

OREGON HEALTH AUTHORITY
IMMUNIZATION PROGRAM
Rabies Inactivated Virus Vaccine
IMOVAX^{®1} (HDCV) and RabAvert^{®2} (PCECV)

Revised 12–2015

- No changes to the PRE—EXPOSURE protocol of 2010
- IMOVAX^{®1} (Sanofi Pasteur) is available for pre-exposure and post-exposure prophylaxis: 1–800–VACCINE (1–800–822–2463) for Sanofi Vax and Rabies Immune Globulin (RIG)
- RabAvert^{®2} (Novartis) is available for pre-exposure and post-exposure prophylaxis from wholesale distributors

1. Oregon Immunization Model Standing Order:

2. Check the ALERT Immunization Information System to determine whether the patient needs this vaccine and any other vaccines.
3. Screen clients for contraindications.
4. Provide a current Vaccine Information Statement (VIS) and answer any questions.
5. Record all required data elements in the client’s permanent health record.
6. Rabies vaccines pre-exposure:
 - a. Give 1mL dose of rabies vaccine intramuscularly (IM) as a three dose series to eligible persons who may be at risk for exposure to the rabies virus on days 0, 7, and 21 or 28.
 - b. Do not remove vaccine from refrigerator until ready to reconstitute it with the diluent supplied.
 - c. Reconstitute only with the supplied diluent. Gently swirl the contents until completely dissolved. Use immediately after reconstitution.
7. Rabies vaccines have not been tested for use with other child or adult vaccines.
8. Ask client to remain seated on the premises for 15 minutes after vaccination to decrease the risk of injury should they faint.

Health Officer Signature

Date

Health Officer Signature

Date

II. LICENSED RABIES VACCINE:

Product name	Vaccine component(s)	Acceptable age range	Preservative
IMOVAX^{®1} Human diploid cell vaccine (HDCV) Sanofi Pasteur	The vaccine is obtained from infected human diploid cells, inactivated by β -propiolactone. One dose (1.0mL) contains <100 mg albumin, <150 μ g neomycin sulfate and 20 μ g of phenol red indicator.	\geq Infancy*	The vaccine contains no preservative or stabilizer. It should be used as a single dose vial.
RabAvert^{®2} Purified chick embryo cell vaccine (PCECV) Novartis	Vaccine is obtained by growing the fixed-virus strain in chicken fibroblasts, which are inactivated with β -propiolactone. One dose (1mL) contains <12 mg polygeline (processed bovine gelatin), <0.3 mg human serum albumin, 1 mg potassium glutamate, 0.3 mg sodium EDTA, <1 μ g neomycin, <20 ng chlortetracycline, and <2ng amphotericin B. Minimal amounts of chicken protein may be present in the final product; albumin content is <3 ng/dose.	In all age groups \diamond	The vaccine contains no preservative.
* Imovax [®] pkg insert, pg. 1, 04-2013 \diamond RabAvert [®] pkg insert, pg. 1, 11-2013			

III. RECOMMENDATIONS FOR USE:

Primary or Pre-exposure Vaccination³

Pre-exposure vaccination should be offered to persons whose activities might bring them into contact with rabies virus or potentially rabid bats, raccoons, skunks, cats, dogs, or other species at risk for having rabies; such as:

- Veterinary students, veterinarians and other animal handlers
- Certain laboratory workers.
- Animal handlers
- Field biologists
- Missionaries and other long-term travelers and expatriates
- Cavers
- International travelers who might come in contact with animals in areas where dogs, monkeys, bats, and cats rabies is enzootic and immediate access to appropriate medical care, including biologics, might be limited.
- Children who are too young to understand either the need to avoid animals or to report a traumatic contact are considered at greater risk of rabid animal exposure and should be offered pre-exposure immunization when travelling to endemic areas.

Routine pre-exposure prophylaxis for other situations might not be indicated.

Pre-exposure prophylaxis is administered for these reasons:

- Although pre-exposure vaccination does not eliminate the need for additional therapy after a rabies exposure, it simplifies therapy by eliminating the need for RIG and decreasing the number of doses of vaccine needed—important for persons at high risk for being exposed to rabies in areas where immunizing products might not be available or where they might be at high risk for adverse reactions.
- Pre-exposure prophylaxis might protect persons whose post exposure therapy is delayed.
- It might provide protection to persons at risk for unapparent exposures to rabies.

Supplies of rabies vaccine have been restored, and the pre-exposure vaccination recommendations should be followed.

IV. VACCINE SCHEDULE:

Dose and Route: 1.0 ml IM in the deltoid^{1, 2, 3}		
Course of vaccination	Recommended Age	Dose Regimen
Primary[*]	All age groups	3 doses at 0, 7, and 21 or 28 days
Booster[◊]	All age groups	1 dose^{§, ‡}

* Immunocompromised Individuals: should postpone pre-exposure vaccinations and consider avoiding activities for which rabies pre-exposure prophylaxis is indicated. When this is not possible, those at risk for rabies should have their antibody titers checked after vaccination with HDCV or PCECV.

◊ Reference Pre-exposure recommendations in section V below to determine which populations might require a booster dose.

§ A pre-exposure booster is indicated if the antibody titer level falls below the minimum acceptable virus neutralization at a 1:5 serum dilution by the rapid fluorescent focus inhibition test. Globally, few laboratories perform the rapid fluorescent focus inhibition test, which is the gold standard test method for measuring rabies antibody levels. Those in the United States are listed on the CDC website www.cdc.gov/rabies/specific_groups/doctors/serology.html.

‡ In the United States, preexposure vaccination consists of a series of 3 injections with human diploid cell rabies vaccine (HDCV) or purified chick embryo cell (PCEC) vaccine.

- Travelers should receive all 3 preexposure immunizations before travel. If 3 doses of rabies vaccine cannot be completed before travel, the traveler should not start the series, as it would be problematic to plan postexposure prophylaxis after a partial immunization series.³
- Preexposure vaccination does not eliminate the need for additional medical attention after a rabies exposure, but it simplifies postexposure prophylaxis.³
- Preexposure vaccination may also provide some degree of protection when there is an unapparent or unrecognized exposure to rabies virus and when postexposure prophylaxis might be delayed.³
- Regardless of whether preexposure vaccine is administered, travelers going to areas where the risk of rabies is high should be encouraged to purchase medical evacuation insurance (see Chapter 2, Travel Insurance, Travel Health Insurance, & Medical Evacuation Insurance).³

Travelers who have completed a 3-dose preexposure rabies immunization series or have received the full postexposure prophylaxis are considered preimmunized and do not require routine boosters, except after a likely rabies exposure. Periodic serum testing for rabies virus neutralizing antibody is not necessary in routine international travelers.³

V. CRITERIA FOR PRE-EXPOSURE RABIES IMMUNIZATION³

Risk category	Nature of risk	Typical populations	Pre-exposure Recommendations
<u>Continuous</u>	Virus present continuously, often in high concentrations. Specific exposures likely to go unrecognized. Bite, non-bite, or aerosol exposure.	Rabies research laboratory workers;* rabies biologics production workers.	Primary course. Serologic testing every 6 months; booster vaccination if antibody titer is below acceptable level. ^o
<u>Frequent</u>	Exposure usually episodic, with source recognized, but exposure also might be unrecognized. Bite, non-bite, or aerosol exposure possible.	Rabies diagnostic lab workers, travelers involved in outdoor and other activities that might bring them into direct contact with dogs, bats, and other mammals e.g. cavers, missionaries, veterinarians and staff, and animal-control and wildlife workers in rabies-enzootic areas. Long-term travelers and expatriates.	Primary course. Serologic testing every 2 years; booster vaccination if antibody titer is below acceptable level. ^o
<u>Infrequent</u> (greater than population at large)	Exposure nearly always episodic with source recognized. Bite or non-bite exposure.	Veterinarians and animal-control and wildlife workers in areas with low rabies rates. Veterinary students. Travelers visiting areas where rabies is enzootic and immediate access to appropriate medical care including biologics is limited.	Primary course. No serologic testing or booster vaccination.
<u>Rare</u> (population at large)	Exposure always episodic with source recognized. Bite or non-bite exposure.	U.S. population at large, including persons in rabies-epizootic areas.	No pre-exposure vaccination necessary.

* Judgment of relative risk and extra monitoring of vaccination status of laboratory workers is the responsibility of the laboratory supervisor. (see <http://www.cdc.gov/biosafety/publications/> for more information).

- ◇ Pre-exposure booster immunization consists of one 1.0 ml dose of human diploid cell (rabies) vaccine (HDCV) or purified chick embryo cell (PCECV) vaccine IM into deltoid. Minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by the rapid fluorescent focus inhibition test. A booster dose should be administered if the titer falls below this level.

VI. CONTRAINDICATIONS

1. In cases of pre-exposure immunization, there are no known specific contraindications other than situations such as developing febrile illness, or previous allergic reaction to any vaccine component.^{1, 2}
2. For post-exposure treatment, there are no known specific contraindications to the use of rabies vaccine.¹⁻³
3. Persons who have experienced “immune complex-like” hypersensitivity reactions should receive no further doses of IMMOVAX[®](HDCV) vaccine unless they are exposed to rabies or likely to be unavoidably or unapparently exposed to rabies virus and have unsatisfactory antibody titers.¹

VII. PRECAUTIONS

1. RabAvert[®]
PCECV: is produced in chick embryo cell culture. Persons with a history of anaphylactic, anaphylactoid, or other immediate reactions (e.g., hives, swelling of the mouth and throat, difficulty breathing, hypotension or shock) subsequent to egg ingestion should not be immunized with this vaccine. IMMOVAX[®] (HDCV) should be administered instead. Rare cases of Guillain-Barré syndrome have been reported with RabAvert[®].¹
2. IMMOVAX[®]
HDCV: serum sickness type reactions have been reported in up to 7% of persons receiving booster doses of IMMOVAX[®].²
Rare cases of Guillain-Barré syndrome have been reported with IMMOVAX[®].²
3. Any suspected or documented bite or scratch from a bat should be grounds for seeking post-exposure prophylaxis.³

VIII. SIDE EFFECTS AND ADVERSE REACTIONS³

- Travelers should be advised that they may experience local reactions after vaccination, such as pain, erythema, swelling, or itching at the injection site, or mild systemic reactions, such as headache, nausea, abdominal pain, muscle aches, and dizziness.
- Approximately 6% of persons receiving booster vaccinations with IMMOVAX[®] (HDCV) may experience an immune complex-like reaction characterized by urticaria, pruritus, and malaise. The likelihood of these reactions is less with RabAvert[®] (PCECV).
- Once initiated, rabies postexposure prophylaxis should not be interrupted or discontinued because of local or mild systemic reactions to rabies vaccine.

IX. 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 of anaphylactic or acute hypersensitivity reaction.^{1, 2}
2. **Immunocompromised:** Corticosteroids, other immunosuppressive agents, antimalarials, and immunosuppressive illnesses can interfere with the development of active immunity after vaccination. For persons with immunosuppression, **pre-exposure** prophylaxis should be administered with the awareness that the immune response might be inadequate. Patients who are immunosuppressed by disease or medications should postpone pre-exposure vaccinations and consider avoiding activities for which rabies pre-exposure prophylaxis is indicated. When this course is not possible, immunosuppressed persons who are at risk for rabies should have their virus neutralizing antibody titers checked after completing the pre-exposure series. A patient who fails to seroconvert after the third dose should be managed in consultation with their physician and appropriate public health officials. No cases of rabies postexposure prophylaxis failure have been documented among persons immunosuppressed because of human immunodeficiency virus infection.^{1, 2}

Immunosuppressive agents should not be administered during postexposure therapy unless essential for the treatment of other conditions. When rabies **postexposure** prophylaxis is administered to persons receiving corticosteroids or other immunosuppressive therapy, or who are immunosuppressed, it is important that a serum sample on day 14 (the day of the fourth vaccination) be tested for rabies antibody to ensure that an acceptable antibody response has been induced. HRIG must not be administered at more than the recommended dose, since active immunization to the vaccine may be impaired.^{4, 5, 6}

- 3. **Pregnancy:** is not a contraindication to post-exposure prophylaxis. If the risk of exposure to rabies is substantial, preexposure prophylaxis might also be indicated during pregnancy.^{4, 5}
- 4. **Lactation:** It is not known whether rabies vaccines are excreted in human milk. Use with caution in nursing mothers.^{1, 2}

X. PRE-EXPOSURE VACCINATION AND SEROLOGIC TESTING

Because the antibody response has been satisfactory after these recommended pre-exposure prophylaxis vaccine regimens, routine serologic testing to confirm sero-conversion is not necessary except for persons suspected of being immunosuppressed. See section IV, page 4, footnote §, for specifics on rabies vaccine titers.

XI. 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

Vaccine	Temp	Storage Issues	Notes
Imovax® 1	Store at 2°–8°C (36°F–46°F)	Do not use if vaccine has been frozen. Report to health educator.	Give within 30 minutes of mixing
Rabavert® 2	Store at 2°–8°C (36°F–46°F)	Do not use after expiration date on package and container Protect from light	Give within 30 minutes of mixing

XII. 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 copies of the report and VAERS ID 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 <http://vaers.hhs.gov/index>.

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 or 711 for TTY. For other questions, consult with the vaccine recipient's primary health care provider or a consulting physician.

Electronic copy of this protocol available at: <http://1.usa.gov/OregonStandingOrders>

REFERENCES

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3. Centers for Disease Control and Prevention. CDC Health Information for International Travel 2016. New York: Oxford University Press; 2015. Chapter 3. Available at: wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/rabies. Accessed 13 August 2015.
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6. CDC. Recommendations of the Advisory Committee on Immunization Practices (ACIP), MMWR 1999; 48 (RR-1) Available at: www.cdc.gov/MMWR/preview/mmwrhtml/00056176.htm Accessed 13 August 2015.