

## Protocol for Yellow Fever Vaccine (YF-VAX®)

### 1. What's New

- A. YF-VAX® (yellow fever vaccine) is now available in the United States. As of May 6, 2021, Stamaril® is no longer available. Providers with a current Oregon Yellow Fever Vaccination Stamp may now order YF-VAX® from the manufacturer.<sup>2</sup>

### 2. Immunization Protocol

- A. Administer a 0.5-mL dose, SQ, of yellow fever vaccine to persons ≥7 years of age if indicated.
- B. YF-VAX®<sup>3</sup> may be given with all other ACIP-recommended vaccines.
- C. **You must be an Oregon-certified Yellow Fever (YF) vaccine provider to administer this vaccine.** More information on Oregon's yellow fever certification can be found at: <https://www.oregon.gov/oha/ph/preventionwellness/vaccinesimmunization/immunization/providerresources/pages/yellfev.aspx>

### 3. Vaccine Schedule

Yellow Fever Vaccine (YF-VAX®) <sup>3</sup> Dose and Route – 0.5-mL SQ		
Dose	Acceptable Age Range	Minimum Acceptable Spacing
1	≥7 years	
Booster <sup>#</sup>		10 years

<sup>#</sup>Not routinely recommended. See Recommendations for use.

### 4. Licensed Vaccine

Product Name	Vaccine Components	Presentation	FDA Approved Age Range	Thimerosal
YF-VAX® <sup>1</sup>	17D-204 strain of YF virus grown in chicken embryos with gelatin and sorbitol as a stabilizer	Vaccine vial, 1 Dose supplied in a package of 5 vials  Diluent vial containing sodium chloride, 0.6 mL, supplied separately in a package of 5 vials  Vaccine vial, 5 Dose supplied in a package of 1 vial  Diluent vial, 3 mL supplied separately in a package of 1 vial	≥9 months	None

### 5. Recommendations for Use

- A. Due to the risk of serious adverse events that can occur following YF vaccine administration, providers should carefully observe the contraindications and consider the precautions to vaccination prior to administration; and vaccinate only persons who are at risk of exposure to YF virus or who require proof of vaccination for country entry.<sup>2</sup>
- B. YF vaccine is recommended for persons aged 7 years and older who are traveling to or living in areas at risk for yellow fever virus (YFV) transmission in Central and South America or Africa.<sup>2</sup>

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- C. Countries or areas with risk of yellow fever transmission are listed at: [wwwnc.cdc.gov/travel/yellowbook/2020/preparing-international-travelers/yellow-fever-vaccine-and-malaria-prophylaxis-information-by-country](http://wwwnc.cdc.gov/travel/yellowbook/2020/preparing-international-travelers/yellow-fever-vaccine-and-malaria-prophylaxis-information-by-country). Vaccination is also recommended for travel outside the urban areas of countries that do not officially report the disease but that lie in a yellow fever-endemic zone.<sup>2</sup>
- D. Yellow fever vaccination may be required for international travel. Some countries in Africa require evidence of YF vaccination from all entering travelers and some countries may waive the requirements for travelers arriving from areas where there is no current evidence of significant risk for contracting yellow fever and will be staying less than 2 weeks. Some countries require an individual, even if only in transit, to have a valid International Certificate of Vaccination if the individual has been in countries either known or thought to harbor yellow fever virus. The certificate becomes valid 10 days after vaccination with YF vaccine.<sup>2</sup>
- E. Laboratory personnel who might be exposed to virulent yellow fever virus or to concentrated preparations of the yellow fever vaccine strain by direct or indirect contact or by aerosols should be vaccinated.<sup>3</sup>
- F. Simultaneous Administration of Other Vaccines or Drugs: No evidence exists that inactivated vaccines and YF vaccine interfere with the immune response to the vaccine. Therefore, inactivated vaccines can be administered either simultaneously or at any time before or after YF vaccination. YF vaccine should be administered either simultaneously or 28 days apart from other live viral vaccines because the immune response to one live virus vaccine might be impaired if administered within 28 days of another live-virus vaccine.<sup>6</sup>
- G. Booster Dose recommendations: As of July 11, 2016, International Health Regulations NO LONGER require revaccination at intervals of 10 years: a completed International Certificate of Vaccination or Prophylaxis is now valid for the lifetime of the vaccinee. Vaccine administrators should check national requirements.<sup>4</sup>
  - a. High-Risk Travel: Travelers who received their last dose of yellow fever vaccine at least 10 years previously and who will be in a higher-risk setting based on season, location, activities, and duration of their travel. This would include travelers who plan to spend a prolonged period in endemic areas or those traveling to highly endemic areas such as rural West Africa during peak transmission season or an area with an ongoing outbreak.
  - b. Hematopoietic stem cell transplant recipients: Persons who received a hematopoietic stem cell transplant after receiving a dose of yellow fever vaccine and who are sufficiently immunocompetent to be safely vaccinated should be revaccinated before their next travel that puts them at risk for yellow fever virus infection.
  - c. HIV Infection: Persons who were infected with human immunodeficiency virus when they received their last dose of yellow fever vaccine should receive a dose every 10 years if they continue to be at risk for yellow fever virus infection.
  - d. Pregnancy: Persons who were pregnant when they received their initial dose of vaccine should receive 1 additional dose before they are next at risk for YF.
  - e. Laboratory workers: Individuals who routinely handle wild-type yellow fever virus should have yellow fever virus-specific neutralizing antibody titers measured at least every 10 years to determine if they should receive additional doses of the vaccine. For laboratory workers who are unable to have neutralizing antibody titers measured, yellow fever vaccine should be given every 10 years as long as they remain at risk.

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### 6. Contraindications<sup>1</sup>

- A. Severe allergic reaction (e.g., anaphylaxis) to a previous dose or to any vaccine component.
- B. History of life-threatening allergic reaction to eating eggs or chicken.
- C. History of thymus disorders associated with abnormal immune cell function, such as thymomas or myasthenia gravis.<sup>3</sup>
- D. Symptomatic HIV infection.<sup>3</sup>
- E. History of primary immunodeficiencies, malignant neoplasms, transplantation, immunosuppressive or immunomodulatory therapies. Persons receiving current or recent radiation therapy or immunosuppressive drugs.<sup>1</sup>
- F. Postpone vaccination in case of an acute or febrile disease.<sup>1</sup>

Vaccine	Contains
YF-VAX® <sup>1</sup>	sorbitol, gelatin, sodium chloride, egg protein

### 7. Warnings and Precautions

#### WARNING

#### **Yellow fever vaccine-associated viscerotropic disease (YEL-AVD)<sup>1</sup>**

YEL-AVD is a severe illness similar to wild-type YF disease, with vaccine virus proliferating and disseminating throughout the host's tissues. To date, two specific risk factors for YEL-AVD have been identified: older age and a history of thymus disease or thymectomy. YEL-AVD has been reported to occur only after the first dose of YF vaccine.

#### **Yellow fever vaccine-associated neurotropic disease (YEL-AND)<sup>1</sup>**

YEL-AND is a serious but rarely fatal adverse event that occurs in first-time YF vaccine recipients. YEL-AND represents a conglomeration of clinical syndromes, including meningoencephalitis, Guillain-Barré syndrome, acute disseminated encephalomyelitis, and cranial nerve palsies.

#### **Adults ≥60 years of age<sup>1</sup>**

Age ≥60 years is a precaution to receiving YF vaccine, particularly a first-ever dose. The risks of YEL-AVD and YEL-AND are higher in this age group.

- A. Avoid vaccinating breastfeeding women against YF. However, when travel of nursing mothers to YF-endemic areas cannot be avoided or postponed, these women should be vaccinated. Some experts recommend breastfeeding women who receive YF vaccine should temporarily suspend breastfeeding, pump, and discard pumped milk for at least 2 weeks after vaccination before resuming breastfeeding. Lactation is a precaution for vaccination, particularly if the breastfeeding infant is <9 months of age, because of the risk of encephalitis.<sup>4</sup>
- B. Pregnancy is a precaution, and pregnant persons should avoid travel to a yellow fever-endemic area. If travel is unavoidable and the vaccination risks outweigh the risks of YFV exposure, pregnant persons should be excused and issued a medical waiver to fulfill health regulations. Pregnant persons who must travel to areas where YFV exposure is likely should be vaccinated.<sup>1</sup>

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- C. Persons ≥60 years of age may be at increased risk for serious adverse events after vaccination, compared with younger persons. The rate of serious adverse events following vaccination is 1.5 times higher than the average rate for persons 60–69 years of age and 3 times higher for persons 70 years or older.  
If travel is unavoidable, the decision to vaccinate travelers aged ≥60 years needs to be weighed against their destination-specific risk for exposure to YFV. Particular caution should be considered for older travelers receiving YF vaccine for the first time.<sup>1</sup>
- D. Asymptomatic HIV infection with moderate immune suppression, i.e., CD4+ T-lymphocyte values of 200 to 499/mm<sup>3</sup> for persons aged ≥6 years old.<sup>4</sup>

### 8. Other Considerations

- A. ACIP recommends that a woman wait 4 weeks after receiving the yellow fever vaccine before conceiving.<sup>3</sup>
- B. Epinephrine hydrochloride solution (1:1,000) and other appropriate agents and equipment must be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs.<sup>5</sup>
- C. HIV-infected persons, because vaccination of asymptomatic HIV-infected persons might be less effective, measurement of their neutralizing antibody response to vaccination should be considered before travel. Contact CDC at 970-221-6400 to discuss serologic testing further.<sup>6</sup>
- D. Allergic Reactions: less severe or localized manifestations of allergy to eggs or to feathers are not contraindications to vaccine administration and do not usually warrant vaccine skin testing.<sup>1</sup>
- E. National YF vaccination requirements are mandatory and are primarily intended to prevent importation into and transmission of YF virus within a given country. Some countries require evidence of vaccination from all entering travelers. International Health Regulations stipulate that a Yellow Fever Stamp-Approved care provider may issue a waiver of yellow fever vaccination to a traveler, if the provider judges that yellow fever vaccination is medically contraindicated. The traveler also should be advised of the possibility that the medical waiver might not be accepted by the destination country. Failure to secure validations can cause a traveler to be quarantined, denied entry, or possibly revaccinated at the point of entry to a country.<sup>4</sup> Country requirements are subject to change at any time; therefore CDC encourages travelers to check with the appropriate embassy or consulate before departure. Because requirements may change, current information should be obtained from the CDC's Travelers' Health website:  
<https://wwwnc.cdc.gov/travel/yellowbook/2020/preparing-international-travelers/yellow-fever-vaccine-and-malaria-prophylaxis-information-by-country>.
- F. All travelers to yellow fever endemic countries should be advised of the risks of the disease and available methods to prevent it, including personal protective measures and vaccine. All travelers should take precautions to avoid mosquito bites to reduce the risk of YF and other vector-borne infectious diseases. These precautions include using insect repellent, wearing permethrin-impregnated clothing, and staying in screened or air conditioned-rooms. Additional information on protection against mosquitoes and other arthropods can be found at: <https://wwwnc.cdc.gov/travel/page/avoid-bug-bites>

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### 9. Side Effects and Adverse Reactions

Adverse Event	Frequency
Local injection site reactions like pain, redness, swelling, rash	Up to 71.9%
Systemic symptoms like fever, tiredness, headache, muscle pain	Up to 30%
Vaccinees over 60 years of age are at increased risk of systemic adverse events and at lower risk of local reactions.	
<b>Yellow Fever Vaccine–Associated Neurologic Disease (YEL-AND)</b>  YEL-AND represents a conglomeration of clinical syndromes, including meningoencephalitis, Guillain-Barré syndrome, acute disseminated encephalomyelitis, and, rarely, cranial nerve palsies	0.8/100,000 doses  <b>Age ≥ 60 years:</b> 2.2/100,000 doses
<b>Yellow Fever Vaccine–Associated Viscerotropic Disease (YEL-AVD)</b>  YEL-AVD is a severe illness similar to wild-type YF disease, with vaccine virus proliferating in multiple organs and often leading to multiorgan dysfunction or failure and occasionally death	0.3/100,000 doses  <b>Age ≥ 60 years:</b> 1.2/100,000 doses

### 10. Storage and Handling

- A. Store medications according to OAR 855-041-1036.

Vaccine	Temp	Storage Issues	Notes
YF-VAX® <sup>1</sup>	2° to 8°C (36°F to 46°F)	Do not use if vaccine has been frozen.	Use immediately. Reconstituted vaccine not used must be discarded after one hour. Discarded vaccine must be either sterilized or disposed in red hazardous waste containers.

### 11. References

1. YF-VAX® February 2019 package insert. Available at: <https://www.fda.gov/media/76015/download> Accessed 13 April 2023.
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3. Yellow fever vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2010. 59(RR07); P 1–32. Available at: [www.cdc.gov/mmwr/pdf/rr/rr5907.pdf](http://www.cdc.gov/mmwr/pdf/rr/rr5907.pdf). Accessed 13 April 2023.
4. CDC. Yellow fever vaccine booster doses: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2015. MMWR 2015;64;647–50. Available at: <https://www.cdc.gov/mmwr/pdf/wk/mm6423.pdf>. Accessed 13 April 2023.
5. CDC. Notes from the field: Fatal yellow fever vaccine-associated viscerotropic disease—Oregon, September 2014. (2015). 64(10);279-81. Available at: <https://www.cdc.gov/mmwr/pdf/wk/mm6410.pdf>. Accessed 13 April 2023.
6. Kroger A, Bahta L, Long S, Sanchez P. General Best Practice Guidelines for Immunization. Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP).

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7. Yellow fever vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2010. 59(RR07); P 1–32. Available at: [www.cdc.gov/mmwr/pdf/rr/rr5907.pdf](http://www.cdc.gov/mmwr/pdf/rr/rr5907.pdf). Accessed 13 April 2023.
  8. CDC. Transmission of yellow fever vaccine virus through breast-feeding— Brazil, 2009. MMWR 2010;59(05);130-132. Available at: [www.cdc.gov/mmwr/preview/mmwrhtml/mm5905a2.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5905a2.htm). Accessed 21 March 2023.
  9. World Health Organization. Vaccine-preventable diseases, Yellow Fever. Available at: <https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/yellow-fever>. Accessed 13 April 2023.

### 12. Appendix

- A. N/A

PROPOSED