

Guidelines on managing rabies postexposure (January 2023)



Contents

Document history	4
A. Introduction	6
Purpose and scope	6
Devolved administrations	7
B. Post-exposure risk assessment: does the person need PET?	8
B1. Patient details	10
B2. Date of exposure	10
B3. Which country?	10
B4. Species of animal: was it a bat, primate, rodent or other terrestrial mammal?	11
B5. Country and/or animal risk	12
B6. Category of exposure	12
B7. Site of bite: additional useful information	14
B8. Imported pets (dogs, cats or ferrets) in UK	14
B9. Suspicion that a pet dog, cat or ferret has been illegally imported	15
B10. Animals in quarantine	16
B11. Exotic pets, and non-indigenous animal in zoos or wildlife centres (in UK)	16
B12. Composite rabies risk	17
C. Significant past medical history	18
C1. Immunosuppression	18
C2. Other relevant history	18
C3. Previous rabies pre-exposure prophylaxis or post-exposure treatment	19
D. Treatment recommendations	20
D1. Treatment based on risk assessment	20
D2. What treatment has already been given?	21
D3. Is vaccine required?	22
D4. Is rabies immunoglobulin (HRIG) required?	23
D5. Administering vaccine and HRIG	24
D6. How soon should treatment be started?	25
D7. Is rabies antibody testing required?	25
E. Logistics	26
E1. Issuing rabies vaccine and HRIG	26

E2. The Rabies and Immunoglobulin Service (RIgS)	26
E3. Issuing HRIG from stockholders	28
F. Governance issues	29
G. Rabies vaccines compatible with UK schedule	30
H. Source documents and useful references	33
Annexe 1. Immunosuppression definitions	34
Annexe 2. Country or animal risk	36
Annexe 3. Summary of risk assessment and treatment	45

Document history

Date	Reason for change	Issue number				
January 2015	PHE version. This updates 'HPA guidelines on managing rabies post-exposure prophylaxis (January 2013)'. Changes to the guidance include a new category of 'partially immune' for those individuals who are not fully immune but have received vaccine in the past, advice on what to do if it is more than 10 years since the last rabies vaccine, and information on dealing with animals imported into the country under the EU PETS passport scheme. The guidance is also reformatted to PHE specifications.	1.0				
June 2015	Rewording of section 'B9 Imported pets (dogs, cats or ferrets)', paragraph 'Background' to clarify that pets from EU or listed countries do not need a blood test, and the waiting period is only 21 days post vaccination.	1.1				
April 2016	Updated information about the new Rabies and Immunoglobulin Service and updated risk assessment to include HRIG for primate category III bites to the head and neck.					
June 2017	Updated contact information. Additional information provided on what to do if a fully immunised patient has received HRIG as part of the management. Revised information on the use of the revised rabies risk assessment form.					
June 2018						
April 2019						
October 2019	-					
August 2020	Updated information on bats in the UK, PET passport scheme on leaving the EU and process for issuing vaccine and immunoglobulin through Colindale.	6.0				

Date	Reason for change	Issue number
September 2021	Updated information on rabies vaccine availability in NHS Trusts in England, importation of animals into UK, definitions of immunosuppression, hours of operation of the RIgS team and availability of HRIG. Reformatted along UKHSA guidelines.	7.0
January 2023	Updated information on timing of blood samples for immunosuppressed patients and importance of taking the potency from the vial and not from the packaging.	8.0

A. Introduction

Rabies is an acute viral encephalomyelitis caused by several members of the Rhabdoviridae family. It transmits through infected saliva via bites or scratches from rabid animals (in particular dogs). It is almost invariably fatal once symptoms develop.

Rabies still poses a significant public health problem in many countries in Asia and Africa where 95% of human deaths occur. Post-exposure treatment (PET) using rabies vaccine with or without rabies immunoglobulin (HRIG) is highly effective in preventing disease if given correctly and promptly after exposure.

The UK has been free of rabies in terrestrial animals since 1922. However, European Bat Lyssavirus 1 (EBLV1) was found for the first time in serotine bats (*Eptesicus serotinus*) in southern England in 2018, and European Bat Lyssavirus 2 (EBLV2), a rabies-like virus, has been found in Daubenton's bats (*Myotis daubentonii*) across the UK. A soprano pipistrelle (*Pipistrellus pygmaeus*) tested positive for lyssavirus antigen in 2020, but there was insufficient RNA to type the virus.

Further information, <u>guidance and the risk assessment form</u> are available on the rabies pages of the UKHSA website.

Purpose and scope

This guidance provides a practical guide to undertaking risk assessment of potential rabies exposures and the correct use of PET. It is aimed at duty doctors at Colindale, health protection teams and other health professionals who may be involved in the assessment and management of potential rabies exposures. It also describes the logistics of issuing vaccines and immunoglobulins as appropriate, and the clinical governance aspects of the Rabies and Immunoglobulin Service (RIgS), Colindale. A separate document deals with the risk assessment of other pathogens associated with animal bites which should be used in conjunction with this document if necessary.

Requests for pre-exposure vaccine or advice on possible human rabies are outside the scope of this document and should be managed as follows:

- A possible case of clinical rabies all calls should be referred to one of the RIgS consultants, UKHSA Colindale (0330 128 1020), or out of hours to Colindale Duty Doctor (0208 200 4400); additional information can be found on the UKHSA website.
- 2. Vaccines prior to travel refer caller to NaTHNaC (the <u>National Travel Health Network and Centre</u>; or for complex queries from health professionals, advice line: 0845 602 6712).
- 3. Vaccines for those with occupational risk (see <u>Green Book</u>) are the responsibility of the employer, and will no longer be provided through UKHSA. Vaccine will only be provided from UKHSA for those who regularly handle bats on a voluntary basis (that is, not part of

employment) – requests should be made using the <u>pre-exposure risk assessment form</u> and returned by secure e-mail to <u>Ig.clerks@nhs.net</u>.

Individual risk assessment of potential rabies prone exposures should be undertaken promptly, so that post-exposure treatment (PET) can be initiated if required. Although treatment should be started promptly, initiating rabies PET is not a medical emergency, and can often wait until the next day (see section D6). In complex cases treatment can be initiated and further advice sought from consultants within RIgS the next working day.

All risk assessments should be <u>completed using the rabies post-exposure risk assessment form</u> and either directly uploaded into HPZone, or emailed to RIgS by secure email. The form can be encrypted using the button on the form, and the password sent in a separate email.

Devolved administrations

Requests for post-exposure treatment from Scotland, Northern Ireland and Wales should be directed to the appropriate services as given in the <u>Green Book</u>. UKHSA and the Department of Health and Social Care does not supply rabies vaccines for Scotland or Northern Ireland (or the Channel Islands).

B. Post-exposure risk assessment: does the person need PET?

The rabies risk assessment comprises 5 main parts:

- 1. Collection of basic information about the exposed person.
- 2. Details of the exposure incident, and an assessment of the composite rabies risk: Green, Amber or Red.
- 3. Any significant past medical history that might affect treatment including immunosuppression, previous rabies immunisation or treatment.
- 4. UKHSA treatment recommendation based on rabies risk and medical history.
- 5. Treatment already given for this exposure, and further treatment required.

For these steps the following information is required to complete the risk assessment:

- patient name, date of birth, age, address, and NHS number if possible
- date of exposure
- · country of exposure
- species and current health status of animal involved
- category of exposure
- site of exposure
- whether the patient is immunosuppressed or has:
 - any allergies
 - o any previous rabies vaccinations, or
 - o immunoglobulin treatment

This should be recorded in the rabies post-exposure form shown below, which can be found in the <u>UKHSA duty doctor pack and on the GOV.UK website</u>. Boxes in pink are mandatory boxes and need to be completed for all risk assessments. All enquiries should be recorded with the patient details, even if vaccine and/or immunoglobulin are not issued. (<u>Screenshot below</u>).

Screenshot of the request form for rabies post-exposure treatment

UK Health	UK	HSA	Rabie	s and	Imm	unogl	obulir	Serv	ice	Print	
Security Agency		Reque	est for	n for R	abies F	ost Exp	oosure	Treatm	ent		
						F	arm version:			31/12/2023	
HPZone Date				Jse ONL	Υ	1111115	or our	Ble	aS No:		
(DD/MM/YYYY)		dd/m	młyyyy			<u>(h</u>	h:mm):		hh:	mm	
Caller details											
Source of call:							Phone		Phone r		
Caller name: Caller							Alt nun				
organication.							Post c	ode:	Post cor	ie	
Patient details Patient name:				C	-		DI.		DI		
		ame	#VALUE!	Surnam Nuc	ne 1		Phone		Phone		
DOB: Patient	dob Uso Ali	- Entor to	get a ne				Alt nur	nber:	Phone r	number	
address:	036 (1)	C-Elicel Co	y get a ne	willie							
	Postco	ode		Countru							
Exposure detai	ils and	l risk a	ssessn	nent							
Date of exposu	ıre:	d	ld/mm/yy	<i>1</i> 99		Rabie	s risk :		#N	I/A	
Country:					Co	ountry /	Animal		#N	I/A	
Species of ani	mal		Other			Exposu	rick ·			WA.	
Site of exposure (Enter sit	e		LXDUSU	e iisk .		-		
Any additional											
information:											
Significant me					1						
la lke palical acaecely akaples E in Geera Baal	ч		, 1	Full details including doses							
Other relevant Hx coagulonathies)	(allergi	ies,									
Previous rabies	s vaco	inatio	n histo	ry:							
Details of previou	ıs						Vacci	nation s	tatus :	Choose an item.	
Treatment reco	ommer	ndation	s (for	UKHSA guidelines cli				#N/A			
	_	_				an item.					
Treatment base given?	eg on	HRIG	Sessin	o of va					.zasina	Choose from list	
Dates and deta	ails of			10 01 10		doses		The Or	vaccine	Choose from list	
previous treatn		dO		d3		d7		d14		1	
Further treatme	ant ro			u ₃		ur		ui4			
Vaccine Requi		quireu		A	JJ11	V L -	4.4- :				
No of doses	ieu:									nto alternate s 0, 3, 7, and	
Start UK sched	ا بد مانیا	d2·		"				21	o aa,	5 0, 0, 1, and	
Immunoglobuli				HRIG I	ot no:	JRC22	032		262	IU/mL	
Weight of patie	_		kg	(HRIG	potenc	20	62 IU/ml	ו	Yol =	2.6 ■	
Dose of Immun			IU	As	much	as poss				bulin to be	
Volume of Imm	-									n. Maximum	
No of vials requ	_	0		aase .	OF ZU N	J per kg		y weigh adad	C. Which	h must not be	
How soon shou									Date		
<i>ndard issue of y</i> Addising a	accine	and R	lG from	Colinda	ale is N	fondar-	Thursday	(before	3:36 ps	n) for nest dag c	
Additional advice!											
information	Ant	ibody t	est requ	ired?							
Doctor/Nurse p	erforr	ning ris	sk asse	ssmen	Entern	ame		Date:			
BEBS& selberieslies	Entern			Signal				GMC N	o:	Enter GMC #	

B1. Patient details

Complete the patient details as indicated. The PET form also acts as the written order if vaccine or immunoglobulin is issued. It is a legal requirement for these cases to record the date of birth (4 digits for the year), age if under 18 years old (the form should calculate this for you), and the patient's address. (Screenshot below).

Firstnar	ne		Family n	ame	Phone nu	ımber:	Phone number
dd/mm/	уууу	######	NHS no:		Alt numb	er:	Phone number
Use Alt-	Enter to (get a new	line				
Postcod	e		Country				
Risk Asses	sment (for recei	nt incide	nts click here)			
	dd/mm/yyyy		yy	Rabi	es Risk :		#N/A
	Ch	hoose from list Country		Country / Anir	Country / Animal risk :		#N/A
	Ch	oose fron	se from list Exposu		ure risk :		Choose an item.
y part):		Enter sit	e				
ation:							
	Use Alt- Postcod Risk Asses y part):	Postcode Risk Assessment (Cr Ch y part):	Use Alt-Enter to get a new Postcode Risk Assessment (for received dd/mm/yy Choose from Choose from y part): Enter sit	Use Alt-Enter to get a new line Postcode Country Risk Assessment (for recent incider dd/mm/yyyy Choose from list Choose from list y part): Enter site	Use Alt-Enter to get a new line Postcode Country Risk Assessment (for recent incidents click here) dd/mm/yyyy Rabi Choose from list Country / Anir Choose from list Exposi y part): Enter site	Use Alt-Enter to get a new line Postcode Country Risk Assessment (for recent incidents click here) dd/mm/yyyy Rabies Risk: Choose from list Choose from list Exposure risk: y part): Enter site	Use Alt-Enter to get a new line Postcode Country Risk Assessment (for recent incidents click here) dd/mm/yyyy Rabies Risk: Choose from list Choose from list Exposure risk: y part): Enter site

B2. Date of exposure

Risk assessment should be undertaken as soon as reasonable following exposure, so that PET, if required, can be started promptly. The incubation period for rabies is typically one to 3 months, but may vary from less than one week to greater than 2 years. Due to the potentially long incubation period for rabies there is no time limit for giving PET and all potential exposures should be risk assessed. This will include knowing what the animal and/or country risk was at the time of the exposure.

If the exposure is more than one year ago, vaccine may still be given although HRIG is not generally indicated. Specialist advice should be sought from the RIgS team.

B3. Which country?

The risk of rabies in each country takes into account the presence or absence of endemic rabies in domesticated cats and dogs (companion animals) and the presence or absence of rabies in wildlife.

All countries should be considered as risk countries for bat exposures, including the UK and Ireland which are considered low risk for bat bites.

The combined risk of rabies according to geographical location (country, island and territory) and animal exposure is updated regularly. This information is incorporated into the <u>Rabies PET form</u> and the most recent version of the combined country and/or animal risks can be found on the UKHSA website.

B4. Species of animal: was it a bat, primate, rodent or other terrestrial mammal?

99% of human rabies cases occur following a deep bite from a rabid dog. However an exposure to infected cats, wild carnivorous species like foxes, raccoons, skunks, jackals and wolves, and insectivorous and vampire bats can also lead to human rabies infection.

All mammals

All warm blooded mammals and bats, including those that are apparently healthy, may pose a risk. Even exposures from vaccinated animals need to be reviewed as transmission of rabies may still be possible. Carnivores generally pose a greater risk for transmitting the virus to humans than herbivores, such as cattle, horses, deer, and so on.

Domestic dogs and cats

The natural history of rabies in domestic dogs and cats is that an animal shedding rabies virus through its saliva will be in the terminal phase of illness, and is unlikely to be behaving normally.

If the animal is observed, remains well and behaves normally 15 days after the date of an exposure it will not have had rabies infection at the time of exposure.

The decision whether to start post-exposure treatment during the 15 day period should be based on a full individual risk assessment of the circumstances of the incident. This includes health and immunisation status of the animal, the nature of the incident (provoked or non-provoked) and how well the animal can be observed, and whether the exposed person is immunocompetent. Generally not starting treatment is only appropriate if it is a family pet, a provoked exposure, and the owners will promptly report any change in animal behaviour, and the individual is not immunosuppressed. If in doubt, start treatment.

Rodents and monkeys

Rabies-infected rodents and primates have been sporadically described in countries where rabies is endemic. Although the risk of transmission of rabies from a rodent (that is, rat or mouse) or primate bite is extremely low, all rodent and primate bites should be assessed.

Bats

All bats, including those in the UK, may carry rabies-related viruses and so careful assessment of potential exposure is required. Bats may carry rabies and related lyssaviruses without signs of disease. Therefore exposure to bats or their secretions may constitute an exposure to virus even in countries which are declared rabies free in terrestrial mammals.

In the UK, bats are the only reservoir of rabies-related lyssaviruses (EBLV1 and EBLV2), but they are a protected species and cannot be destroyed to determine rabies status if caught.

B5. Country and/or animal risk

A combination of the species of mammal and the rabies status of the country is used to determine if the combined country or animal risk is considered to be 'No risk', 'Low risk' or 'High risk'.

All countries apart from the UK and Ireland are considered 'High risk' for a bat exposure: the UK and Ireland are considered 'Low risk' for bat exposures.

All countries where rabies is present in terrestrial animals (either endemic rabies or rabies in wildlife) are considered to be 'Low risk' for rodent and monkey exposures.

In some countries there is an additional risk for some wildlife species, that is, foxes, skunks and raccoons in the USA, and foxes in certain countries in Eastern Europe. In these circumstances the country and/or animal risk would change from 'Low risk' to 'High risk'.

The post-exposure treatment form will automatically determine the country or animal risk based on the information that is entered for the country where the exposure took place and the animal species involved. The information is also available on the Rabies risk by country website and in Annexe 2.

Non-indigenous animals or bats in zoos or wildlife centres will need a separate risk assessment, including whether the animal or bat was bred in captivity, contact with other animals or bats (either wild or recently brought into the zoo or centre) and so on. Further advice can be obtained from the RIgS team.

B6. Category of exposure

The assessment of exposure needs to take into account the risk of direct physical contact with saliva, neural tissue and other body fluids. The assessment will be different for terrestrial mammals and bats.

In the UK most bat bites are felt, not seen, and rarely cause an obvious break in the skin, but should still be considered a direct physical exposure (category 3). UKHSA recommends that all bat bites should be treated.

In the UK and Ireland most bats found in houses and attics are pipistrelles, which are rarely infected with rabies-related viruses. Healthy bats avoid contact with humans, therefore bats behaving normally (that is, flying into a room but not grounded or acting aggressively) do not constitute any risk (category 1). The only exception to this is where the individual, for specific

reasons such as age, intoxication, or mental impairment cannot give a reliable history of a potential bite or other exposure and therefore should be considered a category 2 exposure. For countries outside the UK and Ireland, any bat found in the room of a sleeping or intoxicated person should be considered a category 2 exposure. In the USA, 50% of human rabies with bat-variant rabies virus have resulted from unrecognised bat bites.

Category	Terrestrial mammals	Bats
1	No physical contact with saliva For example: • touching, stroking or feeding animals	No physical contact (that is, no direct contact with the bat's saliva) For example: • touching a dead bat • touching a bat where the person was protected by a barrier capable of preventing saliva contact, such as a boot, shoe, or appropriate protective clothing • a bat in the same room as a person (including a sleeping person) in the UK or Ireland
2	Minimal contact with saliva and/or unable to infiltrate wound with HRIG if needed For example: • bruising or abrasions • licks to broken skin (that is, over insect bites or scratches) • scratches • bites which do not break the skin	 Uncertain physical contact (that is, where there has been no observed direct physical contact (with saliva) but this could have occurred) For example: handling a live bat without appropriate protective clothing (that is, gloves) a bat becoming tangled in hair potential contact with a bat in the UK or Ireland in someone who is unable to give an accurate history of an exposure (that is, intoxicated individual, young child, individual with mental impairment) any bat found in the room of a sleeping person outside of the UK or Ireland)
3	Direct contact with saliva For example: • severe or deep lacerations (that is, down to the muscle) • bites that break the skin • contact of mucous membranes with saliva (for example, licks)	Direct physical contact with bat's saliva For example: all bites or scratches contamination of mucous membrane with saliva or urine

B7. Site of bite: additional useful information

The site of the bite should be given if known. If the bite is to the head or neck and treatment with HRIG required, PET must be started as soon as possible within 12 hours of reporting.

If the animal was a terrestrial mammal (wild or domestic), these details are useful:

- if the animal has died, does laboratory examination of the animal's brain confirm rabies?
- is rabies known or suspected to be present in the species in the locality?
- is there a known owner and are they contactable?
- was the animal behaving normally at the time of the incident?
- had it been immunised against rabies?
- if the animal was a dog or a cat, did it become ill while under observation?
- is the animal non-indigenous or imported? If imported it is important to determine the risk of rabies in both the country of potential exposure and the country of origin of the animal

B8. Imported pets (dogs, cats or ferrets) in UK

There are specific rules for bringing a pet dog, cat or ferret to Great Britain which may allow the animal to enter the UK without quarantine. The pet must have: a microchip, pet passport (this will vary depending on the country the animal is coming from), rabies vaccination and tapeworm treatment if entering from certain countries. Animals should be at least 12 weeks old before receiving rabies vaccine.

If travelling from a Part 1 or Part 2 listed country, a 21 days waiting period must be completed after the rabies vaccine before entry to the UK. If travelling from an unlisted country, the animal requires a blood test 30 days following the date of vaccination and to complete a 3 month waiting period from date of blood sampling. All pets must travel with either a pet passport or an official third country veterinary certificate issued by an authorised vet. Further details on bringing pets into Great Britain can be found on the <u>Bringing your pet dog, cat or ferret to Great Britain</u> web page.

After the UK left the EU, it became categorised as a Part 2 listed country and pet passports issued in Great Britain (England, Wales and Scotland) can no longer be used for travel to an EU country or Northern Ireland. Further information on implications for pet travel to the EU and Northern Ireland can be found on the <u>Taking your pet dog</u>, cat or ferret abroad web page.

B9. Suspicion that a pet dog, cat or ferret has been illegally imported

All suspected illegally imported animals should be reported to, and investigated by, a Trading Standards officer. Vets who are suspicious about the compliance or legality of an imported animal should report this to the local Trading Standards office, or in London boroughs to Animal Health, City of London (through the Heathrow Animal Reception centre: 0208 745 7894). Details of local Trading Standards offices can be found on the Find your local Trading Standards office website.

Suspicion that a pet may have been illegally imported is not the same as suspicion of rabies. Where it is suspected that a pet is not compliant with the pet travel rules the local Trading Standards office should be contacted and they may decide to quarantine the animal.

Suspicion of rabies in an animal

Rabies is a notifiable disease in animals. If suspected, there is a legal requirement to notify the duty vet in the local APHA office (Defra Rural Services Helpline on 03000 200 301). A Notifiable Disease Investigation (NDI) is then started by APHA and an NDI report is sent (as is any follow-up report) to the RIgS team at Colindale, to alert them to the possibility of an animal with suspected rabies. A Defra approved veterinary officer (VO) visits the premises to assess the animal, and may rule out suspicion of rabies at this visit.

If rabies cannot be ruled out during the official veterinary inquiry then the VO will ask for the animal to be euthanised and tested to confirm or rule out a diagnosis of rabies. The animal carcase is sent to the Rabies Reference Laboratory at APHA Weybridge for these diagnostic tests. Initial results are usually available within a few hours of the carcase arriving at the laboratory.

No public health action should be initiated prior to this decision to euthanise and test.

Public health response

The responsibility for advice on the requirement for post-exposure treatment lies only with the RIgS consultant (or Colindale duty consultant if out of hours) in collaboration with the local health protection team, and not Trading Standards or a vet. Where possible, decisions should only be made during working hours.

Exposure to a non-compliant pet animal

All animals suspected to be illegally imported should be reported to, and investigated by, the local Trading Standards office. Post-exposure treatment should not be started solely on the basis that an animal is illegally imported. If the animal is also behaving abnormally it should be

assessed as soon as possible by a vet, and post-exposure treatment should not be initiated until further assessment has taken place (see below).

Exposure to a pet in the UK displaying signs of rabies

The RIgS consultant in collaboration with the Emerging Infections and Zoonoses section and the appropriate local health protection team will coordinate or oversee risk assessment of all persons (owner and household, vet, and so on) who have been exposed to the animal.

(It is possible, however, that the private vet, VO or Trading Standards officer may already have advised individuals in contact with the animal to seek medical advice or vaccination from their general practitioner).

If the risk assessment considers that the exposure does not require immediate treatment (that is, exposures other than head and neck), then decisions about post-exposure treatment can await the initial results of rabies testing in the suspect animal.

In the event of a head and neck exposure then rabies post-exposure treatment may need to be started before results are available.

If rabies is confirmed in the animal by APHA an incident management team will be convened to coordinate public health actions.

B10. Animals in quarantine

All staff working with animals in Defra-authorised quarantine premises should have received pre-exposure vaccination. As the animals are under observation, generally there is no need to treat exposures in quarantine unless rabies is confirmed.

B11. Exotic pets, and non-indigenous animal in zoos or wildlife centres (in UK)

Exotic pets are not illegal in the UK, although a licence is required to keep some types of animal. A full risk assessment should be done, with specific emphasis on ascertaining how long the animal has been in this country, its source (captive bred, wild-caught, and so on), whether the animal has been vaccinated against rabies and the circumstance of the exposure. Importation of animals that are not domestic animals or pets should comply with the Balai Directive on the <u>Guidance on importing and exporting live animals or animal products</u> web page.

B12. Composite rabies risk

Using the combined country or animal risk and the category risk, a composite rabies risk is given a Red, Amber or Green rating. This rating is then used with the past medical history to determine what treatment, if any, is required. All exposures with a Green composite risk rating do not need treatment for this exposure, unless there are extenuating circumstances in the additional information field (see section <u>B7</u>).

Table 1. Composite rabies risk table

Country or animal risk	Category 1 exposure	Category 2 exposure	Category 3 exposure
No risk	Green	Green	Green
Low risk	Green	Amber	Amber
High risk	Green	Amber	Red
Confirmed rabid animal*	Green or amber*	Red	Red

^{*} Advice should be sought from the RIgS team in the assessment of these contacts.

C. Significant past medical history

Information is required in 3 main areas:

- 1. Is the patient severely immunosuppressed?
- 2. Does the patient have a relevant past medical history requiring caution when given vaccines or immunoglobulin?
- 3. Has the patient received any previous (that is before the current incident) rabies vaccines and/or immunoglobulin?

(Screenshot below)

	Significant medical history								
C1	Is the patient severely immunosu (see chapter 6 in Green Book)	ppressed?	Full detai	details including doses					
C2	Other relevant Hx (allergies, coag	julopathies)							
C3	Previous rabies vaccination histo	ory:							
	Details of previous courses			Vaccination status :	Choose an Item.				
	+ 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	BUE THE							

C1. Immunosuppression

Severe immunosuppression is described in <u>chapter 6 of the Green Book</u> as the conditions where the individual should not receive live vaccines (see also <u>Annexe 1</u>).

Anyone who falls into any of the groups listed should be considered to be immunosuppressed and will require treatment with 5 doses of vaccine and HRIG for any Red or Amber exposures, and follow up blood tests at the time of the 5th dose of vaccine (day 30). The vaccines are given by the intramuscular (IM) route at the following intervals: 0, 3, 7, 14 and 30 days. Day 0 is the day of first vaccine **not** necessarily the day of exposure. If vaccination has already been started without HRIG, then because of the potential interference of HRIG with the immune response, the course of vaccines/HRIG should be restarted at d0 with HRIG given no later than the d3 vaccine.

Full details, including doses of medication should be provided on the form so that the degree of immunosuppression can be assessed.

C2. Other relevant history

This should include any history of allergy or bleeding disorders. There are no contra-indications for rabies vaccination and/or HRIG if the risk assessment indicates it is needed. However, if there is a history of allergy to any of the excipients, the vaccine/HRIG should be given under close medical supervision with the ability to appropriately manage anaphylactic reactions.

Intramuscular injection is the preferred route of vaccine administration. However, for individuals with a bleeding disorder vaccinations should be given by subcutaneous injection to reduce the risk of bleeding.

C3. Previous rabies pre-exposure prophylaxis or post-exposure treatment

For those without severe immunosuppression (see section C1) the immune status will be based on history of previous vaccination either as part of rabies post-exposure treatment or pre-exposure prophylaxis given before the current exposure. Ignore any treatment given following the current incident being assessed, as this will only affect what further treatment needs to be given (see section D2). Full information of previous vaccinations should be given on the form.

Immunosuppressed

See section C1.

Fully immunised

At least 3 documented doses of rabies vaccine (on at least 2 separate days, either as a complete primary pre-exposure course or as part of a 4 or 5 dose post-exposure treatment course) or documented rabies virus neutralising antibody (VNA) titres of at least 0.5 IU/ml. If within the last 3 months the patient has completed a rabies post-exposure treatment course (either 4 doses of vaccine, or 2 doses if previously fully immunised), no further treatment is required for a more recent exposure.

Partially immunised

Person who has had an incomplete or inadequate primary vaccination course (that is, less than 3 doses of intramuscular pre-exposure prophylaxis, or anything less than 3 doses of intradermal vaccine over 2 separate days), or VNA never greater than 0.5 IU/ml.

Non immunised

Person who has never received pre- or post-exposure immunisation with rabies vaccine.

D. Treatment recommendations

(Screenshot below)

	Treatment recommendations (for UKHSA guidelines cl								#N/A		
D1	Treatment based o	n risk assessn	nent:		Choose	an item.					
	Treatment already gi	ven? HRIG		No o	f vaccin	e doses		Type of	vaccine?	Choose from list	
D2	Dates and details			-							
	previous treatmen	t: d0		d3		d7		d14			
	Further treatment	required		-		,					
D3	Vaccine Required?	?		04	-l l				:414-		
	No of doses			Stan				_	ınto aite ys 0, 3, 7,	rnate arms by	
	Start UK schedule	at d?:			muan	iusculai i	noculatio	ni on da	73 0, 3, 7,	and 21	
D4	Immunoglobulin R	equire		HRIG lot	no:	JRC22032	2		262	IU/mL	
	Weight of patient (kg):	kg	(HRIG po	tency:		262 IU/ml)	Vol =	2.6 ml	
	Dose of Immunogl	obulin 0	IU	As mu	ch as po	ssible of	the imm	unoglobi	ılin to be	infiltrated at the	
	Volume of Immune	oglobul 0.0	mL	site of the bite/laceration. Maximum dose of 20 IU per kg of body							
	No of vials require	d: 0				weight, w	hich mus	st not be	exceeded	d.	
D6	How soon should t	treatment be st	tarted:						Date		
	NB standard iss	ue of vaccine ar	nd RIG fro	om Colind	ale is Mo	nday-Thui	rsday (bef	ore 3:30 p	m) for ne	kt day delivery	
	Additional advice/										
D7	information	A 411 1 4		10							
יט	given:	Antibody te									
	Doctor/Nurse perfo	orming risk ass	essmen	ıt:	Enter na	ame		Date:			
	UKHSA authorisation	Enter name		Signatu	re:			GMC No	:	Enter GMC #	

D1. Treatment based on risk assessment

A formal risk assessment based on the composite rabies risk and the vaccine status should be performed and this will be shown on the form. This recommendation should be used as a basis, for deciding on the treatment course, and this box must be completed for all risk assessments.

Recommended treatment will generally fall into 5 categories (see the algorithms on following pages):

- 1. no risk and therefore no treatment required
- 2. vaccine only
- 3. vaccine and HRIG
- 4. vaccine, HRIG and blood test with the last dose of vaccine (see section C1)
- 5. observation of animal (domestic cats and dogs only see section B4)

HRIG is not required more than 7 days after the first dose of vaccine, or more than one day after the second dose. HRIG is also not required for partially immunised patients (unless immunosuppressed).

Post-exposure treatment based on composite rabies risk and vaccine status

	Post-exposure treatment										
Composite rabies risk	Non-immunised or partially immunised	Fully immunised	Immunosuppressed								
Green	None	None	None								
Amber	4 doses of vaccine d0, d3, d7, d21	2 doses of vaccine d0, d3-7	HRIG and 5 doses of vaccine d0, d3, d7, d14 and d30**								
Red	HRIG* and 4 doses of vaccine d0, d3, d7, and d21	2 doses of vaccine d0, d3-7	HRIG and 5 doses of vaccine d0, d3, d7, d14 and d30**								

^{*} HRIG is not required more than 7 days after the first dose of vaccine, or more than one day after the second dose. HRIG is not required for partially immunised patients (unless immunosuppressed).

D2. What treatment has already been given?

If treatment has already been started find out details of what has been given, route of administration and timing. Consider whether:

- treatment is appropriate to exposure
- which vaccine (type and name of vaccine if known) is this compatible with vaccines given in the UK? (see <u>section G</u>)
- what vaccine schedule and route has been used is this compatible with the UK schedule?
- has human rabies immunoglobulin (HRIG) been given if not, is this indicated and is there still time to give this?
- Finally, how soon does the patient need to receive their next treatment?

If no treatment has been started, post-exposure treatment at least with vaccine, should ideally be started within 24 hours of contact with UKHSA. However for high risk exposures, such as severe and multiple bites to the head and neck or from a confirmed rabid animal, treatment must be started as soon as possible within 12 hours of reporting. All NHS Trusts in England should have locally available rabies vaccine so prompt treatment can be initiated.

Global vaccines: compatibility with UK vaccines

Most vaccines used globally are now derived from primate or avian diploid cell culture and are compatible with the UK vaccines (see <u>Table 3</u> in section G). However, a wide variety of different

^{**} Send sample for antibody testing.

schedules are used, including multiple doses on the same day, and intramuscular and intradermal administration. Information including dates and route of administration should be collected when possible, and further advice sought from the RIgS team as appropriate.

D3. Is vaccine required?

The UK schedule for immunocompetent individuals is 4 vaccines given by the intramuscular (IM) route at the following intervals 0, 3, 7, 21 days.

Day 0 is the day of first vaccine, **not** necessarily the day of exposure.

Movianto and vaccine holders usually only hold one of the following vaccines (depending on availability), either human diploid cell (HDCV), chick embryo (PCECV), or Vero (PVRV)-derived vaccine, and this will be the only possible vaccine that can be issued. If an individual insists on a particular type of vaccine not held within the UKHSA supply, this will have to be sourced and paid for privately by that individual.

If a dose is missed, or timing has been compromised, the next vaccine should be considered as the missed dose, and subsequent intervals readjusted.

If a person is travelling and has difficulty in achieving the specified interval for PET, it is most important to deliver the first 3 vaccines with plus or minus one day.

The fourth and final dose of rabies vaccine PET must not be given before day 21. If the fourth dose of vaccine has been given before day 21 a fifth dose of vaccine should be administered. This should be 2 weeks after the fourth dose. Enter the date of the fourth vaccine in the d14 box, and change the recommended treatment to 5 doses of vaccine.

In a patient who is partially immunised, a full course of 4 doses of rabies vaccine should be given, but there is no need to issue HRIG.

In a patient who is fully immune at the time of exposure the UK schedule is 2 vaccines at day 0 and day 3 to 7.

If an immunocompetent patient who is fully immune is inadvertently given HRIG they will need a complete 4 dose course of vaccines.

Patients started on alternative regimens

Most of the vaccines available globally are compatible with the UK schedule. If the type of vaccine administered elsewhere is compatible with the UK schedule, then convert timing of doses to closest UK vaccine dose. If the vaccine is not compatible, please contact RIgS for further advice.

If 2 doses of vaccine have been given on the same day, consider this to be a single dose of vaccine rather than 2 doses.

If a dose is missed, or timing has been compromised, the next vaccine should be considered as the missed dose, and subsequent intervals readjusted.

In the UK we no longer give a 28 to 30 or 90-day dose in immunocompetent individuals. If 4 doses of vaccine have been given according to the UK schedule then there is no need to give a dose at day 28 to 30 or day 90.

D4. Is rabies immunoglobulin (HRIG) required?

The mainstay of rabies post-exposure treatment (PET) is rabies vaccine. Human rabies immunoglobulin (HRIG) may provide short term immunity in the first 7 days post initiation of treatment.

The total antibody level induced by active immunisation (vaccine) is many orders of magnitude greater than can be provided by passive immunisation (HRIG). For this reason HRIG is not given more than 7 days after the first dose of rabies vaccine or to an individual who is already partially or previously immunised. HRIG is not indicated if the person has already received 2 doses of rabies vaccine, (that is, d0 and d3 doses) or if the exposure was more than 12 months previously.

HRIG is manufactured from non-UK human blood products. The final formulation is a liquid and the potency of the material is assessed in international units (IU/mI). The maximum dose is 20 IU/kg, adults and children (all ages), and should not be exceeded as it may inhibit the immune response to rabies vaccine.

The packaging of the HRIG will have the minimum quantity and potency of immunoglobulin in the vial. This must not be used for calculating the dose required. Instead the potency recorded on the vial itself must be used.

The preparations of HRIG available for dispensing do vary in potency and volume. It is therefore **critical** to know the following:

- the potency of the current batch in use; information about potency of batches in current use is encoded into the rabies PET form, is available on the UKHSA website, is also available from RIgS team (0330 128 1020), and is on the individual vial itself
- weight of the patient
- volume that is contained in the vials (vials contain 1.5 to 4mls, depending on batch and manufacturer)

If the weight (in kilograms – there is a calculator on the 'Weight converter' page to convert stones and pounds to kilograms if needed) and the lot number of the HRIG to be issued are

entered into the form, the dose, volume and number of vials to be issued will be calculated, and be automatically given on the patients letters.

Alternatively the correct volume for each patient should be calculated as indicated below:

Worked example 1

Child weight 19 kg, potency of BPL product is 180 IU/ml, vials contain 2.5ml Required units total = $19 \times 20 \text{ IU} = 380 \text{ IU}$ Need to administer 380/180 = 2.1mlNeed to supply one vial, there will be some wastage, which should be discarded

Worked example 2

Adult weight 70 kg, potency of Berirab P product is 150 IU/ml, vials contain 2ml Required units total = $70 \times 20 \text{ IU} = 1,400 \text{IU}$ Need to administer 1,400/150 = 9.3 mlNeed to supply 5 vials, there will be some wastage, which should be discarded

Equine immunoglobulin (eRIG) or rabies monoclonal antibody (mAb) products may be used as part of rabies post-exposure treatment in other countries where access to HRIG is limited. If eRIG or mAb have been administered overseas, HRIG is not required.

D5. Administering vaccine and HRIG

Vaccine is given in the deltoid muscle by intramuscular injection. Each sequential dose should be given in alternate deltoids. Suggest starting in nondominant arm. The schedule is indicated in the letter and calendar that should accompany a copy of the risk assessment form.

Immunoglobulin (HRIG) acts to neutralise the virus at the site of the wound and to be effective HRIG must be infiltrated around the site of the wound. If it is not possible to infiltrate the whole volume at the site then any excess can be given by intramuscular injection in the anterolateral thigh. Only in the case of mucous membrane contamination should the whole volume of HRIG be given intramuscularly.

If more than 5ml (2ml in children under 20kg) of HRIG needs to be administered intramuscularly it should be given in divided doses, at different sites.

Vaccine and HRIG should never be given at the same anatomical site.

Adverse reactions to rabies vaccine and immunoglobulin are briefly discussed in the <u>Green</u> Book.

D6. How soon should treatment be started?

Although treatment should be started promptly, initiating rabies PET is not a medical emergency. In most cases rabies vaccine/HRIG can be sent out for administration the next day. However for high risk exposures, such as severe and multiple bites to the head and neck or from a confirmed rabid animal, treatment must be started as soon as possible within 12 hours of reporting. All NHS Trusts in England should have rabies vaccine available so prompt treatment can be initiated, and the vaccine will be replaced if the RIgS team is contacted by the end of the next working day.

Rabies vaccine may also be available through some travel clinics, and they can often provide post-exposure vaccine treatment, although they may charge the patient an administration fee. If vaccine is given for post-exposure treatment, the patient should not be charged for the vaccine itself and the RIgS team can be contacted the next working day, to replace the travel clinic's vaccine.

Vaccines (but not HRIG) can sometimes be obtained from pharmacies on prescription. The patient will be charged, and UKHSA cannot reimburse.

The date of the next vaccine should be completed in the risk assessment form so that the correct schedule can be completed in the accompanying letter and calendar.

D7. Is rabies antibody testing required?

In England, routine measurement of rabies antibody titres post-exposure is not offered for immunocompetent individuals for reasons of expense and practicality. Rabies antibody testing is required for individuals who are immunosuppressed (see section C1) and the blood sample should be taken at the same time as the fifth dose of vaccine (day 30). Depending on the results of testing, further antibody tests may be required. Antibody testing may also be requested in some patients who have started or completed their post-exposure treatment with a vaccine not compatible with the UK schedule, or by the intradermal (ID) rather than the intramuscular (IM) route. Further advice can be sought from the RIgS team.

If antibody testing is recommended by RIgS, a collection pack and prepaid envelope will be sent to the GP surgery for blood collection. The sample (10ml clotted blood or serum sample) should be collected into the tubes provided, the request form completed, and sample and form sent to the Animal and Plant Health Agency (APHA) for testing. The results will be returned to RIgS, who will advise if further treatment or testing is needed.

If there is no clinical indication for testing, the cost will need to be borne by the patient or requesting health facility. If an individual is insistent on this in the absence of clinical indications the cost is approximately £80 and APHA (Rabies Help Line, Monday to Friday 9am to 5pm 0208 415 2280, or main number 0208 225 7611) should be contacted directly to arrange this. Samples should be sent directly to APHA and testing will be charged to the sender.

E. Logistics

(Screenshot below)

				FOR AL	L ISSU	ES					
Vials of HRIG required		0		Dose	Doses of vaccine required			0			
Is this a split issue?				How many issues?				If more than 2 - linked form #			
Issue 1 from Movianto:	N	lo	Mov. #:			İssı	ue 1 from	issuing	centre:	Which centre?	
Recipient doctor #1:	Title an	d name			Telephone number: Telephone -1						
Department (#1)	Enter d	lepartme	ent		Е	E-mail addresses : E-mail address -1					
Delivery address (#1):	Delivery address							E-mail ad	ldress - 2		
	Post co	ode:			Country:			Custome	r verified:		
lmmunoglobulin Issue (#1)		vials of	oglobulin		В	Batch no: SKU: 24RI0			JRC19254 RIG_JRC19254 Exp 30/03/2021		
Vaccine Issue (#1)		vials of	vaccine	sku:				2	4RABIPU	IR	
Movianto #1 Order date		dd/m	m/yyyy		Movian	to #1 Re	ference	Number			

E1. Issuing rabies vaccine and HRIG

Rabies vaccine should be widely available so that post-exposure treatment can be started promptly if needed. All NHS trusts in England should have access to rabies vaccine. Any rabies vaccine that is issued in good faith for rabies post-exposure treatment will be replaced through the Rabies and Immunoglobulin Service (RIgS) at Colindale if notified by the end of the next working day. There is no need to contact the RIgS team for permission to issue.

Vaccines for the completion of the course will be sent out through Movianto.

HRIG is only available at a limited number of stock-holders and through the Rabies and Immunoglobulin Service. It is not available through pharmacies

E2. The Rabies and Immunoglobulin Service (RIgS)

The Rabies and Immunoglobulin Service (RIgS) at Colindale is a cross-divisional service supporting the post-exposure treatment of serious infections, through the development of guidance, provision of clinical advice and issuing of immunoglobulins and antitoxins following a detailed risk assessment. This includes post exposure treatment and clinical management for rabies. RIgS is a busy service, and in the financial year 2019 to 2020 there were over 3,400 calls relating to rabies prophylaxis or post-exposure treatment.

Rabies vaccine and immunoglobulin are procured by UKHSA using the programme budget delegated by the Department of Health and Social Care. Stock is held centrally at Movianto and a small number of stock holders distributed throughout the country.

Colindale is no longer a stock holder, and all product ordered through Colindale will be delivered via Immform. In addition, there are no facilities at Colindale for the administration of vaccine and/or immunoglobulin. The responsibility for arranging administration of vaccine and/or immunoglobulin lies with the requesting clinician.

UKHSA cannot issue vaccines or HRIG for patients outside of England.

The Falsified Medicine Directive (FMD) and Delegated Regulation came into force on 9 February 2019. Vaccines and immunoglobulins provided through RIgS in FMD-compliant packs are subject to the requirements of the Delegated Regulation.

Routine service

RIgS operates between 8am to 5:30pm Monday to Friday. All requests for replacement vaccine and advice about issuing should be directed to this service: 0330 128 1020.

Requests for immunoglobulin or vaccine Monday to Friday will be ordered through Movianto for delivery to a named responsible clinician to arrive the next working day before 2pm. However, there may occasionally be specific urgent situations where HRIG is needed sooner than this, and in these circumstances UKHSA can issue immunoglobulin through a more rapid delivery.

Out of hours service

Clinical advice is available through the Colindale Duty Doctor service, between 9am and 7pm at weekends and bank holidays. Most calls can wait until the next day, so callers after 5:30pm are encouraged to call back the next morning to speak to RIgS or the Colindale Duty Doctor service (see <u>Table 2</u>). Vaccine should be sourced locally, and will be replaced through RIgS the next working day. There is no need to talk to the RIgS team or Colindale before arranging this.

If HRIG is required out of working hours and cannot wait till the next working day, the product may be able to be collected from a local stock-holder or be issued out of hours for delivery the next day. Arrangements for urgent delivery on non-working days should be made by calling the duty doctor between 9am and 7pm.

Table 2. Clinical advice, ordering and issuing of products from Colindale

	Advice, delivery and administration
Weekday working hours	
Monday to Friday, 8am to 5:30pm	Contact RIgS
Monday to Friday, 5:30pm to 7pm	Contact Colindale out of hours duty doctor service
Weekday out of hours	
Monday to Thursday, 7pm to 8am	Administer vaccine
	Contact RIgS the next morning
Weekend out of hours	
Friday 7pm to Saturday 9am	Administer vaccine and contact Colindale out of hours Duty Doctor service the next morning
Saturday and Sunday 9am to 7pm	Contact Colindale out of hours duty doctor service
Saturday 7pm to Sunday 9am	Administer vaccine and contact Colindale out of hours Duty Doctor service the next morning (after 9am)
Sunday, 7pm to 8am	Administer vaccine and contact RIgS the next morning

E3. Issuing HRIG from stockholders

HRIG is held at Movianto and also in various stock holders throughout England. If urgent HRIG is needed it may be more convenient to collect from one of the centres, as opposed to delivery through Movianto. Stock holders provide a collection only service; they do not provide postal delivery.

Current HRIG stock-holders in England are:

- Birmingham
- Cambridge
- Manchester

For UKHSA staff please see the Intranet Rabies Duty Doctor Pack.

F. Governance issues

(Screenshot below)

Doctor/Nurse perf	orming risk assessmer	nt: Enter name	Date:	
UKHSA authorisation	Enter name	Signature:	GMC No:	Enter GMC #
UKHSA Audit				
Consultant name	Enter name	Signature:	Date:	
GMC number	Enter GMC #	Comment		

Colindale calls

All calls must be logged in HPZone and the form uploaded by the end of each working day at the latest.

If calls are taken out of hours, the call should still be recorded in HPZone, the form uploaded, required actions listed and the RIgS clerks informed as soon as possible the next working day.

All calls relating to the provision of rabies clinical advice are subject to audit and must be documented (in HPZone or equivalent) whether vaccine is issued or not. The forms will be regularly reviewed and audited by an UKHSA consultant or member of the RIgS team. This should not delay the issue of vaccine or immunoglobulin as it may take place 24 to 48 hours later.

All those participating in the Colindale duty doctor service should have completed relevant training on risk assessments for rabies post-exposure treatment, for example, viewing the rabies webinar. Participation in Colindale clinical audit and duty doctor training on a regular basis is required.

Initial training for registrars or trainees and new consultants can be arranged through the RIgS team and is an essential requirement for participation in the Colindale duty rota.

Issuing centres

All issues should be recorded and the forms returned to Colindale for audit. In addition all vaccine and HRIG that is used must be recorded in Immform, including any discarded or out of date stock.

G. Rabies vaccines compatible with UK schedule

The table below provides a generic classification of types of vaccine available globally and their compatibility with UK vaccines. Most vaccines available in Europe, N America, Australia, and New Zealand are either HDCV, PCECV or vaccines grown on mammalian cells (PVRV). Further information can be found in the <u>World Health Organization's Expert Consultation on Rabies, third report (2018)</u>.

Table 3. Rabies vaccines available globally and compatibility with UK vaccines

Rabies vaccine/lg	Comment	Manufacturer and likely distribution	Compatible with UK
Human diploid cell vaccine (HDCV)	Immunogenicity efficacy data does exist for this.	Imovax, Pasteur Mérieux Group, Sanofi Pasteur MSD Ltd UK Chengdu Kanghua, Rabivax	*
Purified chick embryo cell vaccine (PCECV)	Immunogenicity efficacy data does exist for this.	(UK licence) Rabavert, Rabipur, Vaxirab-N Chiron vaccines	✓
Purified vero cell vaccine (PVRV)	Vaccine is made on mammalian cells (VERO cells) as an alternative cell substrate to fibroblast cells. This is a licensed vaccine produced in many parts of the world (although unlicensed in the UK), for which formal efficacy data does not exist, but the potency and immunogenicity is evaluated similarly to HDCV and PCECV vaccines. These are generally reliable vaccines.	Variety of manufacturers make this. Possible trade names include Verorab. Abhayrab, Indirab (India) SII Rabivax (India) SPEEDA (CELBIO)	✓

Rabies vaccine/lg	Comment	Manufacturer and likely distribution	Compatible with UK
Purified duck embryo vaccine (PDEV)	The vaccine uses duck embryo cells as substrate. These are inactivated by ß-propiolactone and purified by ultracentrifugation. PDEV contains thiomersal.	Lyssavac, Vaxirab	✓
Primary Syrian hamster kidney cell (PHKCV)	Uses the Beijing strain of the rabies virus and is inactivated with formalin and adsorbed to aluminium hydroxide. The vaccine contains thiomersal.	Local producers in China	✓
Baby hamster kidney cells (BHKV)	The vaccine uses baby hamster kidney cells as substrate and is produced in Russia	Kokav (Russia)	√
Suckling mouse brain vaccine (SMBV)	Vaccines of this sort are generally reliable but may have marginally reduced efficiency with increased risk of side effects.	Used in some countries in S America, including Bolivia	х
Nervous tissue vaccine (sheep, goat)	Nerve tissue vaccines induce more severe adverse reactions and are less immunogenic than cell culture and embryonated egg vaccines; therefore their production and use is not recommended by WHO.	Used in Asia, Ethiopia and Argentina but being phased out	x
Horse Serum (equine RIG or eRIG)	Trade name is not always clear. May be given as treatment alone or with vaccine. Most often found in certain South American and Middle East countries, and India. If this is the only treatment given, need to start PET (Omit HRIG).	EquiRab, CARIG, Rabix IG, Abhay-RIG, Pars, Plasmarab, PremiRab, VINRIG, VINRAB, TRCS eRIG	X

Rabies vaccine/lg	Comment	Manufacturer and likely distribution	Compatible with UK
HRIG		Berirab-P	
		Bayrab	✓
		HyperRab S/D	
		Imogan HRIG	
		Kendrab, KamRAB, KedRABImogram	
		Rabies HT, Rabigam, Rabishield	
		Rabglob	

H. Source documents and useful references

- Immunisation against infectious disease, 'The Green Book'
- Immunisation of individuals with underlying medical conditions, 'The Green Book'
- WHO Expert Consultation on Rabies: third report, April 2018
- Rabies vaccines: <u>WHO position paper: weekly epidemiological record (WER)</u> April 2018, volume 93, pages 201 to 220
- British National Formulary
- Terrestrial animal health code, World Organisation for Animal Health (OIE)
- PETS animal passport scheme
- Falsified Medicines Directive

Further documents relating to rabies, rabies pre-exposure prophylaxis and rabies post-exposure prophylaxis are also <u>available on the rabies page of the duty doctor pack on the Intranet</u> and <u>on the UKHSA website</u>.

Annexe 1. Immunosuppression definitions

Individuals with primary or acquired immunodeficiency states due to conditions including:

- acute and chronic leukaemias, and clinically aggressive lymphomas (including Hodgkin's lymphoma) who are less than 12 months since achieving cure
- individuals under follow up for a chronic lymphoproliferative disorders including haematological malignancies such as indolent lymphoma, chronic lymphoid leukaemia, myeloma, Waldenstrom's macroglobulinemia and other plasma cell dyscrasias (please note: this list not exhaustive)
- immunosuppression due to HIV/AIDS with a current CD4 count of below 200 cells/μl (aged 5 years or less, with a CD4 count below 500 cells/μl) and/or detectable HIV viraemia
- primary or acquired cellular and combined immune deficiencies those with lymphopaenia (less than 1,000 lymphocytes/ul), including aplastic anaemia, or with a functional lymphocyte disorder
- those who have received an allogeneic (cells from a donor) or an autologous (using their own cells) stem cell transplant in the previous 24 months
- those who have received a stem cell transplant more than 24 months ago but have ongoing immunosuppression or graft versus host disease (GVHD)
- persistent agammaglobulinaemia (IgG less than 3g/L) due to primary immunodeficiency (for example, common variable immunodeficiency) or secondary to disease or therapy

Individuals on immunosuppressive or immunomodulating therapy including:

- those who are receiving or have received in the previous 6 months immunosuppressive therapy for a solid organ transplant
- those who are receiving or have received in the previous 3 months targeted therapy
 for autoimmune disease, such as JAK inhibitors or biologic immune modulators
 including B-cell targeted therapies (including rituximab but for which a 6 month period
 should be considered immunosuppressive), monoclonal tumor necrosis factor
 inhibitors (TNFi), T-cell co-stimulation modulators, soluble TNF receptors, interleukin
 (IL)-6 receptor inhibitors, IL-17 inhibitors, IL 12/23 inhibitors, IL 23 inhibitors (N.B: this
 list is not exhaustive)
- those who are receiving or have received in the past 6 months immunosuppressive chemotherapy or radiotherapy for any indication

Individuals with chronic immune mediated inflammatory disease who are receiving or have received immunosuppressive therapy:

- moderate to high dose corticosteroids (equivalent greater than or equal to 20mg prednisolone per day; children 1 mg/kg/day) for more than 10 days in the previous month
- long term moderate dose corticosteroids (equivalent to greater than or equal to 10mg prednisolone per day or children 0.5 mg/kg/day for more than 4 weeks) in the previous 3 months
- adults on non-biological oral immune modulating drugs, for example, methotrexate greater than 20mg per week (oral and subcutaneous), azathioprine greater than 3.0mg/kg/day; 6-mercaptopurine greater than 1.5mg/kg/day, mycophenolate greater than 1g/day, in the previous 3 months
- children on any dose of non-biological oral immune modulating drugs
- certain combination therapies at individual doses lower than stated above, including
 those on greater than or equal to 7.5mg prednisolone per day in combination with
 other immunosuppressants (other than hydroxychloroquine or sulfasalazine) and
 those receiving methotrexate (any dose) with leflunomide in the previous 3 months

Individuals who have received a short course of high dose steroids (equivalent or greater than 40mg prednisolone per day or children 2 mg/kg/day for more than a week) for any reason in the previous month.

Individuals who had received brief immunosuppression (less than or equal to 40mg prednisolone per day) for an acute episode (for example, asthma, COPD or coronavirus (COVID-19)) and individuals on replacement corticosteroids for adrenal insufficiency are not considered severely immunosuppressed and can be treated with the standard post exposure treatment.

Annexe 2. Country or animal risk

This list is accurate as of 27 October 2022 and may not represent the most up to date list of country or animal risks if printed. The most up to date list is available on the UKHSA website. The country or animal risks presented here represent risks assessed by UKHSA for use in rabies post-exposure risk assessments and incorporate the presence or absence of rabies in domestic and wild animals, surveillance systems in place and consideration of UK traveller behaviours.

Bats

Bats may carry rabies-like viruses in countries which are declared rabies-free in terrestrial animals. Therefore exposure to bats or their secretions should be considered as a potential rabies risk wherever in the world this has occurred.

All countries worldwide are considered high risk for bat exposures, apart from the UK and Ireland which are low risk for bats.

Primates and rodents

The risk of rabies transmission to humans from primates or rodents is considerably lower than the risks associated with exposures from other animals, particularly carnivores. All countries where rabies is present in terrestrial animals (that is, low or high risk ratings) are considered to be low risk for any exposures from primates and rodents.

For all other terrestrial animals use the table below:

Table of rabies risk

Country	Risk level
Afghanistan	High risk
Albania	High risk
Algeria	High risk
American Samoa	No risk
Andaman and Nicobar Islands	High risk
Andorra	No risk
Angola	High risk
Anguilla	No risk
Antarctica	No risk
Antigua and Barbuda	No risk

Country	Risk level
Argentina	High risk
Armenia	High risk
Aruba	No risk
Ascension Island	No risk
Australia	No risk
Austria	No risk
Azerbaijan	High risk
Azores	No risk
Bahamas	No risk
Bahrain	Low risk
Balearic islands	No risk
Bali	High risk
Bangladesh	High risk
Barbados	No risk
Belarus	High risk
Belgium	No risk
Belize	High risk
Benin	High risk
Bermuda	No risk
Bhutan	High risk
Bolivia	High risk
Borneo	High risk
Bosnia and Herzegovina	High risk
Botswana	High risk
Brazil	High risk
British Virgin Islands	No risk
Brunei Darussalam	Low risk
Bulgaria	Low risk, but foxes are high risk
Burkina Faso	High risk
Burma / Myanmar	High risk
Burundi	High risk
Cabrera	No risk
Cambodia	High risk

Country	Risk level
Cameroon	High risk
Canada	Low risk, but foxes, skunks and racoons are high risk
Canary Islands	No risk
Cape Verde	No risk
Cayman Islands	No risk
Central African Republic	High risk
Chad	High risk
Channel Islands	No risk
Chile	Low risk
China	High risk
Christmas Island	No risk
Cocos (Keeling) Islands	No risk
Colombia	High risk
Comoros	High risk
Congo (Republic)	High risk
Congo (Democratic Republic of)	High risk
Cook Islands	No risk
Corsica	No risk
Costa Rica	High risk
Côte d'Ivoire	High risk
Croatia	Low risk, but foxes are high risk
Cuba	High risk
Cyprus	No risk
Czech Republic	No risk
Czech Republic, within 50km border Poland / Slovakia*	Low risk, but foxes are high risk
Democratic Republic of the Congo	High risk
Denmark	No risk
Djibouti	High risk
Dominica	No risk
Dominican Republic	High risk
East Timor	Low risk
Easter Island	No risk

Country	Risk level
Ecuador	High risk
Egypt	High risk
El Salvador	High risk
Equatorial Guinea	High risk
Eritrea	High risk
Estonia	Low risk, but foxes are high risk
Ethiopia	High risk
Faeroe Islands	No risk
Falkland Islands	No risk
Fiji	No risk
Finland	No risk
Formentera	No risk
France	No risk
French Guiana	High risk
French Polynesia	No risk
Gabon	High risk
Galapagos Islands	No risk
Gambia, The	High risk
Georgia	High risk
Germany	No risk
Ghana	High risk
Gibraltar	No risk
Greece	No risk
Greenland	High risk
Grenada	Low risk
Guadeloupe	No risk
Guam	No risk
Guatemala	High risk
Guinea	High risk
Guinea-Bissau	High risk
Guyana	High risk
Haiti	High risk
Hawaii	No risk

Country	Risk level
Honduras	High risk
Hong Kong	Low risk
Hungary*	Low risk, but foxes are high risk
Ibiza	No risk
Iceland	No risk
India	High risk
Indonesia	High risk
Iran	High risk
Iraq	High risk
Ireland	No risk
Isle of Man	No risk
Israel	High risk
Italy	No risk apart from Arezzo (see website)
Jamaica	No risk
Jan Mayen and Svalbard (Norway)	High risk
Japan	No risk
Jordan	High risk
Kazakhstan	High risk
Kenya	High risk
Kiribati	No risk
Korea, North	High risk
Korea, South	High risk
Kosovo	High risk
Kuwait	Low risk
Kyrgyzstan	High risk
Laos	High risk
La Reunion	No risk
Latvia	Low risk, but foxes are high risk
Lebanon	High risk
Lesotho	High risk
Liberia	High risk
Libya	High risk
Liechtenstein	No risk

Country	Risk level
Lithuania	High risk
Luxembourg	No risk
Macau SAR	High risk
Macedonia	High risk
Madagascar	High risk
Madeira Islands	No risk
Majorca	No risk
Malawi	High risk
Malaysia	High risk
Maldives	No risk
Mali	High risk
Malta	No risk
Margarita Island	High risk
Marshall Islands	No risk
Martinique	No risk
Mauritania	High risk
Mauritius	No risk
Mayotte	No risk
Menorca	No risk
Mexico	High risk
Micronesia	No risk
Moldova	High risk
Monaco	No risk
Mongolia	High risk
Montenegro	High risk
Montserrat	No risk
Morocco	High risk
Mozambique	High risk
Myanmar (Burma)	High risk
Namibia	High risk
Nauru	No risk
Nepal	High risk
Netherlands	No risk

Country	Risk level
Netherlands Antilles	No risk
New Caledonia	No risk
New Zealand	No risk
Nicaragua	High risk
Niger	High risk
Nigeria	High risk
Niue	No risk
Norfolk Island	No risk
Northern Mariana Islands	No risk
Norway (mainland only)	No risk
Oman	High risk
Pakistan	High risk
Palau	No risk
Palestine	High risk
Panama	High risk
Papua New Guinea	No risk
Paraguay	High risk
Peru	High risk
Philippines	High risk
Pitcairn Islands	No risk
Poland	High risk
Portugal	No risk
Puerto Rico	High risk
Qatar	Low risk
Republic of Korea (South Korea)	High risk
Reunion	No risk
Romania	High risk
Russian Federation	High risk
Rwanda	High risk
Saint Helena	No risk
Saint Kitts and Nevis	No risk
Saint Lucia	No risk
Saint Martin / Sint Maarten	No risk

Country	Risk level
Saint Pierre and Miquelon	No risk
Saint Vincent and the Grenadines	No risk
Samoa	No risk
San Marino	No risk
Sao Tome and Principe	Low risk
Saudi Arabia	High risk
Senegal	High risk
Serbia	High risk
Seychelles	No risk
Sierra Leone	High risk
Singapore	No risk
Slovakia	Low risk, but foxes are high risk
Slovenia	Low risk, but foxes are high risk
Solomon Islands	No risk
Somalia	High risk
South Africa	High risk
South Georgia and the South Sandwich Islands	No risk
South Sudan	High risk
Spain: mainland, Balearic and Canary Islands	No risk
Spain: north African territories of Ceuta and Melila	High risk
Sri Lanka	High risk
Sudan	High risk
Suriname	High risk
Svalbard	High risk
Swaziland / Eswatini	High risk
Sweden	No risk
Switzerland	No risk
Syria	High risk
Tahiti	No risk
Taiwan	Low risk
Tajikistan	High risk

Country	Risk level	
Tanzania	High risk	
Thailand	High risk	
Tibet	High risk	
Timor-Leste	Low risk	
Togo	High risk	
Tokelau	No risk	
Tonga	No risk	
Trinidad and Tobago	Low risk	
Tunisia	High risk	
Türkiye	High risk	
Turkmenistan	High risk	
Turks and Caicos Islands	No risk	
Tuvalu	No risk	
Uganda	High risk	
Ukraine	High risk	
United Arab Emirates	Low risk	
United Kingdom	No risk	
	Low risk for bats	
United States of America	Low risk but foxes, skunks and racoons are high risk	
Uruguay	High risk	
Uzbekistan	High risk	
Vanuatu	No risk	
Venezuela	High risk	
Vietnam	High risk	
Virgin Islands	No risk	
Wake Island and the US Pacific Islands	No risk	
Wallis and Futuna Islands	No risk	
Western Sahara	High risk	
Yemen	High risk	
Zambia	High risk	
Zanzibar	High risk	
Zimbabwe	High risk	

This list is accurate as of 13 December 2022 and may not represent the most up-to-date list of country or animal risks if printed. The <u>most up-to-date list</u> is available on the UKHSA website.

Annexe 3. Summary of risk assessment and treatment

- 1. Determine the combined country or animal risk.
- 2. Determine the category of exposure.

Category	Terrestrial mammals	Bats
1	No physical contact with saliva	No physical contact (that is, no direct contact with the bat's saliva)
2	Minimal contact with saliva and/or unable to infiltrate wound with HRIG if needed	Uncertain physical contact (that is, where there has been no observed direct physical contact (with saliva) but this could have occurred)
3	Direct contact with saliva	Direct physical contact with bat's saliva

3. Determine the composite rabies risk

Country or animal risk	Category 1 exposure	Category 2 exposure	Category 3 exposure
No risk	Green	Green	Green
Low risk	Green	Amber	Amber
High risk	Green	Amber	Red
Confirmed rabies	Green or amber	Red	Red

^{*} Specific advice regarding the risk from certain animals or bats in different countries should be taken into account when using these summary tables.

4. Determine the post-exposure treatment required

	Post-exposure treatment			
Composite rabies risk	Non immunized or partially immunised	Fully immunised	Immunosuppressed	
Green	None	None	None	
Amber	4 doses of vaccine d0, d3, d7, d21	2 doses of vaccine d0, d3-7	HRIG and 5 doses of vaccine d0, d3, d7, d14 and d30	
Red	HRIG* and 4 doses of vaccine d0, d3, d7, and d21	2 doses of vaccine d0, d3-7	HRIG and 5 doses of vaccine d0, d3, d7, d14 and d30	

^{*} HRIG not required if more than 7 days after first dose of vaccine, or more than one day after the second dose or for partially immunised patients (unless immunosuppressed).

About the UK Health Security Agency

UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation's health secure.

<u>UKHSA</u> is an executive agency, sponsored by the <u>Department of Health and Social Care</u>.

© Crown copyright 2023 Version 8

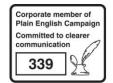
Prepared by: Katherine Russell and Kevin Brown
For queries relating to this document, please contact: Rabies and Immunoglobulin Service
(RIgS) at RIgS@ukhsa.gov.uk

Published: January 2023

Publishing reference: GOV-14000

OGL

You may re-use this information (excluding logos) free of charge in any format or medium, under the terms of the Open Government Licence v3.0. To view this licence, visit <u>OGL</u>. Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.



UKHSA supports the Sustainable Development Goals

