

**OREGON HEALTH AUTHORITY
IMMUNIZATION PROGRAM
TYPHOID: INJECTABLE AND LIVE ORAL VACCINES**

03-27-2015 ACIP recommended the following:¹

- Typhoid vaccine is no longer recommended for travelers to certain Eastern European and Asian countries. See travel site at: wwwnc.cdc.gov/travel/
- Neither typhoid vaccine available in the U. S. is licensed by the FDA for the prevention of paratyphoid fever
- Even if vaccinated, infections with drug-resistant typhoid strains can be fatal
- Updates to Vivotif[®] concomitant usage, storage, and handling²

I. Oregon Model Standing Order:

1. Check the ALERT Immunization Information System (IIS) to determine whether the patient needs this vaccine and any other vaccines.
2. Screen clients for contraindications.
3. Provide a current Vaccine Information Sheet (VIS), and answer any questions.
4. Record all required data elements in the client's permanent health record.
5. TyphimVi[®] Polysaccharide Inactivated:
 - a. Give 0.5mL intramuscularly (**IM**) to eligible clients at least 2 weeks before potential exposure.
6. Ask client to remain seated on the premises for 15 minutes after vaccination to decrease the risk of injury should they faint.
7. Vivotif[®] Live Oral:
 - a. Give 4–capsule blister pack to eligible clients at least 2 weeks before potential exposure.

Each capsule should be taken by mouth with cool water no warmer than 98.6°F (37.0°C) approximately 1 hour before a meal, every 48 hours: day 1, 3, 5 and 7.

Health Officer Signature

Date

Health Officer Signature

Date

II. LICENSED VACCINES

Product Name	Vaccine Components	FDA-Approved Age Range	Route	Re-vaccination
<p>Vivotif^{®2} (VaxPax)</p>	<p><i>Salmonella</i> Typhi Ty21a: 2.0–10.0x10⁹ colony-forming units</p> <p>Nonviable <i>S. Typhi</i> Ty21a: 5–50x10⁹ bacterial cells</p> <p>Sucrose: 3.3–34.2 mg</p> <p>Ascorbic acid: 0.2–2.4 mg</p> <p>Amino acid mixture: 0.3–3.0 mg</p> <p>Lactose: up 200 mg</p> <p>Magnesium stearate: 3.6–4.0 mg</p>	<p>≥6 years of age</p>	<p>PO</p>	<p>Every 5 years</p>
<p>Typhim Vi^{®3} (sanofi)</p>	<p><i>Salmonella</i> Typhi Ty2 strain: 25 µg</p> <p>Formaldehyde: ≤100 µg</p> <p>Phenol: 0.25%</p> <p>Sodium Chloride: 4.150 mg</p> <p>Disodium phosphate: 0.065 mg</p> <p>Monosodium phosphate: 0.023 mg</p>	<p>≥2 years of age</p>	<p>IM</p>	<p>Every 2 years</p>

III. A. GENERAL RECOMMENDATIONS FOR USE

1. Typhoid vaccines are not indicated for routine immunization of individuals in the United States. Immunization against typhoid fever is indicated for the following groups:
 - a. Travelers to areas in which there is a recognized risk of exposure to *S. Typhi*, particularly those who will have prolonged exposure to potentially contaminated food and drink.
 - b. Persons with intimate exposure (e.g., continued household contact) to a documented *S. Typhi* carrier
 - c. Microbiology laboratorians who frequently work with *S. Typhi*.¹
2. Current CDC advisories should be consulted with regard to areas with a risk of exposure to *S. Typhi*. Travelers should use caution in selecting food and water, even if vaccinated. Infections with drug resistant strains can be fatal. See also travel apps for: TravWell, Can I Eat This?, and the 2016 Yellow Book.⁵
3. Typhoid vaccines will not protect against serotypes of *Salmonella* other than Typhi.^{2,3}

III. B. SPECIFIC RECOMMENDATIONS FOR USE

Vivotif^{®2}

1. Oral typhoid vaccine is indicated for persons six years of age or older.¹
2. Oral vaccines can be administered simultaneously or at any interval before or after other live vaccines (injectable or intranasal) if indicated. This includes Yellow Fever live, attenuated vaccine or immune globulin if indicated.¹
3. Immunization (i.e., ingestion of all four doses) should be completed at least one week prior to potential exposure to *Salmonella Typhi*.¹
4. Re-immunization is recommended every five years for persons under conditions of repeated or continued exposure to *Salmonella Typhi*.^{1,2}

TyphimVi®³

1. Injectable typhoid vaccine is indicated for persons two years of age or older.^{1,3}
2. Re-immunization is recommended every two years for persons under conditions of repeated or continued exposure to *Salmonella* Typhi.^{1,3}
3. Immunization should occur at least two weeks prior to potential exposure to *Salmonella* Typhi.^{1,3,4}

IV. VACCINE SCHEDULE

Vaccine ^{2, 3}	FDA-Approved Age Range	Dose, Route or Administration	Number of Doses	Spacing Interval	Re-vaccination *
Vivotif® (PaxVax)	≥6 years	1 enteric coated capsule taken by mouth on alternate days (day 1,3, 5, 7) for a total of 4 capsules [§]	4 [‡]	48 hours between doses [◊]	The complete 4-dose series every 5 years
Typhim Vi® (sanofi)	≥2 years	IM	1		One injection every 2 years

*When continued or renewed exposure is expected.

◊**Vivotif®**: Missed doses: prolonging the interval between doses by 2–4 days does not interfere with immunity achieved after the concluding dose of the basic series. Ingest all 4 capsules within 10 days.⁶

§Instruct patient and review the following instructions. Provide manufacturer’s instruction card:²

- a) Inspect blister pack to ensure that foil seal and capsule are intact.
- b) Each capsule should be taken on an empty stomach. Swallow one capsule one hour before a meal with cold or lukewarm water ($\leq 37^{\circ}\text{C}$ or 98.6°F), on alternate days (day 1, 3, 5, 7). Indicate days on instruction card.
- c) Do not chew capsule.
- d) Swallow as soon as possible after placing in mouth.
- e) Do not expose capsule to direct sunlight.²
- f) It is essential to replace unused vaccine in the refrigerator between doses.²
- g) Patient should call vaccine administrator if vaccine is taken incorrectly or mishandled.

‡ **Dispense vaccine with prescription label and provide client with adequate insulation for safe transport** (e.g., provide sufficient ice on warm days to protect vaccine until client can get the vaccine into cold storage). Do not freeze.²

V. A. GENERAL CONTRAINDICATIONS

1. History or hypersensitivity to any component of the vaccine.^{2,3}

V. B. VACCINE-SPECIFIC CONTRAINDICATIONS

Vivotif^{®2}

1. Do not give during an acute febrile illness. Postpone if persistent diarrhea or vomiting is occurring.^{1,2}
2. Safety of the vaccine has not been demonstrated in persons deficient in their ability to mount a humoral or cell-mediated immune response, due to either a congenital or acquired immunodeficient state including treatment with immunosuppressive or antimetabolic drugs. The vaccine should not be administered to these persons regardless of benefits.^{1,2}
3. Oral typhoid vaccine should not be given to people taking antibacterial agents as these may inactivate the vaccine. Vivotif[®] should not be given until at least 3 days after the last dose of antimicrobial agent and, if possible, antimicrobial agents should not be started within 3 days of the last dose of Vivotif[®] vaccine. A longer interval should be considered for long-acting antimicrobials (e.g., azithromycin).^{1,2,7}
4. Do not administer to children less than six years of age.^{1,2}

V. B. VACCINE SPECIFIC CONTRAINDICATIONS Cont.**TyphimVi®³**

1. Typhim Vi should be given to a pregnant woman only if clearly needed.³
2. When possible, delaying vaccination with TyphimVi® until the second or third trimester to minimize the possibility of teratogenicity is a reasonable precaution.³

VI. A. PRECAUTIONS**Vivotif®²**

1. The antimalarial agents mefloquine and chloroquine and the combinations atovaquone/proguanil and pyrimethamine/sulfadoxine can, at doses used for prophylaxis, be administered together with Vivotif®; however, the manufacturer advises that other antimalarial agents only be administered at least 3 days after the last vaccine dose.

When needed, administer higher doses of proguanil at least 10 days after the last dose of Vivotif®.^{1,2,6}

TyphimVi®³

1. Acute or febrile illness may be reason for delaying use of this vaccine except when, in the opinion of the physician, withholding the vaccine entails a greater risk.³
2. TyphimVi® should not be used to treat a patient with typhoid fever or a documented carrier.

VII. SIDE EFFECTS AND ADVERSE REACTIONS

Vivotif^{®2}

Number followed for Safety *	Adverse Reaction % after 3 doses (n = 483)
Systemic Complaints	
Abdominal Pain	6.4%
Nausea	5.8%
Diarrhea	2.9%
Vomiting	1.5%
Fever	3.3%
Headache	4.8%
Rash	1.0%
* Package insert, page 4 ²	

VII. SIDE EFFECTS AND ADVERSE REACTIONS AMONG ADULTS

TyphimVi^{®3}

Number followed for Safety *	Adverse reactions within 48 hours n (%)	
	Trial 1 1 lot (n = 54)	Trial 2 2 lots combined (n = 98)
Local Reaction, Injection site		
Pain	22 (40.7%)	26 (26.5%)
Redness	2 (3.7%)	5 (5.1%)
Swelling	8 (14.8%)	5 (5.1%)
Systemic Complaints		
Fever ≥100°F	1 (1.9%)	0
Nausea	1(1.9%)	8 (8.2%)
Vomiting	1 (1.9%)	0
Diarrhea	0	3 (3.1%)
Tiredness (malaise)	13 (24%)	4 (4.1%)
Headache	11 (20.4%)	16 (16.3%)
Muscle pain	4 (7.4%)	3 (3.1%)

* Patients were 18–40 years of age. Data from package insert, page 16, Table 3

VII. SIDE EFFECTS AND ADVERSE REACTIONS AMONG CHILDREN

TyphimVi^{®3}

	Adverse reactions within 48 hours n (%) n = 175
Number followed for Safety *	
Local Reaction, Injection site	
Pain	25 (14.3%)
Redness	12 (6.9%)
Swelling	5 (2.9%)
Systemic Complaints	
Reported feverishness	5(2.9%)
Impaired limb use	0
Decreased activity	3 (1.7%)
Headache	0
* Patients were 1–12 years of age. Package insert, page 17, Table 4,	

IX. OTHER CONSIDERATIONS

1. Epinephrine hydrochloride solution (1:1,000) and other appropriate agents and equipment must be available for immediate use in case of anaphylactic or acute hypersensitivity reaction.^{1,2}
2. Individuals with altered immunocompetence may have reduced immune responses.^{1,2}
3. It is not known whether typhoid vaccines are excreted in human milk. Use with caution in nursing mothers.^{1,2}
4. Vivotif[®] vaccine can be administered simultaneously or at any interval before or after other live vaccines (injectable or intranasal) or immune globulin if indicated.¹
5. The importance of vaccination and other preventive measures for typhoid fever is heightened by increasing resistance of *Salmonella* serotype Typhi to antimicrobial agents, including fluoroquinolones, in many parts of the world. Even if vaccinated, infections with drug-resistant typhoid strains can be fatal.¹
6. Paratyphoid fever, caused primarily by *Salmonella enterica* serotype Paratyphi A, but also by serotypes Paratyphi B (tartrate negative) and C, is an illness clinically indistinguishable from typhoid fever and responsible for as many as 50% of enteric fever cases in many countries. Neither typhoid vaccine is labeled in the U. S. for prevention of paratyphoid fever.¹
7. Either vaccine can be used for revaccination, within the appropriate time interval.¹
8. Typhim Vi[®]: Persons deficient in producing antibodies, whether due to genetic defect, immunodeficiency disease, or immunosuppressive therapy, may not obtain the expected immune response. This includes patients with asymptomatic or symptomatic HIV-infection, severe combined immunodeficiency, hypogammaglobulinemia, or agammaglobulinemia; altered immune states due to diseases such as leukemia, lymphoma, or generalized malignancy; or an immune system compromised by treatment with corticosteroids, alkylating drugs, antimetabolites or radiation.³
9. No data have been reported on the use of either vaccine in pregnant women. In general, live vaccines (Vivotif[®])² are contraindicated in pregnant women.^{1, 2}
10. Polysaccharide vaccine (TyphimVi[®])³ should be given to pregnant women only if clearly needed.¹

X. STORAGE AND HANDLING

All clinics and pharmacies enrolled with the VFC program must **immediately** report any storage and handling deviations to their Oregon Immunization Program health educator. The health educator assignment map is located at: http://bit.ly/HE_Map

TyphimVi[®]:³

- TyphimVI[®] is a clear, colorless solution
- Store at 2°–8°C (36°–46°F)
- Do not freeze
- Do not use after expiration date

Vivotif[®]:²

- Vivotif[®] is not stable when exposed to ambient temperatures
- Ship and store between 2°C and 8°C (36°F–46°F)
- Expiration date is valid only if the product has been maintained at 2°C–8°C (36°F–46°F).
- Do not use after expiration date
- Do not expose capsule to direct sunlight.²

See excursion table next page.

X. STORAGE AND HANDLING Cont.

Short-term exposure to temperatures outside the registered storage conditions (2°–8°C) is not critical for the stability and efficacy of Vivotif®.

Following a temperature excursion the product must be returned immediately to the registered storage conditions. See table below to determine if the vaccine can still be administered.

Temperature *	Duration	Action
>8°C but not >25°C	≤24 hours	Administer as normal
>8°C but not >25°C	>24 hours	Do not use
>25°C	Any duration	Do not use
<2°C but not <-20°C	≤72 hours	Administer as normal
<2°C but not <-20°C	>72 hours	Do not use
<-20°C	Any duration	Do not use

This table is valid for only the first excursion. If a repeat excursion occurs then the vaccine must not be used. Report further excursions to a PaxVax (formerly Crucell) representative at 1-800-533-5899. Current as of 2015 per company representative.^{6,8}

Temperature	Conversion *	
	To	F°
-20°C	=	-4°F
2°C	=	36°F
8°C	=	46°F
25°C	=	77°F

X.ADVERSE EVENTS REPORTING

Public providers are to complete the Vaccine Adverse Events Reporting System (VAERS) report online at <https://vaers.hhs.gov/esub/step1>. Save a copy of the report number for your records, and send a copy and the report number to the Oregon Immunization Program Vaccine Safety Coordinator via confidential email at ORVAERS.Reports@state.or.us or fax (971-673-0278). Private providers are to report events directly to VAERS and can read about options on how to do so at www.vaers.hhs.gov.

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.

Electronic copy of this standing order is available at:

<http://1.usa.gov/OregonStandingOrders>

References

1. CDC. Updated recommendations for the use of Typhoid Vaccine – Advisory Committee on Immunization Practices, United States, 2015. MMWR 2015; 64:305–8. Available at: www.cdc.gov/mmwr/pdf/wk/mm6411.pdf. Accessed 21 July 2015.
2. Typhoid Vaccine Live Oral Ty21a (Vivotif[®]) package insert 2013. Available at: www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142807.pdf. Accessed 21 July 2015.
3. Typhoid VI Polysaccharide Vaccine (TyphimVI[®]) package insert 2014. Available at: www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142811.pdf. Accessed 21 July 2015.
4. CDC. General Recommendations on Immunizations. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2011; 60 (RR-2). Available at: www.cdc.gov/mmwr/pdf/rr/rr6002.pdf. Accessed 21 July 2015
5. CDC. Travelers' Health. Mobile apps. TravWell, Can I Eat This, 2014 Yellow Book. Available at: wwwnc.cdc.gov/travel/page/apps-about. Accessed 21 July 2015
6. Kantele A, Kantele JM, Arvilommi H, Mäkelä PH. Active immunity is seen as a reduction in the cell response to oral live vaccine. Vaccine. 1991 Jun;9:428–31. Abstract available at: www.ncbi.nlm.nih.gov/pubmed/1887674. Accessed 21 July 2015.
7. CDC. Yellow Book of Travel Medicine. 2016. Available at wwwnc.cdc.gov/travel/page/yellowbook-home. Accessed 21 July 2015.
8. PaxVax Berna of Switzerland (formerly Crucell), phone: 1-800-533-5899, 8:00 AM to 5:00 PM Eastern Standard Time; ask for the Medical Department.