

# Rabies Vaccine

Revision Date: April 4, 2018

## Rationale for Update:

- Rationale for Policy Update: Removed Rabies Pre-Exposure form.

Please consult the Product Monograph <sup>1,2</sup> for further information about the vaccine.		
	<b>IMOVAX® Rabies</b>	<b>RabAvert®</b>
<b>Manufacturer</b>	Sanofi Pasteur SA - distributed by Sanofi Pasteur Limited	GlaxoSmithKline Inc.
<b>Authorization and access</b>	<p><b>Special authorization and access procedures must be followed.</b></p> <ul style="list-style-type: none"> <li>• Pre-exposure immunization: Vaccine must be obtained by special order through Alberta Health Provincial Vaccine Depot.</li> <li>• Post-exposure prophylaxis (PEP):             <ul style="list-style-type: none"> <li>➤ See <a href="#">Rabies Post-exposure - Authorizing and Obtaining Rabies Post-exposure Biologicals</a>.</li> </ul> </li> </ul> <p>For disease investigation, assessment of exposure and reporting requirements refer to <i>Public Health Notifiable Disease Management Guidelines: Rabies</i>.<sup>3</sup></p>	
<b>Licensed use</b>	<p><b>Pre-exposure:</b></p> <p>1.0 mL administered by intramuscular route to all eligible individuals.</p>	
<b>Off-license use</b>	<p><b>Pre-exposure:</b></p> <p>0.1 mL administered by intradermal route to individuals who are not immune compromised and are not taking steroid or antimalarial medications.</p>	
<b>Indications for use of provincially funded vaccine</b>	<p><b>Pre-exposure:</b></p> <p><b>High-risk occupations including:</b></p> <ul style="list-style-type: none"> <li>• Workers routinely caring for animals including veterinarians, veterinary health technicians, veterinary assistants, Humane Society/SPCA workers.</li> <li>• Animal research workers including rabies laboratory workers and those in other laboratories working with rabies-prone species.</li> <li>• Animal control workers including bylaw officers, animal control (dog pound) workers and zoo workers.</li> <li>• Wildlife workers including fish and wildlife workers and foresters.</li> <li>• Spelunkers (cavers): Albertans involved in work-related spelunking.</li> </ul> <p><b>Notes:</b></p> <ul style="list-style-type: none"> <li>• Employees under federal jurisdiction including Canadian Food and Inspection Agency (CFIA) and Parks Canada are not eligible to receive provincially funded rabies vaccine.</li> <li>• Recreational spelunkers and those at risk due to international travel are not eligible to receive provincially funded rabies vaccine.</li> </ul>	

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	<p><b>Post-exposure:</b></p> <ul style="list-style-type: none"> <li>• Rabies PEP must be considered if potential exposure to rabies virus has occurred. The animal species, the incident and the type of exposure must be considered.</li> <li>• Pre-exposure rabies immunization does not eliminate the need for prompt PEP when a significant exposure occurs. It does eliminate the need for rabies immune globulin (RIG) and reduces the number of vaccine doses required for PEP.</li> </ul> <p>For disease investigation, assessment of exposure and reporting requirements refer to: <i>Public Health Notifiable Disease Management Guidelines – Rabies</i><sup>3</sup></p> <p><b>Note:</b> Individuals from out of province requiring rabies PEP should be referred to the Alberta Health Immunization Program. The Nurse Consultant will send a referral to the appropriate jurisdiction to ensure follow-up is completed.</p>
<b>Dose</b>	<p><b>Pre-exposure:</b></p> <ul style="list-style-type: none"> <li>• 0.1 mL Intradermal (ID) OR</li> <li>• 1.0 mL Intramuscular (IM) if ID administration is contraindicated</li> </ul> <p><b>Post-exposure:</b></p> <ul style="list-style-type: none"> <li>• 1.0 mL IM</li> </ul>
<b>Route</b>	<p><b>Pre-exposure:</b></p> <p><b>Intradermal injection or intramuscular injection if ID is contraindicated:</b></p> <ul style="list-style-type: none"> <li>• ID (unless contraindicated see note below) is the preferred method for pre-exposure immunization (primary series and booster doses) using provincially funded vaccine. Book groups of six or more individuals at the same time, as much as possible. When risk of exposure is high and immediate immunization is required, please consult the Alberta Health, Immunization Program before proceeding with an IM dose for one individual.</li> <li>• Although rabies vaccine is not specifically licensed in Canada for ID administration, the World Health Organization (WHO) considers the ID regimen an acceptable alternative to IM administration as it uses less vaccine to produce a comparable degree of protection against rabies.<sup>4</sup></li> </ul> <p><b>Note:</b> The ID route is contraindicated for some individuals. Those who are immune compromised or taking steroid medications or taking anti-malarial medications, should have the vaccine administered by the IM route only.<sup>4</sup></p> <p><b>Post-exposure:</b></p> <p>Intramuscular injection (i.e., the deltoid in children and adults or the anterolateral aspect of the mid thigh in infants and young children).<sup>4</sup></p> <p><b>Note:</b> The gluteal region should never be used for IM administration of rabies vaccine since administration in this area can result in a lower antibody response.<sup>1,2</sup></p>
<b>Schedule</b> <b>Pre-exposure</b>	<p><b>Pre-exposure primary series</b> (3 doses):</p> <ul style="list-style-type: none"> <li>❖ Dose 1: day 0</li> <li>❖ Dose 2: day 7</li> <li>❖ Dose 3: day 21 - 28</li> </ul> <p><b>Notes:</b></p> <ul style="list-style-type: none"> <li>• When ID administration of the vaccine is used, serology should be checked at least two weeks after completion of the vaccine series or after a booster dose to ensure adequate protection.<sup>4</sup></li> </ul>

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	<ul style="list-style-type: none"> <li>Immune compromised individuals should have serology 7 – 14 days post-immunization to ensure an acceptable antibody concentration has been achieved.<sup>4</sup> If an acceptable response is not obtained, a second series of vaccine should be administered followed by serologic testing.<sup>4</sup></li> </ul> <p><b>Pre-exposure reinforcing doses:</b></p> <ul style="list-style-type: none"> <li>Determination of immunity is recommended every two years for individuals at continuing risk (occupations listed under indications) of rabies exposure.<sup>4</sup> Antibody determination should precede any reinforcing dose of vaccine.</li> <li>Research lab workers working with live rabies virus at risk of unapparent exposure should be tested for rabies immunity every six months.<sup>4</sup></li> <li>Rapid fluorescent-focus inhibition test (RFFIT) results of less than 0.5 IU/mL indicate the need for a booster dose. However, due to inherent imprecision in the rabies assay (RFFIT)<sup>5</sup> when test results are reported as between 0.5 IU/mL – 1 IU/mL, individuals at increased or continuing risk of rabies exposure should be offered a reinforcing dose of rabies vaccine.</li> </ul>
<p><b>Schedule</b></p> <p><b>Post-exposure</b></p>	<p><b>Post-exposure prophylaxis (PEP):</b></p> <p><b>Previously unimmunized</b></p> <ul style="list-style-type: none"> <li><b>Immune competent individuals:</b> Four doses of 1.0 mL each administered IM.<sup>4</sup> <ul style="list-style-type: none"> <li>❖ Dose 1: day 0 (day 0 is the day the first dose is administered)</li> <li>❖ Dose 2: day 3</li> <li>❖ Dose 3: day 7</li> <li>❖ Dose 4: day 14</li> </ul> </li> <li><b>Immune compromised individuals</b> (due either to immune suppressive agents or illness) and individuals taking antimalarial medications: Five doses of 1.0 mL each administered IM.<sup>4</sup> <ul style="list-style-type: none"> <li>❖ Dose 1: day 0 (day 0 is the day the first dose is administered)</li> <li>❖ Dose 2: day 3</li> <li>❖ Dose 3: day 7</li> <li>❖ Dose 4: day 14</li> <li>❖ Dose 5: day 28</li> </ul> </li> </ul> <p><b>Notes:</b></p> <ul style="list-style-type: none"> <li>RIG should be administered to previously unimmunized individuals on day 0 at the same time as dose 1 of rabies vaccine but at a different anatomical site from the vaccine.<sup>4</sup> See <u>Rabies Immune Globulin</u>.</li> <li>Rabies post-exposure vaccine schedules should be adhered to as closely as possible and it is essential that all recommended doses of vaccine be administered.<sup>4</sup> It is critical that the first three doses be spaced according to the schedule. Prolonging the interval between doses may seriously delay achieving the protective antibody titres, with potentially fatal consequences.<sup>6</sup></li> </ul> <p><b>Previously completely immunized persons:</b></p> <p>Two doses of 1.0 mL each administered IM</p> <ul style="list-style-type: none"> <li>❖ Dose 1: day 0</li> <li>❖ Dose 2: day 3</li> </ul> <p><b>Notes:</b></p> <ul style="list-style-type: none"> <li>RIG should not be administered.</li> </ul>

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	<ul style="list-style-type: none"> <li>• Appropriate rabies protection consists of: <ul style="list-style-type: none"> <li>➢ Documentation of a complete course of pre- or post-exposure prophylaxis with a human diploid cell vaccine (HDCV) as in IMOVAX® Rabies or purified chick embryo cell vaccine (PCECV) as in RabAvert®.<sup>4</sup></li> <li>➢ Documentation of complete immunization with other types of rabies vaccine or with HDCV or PCECV according to unapproved schedules with demonstration of antibody response (0.5 IU/mL or greater) following completion of the immunization.<sup>4</sup></li> </ul> </li> <li>• If vaccine other than HDCV or PCECV was used for pre-exposure immunization and the person's immune status is not known, a full course of treatment, including RIG, should be initiated. A serum sample may be collected before the vaccine is administered, and if the antibody is demonstrated, the vaccine series may be discontinued, provided at least two doses of vaccine have been administered.<sup>4</sup></li> </ul> <p><b>Recommendations for Post-exposure series initiated in another country:</b></p> <ul style="list-style-type: none"> <li>• If the post-exposure series initiated meets the World Health Organization (WHO) approved vaccine, was administered I.M., and meets WHO approved schedule - complete the series as appropriate.</li> </ul> <p>See attached links for additional information:</p> <ul style="list-style-type: none"> <li>➢ WHO Guide for post-exposure prophylaxis <a href="http://www.who.int/rabies/human/postexp/en/">www.who.int/rabies/human/postexp/en/</a>.<sup>7</sup></li> <li>➢ CATMAT Rabies Statement.<sup>8</sup></li> </ul> <p>RIG can be offered if the client has not already received RIG and it can be administered within seven days of the first dose of I.M. rabies vaccine.<sup>4</sup></p> <ul style="list-style-type: none"> <li>• For uncertain vaccines, vaccines given I.D., or unknown schedule, including no clear documentation - restart series and offer RIG.</li> </ul> <p><b>Notes for Post-exposure (unimmunized and immunized):</b></p> <ul style="list-style-type: none"> <li>• Individuals, who have immune suppressive illnesses or those receiving steroids or immune suppressive therapy, should have a rabies antibody determination following completion of PEP to ensure that an acceptable level has been achieved.<sup>4</sup></li> <li>• If a person needs to complete the post-exposure series outside of Alberta, contact Alberta Health Immunization Program for assistance in making the arrangements to complete the vaccine series.</li> </ul>
<b>Contraindications</b>	<p><b>Pre-exposure:</b></p> <ul style="list-style-type: none"> <li>• Known severe hypersensitivity to any of the components of the vaccine or the vaccine container.</li> <li>• Anaphylaxis or other severe allergic reaction to a previous dose of vaccine containing rabies antigen.</li> </ul> <p><b>Post-exposure:</b></p> <p>Because rabies disease is almost always fatal, there is no contraindication to PEP. However, expert opinion should be sought in the management of individuals who are hypersensitive to the vaccine or any ingredients in the formulation or the vaccine container.<sup>4</sup> See the Product Monograph for details.</p>
<b>Precautions</b>	<ul style="list-style-type: none"> <li>• Immune compromised persons may have a suboptimal immune response to rabies vaccine.</li> <li>• Immune suppressive agents should not be administered during post- exposure prophylaxis unless essential for the treatment of other conditions.<sup>6</sup></li> </ul>

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	<ul style="list-style-type: none"> <li>Persons eligible for pre-exposure vaccine with a history of severe hypersensitivity reactions to egg or egg products should be given an HDCV vaccine as in Imovax® Rabies.<sup>4</sup></li> </ul>
<b>Possible reactions</b>	<p><b>Common:</b></p> <ul style="list-style-type: none"> <li>Pain, erythema, swelling, and itching at the injection site.<sup>1,2</sup></li> <li>Headache, nausea, abdominal pain, vomiting, diarrhea, asthenia, muscle aches, arthralgia, malaise, fever, chills, adenopathy, rash and dizziness.<sup>1,2</sup></li> </ul> <p><b>Note:</b></p> <ul style="list-style-type: none"> <li>Systemic allergic reactions characterized by generalized urticaria and accompanied in some cases by arthralgia, angioedema, fever, nausea and vomiting have been reported.<sup>4</sup> These reactions are uncommon in people receiving primary immunization but have occurred in up to 7% of those receiving a booster dose, with onset after 2 to 21 days.<sup>4</sup></li> </ul> <p><b>Rare:</b></p> <ul style="list-style-type: none"> <li>Anaphylaxis (Immediate anaphylactic reactions have occurred in 1 in 10,000 people given HDCV.<sup>4</sup>)</li> </ul> <p><b><u>For Imovax® Rabies only:</u></b></p> <ul style="list-style-type: none"> <li>The following additional adverse events following immunization have been reported from post-marketing surveillance:</li> <li>Pruritus, paraesthesia, neuropathy, asthenia and serum sickness type reactions.<sup>1</sup></li> <li>Two cases of neurologic illness resembling Guillain-Barré syndrome temporally associated with HDCV.<sup>1</sup></li> </ul> <p><b><u>For RabAvert® only:</u></b></p> <ul style="list-style-type: none"> <li>The following additional adverse events following immunization have been reported from post-market surveillance: Chills, sweating, palpitations or hot flash, vertigo, visual disturbance, paraesthesia, nervous system disorders (such as encephalitis, transient paralysis or Guillain-Barré syndrome), allergic reactions (such as anaphylaxis, anaphylactic shock, bronchospasm, edema or pruritis) and pain or swelling in limbs.<sup>2</sup></li> </ul>
<b>Pregnancy</b>	Pregnancy is not a contraindication to post-exposure rabies immunization. If there is a substantial risk of exposure to rabies, pre-exposure immunization may be indicated during pregnancy. <sup>1,2,4</sup>
<b>Lactation</b>	Breastfeeding is not a contraindication to rabies immunization. It is not known whether rabies vaccine or corresponding antibodies cross into breast milk. <sup>1,2,6</sup>
<b>Program Notes</b>	<ul style="list-style-type: none"> <li>1980 January 1 – Rabies vaccine introduced into program.</li> <li>1999 August – Imovax® introduced.</li> <li>2005 June 1 – RabAvert® introduced.</li> <li>2013 August 29 – Schedule change for Rabies PEP four doses of vaccine instead of five doses of vaccine for unimmunized, immune competent individuals.</li> <li>2016 November 16 – Recommendations included for post-exposure series initiated in another country.</li> </ul>

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## References

- <sup>1</sup> Sanofi Pasteur Limited. (2006, March). IMOVAX® Rabies: Rabies vaccine inactivated (DCO). *Product Monograph*.
- <sup>2</sup> GlaxoSmithKline Inc. (2017, March 15) RabAvert®: Rabies vaccine. *Product Monograph*.
- <sup>3</sup> Alberta Health. Public Health Notifiable Disease Management Guidelines: Rabies. [www.health.alberta.ca/professionals/notifiable-diseases-guide.html](http://www.health.alberta.ca/professionals/notifiable-diseases-guide.html)
- <sup>4</sup> National Advisory Committee on Immunization. (2016). *Canadian Immunization Guide* (Evergreen ed.). Ottawa, ON: Public Health Agency of Canada. [www.canada.ca/en/public-health/services/canadian-immunization-guide.html](http://www.canada.ca/en/public-health/services/canadian-immunization-guide.html)
- <sup>5</sup> Personal communication between Dr. Lavoie and the National Microbiology Laboratory. (2015-01).
- <sup>6</sup> Grabenstein, J. D. (2012). *ImmunoFacts: Vaccines and Immunologic Drugs 2013*. St. Louis, MO: Wolters Kluwer Health.
- <sup>7</sup> World Health Organization. (2016). Rabies - Guide for post-exposure prophylaxis. [www.who.int/rabies/human/postexp/en/](http://www.who.int/rabies/human/postexp/en/).
- <sup>8</sup> CATMAT. (2002) Statement on Travellers and Rabies Vaccine. *CCDR 1 March 201, Volume 28, ACS4*.