OREGON HEALTH AUTHORITY
IMMUNIZATION PROTOCOL FOR PHARMACISTS
RABIES INACTIVATED VIRUS VACCINE
FOR PRE-EXPOSURE PROPHYLAXIS ONLY

Review 04-2013
- No changes to the PRE-EXPOSURE protocol of 2008.
- Supplies of rabies vaccine are currently restricted.
- RabAvert (Novartis) is available for pre-exposure and postexposure prophylaxis from wholesale distributors.
- IMOVAX (Sanofi Pasteur) is currently available for postexposure prophylaxis

I. Order:
1. Check the ALERT Immunization Information System to determine whether the patient needs this vaccine and any other vaccines.
2. Screen clients ≥11 years for contraindications.
3. Provide an Adolescent Well Visit Flyer to those 11—18 years of age.
4. Provide a current Vaccine Information Sheet (VIS) answering any questions.
5. Obtain a signed Vaccination Administration Record (VAR)
6. Do not remove vaccine from refrigerator until ready to reconstitute it with the diluent supplied.
7. Reconstitute only with the supplied diluent. Gently swirl the contents until completely dissolved. It should be used immediately after reconstitution, and if not administered promptly, discard contents.
8. Give 1ml dose of vaccine intramuscularly (IM) as a three dose series to eligible persons ≥11 years of age who may be at risk for exposure to the rabies virus on days 0, 7, and 21 or 28.
   a. May be given simultaneously with all other vaccines.
II. LICENSED RABIES VACCINE:

<table>
<thead>
<tr>
<th>Product name</th>
<th>Vaccine component(s</th>
<th>Acceptable age range</th>
<th>Preservative</th>
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</thead>
<tbody>
<tr>
<td>IMOVAX® Rabies Human diploid cell vaccine (HDCV) Sanofi Pasteur</td>
<td>The vaccine is obtained from infected human diploid cells, inactivated by β-propiolactone. It also contains &lt;100 mg albumin, &lt;150 μg neomycin sulfate and 20 μg of phenol red indicator.</td>
<td>≥Infancy&lt;sup&gt;1&lt;/sup&gt;</td>
<td>The vaccine contains no preservative or stabilizer. It should be used as a single dose vial.</td>
</tr>
<tr>
<td>RabAvert® Purified chick embryo cell vaccine (PCECV) Novartis</td>
<td>Vaccine is obtained by growing the fixed-virus strain in chicken fibroblasts, which are inactivated with β-propiolactone. One dose (1ml) contains &lt;12 mg polygeline (processed bovine gelatin), &lt;0.3 mg human serum albumin, 1 mg potassium glutamate, 0.3 mg sodium EDTA, &lt;1μg neomycin, &lt;20 ng chlortetracycline, and &lt;2ng amphotericin B. Minimal amounts of chicken protein may be present in the final product; albumin content is &lt;3 ng/dose.</td>
<td>In all age groups&lt;sup&gt;2&lt;/sup&gt;</td>
<td>The vaccine contains no preservative.</td>
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<sup>1</sup> Imovax® pkg insert, pg. 5, 12-2005
<sup>2</sup> RabAvert® pkg insert, pg. 2, 10-2006
### III. RECOMMENDATIONS FOR USE:

**Primary or Pre-exposure Vaccination**

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
- 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.

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.

\(^1\)Source: The Yellow Book, September 2012
### IV. VACCINE SCHEDULE:

<table>
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<tr>
<th>Course of vaccination</th>
<th>Recommended Age</th>
<th>Dose Regimen</th>
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<tbody>
<tr>
<td>Primary</td>
<td>≥11 years²</td>
<td>3 doses at 0, 7, and 21 or 28 days</td>
</tr>
<tr>
<td>Booster³</td>
<td>≥11 years²</td>
<td>1 dose only⁴,⁵</td>
</tr>
</tbody>
</table>

³Immunocompromised 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.

²While this vaccine is licensed for persons ≥infancy, Oregon pharmacist’s, by law, currently can’t administer this vaccine to persons ≤10 years of age.

³Reference Pre-exposure recommendations in section V below to determine which populations might require a booster dose.

⁴A 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.

⁵In 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. The schedule for this series is given in Table 3-15. 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. Preexposure vaccination does not eliminate the need for additional medical attention after a rabies exposure, but it simplifies postexposure prophylaxis. 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.

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.
### V. CRITERIA FOR PRE-EXPOSURE RABIES IMMUNIZATION

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Nature of risk</th>
<th>Typical populations</th>
<th>Pre-exposure Recommendations</th>
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<tbody>
<tr>
<td>Continuous</td>
<td>Virus present continuously, often in high concentrations. Specific exposures likely to go unrecognized. Bite, non-bite, or aerosol exposure.</td>
<td>Rabies research laboratory workers,(^1) rabies biologics production workers.</td>
<td>Primary course. Serologic testing every 6 months; booster vaccination if antibody titer is below acceptable level. (^2)</td>
</tr>
<tr>
<td>Frequent</td>
<td>Exposure usually episodic, with source recognized, but exposure also might be unrecognized. Bite, non-bite, or aerosol exposure possible.</td>
<td>Rabies diagnostic lab workers, (^1) cavers, missionaries, veterinarians and staff, and animal-control and wildlife workers in rabies-enzootic areas.</td>
<td>Primary course. Serologic testing every 2 years; booster vaccination if antibody titer is below acceptable level. (^2)</td>
</tr>
<tr>
<td>Infrequent (greater than population at large)</td>
<td>Exposure nearly always episodic with source recognized. Bite or non-bite exposure.</td>
<td>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.</td>
<td>Primary course. No serologic testing or booster vaccination.</td>
</tr>
<tr>
<td>Rare (population at large)</td>
<td>Exposure always episodic with source recognized. Bite or non-bite exposure.</td>
<td>U.S. population at large, including persons in rabies-epizootic areas.</td>
<td>No pre-exposure vaccination necessary.</td>
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</tbody>
</table>

\(^1\) Judgment of relative risk and extra monitoring of vaccination status of laboratory workers is the responsibility of the laboratory supervisor. (see www.cdc.gov/biosafety/publications/bmbl5 for more information).

\(^2\) 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.
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<tr>
<th>VI. CONTRAINDICATIONS</th>
<th>VII. PRECAUTIONS</th>
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<tbody>
<tr>
<td>1. In cases of pre-exposure immunization, there are no known specific contraindications other than situations such as developing febrile illness, etc.</td>
<td>1. RabAvert® (PCECV) vaccine 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. HDCV should be administered instead.</td>
</tr>
<tr>
<td>2. For post-exposure treatment, there are no known specific contraindications to the use of rabies vaccine.</td>
<td>2. When chloroquine phosphate was used routinely for malaria prophylaxis, investigators discovered that the drug decreased the antibody response to concomitantly administered HDCV. Although interference with the immune response to rabies vaccine by other antimalarials structurally related to chloroquine (e.g., mefloquine) has not been evaluated, precautions for persons receiving these drugs should be followed.</td>
</tr>
<tr>
<td>3. Pregnancy is not a contraindication to post-exposure prophylaxis.</td>
<td>3. Immune suppression, such as corticosteroid treatment or immunosuppressive illness, can interfere with the development of active immunity.</td>
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<tr>
<td></td>
<td>4. Pre-exposure vaccination is not usually recommended during pregnancy, but may be indicated if there is substantial risk. Consult with health care provider.</td>
</tr>
<tr>
<td></td>
<td>5. Any suspected or documented bite or scratch from a bat should be grounds for seeking post-exposure prophylaxis.</td>
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</tbody>
</table>
VIII. SIDE EFFECTS AND ADVERSE REACTIONS

- 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 HDCV (IMOVAX®) may experience an immune complex-like reaction characterized by urticaria, pruritus, and malaise. The likelihood of these reactions is less with PCECV (RabAvert®).
- Once initiated, rabies postexposure prophylaxis should not be interrupted or discontinued because of local or mild systemic reactions to rabies vaccine.

1Yellow Book 2012, Chapter 3 available at wwwnc.cdc.gov/travel/yellowbook/2012/chapter-3-infectious-diseases-related-to-travel/rabies.htm

IX. OTHER CONSIDERATIONS

Persons who have experienced “immune complex-like” reactions should receive no further doses of HDCV vaccine unless they are exposed to rabies or likely to be unavoidably or unapparently exposed to rabies virus and have unsatisfactory antibody titers.

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. Patients who are immunosuppressed by disease or medications should postpone pre-exposure prophylaxis vaccinations and consider avoiding activities for which rabies pre-exposure prophylaxis is indicated. When that is not possible, immunosuppressed persons who are at risk for exposure to rabies should be vaccinated and their antibody titers checked. In these cases,
failures to seroconvert after the third dose should be managed in consultation with appropriate public health officials.

XI. STORAGE AND HANDLING

The freeze-dried vaccine should be protected from light and stored in a refrigerator between 2º-8ºC (35º to 47ºF). Do not freeze. It should be used immediately after reconstitution.

XII. ADVERSE EVENTS REPORTING

Adverse events following immunization must be reported to the Vaccine Adverse Events Reporting System (VAERS) at 1-800-822-7967. Forms and procedures can be found at the VAERS website: www.vaers.hhs.gov. In addition, a copy of the reporting form should be reported to the patient’s primary provider, per Oregon Revised Statute (ORS) 855-019-0280(4).

REFERENCES


2. CDC. Use of a reduced (4-dose) vaccine schedule for postexposure prophylaxis to prevent human rabies. MMWR 2010:59 (RR02); 1-9. Available at: www.cdc.gov/mmwr/preview/mmwrhtml/rr5902a1.htm

3. 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


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: 1.usa.gov/PharmacyImmunizationProtocols

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