 weeks. If the 3rd HepB dose is administered before 24 weeks of age, then a 4th dose is required at ≥ 6 months of age to complete the series.

Note: For low-birth-weight infants born to women of unknown status, every effort should be made to determine maternal HBsAg status at the hospital within 12 hours of delivery. If the mother's status remains unknown after 12 hours following delivery, proceed with hepatitis B prophylaxis (vaccine and HBIG).

B. Routine Infant and Child Vaccine Schedule
Minimum Age and Dosage Intervals for Single and Combination Vaccines[1,2]

Vaccine 0.5 ml Dose	Minimum age at first dose	Minimum interval from dose 1 to 2	Minimum interval from dose 2 to 3	Minimum interval from dose 1 to 3	Minimum Age at third dose
Infants and children					
Hepatitis B 3-dose schedule with pediatric single antigen	Birth[2,3,4]	4 weeks	8 weeks	16 weeks	24 weeks[5]
COMVAX®[6,7,8]	6 weeks	4 weeks	8 weeks	16 weeks	24 weeks[5,]
PEDIARIX™[6,7,9]	6 weeks	4 weeks	8 weeks	16 weeks	24 weeks[5]

[1] For retrospective checking, doses that violate the minimum spacing or age by 4 or fewer days do not need to be repeated. Doses administered 5 days or earlier than the minimum interval or age should be repeated as age appropriate.

[2] All infants should receive the first dose of HepB vaccine soon after birth and before hospital discharge. The 1st dose may be delayed until age 2 months if the infant's mother is HBsAg-negative.

[3] Infants born to HBsAg-positive mothers need 0.5 ml Hep B Immune Globulin (HBIG) administered IM concurrently with hepatitis B vaccine at different sites, within 12 hours of birth. Efficacy of HBIG given at 12-48 hours is presumed. DHS does not provide HBIG.

[4] Mothers who are HBsAg-unknown should be tested when they arrive for delivery. While test results are pending, newborns should receive the first dose of hepatitis B vaccine. If the mother is found to be HBsAg-positive, the infant should also receive 0.5 ml HBIG as soon as possible but not more than 7 days after birth.

[5] The last dose of hepatitis B vaccine should not be given to infants before 24 weeks of age. If a 3rd dose is administered before 24 weeks of age, then a 4th dose is required at $\geq$ 6 months of age to complete the series. Recommended age for receipt of the 3rd dose of hepatitis B vaccine is 6-18 months of age.

[6] Three doses of combination vaccines may be given to complete the hepatitis B vaccine series after the preferred dose at birth. Combination vaccines cannot be given before 6 weeks of age. Four doses of a HepB-containing vaccine may be administered when the HepB birth dose is given.

[7] Comvax® and Pediarix™ are approved by ACIP for use in children born to HBsAg+ and HBsAg unknown women, but not for the HepB birth dose.

[8] If Comvax® is given for the first two doses of the Hib and HepB vaccine (recommended age is 2 months for dose #1 and 4 months for dose #2), the third dose for both should be given at 12-15 months of age.

[9] The recommended ages for the three dose Pediarix™ series in infants are; 2 months, 4 months, and ≥6 months. However, Pediarix™ can be used for children behind schedule as long as given for only doses 1,2 or 3 of Hep-B, DTaP, and IPV series and child is < 7 years old.

C. Routine Adolescent Vaccine Schedule (11 through 19 years)[1,2]
Minimum Age and Dosage Intervals for
Single and Combination vaccines[3]

Vaccine & Dose	Minimum age at first dose	Minimum interval from dose 1 to 2	Minimum interval from dose 2 to 3 (when applicable)	Minimum interval from dose 1 to 3 (when applicable)
Hepatitis B 3-dose schedule with pediatric single antigen (0.5 ml dose)[2]	N/A	4 weeks	8 weeks	16 weeks
Hepatitis B 2-dose schedule with adult 1.0 ml dose for 11-15 yr. Olds[4,5]	11 years	16 weeks	N/A	N/A
Hepatitis B 3-dose schedule as combined Hep A and Hep B vaccine (Twinrix®)[6] (1.0 ml dose)	18 years	4 weeks	8 weeks	6 months

[1] If 317- funded adolescents start any HepB series before their 19th birthday, they may complete the series with state-supplied vaccine until they turn 20.

[2] If using Engerix-B® to vaccinate an 11-19 year old high-risk client (kids born to HBsAg + moms, sexual contacts, sexually active travelers to endemic areas, needle-stick victims, etc.) a 1.0 ml dose is recommended.

[3] For retrospective checking, doses that violate the minimum spacing or age by 4 or fewer days do not need to be repeated. Doses administered 5 days or earlier than the minimum interval or age should be repeated as age appropriate.

[4] This schedule approved only for use with Merck's Recombivax HB® vaccine. This 2-dose schedule should be completed by 16 years of age.

[5] If the schedule is started with 1.0 ml of Recombivax HB vaccine, the 2nd dose must also be 1.0 ml of Recombivax HB®. If Recombivax® is not available for dose #2, you must return to a 3-dose schedule and a pediatric dosage to complete the series, regardless of vaccine brand.

[6] The use of a combined vaccine containing HepB is acceptable as long as one antigen is indicated and the other antigen is not contraindicated.

D. Routine Adult Vaccine Schedule[1]
Dose Volume for clients ≥20 yrs = 1.0 ml[2]
Route: IM into the deltoid

DOSE	MINIMUM SPACING [3]	MINIMUM AGE
1		20 years
2	4 weeks after dose #1	NA
3	8 weeks after dose #2 and 16 weeks after dose #1	NA

1The usual schedule for adults is two doses separated by no less than 4 weeks, and a third dose 4-6 months after the second dose. If an accelerated schedule is needed, minimum spacing can be used.

2 The adult formulation (1.0ml) of Engerix-B® may be used in adolescents 11-19 years following the regular 0,1,6 month schedule.

3 For retrospective checking, doses that violate the minimum spacing or age by 4 or fewer days do not need to be repeated. Doses administered 5 days or earlier than the minimum interval or age should be repeated as age-appropriate.

E. Hemodialysis and other Immunocompromised Persons Schedule	**Single-Antigen Vaccine**			
	Recombivax HB		**Engerix-B**	
	Dose (mcg)	**Volume (ml)**	**Dose (mcg)**	**Volume (ml)**
<20 years[1]	**5**	**0.5**	**10**	**0.5 ml**
≥20 years	**40[2]**	**1.0**	**40[3]**	**2.0 ml**

[1]Higher doses might be more immunogenic, but no specific recommendations have been made.
[2]Dialysis formulation administered on a 3-dose schedule at age 0, 1, and 6 months.
[3]Two 1.0 ml doses administered in 1 or 2 injections on a 4-dose schedule at 0, 1, 2, and 6 months.

Source: *Epidemiology and Prevention of Vaccine-Preventable Diseases* ("Pink Book"). Atkinson W, Hamborsky J, Wolfe S, 10th ed, 2007; **table on p. 221.**

V. Postexposure Prophylaxis Guidelines

Table 1. Postexposure prophylaxis for perinatal and sexual exposures to HBsAg+ source

	HBIG		VACCINE	
Exposure	**Dose**	**Recommended timing**	**Dose**	**Recommended timing**
Perinatal*	0.5 ml IM	Within 12 hours of birth	0.5 ml IM	Within 12 hours of birth
Sexual	0.06 ml/kg IM	Single dose ASAP, but not more than 14 days after last sexual contact	Varies**	First dose at same time as HBIG; in different site

*For premature infants born to positive moms, see Section IV. Table A.
** For age-specific dose, see Section IV. Tables B, C, and D.

Table 2. Postexposure prophylaxis following percutaneous or permucosal exposure

Exposed person	**Source HBsAg positive**	**Source HBsAg negative**	**Source status unknown**
Unvaccinated	HBIG x 1 and start HB vaccine	Start vaccine	Start vaccine
Previously Vaccinated			
Documented responder	No treatment	No treatment	No treatment
Documented non-responder to single series	HBIG x1 plus 1 dose vaccine; test for anti-HBs 4-6 mo. later. If inadequate titer give additional 2 doses of vaccine	No treatment	If known high-risk source, may treat as if HBsAg +
Documented non-responder to 4 or more doses	HBIG x2 (1 month apart)	No treatment	If known high-risk source, may treat as if HBsAg +
Response never documented	Test exposed for anti-HBs: if adequate, no treatment; if inadequate, HBIG x 1 plus HB vaccine booster dose; test 4–6 mo. later	No treatment	Test exposed for anti-HBs: if adequate, no treatment; If inadequate, HB vaccine booster dose.

Source: Oregon Public Health Division. Hepatitis B Investigative Guideline, July 2007: p. 8. Available at: http://egov.oregon.gov/DHS/ph/acd/reporting/guideln/hepb.pdf

VI. CONTRAINDICATIONS

A. Hypersensitivity to baker's yeast, the preservative thimerosal, or any other component of the vaccine.

B. Severe allergic reaction/anaphylactic response after a previous dose.

C. Moderate or severe acute illness with or without fever should be deferred until illness resolves.

VII. SIDE EFFECTS AND ADVERSE REACTIONS

Event	Adults	Infants and children
Pain at injection site	13% - 29%	3% - 9%
Mild systemic complaints (fatigue, headache)	11% - 17%	0 –20%
Temperature >37.7 C	1%	0.4% -6%
Severe systemic reactions	Rare	Rare

Source: *Epidemiology and Prevention of Vaccine-Preventable Diseases*, January 2004; 210.

VIII. OTHER CONSIDERATIONS

A. Pregnancy should **not** be considered a contraindication to vaccination. There is no apparent risk of adverse effects to developing fetuses when hepatitis B vaccine is given to pregnant women (CDC, unpublished data). Hepatitis B infection in a pregnant woman may result in serious disease for the mother and chronic infection of the newborn.

B. DO NOT RESTART A SERIES. Count the number of doses the recipient has had and give the next dose due, observing minimum spacing and ages.

C. Breast feeding is not a contraindication to vaccination for mother or infant. HBsAg-positive women should be encouraged to breast feed; breast-feeding does not pose any additional risk of exposure to the infant.

D. Hemodialysis patients require special formulation and/or dosage. See Section IV. E, page 7.

E. Internationally adopted children should undergo serological testing for hepatitis B surface antigen; If positive they should be monitored for development of liver disease. (MMWR 2002: Vol 51(RR-2). Household members of HBsAg-positive children should be vaccinated. Adoptees whose records indicate receipt of ≥ 3 doses of vaccine can be considered protected if ≥1 dose was administered at age ≥ 6 months.

F. Immune response when one or two doses of vaccine from one manufacturer are followed by subsequent doses from a different manufacturer has been shown to be comparable to a full course of vaccination with a single vaccine.

G. Booster doses: For children and adults with normal immune status, a booster dose is not recommended, nor is serologic testing to assess antibody levels. The possible need for booster doses will be assessed as additional information becomes available.

H. For someone with a history of fainting with injections, a 15-minute observational period is recommended post immunization.

IX. POST-VACCINATION SEROLOGY

1. Following perinatal exposure, testing is necessary for infants born to HBsAg-positive mothers at least 3 months and no later than 9 months following the completion of the series.

2. Testing for persons exposed via household, sexual or percutaneous routes: HBsAb testing is advised 1-2 months after the completion of the vaccine series for:
    a. Persons whose subsequent clinical management depends on knowledge of their immune status, such as dialysis patients and staff, and persons with HIV infection.
    b. Persons at occupational risk who may have exposures from injuries with sharp instruments. Knowledge of their antibody response will aid in determining appropriate post-exposure prophylaxis

3. Post-vaccination testing includes serological screening for two different markers, each for a specific reason:
    a. **HBsAg:** to determine whether they have become infected with the hepatitis B virus; **AND**
    b. **HBsAb (Anti-HBs):** to determine whether the vaccine was effective in mounting an immune response in the recipient.

4. Vaccine recipients who do not develop a serum antibody response (a HBsAb titer of ≥10mIU/ml or "positive" result) after the primary series should be revaccinated with a complete series prior to re-testing

5. Testing is available free to local health departments through the Oregon State Public Health Lab; see the OSPHL's "Guide to Services" manual or visit website at www.oregon.gov/DHS/ph/phl/docs/guide.pdf. There is a small charge for testing ordered by private providers.

X. ADVERSE EVENT REPORTING

Adverse events following immunization should be reported by public providers to the Immunization Program, Health Services, using a Vaccine Adverse Events Reporting System (VAERS) form, according to state guidelines. Private providers report all adverse events directly to VAERS by phone, mail, or on-line. VAERS phone number: (800) 822-7967, and the website address is www.vaers.org

Table C. Events Reportable to VAERS

Vaccine	Illness, disability, injury or condition covered	Time period until first symptom or the onset of significant reactions following vaccine administration
Vaccines containing Hepatitis B	1. Anaphylaxis or anaphylactic shock 2. Any acute sequela (including death)	4 hours Not applicable

XI. REFERENCES

1. CDC. Hepatitis B virus: A Comprehensive Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States: Immunization of Adults. MMWR, 2006: 55(RR-16).
2. CDC. A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States: Immunization of Infants, Children, and Adolescents, MMWR 2005; 54(RR-16).
3. Hepatitis B. In: Pickering LK, ed. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2006: 335-55.
4. Hepatitis B. In: *Epidemiology and Prevention of Vaccine-Preventable Diseases* ("Pink Book"). Atkinson W, Hamborsky J, Wolfe S, eds. 10th ed. Washington, DC: Public Health Foundation, 2007: 211-34.
5. Oregon Public Health Division. Hepatitis B investigative guideline Available at: http://egov.oregon.gov/DHS/ph/acd/reporting/guideln/hepb.pdf
6. Hep-B-containing-vaccine package inserts.

For more information or to clarify any part of the above order, consult with your health officer or contact the DHS Immunization Program at (971) 673-0300.

To download a copy visit our website at
http://oregon.gov/DHS/ph/imm/provider/stdgordr.shtm
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