PHE guidelines on rabies post-exposure treatment (June 2017)
PHE guidelines on managing rabies post-exposure (June 2017)

**Document information**

<table>
<thead>
<tr>
<th>Title</th>
<th>PHE guidelines on managing rabies post-exposure cases (June 2017)</th>
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<tbody>
<tr>
<td>Authors</td>
<td>Kevin Brown, ,</td>
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<tr>
<td>Reviewed by</td>
<td>David Brown, Katerine Russell, Mary Ramsay</td>
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<tr>
<td>Version</td>
<td>Final</td>
</tr>
<tr>
<td>Date of Issue</td>
<td>June 2017</td>
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**Document history**

<table>
<thead>
<tr>
<th>Date</th>
<th>Reason for change</th>
<th>Issue number</th>
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<tbody>
<tr>
<td>January 2015</td>
<td>PHE version. This updates &quot;HPA guidelines on managing rabies post-exposure prophylaxis (January 2013)&quot;. 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.</td>
<td>1.0</td>
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<tr>
<td>June 2015</td>
<td>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.</td>
<td>1.1</td>
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<tr>
<td>April 2016</td>
<td>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.</td>
<td>1.2</td>
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<tr>
<td>June 2017</td>
<td>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.</td>
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Document review plan

**Responsibility for review** (disease group lead)  
Kevin Brown

**Next review date**  
2018

**Next issue date**  
-

**QPulse number**  
IMW23301

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About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. It does this through world-class science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. PHE is an operationally autonomous executive agency of the Department of Health.

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Published June 2017
PHE publications gateway number: 2014684
Contents

Document information 2
Document history 2
Document review plan 3
Contact information 3

About Public Health England 4

Contents 4

A. Introduction 7

Purpose and scope 7
Devolved administrations 8

B. Post-exposure risk assessment: does the person need PET? 9

B1. Patient details 10
B2. Relevant medical history 10
B3. Date of exposure 10
B4. Has the person been previously vaccinated against rabies? 11
B5. Which country? (no risk / low risk / high risk for terrestrial rabies) 11
B6. Species of animal: was it a bat, primate, rodent or other terrestrial mammal? 12
B7. Nature of exposure?
   Terrestrial mammals 13
   Bats 14

B8. Additional useful information 15

B9. Imported pets (dogs, cats or ferrets) 15
   Background 15
   Suspicion that a pet dog, cat or ferret has been illegally imported 15
   Suspicion of rabies in an animal 16
   Public health response 16
   Exposure to a non-compliant pet animal 16
   Exposure to a pet displaying signs of rabies 17

B10. Animals in quarantine 17

B11. Exotic pets (in UK) 17

C. Treatment recommendations 18

C1. Treatment based on risk assessment 18
C2. What treatment has already been given 21
   Global vaccines – compatibility with UK vaccines 21
C3. Is vaccine required? 21
   Patients started on alternative regimens 22
   Rabies antibody testing 23
C4. Is rabies immunoglobulin (HRIG) required 23
C5. Administering vaccine and immunoglobulin 24
C6. How soon should treatment be started?  
D. Logistics  
D.1 Issuing rabies vaccine/HRIG from Colindale  
  Routine service  
  Urgent service  
D.2 Issuing rabies vaccine/HRIG from stockholders  
E. Governance issues  
  Colindale issues  
F. Rabies vaccines compatible with UK schedule  
G. Source documents and useful references
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 2 (EBLV2), a rabies-like virus, has been found in Daubenton's bats (Myotis daubentonii) across the UK.

Further information, guidance and the risk assessment form are available on the rabies pages of the PHE 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 PHE Rabies and Immunoglobulin Service (RIGS), Colindale. A separate document deals with the risk assessment of monkey bites which should be used in conjunction with this document if necessary. (Add link)

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 VRD consultants, PHE Colindale (0208 327 6204), or out of hours to Colindale Duty Doctor (0208-200-4400); additional information can be found on the PHE website
- vaccines prior to travel - refer caller to NaTHNaC (website: https://www.nathnac.net) or for complex queries, advice line 0845 602 6712)
• vaccines for those with occupational risk (see Green Book) — requests should be made in writing by email or fax to Rabies and Immunoglobulin Service, PHE Colindale (Rlgs; RIGS@phe.gov.uk or 020 8327 7404).

Individual risk assessment of potential rabies prone exposures should be undertaken as soon as possible, 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 C6). In complex cases treatment can be initiated and further advice sought from consultants at the PHE Rabies and Immunoglobulin Service/Virus Reference Department on the next working day.

All risk assessments should be completed using the rabies post-exposure risk assessment form (https://www.gov.uk/government/publications/rabies-post-exposure-risk-assessment-form-and-calendar) and either directly uploaded into HPZone, or emailed to the Rabies and Immunoglobulin Service by secure email. The form can be encrypted using the button on the form, and the password sent in a separate email.

Devolved administrations

PHE/Department of Health does not supply rabies vaccines for Scotland or Northern Ireland (or Channel Islands). Requests from Scotland should be referred to the local infectious diseases consultant (see Green Book for details), and from Northern Ireland to the regional virology service or public health agency duty room (see Green Book for details: https://www.gov.uk/government/publications/rabies-the-green-book-chapter-27).

Requests for post-exposure treatment for patients in Wales should be referred to the duty virologist, University Hospital of Wales, Cardiff (029 20 747 747).
B. Post-exposure risk assessment: does the person need PET?

The following information is required to complete the risk assessment:

- patient name, date of birth, age and address
- date of exposure
- species and current health status of animal involved
- country of exposure
- type of exposure
- site of exposure
- any previous rabies vaccinations

This should be recorded in the rabies post-exposure form which can be found in HPZone and on the PHE website (https://www.gov.uk/government/publications/rabies-post-exposure-risk-assessment-form-and-calendar).

All enquiries should be recorded, even if vaccine and/or immunoglobulin are not issued.
B1. Patient details

Complete the patient details as indicated. The PET form also acts as the prescription 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 and the patient’s address.

<table>
<thead>
<tr>
<th>Patient details</th>
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</thead>
<tbody>
<tr>
<td>Patient name:</td>
</tr>
<tr>
<td>DOB:</td>
</tr>
<tr>
<td>Patient address:</td>
</tr>
</tbody>
</table>

B2. Relevant medical history

There are no absolute contra-indications to rabies post-exposure treatment. However, in certain circumstances i.e. immunosuppression special follow up may be required, and further advice should be sought in hours from PHE Rabies Service, Colindale. Advice about precautions in giving treatment if there has been a previous hypersensitivity reaction are given in the Green Book.

B3. Date of exposure

Risk assessment should be undertaken as soon as possible following exposure, so that PET, if required, can be started promptly. The incubation period for rabies is typically 1–3 months, but may vary from <1 week to >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.

If the exposure is more than one year ago, HRIG is not generally indicated and specialist advice should be sought from the PHE Rabies and Immunoglobulin Service, Colindale.
B4. Has the person been previously vaccinated against rabies?

Immune status for rabies will be based on history of vaccination and whether the person is immunocompetent and will determine the PET required. Immunity should be assessed as follows:

**Fully immunised:** At least three documented doses of rabies vaccine (either a complete primary pre-exposure course or as part of a five dose postexposure course) or documented rabies antibody (VNA) titres of at least 0.5 IU/ml.

If the patient has recently completed a rabies post-exposure course of treatment (either 5 doses of vaccine, or 2 doses if previously fully immunised) within the last 6 months, no treatment is required for a more recent exposure.

If vaccination was more than 10 years ago, treat as fully immunised (2 doses of vaccine only) and check antibody levels 1 week after last dose. If exposure to a known rabid animal, or multiple severe bites to head and neck, then start PET and seek specialist advice from PHE Rabies and Immunoglobulin Service, Colindale on further management.

If the person is immunosuppressed (as defined in Green Book, chapter 6; https://www.gov.uk/government/publications/contraindications-and-special-considerations-the-green-book-chapter-6), treat as though nonimmune and consider testing antibody levels 1 week post vaccination.

**Partially immune:** Person who has had incomplete / inadequate primary vaccination course, or VNA never >0.5IU/ml.

**Non immune:** Person who has never received pre- or postexposure immunisation with rabies vaccine.

B5. Which country? (no risk / low risk / high risk for terrestrial rabies)


A country may be considered free from rabies when:
- the disease is notifiable
- an effective system of disease surveillance is in operation
- all regulatory measures for the prevention and control of rabies have been implemented including effective importation procedures
- no case of indigenously acquired rabies infection has been confirmed in man or any animal species during the past 2 years; however, this status would not
be affected by the isolation of a bat lyssavirus such as European bat lyssavirus (EBL1 or EBL2)
• no imported case in carnivores has been confirmed outside a quarantine station for the past 6 months

The risk of rabies from terrestrial mammals according to geographical location (country, island and territory) is updated regularly. This information is incorporated into the Rabies PET form, the most recent version of which can be found on the PHE website at: https://www.gov.uk/government/publications/rabies-risks-by-country.

All countries should be considered as high risk countries for bat exposures, including the UK.

B6. Species of animal: was it a bat, primate, rodent or other terrestrial mammal?

“The most frequent way that humans become infected with rabies is through the bite of infected dogs and cats, wild carnivorous species like foxes, raccoons, skunks, jackals and wolves, and insectivorous and vampire bats. Cattle, horses, deer and other herbivores can become infected with rabies and although they could potentially transmit the virus to other animals and to people, this rarely occurs.”

All animals: All warm blooded animals and bats, including those that are apparently healthy, may pose a risk. Even vaccinated animals need to be reviewed as transmission of rabies may still be possible.

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 postexposure 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. Generally this is only appropriate if it is a family pet, a provoked exposure, and the owners will promptly report any change in animal behaviour. If in doubt, start treatment.

1 http://www.who.int/mediacentre/factsheets/fs099/en/
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 or primate bite is extremely low, rodent and primate bites occurring in low or high risk countries should receive PET with vaccine only. The only exception is category III primate bites from high risk countries to the head and neck where HRIG should be administered if within 7 days of starting vaccine.

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 in countries which are declared rabies free in terrestrial animals.

In the UK, bats are the only reservoir of rabies or related lyssavirus, but they are a protected species and cannot be destroyed to determine rabies status if caught.

B7. Nature 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.

**Terrestrial mammals**

<table>
<thead>
<tr>
<th>Category</th>
<th>Terrestrial mammal: <strong>categories of exposure</strong> (adapted from WHO)</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>Touching or stroking animals</td>
</tr>
<tr>
<td>II</td>
<td>Licks of the skin or other contact with saliva (eg feeding animals)</td>
</tr>
<tr>
<td></td>
<td>Minor scratches, bruising or abrasions without bleeding</td>
</tr>
<tr>
<td></td>
<td>Minor bites without breaking of the skin (covered areas of arms, trunk and legs)</td>
</tr>
<tr>
<td></td>
<td>All bites, licks and scratches from rodents and primates</td>
</tr>
<tr>
<td>III</td>
<td>Single or multiple transdermal bites or scratches, licks on broken skin</td>
</tr>
<tr>
<td></td>
<td>Major bites (multiple or on face, head, finger or neck)</td>
</tr>
<tr>
<td></td>
<td>Contact of mucous membranes with saliva (eg licks)</td>
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</tbody>
</table>
Bats

<table>
<thead>
<tr>
<th>Category</th>
<th>Bats: categories of exposure (adapted from WHO)</th>
</tr>
</thead>
</table>
| I        | No physical contact:  
ie no direct physical contact with the bat’s saliva or neural tissue, or the person was protected by a barrier capable of preventing such contact, such as a boot, shoe, or appropriate protective clothing |
| II       | Uncertain physical contact: (may be common with bat exposures):  
ie where there has been no observed direct physical contact (with saliva) but this could have occurred, a young child found in a room with a bat, or in the UK a grounded or aggressive bat found in a room of a sleeping (or intoxicated) person* |
| III      | Direct physical contact with bat’s saliva or neural tissue  
Single or multiple transdermal bites or scratches and bruising  
Minor bites without breaking of the skin (covered areas of arms, trunk and legs)  
Major bites (multiple or on face, head, finger or neck)  
Contamination of mucous membrane with saliva or bat droppings/urine |

* Bat species found in houses and attics in the UK are unlikely to be infected with rabies-related viruses. Healthy bats avoid contact with humans, therefore bats behaving normally (ie flying into a room, but not grounded or acting aggressively) do not constitute a risk. However, as the risk cannot be completely excluded, bat bites occurring in attics of houses in the UK should be treated.

For countries outside of the UK, any bat, regardless of behaviour, found in the room of a sleeping or intoxicated person, should be considered a category II exposure, In the USA 50% of human cases with bat-variant virus have resulted from unrecognised bat bites.

Most bat bites are felt, not seen. Bat bites rarely cause an obvious break in the skin, and are often felt rather than seen, but should still be considered a direct physical exposure (category III). PHE recommends that all bat bites, even if said to be from a pipistrelle, should be treated.
B8. Additional useful information

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

- Is rabies known or suspected to be present in the species in the locality?
- Is there an owner known and 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?
- If the animal has died, does laboratory examination of the animal’s brain confirm rabies?
- Is the animal non-indigenous or imported? If imported it is important to determine the risk of rabies (no risk / low risk / high risk) in both the country of potential exposure and the country of origin of the animal.

B9. Imported pets (dogs, cats or ferrets)

Background

In 2012 the UK harmonised with the EU pet travel scheme (having launched its own pet travel scheme in 2000). This regime allows people who are travelling with a pet dog or cat (or ferret) to enter the UK without quarantine so long as they fulfil the conditions of the scheme depending on the country they are travelling into the UK from. This requires the pet to have: a microchip and rabies vaccination; if travelling to or from an unlisted country, a blood test 30 days following the date of vaccination; and to complete a waiting period prior to travel (21 days from the date of vaccination if travelling to/from an EU or ‘listed’ country, or a three month wait from date of blood sampling if travelling from an ‘unlisted’ country). All pets must travel with either a pet passport or an official third country veterinary certificate issued by an authorised vet. Further information is available here: https://www.gov.uk/pet-travel-information-for-pet-owners. The number of pets found to be non-compliant and subsequently quarantined by Trading Standards has increased since 2012 (from 127 in 2011 to 417 in 2012 and 459 in 2013).

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

The policy underpinning the pet travel scheme is managed by Defra and operationalised by the Animal and Plant Health Agency (APHA). The regime is enforced by local authorities. These organisations work closely together to monitor the effectiveness of the scheme.
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 Trading Standards, 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 at: https://www.gov.uk/find-local-trading-standards-office

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 Trading Standards should be contacted and they may decide to quarantine the animal.

Suspicion of rabies in an animal

Rabies is a notifiable disease. If suspected, there is a legal requirement to notify the duty vet in the local APHA office. A Notifiable Disease Investigation (NDI) is then started and an NDI1 report is sent (as is any follow-up report) to PHE’s Emerging Infections and Zoonoses team (EIZ) and Virus Reference Department (VRD) 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 PHE Rabies and Immunoglobulin Service 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, Trading Standards. 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 displaying signs of rabies**

The PHE Rabies and Immunoglobulin consultant in collaboration with EIZ and the appropriate local health protection team will coordinate/oversee risk assessment of all persons (owner and household, vet etc) who have been exposed to the animal. *(It is possible however that the 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 (ie exposures other than head and neck), then decisions about postexposure treatment can await the initial results of rabies testing in the suspect animal.

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

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

**B10. Animals in quarantine**

All staff working with animals in quarantine 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 (in UK)**

Exotic pets are not illegal in the UK. 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 etc), whether the animal has been vaccinated against rabies and the circumstance of the exposure.
C. Treatment recommendations

### C1. Treatment based on risk assessment

A formal risk assessment based on the collected information should be performed; Recommended treatment will generally fall into five categories (see algorithms on following pages):

- no risk and therefore no treatment
- vaccine and HRIG
- vaccine only
- vaccine and blood test 1 week after last dose – see section C3
- observation of animal (domestic cats and dogs only – see section B6)
If last dose of vaccine was more than 10 years ago, arrange antibody test 1 week after 2nd vaccine.
If last dose of vaccine was more than 10 years ago, arrange antibody test 1 week after 2nd vaccine.
C2 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?
- 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 their next treatment?

If no treatment has been started, post exposure treatment should be started within two working days. However for high risk exposures, such as severe and multiple bites to the head and neck or from a confirmed rabid animal, treatment should be started as soon as possible.

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 Table 1: Section F). However, a wide variety of different 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 PHE Rlgs as appropriate.

C3. Is vaccine required?

The UK schedule is 5 vaccines at the following interval 0, 3, 7, 14, 28-30 days given by the i.m. route.

Day 0 is the day of 1st vaccine NOT necessarily the day of exposure.

Vaccine issuing centres, including Colindale, 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 PHE 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/minus one day.

The 5th final dose of rabies vaccine PET should not be given before day 26.

In a patient who is partially immune, a full course of 5 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 3-7. If the last dose of vaccine was more than 10 years ago, antibody testing should be arranged through Rlgs to ensure that there is an adequate antibody response. A collection pack and prepaid envelope will be sent to the GP surgery for collection. The sample (10ml clotted blood or serum sample) should be collected one week after vaccination, the request form completed and sample and form sent to APHA for testing. The results will be returned to Rlgs who will advise if further treatment is needed.

Patients started on alternative regimens

If the type of vaccine is compatible with the UK schedule, then convert timing of doses to closest UK vaccine dose.

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

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 90-day dose. If 5 doses of vaccine have been given according to the UK schedule then there is no need to give a dose at day 90.

If a vaccine course has been started /completed with a vaccine not compatible with the UK schedule, or by the intradermal (id) rather than the intramuscular (im) route, complete vaccine course on UK schedule and then test antibodies, one week after completion.

If a patient, despite being previously immunised against rabies is treated with rabies immunoglobulin following their exposure, they should complete a full 5 dose course of rabies vaccination.
Rabies antibody testing

In England routine measurement of rabies antibody titres postexposure is not offered for reasons of expense and practicality. If testing is recommended by PHE Rlgs, Colindale, a collection pack and prepaid envelope will be sent to the GP surgery for 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 APHA for testing. The results will be returned to PHE Rlgs, Colindale, who will advise if further treatment 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 01932 357345, or main number 01932 341111) should be contacted directly to arrange this. Samples should be sent directly to APHA and testing will be charged to the sender.

If antibody testing for immunity is needed following a pre-exposure course of vaccines, samples should be collected at least 2 weeks after the last dose of vaccine.

C4. Is rabies immunoglobulin (HRIG) required?

The mainstay of rabies postexposure treatment (PET) is rabies vaccine. Human rabies immune globulin (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 after 7 days post initiation of rabies PET vaccination or to an individual who is already partially or previously immunised.

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/ml). The recommended dose is 20IU/kg, adults and children (all ages)

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 and is also available from Rlgs team (0208 327 6204).
- weight of the patient
volume in vials (vials contain 1-4mls, depending on batch and manufacturer)

If the weight (in kg – there is a calculator on the ‘Weight converter’ page to convert stones and lbs to kg 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. Alternatively the correct volume for each patient should be calculated as indicated below:

Worked example 1
Child wt 19kg, potency of BPL product is 180IU/ml, vials contain 2.5ml
Required units total = 20 x 19IU = 380IU
Need to administer (380/180 = 2.1ml)
Need to supply 1 vial, there will be some wastage

Worked example 2
Adult wt 70 kg potency of Berirab P product is 150 IU/ml, vials contain 2ml
Required units total = 70 x 20 = 1400IU
Need to administer 1400/150 = 9.3ml
Need to supply 5 vials

C5. Administering vaccine and immunoglobulin

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

All immunoglobulin (HRIG) is given at the site of the wound, infiltrated around the site of the wound. If this is difficult or the wound has healed and the site is unclear, then this can be given by intramuscular injection in the anterolateral thigh (this advice is based on the most recent WHO position paper on rabies vaccine (Aug 2010) and may contradict advice in the rabies immunoglobulin product leaflet, which has not been updated).

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

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

C6. 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 mailed out for administration the next day. However for head and neck bites, treatment should ideally be started within 12 hours of reporting.

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

Rabies vaccine is also available through some travel clinics, and they can often provide postexposure vaccine treatment, although they may charge the patient an administration fee. If arranged with RlgS before administration, RlgS can replace the vaccine.

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.
D. Logistics

D.1 Issuing rabies vaccine/HRIG from Colindale

The Rabies and Immunoglobulin Service is a combined service with responsibility to support the post-exposure treatment of serious infections, through the production of guidance and by undertaking risk assessments, providing clinical advice and issuing of immunoglobulins and antitoxins. These rare products are procured by PHE from a range of producers, using the programme budget delegated by the Department of Health for the national immunisation programmes. Stock is held at Colindale as part of the RlgS service but also at a number of stock holders distributed throughout the country. RlgS is a busy service; in the financial year 2016/7 there were over almost 2000 calls related to rabies post-exposure treatment (vaccine and or human rabies immunoglobulin), and approximately 1000 calls for rabies pre-exposure.

Routine service

The PHE Rabies and Immunoglobulin service operates between 9am-5pm Monday to Friday. All requests for stock and advice about issuing should be directed to this service (tel 020 8327 6204).
Requests for immunoglobulin / vaccine received before 4pm Monday-Friday will be posted to a named responsible clinician to arrive on the next working day. Requests received after 4pm will not be posted until the next working day. (Posting of immunoglobulin / vaccine on a Friday will only be possible if the delivery address is open on a Saturday. If this is not the case a courier would need to be arranged or the issue would need to wait until the next working day).

Where product is needed sooner, PHE can issue stock from Colindale during working hours for providers to collect using a courier or taxi service (paid by the provider) or for the patient to pick up and return to them. The site is open for collection 24 hours a day, seven days a week.

Alternatively stock can be collected from the nearest stock-holder – RlgS can provide the contact details.

**Urgent service**

PHE can issue immunoglobulin from Colindale between 9 am and 3pm at weekends and bank holidays for the requestor to arrange collection (generally using a courier or the patient picking up the package). Therefore, for the majority of patients, it is preferable to make arrangements for collection and administration of the immunoglobulin product on the next day.

Requests to issue immunoglobulin at other times will only be considered where there is an immediate threat to life – for rabies vaccine/immunoglobulin this would be for high risk exposures for previously untreated rabies exposures to the head and neck.

PHE does not issue vaccines or HRIG for administration to patients outside of England.

**D.2 Issuing rabies vaccine/HRIG from stockholders**

Vaccines and HRIG are also held in various centres throughout England. It may be more convenient to issue vaccine and HRIG from an alternative supply centre, once the decision has been made that vaccine/immunoglobulin are appropriate. However vaccine supply centres elsewhere may be used for collection only of vaccines and RIG; they do not provide postal delivery. If a split issue is required, the second part of the issue can be sent out from Colindale.
Current issuing centres in England are:
- Birmingham
- Cambridge
- Leeds
- Liverpool
- Manchester
- Oxford
- Newcastle
- Norwich
- Southampton

For PHE staff a complete listing of issuing centres with contact details is available in the PHE Intranet Duty Doctor Pack and in HPZone:
Rabies vaccine and Ig issuing centres.doc
E. Governance issues

Colindale issues

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 and the RIgS clerks informed as soon as possible the next working day.

All forms need to be signed by a medical doctor (prescribing clinician) and GMC number recorded before issue.

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 reviewed by the duty VRD consultant on the next working day. This should not delay the issue of vaccine as it may take place 24-48 hours later.

All those participating in the rabies service should have completed the rabies e-learning course (https://lms.kallidus.com/PublicHealthEngland).

Initial training for SpRs and new consultants will be arranged on an individual/ad hoc basis, but is an essential requirement for participation in the Colindale duty doctor/on call rabies service.

Participation in Colindale clinical audit and duty doctor training on a regular basis is required.
F. Rabies vaccines compatible with UK schedule

Table 1 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).

Table 1. Types of rabies treatment used globally for rabies PET

<table>
<thead>
<tr>
<th>Rabies vaccine/lg</th>
<th>Comment</th>
<th>Manufacturer and likely distribution</th>
<th>Compatible with UK*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human diploid cell vaccine (HDCV)</td>
<td>Immunogenicity efficacy data do exist for this.</td>
<td>IMOVAX Pasteur Mérieux Group, Sanofi Pasteur MSD Ltd UK</td>
<td>√</td>
</tr>
<tr>
<td>Purified chick embryo cell vaccine (PCECV)</td>
<td>Immunogenicity efficacy data do exist for this.</td>
<td>(UK licence) Chiron vaccines</td>
<td>√</td>
</tr>
<tr>
<td>Purified vero cell vaccine (PVRV)</td>
<td>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 do not exist, but the potency and immunogenicity is evaluated similarly to HDCV and PCECV vaccines. These are generally reliable vaccines.</td>
<td>Variety of manufacturers make this. Possible trade names include VERORAB. ABHAYRAB (India) SII Rabivax (India) Speeda (CELBIO)</td>
<td>√</td>
</tr>
<tr>
<td>Purified duck embryo vaccine (PDEV)</td>
<td>The vaccine uses duck embryo cells as substrate. These are inactivated by β-propiolactone and purified by ultracentrifugation. PDEV contains thiomersal.</td>
<td>Variety of manufacturers in India under license from Berna Biotech</td>
<td></td>
</tr>
<tr>
<td>Primary Syrian hamster kidney cell (PHKCV)</td>
<td>Uses the Beijing strain of the rabies virus and is inactivated with formalin and adsorbed to aluminium hydroxide. The vaccine contains thiomersal.</td>
<td>Local producers in China</td>
<td></td>
</tr>
<tr>
<td>Vaccine Type</td>
<td>Description</td>
<td>Region/Recommendation</td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Suckling mouse brain vaccine (SMBV)</td>
<td>Vaccines of this sort are generally reliable but may have marginally reduced efficiency with increased risk of side effects.</td>
<td>Used in S America</td>
<td></td>
</tr>
<tr>
<td>Nervous tissue vaccine (sheep, goat)</td>
<td>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.</td>
<td>Used in Asia but being phased out</td>
<td></td>
</tr>
<tr>
<td>Horse Serum</td>
<td>Trade name not clear. May be given as treatment alone or with vaccine. Most often found in certain S American and middle East countries. If this is the only treatment given, need to start PET (Omit HRIG).</td>
<td>EquiRIG Unknown</td>
<td></td>
</tr>
<tr>
<td>HRIG</td>
<td>Berirab Bayrab HyperRab S/D Imogan HRIG USA Imogan Rabies HT</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*See section C3*
G. Source documents and useful references

Current WHO Guide for Rabies Pre and Post Exposure Treatment in Humans
Rabies vaccines: WHO Position Paper :Weekly Epidemiological Record (WER) 6

Immunisation against infectious disease - "The Green Book"

British National Formulary
http://www.bnf.org

Rabies e-Health learning module
eHealth can be accessed by registering at https://lms.kallidus.com/PublicHealthEngland
To find the rabies module, enter the HPA Emergency Response Portal.

Terrestrial animal health code
http://web.oie.int/eng/normes/mcode/en_chapitre_1.8.10.htm

PETS animal passport scheme

Management of a human rabies case
HPA Public Health Management of suspected case of human rabies, A standard
operating procedure for communication and action 30/11/2004 (updated 2009)
of-a-suspected-case

DH memorandum on rabies: Memorandum on Rabies Prevention and Control (Feb
2000)
consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4080657.pdf

Further documents relating to rabies, rabies pre-exposure prophylaxis and rabies
postexposure prophylaxis are also available on the rabies page of the duty doctor pack
on the Intranet, and on the PHE website:
treatment-management