

# Rabies Vaccine

Revision Date: February 28, 2022

## Rationale for Update:

- Clarified recommendation for individuals being assessed for pre-exposure rabies vaccine reporting undocumented rabies immunization series.

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> <p>Pre-exposure immunization:</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> </ul> <p>Post-exposure prophylaxis (PEP):</p> <ul style="list-style-type: none"> <li>➤ The MOH/designate within the AHS Zone will authorize the release of rabies immune globulin (RIG) or rabies vaccine for an individual.</li> <li>➤ The Office of the Chief Medical Officer of Health (OCMOH) is available for consultation if desired by the MOH.</li> </ul> <p>For disease investigation, assessment of exposure and reporting requirements refer to <i>Rabies Prevention and Control Manual Guidance for Public Health and Veterinary Professionals</i>.<sup>3</sup></p>	
<b>Licensed use</b>	<p><b>Pre-exposure and Post-exposure:</b></p> <ul style="list-style-type: none"> <li>• 1.0 mL administered by intramuscular route to all eligible individuals.</li> </ul>	
<b>Off-license use</b>	<p><b>Pre-exposure :</b></p> <ul style="list-style-type: none"> <li>• 0.1 mL administered by intradermal route to eligible individuals.</li> </ul> <p><b>Post-exposure:</b></p> <ul style="list-style-type: none"> <li>• 0.1 mL administered by intradermal route to two anatomical sites to eligible individuals (for a total of 0.2 mL).</li> </ul>	
<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> </ul>	

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	<ul style="list-style-type: none"> <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> <li>• Students attending a post-secondary institution and enrolled in a veterinarian, veterinary health technician or veterinarian assistant program.</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>• Volunteers, recreational spelunkers and those at risk due to international travel are not eligible to receive provincially funded rabies vaccine.</li> </ul> <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>REFER to: <i>Rabies Prevention and Control Manual Guidance for Public Health and Veterinary Professionals</i><sup>3</sup> for risk assessment to determine if PEP is indicated.</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>• 0.1 mL Intradermal (ID) at two anatomical sites (total of 0.2 mL) OR</li> <li>• 1.0 mL IM (if ID administration is contraindicated or not operationally feasible)</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 reinforcing 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>• After reconstitution, the vaccine must be used as soon as possible and within 6 hours.<sup>4</sup></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>4,5</sup></li> </ul>

	<p><b>Post-exposure:</b></p> <p><b>Intradermal injection or intramuscular injection if ID is contraindicated or not operationally feasible.</b></p> <ul style="list-style-type: none"> <li>• <b>Intradermal injection</b> (ID in the deltoid)</li> </ul> <p><b>Notes:</b></p> <ul style="list-style-type: none"> <li>○ After reconstitution, the vaccine must be used as soon as possible and within 6 hours.<sup>4</sup></li> <li>○ The ID route is contraindicated for individuals who are immunocompromised due to illness or immunosuppressive agents, or for individuals taking chloroquine or hydroxychloroquine. The immune response to receiving the vaccine ID may not be protective under these circumstances.<sup>5</sup> Therefore for these individuals, the vaccine should be administered by the IM route only.<sup>5,6</sup></li> </ul> <ul style="list-style-type: none"> <li>• <b>Intramuscular injection</b> (i.e., the deltoid in children and adults or the anterolateral aspect of the mid thigh in infants and young children).<sup>5</sup></li> </ul> <p><b>Notes:</b></p> <ul style="list-style-type: none"> <li>○ 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></li> </ul>
<p><b>Schedule</b></p> <p><b>Pre-exposure</b></p>	<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 reinforcing dose to ensure adequate protection.<sup>4</sup></li> <li>• Immunocompromised individuals should have serology 7 – 14 days post-immunization to ensure an acceptable antibody concentration has been achieved.<sup>5</sup> If an acceptable response is not obtained, a second series of vaccine should be administered followed by serologic testing.<sup>5</sup></li> <li>• Individuals who have received an undocumented rabies immunization series and who present with rabies serology indicating inadequate immunity should be offered a reinforcing dose. If serology following the reinforcing dose indicates inadequate immunity, offer two more doses to complete a series.</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>5</sup> Antibody determination should precede any reinforcing dose of vaccine.<sup>5,6</sup></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>5</sup></li> <li>• Rapid fluorescent-focus inhibition test (RFFIT) results of less than 0.5 IU/mL indicate the need for a reinforcing dose. However, due to inherent imprecision in the rabies assay (RFFIT)<sup>7</sup> when test results are reported as 0.5 IU/mL up to and including 1 IU/mL, individuals at increased or continuing risk of rabies exposure should be offered a reinforcing dose of rabies vaccine.</li> </ul>

<b>Schedule</b> <b>Post-exposure</b>	<b>Post-exposure prophylaxis (PEP):</b> <b>Unimmunized Individuals:</b>
	<b>Immunocompetent individuals</b> <b>IM</b> – 1.0 mL each <sup>4</sup> OR <b>ID</b> – 0.1 mL each at two anatomical sites (for a total of 0.2 mL). <sup>7</sup>  ❖ Dose 1: day 0 (day 0 is the day the first dose is administered) ❖ Dose 2: day 3 ❖ Dose 3: day 7 ❖ Dose 4: day 14  <b>Notes:</b> <ul style="list-style-type: none"><li>ID administration is the preferred route of administration (unless contraindicated) when operationally feasible and clients can be clustered.</li><li>Series may be completed using a mixed IM/ID schedule as long as the scheduling is maintained.</li></ul>
	<b>Immunocompromised individuals</b> (due either to immunosuppressive agents or illness) <b>OR Individuals taking chloroquine or hydroxychloroquine</b> Five doses of 1.0 mL each administered IM. <sup>5</sup>  ❖ Dose 1: day 0 (day 0 is the day the first dose is administered) ❖ Dose 2: day 3 ❖ Dose 3: day 7 ❖ Dose 4: day 14 ❖ Dose 5: day 28  <b>Notes:</b> <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>5</sup> See Biological Products <a href="#">Rabies Immune Globulin</a>.</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>5</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>8</sup></li></ul>
	<b>Previously appropriately immunized individuals:</b> <b>IM</b> – 1.0 mL each <sup>5</sup> OR <b>ID</b> – 0.1 mL each at two anatomical sites (for a total of 0.2 mL). <sup>7</sup>  ❖ Dose 1: day 0 ❖ Dose 2: day 3  <b>Notes:</b> <ul style="list-style-type: none"><li>RIG should not be administered.<sup>5,6</sup></li><li>Appropriate rabies immunization consists of:</li></ul>

	<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>5</sup></li> <li>➤ Documentation of complete immunization series with: <ul style="list-style-type: none"> <li>▪ Other types of rabies vaccine, OR</li> <li>▪ HDCV or PCECV according to unapproved schedules<sup>5</sup>, OR</li> <li>▪ I.D. rabies series with HDCV or PCECV vaccine</li> </ul> </li> </ul> <p>AND</p> <ul style="list-style-type: none"> <li>▪ Serology demonstrating an antibody response (0.5 IU/mL or greater) following completion of the immunization series.<sup>5</sup></li> </ul> <ul style="list-style-type: none"> <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>5</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 vaccines*, and meets WHO approved schedule – complete the series as appropriate.</li> </ul> <p>*WHO approved vaccines: cell culture vaccines (purified chicken embryo vaccine, purified Vero cell rabies vaccine and human diploid cell vaccine) and duck embryo vaccine.<sup>9</sup></p> <p>See attached links for additional information:</p> <ul style="list-style-type: none"> <li>➤ <a href="#">WHO Expert Consultation on Rabies:</a><sup>9</sup></li> <li>➤ <a href="#">CATMAT Rabies Statement.</a><sup>9</sup></li> </ul> <p>RIG can be offered if the individual has not already received RIG and it can be administered within seven days of the first dose of rabies vaccine.<sup>5</sup></p> <ul style="list-style-type: none"> <li>• For uncertain vaccines, 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>• Immunocompromised individuals (due to illness or immunosuppressive agents) or those taking chloroquine or hydroxychloroquine, should have a rabies antibody determination following completion of PEP to ensure that an acceptable level has been achieved.<sup>5,6</sup></li> <li>• If an individual 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.<sup>5</sup></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>5</sup> See Product Monograph for details.</p>

<b>Precautions</b>	<ul style="list-style-type: none"> <li>Immunocompromised persons may have a suboptimal immune response to rabies vaccine.<sup>5</sup></li> <li>Immunosuppressive agents should not be administered during post-exposure prophylaxis unless essential for the treatment of other conditions.<sup>8</sup></li> <li>Individuals with a history of severe hypersensitivity reactions to egg or egg products should be given an HDCV vaccine as in Imovax® Rabies.<sup>5</sup></li> </ul>
<b>Possible reactions</b>	See Product Monograph
<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>1,2,5</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</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> <li>2019 October - Alternate route and dose of post-exposure rabies vaccine. Vaccine to be administered I.D. (2-site 0.1 mL) when operationally feasible with the exception of immunocompromised individuals.</li> <li>2022 February 28 - Clarified recommendation for individuals being assessed for pre-exposure rabies vaccine reporting undocumented rabies immunization series.</li> </ul>

## References

- Sanofi Pasteur Limited. (2006, March 9). Imovax® Rabies: Rabies vaccine inactivated (DCO). *Product Monograph*.
- GlaxoSmithKline Inc. (2019 February 25) RabAvert®: Rabies vaccine. *Product Monograph*.
- Alberta Health. Rabies Prevention and Control Manual: Guidance for Public Health and Veterinary Professionals. <https://open.alberta.ca/publications/9781460142639>.
- Personal communication from Sanofi regarding stability of Imovax® Rabies vaccine. (2019-10-17)
- National Advisory Committee on Immunization. (2018). *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)
- World Health Organization (2018) Frequently asked questions about rabies for Clinicians. Retrieved from: [http://www.who.int/rabies/Rabies\\_Clinicians\\_FAQs\\_21Sep2018.pdf?ua=1](http://www.who.int/rabies/Rabies_Clinicians_FAQs_21Sep2018.pdf?ua=1)
- WHO. *Rabies vaccines and immunoglobulins: WHO position April 2018*. Retrieved from: [https://www.who.int/immunization/policy/position\\_papers/pp\\_rabies\\_summary\\_2018.pdf?ua=1](https://www.who.int/immunization/policy/position_papers/pp_rabies_summary_2018.pdf?ua=1)
- Grabenstein, J. D. (2012). *ImmunoFacts: Vaccines and Immunologic Drugs 2013*. St. Louis, MO: Wolters Kluwer Health.
- WHO Expert Consultation on Rabies, third report: WHO Technical Series Report No. 1012, Geneva, 2018. Retrieved from: <https://apps.who.int/iris/bitstream/handle/10665/272364/9789241210218-eng.pdf?sequence=1&isAllowed=y>.
- CATMAT. (2002) Statement on Travellers and Rabies Vaccine. *CCDR 1 March 201, Volume 28, ACS4*. <http://publications.gc.ca/collections/Collection/H12-21-2-28-4.pdf>