

**OREGON HEALTH AUTHORITY  
IMMUNIZATION PROTOCOL FOR PHARMACISTS**

<b>Yellow Fever</b>	
Last Reviewed	26 March 2019
Last Revised	26 March 2019
This order expires	31 July 2021

No changes from previous version.

**I. OREGON IMMUNIZATION PHARMACY PROTOCOL:**

You must be in possession of a Yellow Fever Stamp in order to administer this vaccine.

1. Check the ALERT Immunization Information System to determine whether the patient needs this vaccine and any other vaccines.
2. Screen for contraindications. See warning box on page 3.
3. Provide a current Vaccine Information Sheet (VIS) answering any questions.
4. Record all required data elements in patient's permanent health record.
5. See page 10 for vaccine preparation and storage.
6. Verify needle length for SQ injection into the deltoid muscle.
7. Avoid injecting in the upper third of the deltoid muscle.
8. Both client and vaccinator must be seated for vaccine administration.
9. Give Yellow Fever<sup>1A, 1B</sup> vaccine (0.5 ml) **subcutaneously** (SC) as a single dose to individuals  $\geq 7$  years of age.
10. This vaccine may be given simultaneously with all other ACIP-recommended child and adult vaccines, including travel vaccines.
11. Ask client to remain seated on the premises for 15 minutes after vaccination to decrease the risk of injury should they faint.

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Immunizing Pharmacist

Date

**II. VACCINE SCHEDULE** <sup>1A, 1B, 2</sup>

<b>Dose and Route: 0.5 ml SC</b>		
<b>DOSE</b>	<b>PREFERRED AGE</b>	<b>MINIMUM ACCEPTABLE SPACING BETWEEN PRIMARY VACCINE &amp; ADDITIONAL DOSES</b>
1	≥7 years of age	10 years <sup>*</sup>

\*The International Health Regulations NO LONGER requires revaccination at intervals of 10 years. Additional doses of Yellow Fever vaccine may be indicated for certain populations. See Section II. In 2014, the World Health Assembly (of the WHO) adopted the recommendation to remove the 10-year booster dose requirement from the IHR as of June 2016. Once this change is instituted, a completed International Certificate of Vaccination or Prophylaxis will be valid for the lifetime of the vaccinee. It is uncertain when and if all countries with yellow fever vaccination entry requirements will adopt this change.<sup>2, 5</sup>

### III. LICENSED YELLOW FEVER VACCINE

Product Name	Vaccine components	Minimum Acceptable Age Range*	Preservatives	Booster Dose
YF-VAX <sup>®1A</sup> (sanofi-pasteur)	17D-204 strain of YF virus grown in chicken embryos with gelatin and sorbitol as a stabilizer	≥7 years of age <sup>1, 2</sup>	None	As Indicated* <sup>-</sup> ◇◇
Stamaril <sup>1B</sup> (sanofi-pasteur)				
* See Precautions, Section VI. Page 6				

\* ≥60 years of age is a precaution<sup>3</sup>

◇A booster dose may be given to 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.<sup>2</sup>

§Women who were pregnant (regardless of trimester) when they received their initial dose of yellow fever vaccine should receive 1 additional dose of yellow fever vaccine before their next travel that puts them at risk for yellow fever virus infection.<sup>2</sup>

‡ 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.<sup>2</sup>

\*\* 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.<sup>2</sup>

◇◇ Laboratory workers 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.<sup>2</sup>

### WARNING

**1. Yellow fever vaccine-associated viscerotropic disease (YEL–AVD)** previously described as multiple organ system failure, is a rare adverse reaction that is similar to fulminant yellow fever caused by wild-type yellow fever virus. More common in adults  $\geq 60$  years of age. YEL–AVD has a world-wide case fatality rate of 60%.<sup>3, 4</sup>

**2. Yellow fever vaccine-associated neurotropic disease (YEL–AND)**, represents a conglomerate of clinical syndromes, including meningoencephalitis, Guillain-Barré syndrome, acute disseminated encephalomyelitis, and rarely, cranial nerve palsies. Historically, YEL–AND was seen primarily among infants as encephalitis, but more recent reports have been among people of all ages, especially those  $\geq 60$  years of age. The onset of illness for documented cases is 3–28 days after vaccination, and almost all cases were in first-time vaccine recipients. YEL–AND is rarely fatal.<sup>3</sup>

**3. Individuals  $\geq 65$  years of age** who are traveling to or reside in known yellow fever endemic or epidemic areas, because of the increased risk for systemic adverse events in this age group, should be carefully monitored for adverse events for 10 days post-vaccination.<sup>3, 5, 7</sup>

**To minimize the risk for serious adverse events, health-care providers should observe the contraindications, consider the precautions to vaccination before administering vaccine, and issue a medical waiver if indicated.**<sup>6</sup>

## IV. RECOMMENDATIONS FOR USE:

### A. Risks and Regulations

1. Due to the risk of serious adverse events that can occur following YF vaccine administration, Yellow Fever Stamp-Approved care providers should carefully observe the contraindications and consider the precautions to vaccination prior to administration and vaccinate only persons who:
  - a) are at risk of exposure to YF virus, or
  - b) require proof of vaccination for country entry<sup>3</sup>

### B. Vaccination for International Travel and Persons Living in Endemic Areas

1. Persons  $\geq 9$  months of age traveling to or living in areas of South America or Africa where yellow fever infection is officially reported should be vaccinated.<sup>1A, 1B</sup> Countries or areas with risk of yellow fever transmission are listed on the CDC Travelers' Health website<sup>3</sup> at: [wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/yellow-fever](http://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/yellow-fever) Accessed 29 June 2017. 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>1A, 1B</sup>
2. Yellow fever vaccination may be required for international travel. Some countries in Africa require evidence of vaccination from all entering travelers and some countries may waive the requirements for travelers staying less than 2 weeks that are coming from areas where there is no current evidence of significant risk for contracting yellow fever. 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-VAX vaccine.<sup>1A, 1B, 3</sup>

### C. Laboratory Personnel

1. Those 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>1A, 1B, 3</sup>

## V. CONTRAINDICATIONS

1. Persons who have ever had a life-threatening allergic reaction to eggs, chicken, gelatin or a previous yellow fever vaccine.<sup>1A, 1B</sup>
2. Vaccination should be postponed in case of an acute or febrile disease.<sup>1A, 1B</sup>
3. Symptomatic HIV infection or CD4<sup>+</sup> T-lymphocyte values <200/mm<sup>3</sup> or <15% total lymphocytes for children <6 years old.<sup>3, 7</sup>
4. YF vaccine is contraindicated for persons with thymus disorders that are associated with abnormal immune cell function, such as thymomas or myasthenia gravis.<sup>3, 5</sup>
5. Primary immunodeficiencies<sup>3, 5</sup>
6. Malignant neoplasms<sup>3, 5</sup>
7. Transplantation<sup>3, 5</sup>
8. Immunosuppressive and Immunomodulatory therapies.<sup>3, 5</sup>

YF vaccine is contraindicated for persons whose immunologic response is either suppressed or modulated by current or recent radiation therapy or drugs.<sup>3, 5</sup>

## VI. PRECAUTIONS

1. As there is a theoretical risk of transmission of vaccine components to the infants from breast-feeding mothers, lactation constitutes a precaution, particularly when infants are below 9 months of age because of the risk of encephalitis.<sup>3, 4, 7</sup>
2. Pregnancy is a precaution for yellow fever vaccine administration. If travel is unavoidable and the vaccination risks are felt to outweigh the risks of YFV exposure, pregnant women should be excused from immunization and issued a medical waiver to fulfill health regulations. Pregnant women who must travel to areas where YFV exposure is likely should be vaccinated. Although there are no specific data, ACIP recommends that a woman wait 4 weeks after receiving the yellow fever vaccine before conceiving.<sup>3, 5</sup>
3. Refer adults ≥60 years to private provider before immunizing.<sup>3, 5</sup>
4. Persons ≥60 years of age maybe 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  $\geq 60$  years needs to be weighed against their destination-specific risk for exposure to YFV.<sup>3, 7</sup>

5. Asymptomatic HIV infection with moderate immune suppression, i.e., CD4<sup>+</sup> T-lymphocyte values of 200 to 499/ mm<sup>3</sup> for persons aged  $\geq 6$  years old or 15%-24% total lymphocytes for children aged  $< 6$  years.<sup>5, 6</sup>

## VII. OTHER CONSIDERATIONS

1. **Adverse Events:** 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>
2. **Immunocompromised:** 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 1-970-221-6400 to discuss serologic testing further.<sup>3, 6</sup>
3. **Valid Yellow Fever Vaccine:** For purposes of international travel, yellow fever vaccines produced by different manufacturers worldwide must be approved by the World Health Organization (WHO) and administered at an approved Yellow Fever Vaccination Center. Vaccinees should receive an International Certificate of Vaccination that has been completed, signed, and validated with the center's stamp where the vaccine is given. The certificate becomes valid 10 days after vaccination with YF-VAX vaccine.<sup>3, 8</sup>
4. **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>1A</sup>
5. **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>6</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: [wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/yellow-fever-malaria-information-by-country](http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/yellow-fever-malaria-information-by-country)<sup>3</sup>

Updates posted to the World Health Organization website at <http://www.who.int/ith/en/><sup>8</sup>

**6. Vector Control:**

A. 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.<sup>3, 9</sup>

B. 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 <http://wwwnc.cdc.gov/travel/yellowbook/2016/the-pre-travel-consultation/protection-against-mosquitoes-ticks-other-arthropods><sup>9</sup>

**VIII. A. SIDE EFFECTS AND ADVERSE EVENTS**

2001	Vaccine Name
Number followed for Safety	Study Number
	N =725
	Adverse Reaction %
Age in Years ≥18 years *	
Local Reaction, Injection site	
Pain	71.9 <sup>◇</sup> §
Redness	
Swelling	
Rash	3.2
Systemic Complaints	
Fever †	10–30 <sup>◇</sup>
Tiredness	
Headache	
Muscle pain	
Package insert page 17, 18	

\* Patients aged 65 or older are at increased risk for systemic adverse events temporally associated with vaccination compared to 25– to 44– year–old age group. For patients 65–74 the rate of systemic adverse events occurring post-vaccination was 2.5 times higher than the rate for individuals 25–44 years of age, based on incidence rates of 6.21 and 2.49 per 100,000 doses of vaccine in the two groups respectively.<sup>1A</sup>

◇ 4 local reactions were considered severe.

§ These reactions were significantly lower in subjects >60<sup>§</sup> years compared to younger subjects.

† Reported events typically include low-grade fever, headache, and myalgias that begin within days after vaccination and last 5–10 days. Approximately 1% of vaccinees temporarily curtail their regular activities because of these reactions.<sup>3</sup>

## VIII. B. SIDE EFFECTS AND ADVERSE EVENTS:

1. **Yellow fever vaccine-associated viscerotropic disease (YEL–AVD)** previously described as multiple organ system failure, is a rare adverse reaction that is similar to fulminant yellow fever caused by wild-type yellow fever virus. More common in adults  $\geq 60$  years of age. YEL–AVD has a world-wide case fatality rate of 60%.<sup>3, 4</sup>
2. **Yellow fever vaccine-associated neurotropic disease (YEL–AND)**, represents a conglomerate of clinical syndromes, including meningoencephalitis, Guillain-Barré syndrome, acute disseminated encephalomyelitis, and rarely, cranial nerve palsies. Historically, YEL–AND was seen primarily among infants as encephalitis, but more recent reports have been among people of all ages, especially those  $\geq 60$  years of age. The onset of illness for documented cases is 3–28 days after vaccination, and almost all cases were in first-time vaccine recipients. YEL–AND is rarely fatal.<sup>3</sup>
3. **Individuals  $\geq 65$  years of age** who are traveling to or reside in known yellow fever endemic or epidemic areas, because of the increased risk for systemic adverse events in this age group, should be carefully monitored for adverse events for 10 days post-vaccination.<sup>3, 5, 6,</sup>

## IX. STORAGE AND HANDLING <sup>1A, 1B</sup>

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).

Preparation:

1. Do not remove vaccine from refrigerator until ready to reconstitute it with the diluent supplied.
2. Add diluent slowly, let sit one to two minutes, then carefully swirl mixture to obtain a uniform suspension (avoid vigorous shaking, as this causes foaming). Suspension is a slight pink-brown.
3. Vaccine must be kept cool and used within 60 minutes following reconstitution.

Vaccine	Temp	Storage Issues	Notes
Yellow Fever <sup>®</sup> 1A	Store at 2°–8°C (36°F–46°F)	Do not use if vaccine has been frozen. Report to health educator.  Do not use after expiration date	Any reconstituted vaccine not used must be discarded after one hour: either sterilized or disposed in red hazardous waste containers.  Half-life is reduced from approximately 14 days at 35°–37°C to 3–4 days at 45° to 47°C.
Stamaril <sup>1B</sup>			Use Immediately

## X. ADVERSE EVENTS REPORTING

Private providers are to report events directly to VAERS and can read about options on how to do so at <https://vaers.hhs.gov/reportevent.html>

A pharmacist who administers any vaccine must report the following elements to the OHA ALERT Immunization Information System in a manner prescribed by OHA within 15 days of administration. This replaces the former requirement to notify the primary health care provider. A pharmacist is not required to notify the primary health care provider. Oregon Administrative Rule 855-019-0290-(2)(3).<sup>10</sup>

Electronic copy of this standing order is available at:  
[1.usa.gov/PharmacyImmunizationProtocols](https://www.1.usa.gov/PharmacyImmunizationProtocols)

To request this material in an alternative format (e.g., Braille) or to clarify any part of the above order, contact the Oregon Health Authority Immunization Program at 971.673.0300 and 711 for TTY. For other questions, consult with the vaccine recipient's primary health care provider or a consulting physician.

## REFERENCES

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