



Annex 2: CDC suggested SOP for Rabitec Oral Rabies Vaccination Bait Contacts

Version 1, July 2023

This document is an annex to the 'Oral vaccination of dogs against rabies: Recommendations for field application and integration into dog rabies control programmes' document published by FAO, WHO and WOA in 2023.

Preamble

Mongoose are the primary reservoir for rabies in Puerto Rico and are responsible for hundreds of human rabies exposures annually and several human rabies deaths over the last 10 years. Rabitec is a live oral rabies virus vaccine that is licensed and used in wildlife in Europe to control fox-mediated rabies. This vaccine has been shown safe and effective at vaccinating mongoose, leading to the hopes that rabies virus elimination in Puerto Rico may be possible in the near future. The US Department of Agriculture (USDA), working in collaboration with CDC, began extensive feasibility studies in 2012 including population studies, bait density studies, and placebo vaccination trials. The results are promising and elucidates a pathway for a successful mongoose vaccination program. The following Standard Operating Procedure was developed at the request of USDA to be included in the National Environmental Policy Act (NEPA) application for experimental licensing of Rabitec in mongoose. While the information contained in this document is not intended for public distribution, it is likely to be referenced by state and territorial health experts to inform their local recommendations for addressing human contacts with Rabitec vaccines.

SUGGESTED SOP FOR RABITEC ORAL RABIES VACCINATION BAIT CONTACTS (HUMAN)

**Please note this is a suggested SOP based on currently available evidence. State and county Health Departments are not required to follow this SOP and may alter the components to accommodate their program.*

Rabitec is a 3rd generation live-attenuated rabies vaccine. Safety studies conducted in line with criteria established by the World Health Organization (WHO) and World Organisation for Animal Health (OIE) have found that this product is highly effective at vaccinating target species, while posing no known health risks to the general public. This vaccine construct has been used to control fox-mediated rabies in Europe since 2017, with no reported adverse events in humans. In rare cases, in studies involving severely immune-compromised animals, adverse events were observed. While these adverse events have never been seen in humans, the following guidance provides public health recommendations for human exposure to Rabitec oral rabies vaccines with these rare risks in immune-compromised animals in mind.

Persons with contact to the Rabitec vaccine should seek medical advice and report the exposure and any resulting adverse events to public health authorities. Contact with an intact vaccine bait is **not** considered an exposure. Vaccine exposures may be *direct* (e.g., exposure to the interior contents of a non-intact vaccine sachet) or *indirect* (e.g., scratch or bite from an animal exposed to Rabitec within the preceding 48 hours). Vaccine exposures can also be *minor* (e.g., mucosal, subcutaneous) or *severe* (e.g., intra-muscular, intra-peritoneal, intra-cranial). Thorough washing of vaccine-exposed skin is always recommended. Rabies post-exposure prophylaxis (PEP) may be indicated, depending on the nature of the vaccine contact and the immune status of the individual. Saliva from animals that consumed Rabitec should be avoided for up to 48 hours, as latent residual vaccine may still be present in oral secretions.



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- Rabies PEP is **not** indicated for contact with **intact** vaccine bait. An intact vaccine bait is not considered vaccine contact.
- Rabies PEP is **not** indicated for *immune-competent persons*, regardless of the nature of the exposure. In animal studies, no risks were identified when immune-competent subjects had either minor or severe vaccine exposures.
- Rabies PEP should be **considered** on a case-by-case basis for *immune-compromised persons* with minor vaccine exposure to Rabitec (e.g., Type III, Table 1). In animal studies, no risks were identified when minor exposures occurred. Out of an abundance of caution, PEP can be considered depending on the nature of exposure and degree of immunosuppression.
- Rabies PEP **is** indicated for *immune-compromised persons* who have had a severe vaccine exposure to Rabitec (e.g., Type IV, Table 1). Severe exposures occur when the vaccine is introduced via the intra-muscular, intra-peritoneal, or intra-cranial route. The most likely cause of a severe exposure is from a bite from an animal exposed to the vaccine within the past 48 hours. There are no reports of Rabitec vaccine-related adverse events in humans, but animal studies suggest that such events are possible. Out of an abundance of caution, rabies PEP should be initiated immediately.

This guidance is intended for potential exposures to the general public. Unpublished studies have shown a risk of illness associated with aerosol inoculation into the nasal cavity which may occur during specialized procedures performed in a laboratory (i.e., are not exposures that would be incurred by the general public). Laboratory workers with intranasal or high-dose aerosol exposures should immediately consult their occupational health service and initiate PEP.

This guidance only considers risks associated with exposure to Rabitec vaccine. Additional PEP considerations may be necessary based on the risk of rabies virus exposure as a result of contact with wild or domestic mammals. Persons exposed to an animal suspected to be infected with rabies virus should thoroughly wash the wound and immediately seek medical evaluation.



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Table 1. Type of vaccine-bait contact and subsequent treatment

	Definition	Common routes of exposure	Recommendation
I	Contact with an intact bait	Touching a bait that has no defects	1. No action necessary. Return bait to the location it was found or to a location where people and/or pets will not find the bait (e.g., wooded area).
II	Contact with vaccine virus to intact (unbroken) skin	Lick by an animal* on intact skin Touching a damaged bait	1. Immediate washing of skin with soap and running water 2. Rabies PEP is not necessary
IIIa	Contact with vaccine virus on non-intact (broken) skin Contamination of mucous membranes or conjunctiva with vaccine virus	Licked or scratched by an animal* on non-intact (broken) skin Contamination of mucous membranes or open skin wounds with saliva of animals*	Immune Competent Persons 1. Immediate flushing and washing the wound(s) and adjoining areas with soap and water, preferably under a running tap, for at least 15 minutes. 2. Rabies PEP is not necessary
IIIb			Immune Compromised** 1. Immediate flushing and washing the wound(s) and adjoining areas with soap and water, preferably under a running tap, for at least 15 minutes. 2. While there is no known risk for an adverse event, rabies PEP may be considered based on the severity of immune disorder and degree of vaccine virus exposure
IVa	Penetration of vaccine virus into muscular tissue, or peritoneal or cranial spaces	Severe bites from animals*	Immune Competent Persons 1. Immediate flushing and washing the wound(s) and adjoining areas with soap and water, preferably under a running tap, for at least 15 minutes. 2. Rabies PEP is not necessary
IVb			Immune Compromised** 1. Immediate flushing and washing the wound(s) and adjoining areas with soap and water, preferably under a running tap, for at least 15 minutes. 2. Immediate initiation of rabies PEP

*Animals – animals that have chewed on a vaccine bait and/or vaccine blister during the last 48 hours.

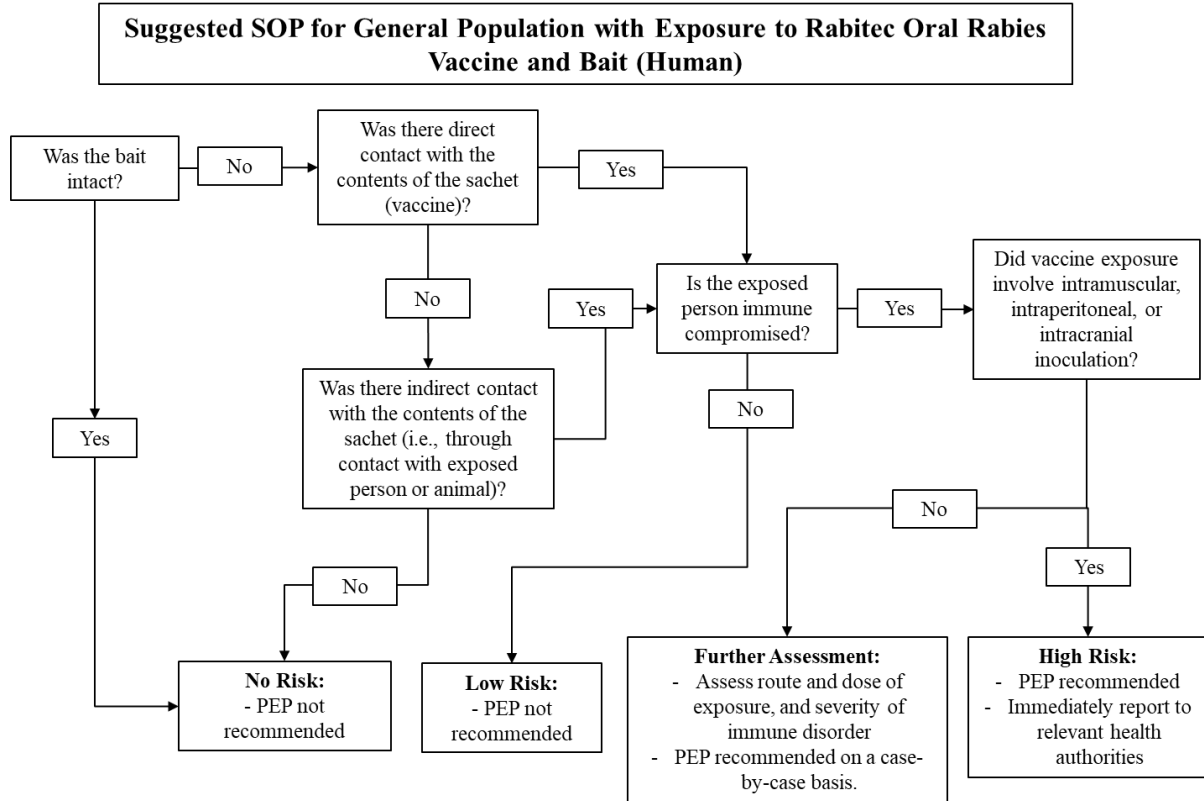
** Interpretation of the severity of immune compromising conditions should be made in consultation with the exposed person's clinician. In animal studies, adverse events were only reported in animals with severe deficiencies in both B or T cell functionality.



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Supplemental Information: Summary of data considered in the development of this suggested guidance

Risk Level	Criteria	Recommendation	Quality of Evidence
I	- Contact with intact bait	- No PEP recommended	Not Applicable
II	- Contact with vaccine to intact skin	- No PEP recommended - Alert appropriate health officials	Not Applicable
Mild Vaccine Exposures (mucosal & subcutaneous contact)			
IIIa	- Immune competent individual	- No PEP recommended - Alert appropriate health officials	Lab: STRONG (n = 305) Field*: STRONG
IIIb	- Immune compromised	- No known risk associated with mild exposure: Assess degree of exposure, severity immune disorder, and recommend PEP on a case-by-case basis. - Alert appropriate health officials	Lab: MODERATE (n = 47) Field*: WEAK
Severe Vaccine Exposures (intra-muscular, intra-peritoneal, intra-cranial contact)			
IVa	- Immune competent	- No PEP recommended - Alert appropriate health officials	Lab: STRONG (n = 259) Field*: STRONG
IVb	- Immune compromised	- PEP recommended - Alert appropriate health officials	Lab: STRONG (n = 129) Field*: WEAK

* Field evidence is based on reports from European Union related to bait contact and reported adverse events to Rabitec. Since data regarding bait contact and immune status has not been made available, this evidence was deemed "weak" for those populations.



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