



UK Health
Security
Agency



9304

Rare and Imported Pathogens Laboratory (RIPL)

Specimen referral guidelines and service user manual

UKHSA Porton

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General information

RIPL history

The Rare and Imported Pathogens Laboratory (RIPL) is now incorporated into the functions of the UK Health Security Agency (UKHSA), which was established on 1 October 2021 and superseded Public Health England. Previously, RIPL operated within the Health Protection Agency's (HPA) Microbiology Services Porton and until November 2011 was as the Special Pathogens Reference Unit (SPRU). From 2005 to 2009, SPRU operated as part of the Novel and Dangerous Pathogens Department at the HPA Centre for Emergency Preparedness and Response (CEPR), then later as part of the Medical Affairs Department.

RIPL provides a clinical diagnostic service for rare and/or imported pathogens such as pathogenic arboviruses, haemorrhagic fever viruses and a number of Hazard Group 3 bacterial pathogens including rickettsiae, *Coxiella burnetii* and *Bacillus anthracis*.

RIPL is the frontline laboratory providing diagnostics for the Imported Fever Service following its inception in June 2012.

RIPL also provides an environmental detection service for investigation and identification of anthrax.

The Lyme disease testing service was transferred from HPA Southampton to RIPL on 1 June 2012. See [Appendix 1](#) for details.

The *Leptospira* diagnostic service was transferred from Hereford to UKHSA laboratories at Porton on 1 April 2015.

Population served

RIPL provides specialist expertise and advice to UKHSA, the NHS, government departments, the commercial sector, and to clinical, veterinary and environmental services throughout the UK, Europe and elsewhere in the world.

RIPL is the core component of the World Health Organization (WHO) Collaborating Centre for Virus Reference and Research (Special Pathogens) at Porton Down.

Contact details and where to find RIPL

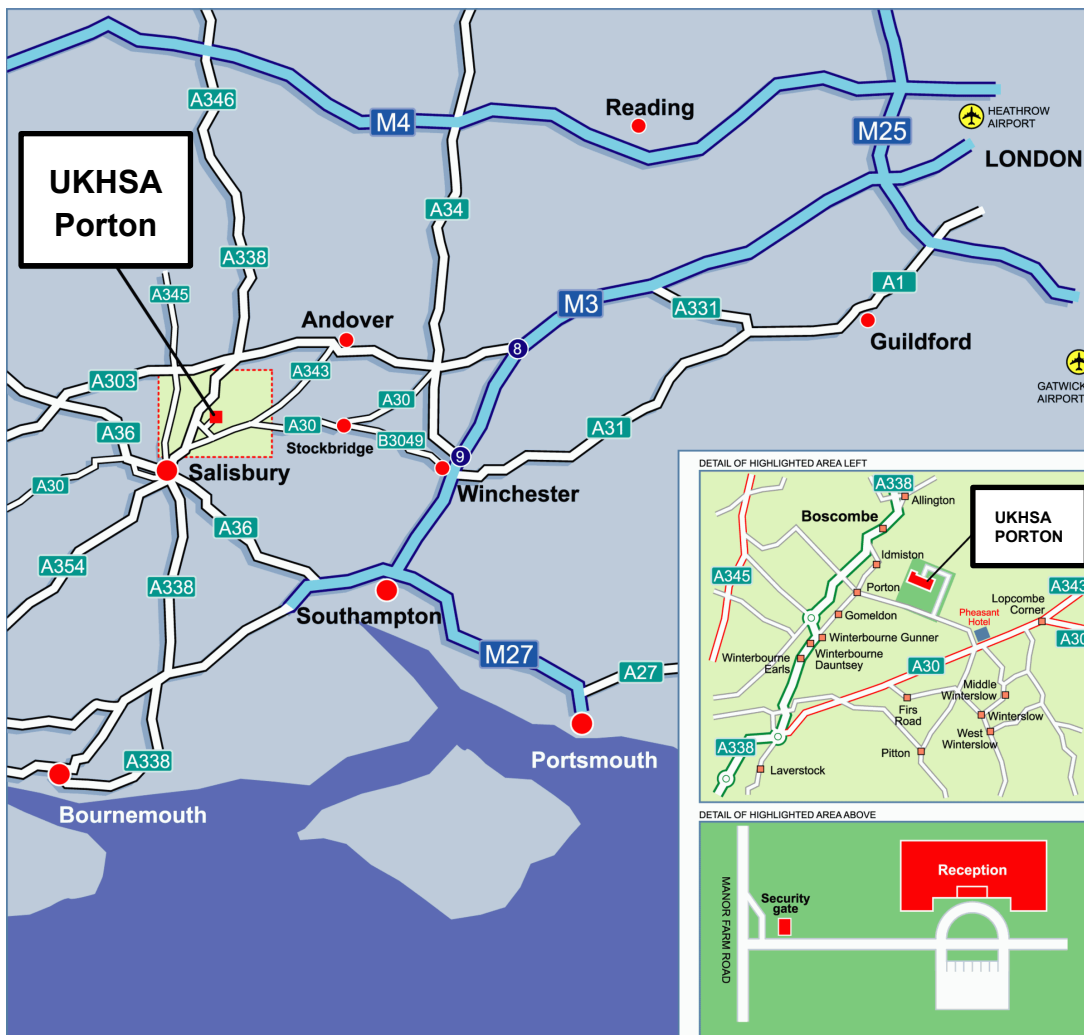
Address

Rare and Imported Pathogens Laboratory (RIPL)
UK Health Security Agency
Porton Down
Salisbury
Wiltshire
SP4 0JG
United Kingdom

Sat Nav users

Specify 'Manor Farm Road, Porton Down' rather than the address postcode SP4 0JG, and approach via Winterslow Road to avoid being directed to the wrong entrance. Actual co-ordinates for the entrance to the site are 51°07'46.7"N, 1°42'21.3"W.

Figure 1. Map showing location of Porton Down



DX address

DX 6930400 Salisbury92/SP

Telephone

9am to 5pm weekdays: +44 (0) 1980 612348

Out-of-hours (Porton reception): +44 (0) 1980 612100

UK Imported Fever Service telephone line: 0844 77 88 990

Email

ripl@ukhsa.gov.uk (checked on weekdays only)

Websites

- [UKHSA](#)
- [Rare and imported pathogens laboratory \(RIPL\)](#)

Research

The laboratory and associated research groups included in the WHO Collaborating Centre undertake a wide range of research activities. This extends from investigation of clinical isolates from specific cases and outbreaks by isolation, phenotypic and genotypic characterisation through to assessment and development of new diagnostic tests and platforms for use within the conventional and field laboratory.

Research also includes development and assessment of interventions in models of infection. We also welcome participation in prospective and retrospective clinical studies, serosurveillance and disease prevalence studies as well as therapeutic studies for a number of potential pathogens with partners worldwide.

Personnel and contact details

Table 1. Personnel and contact details

Name	Designation	Email
Dr Tim Brooks	Consultant Microbiologist and Clinical Services Director	tim.brooks@ukhsa.gov.uk
Dr Claire Gordon	Consultant, Microbiology and Infectious Diseases	claire.gordon@ukhsa.gov.uk
Dr Tommy Rampling	Consultant, Medical Virology and Infectious Diseases	tommy.rampling@ukhsa.gov.uk

Name	Designation	Email
Dr Catherine Houlihan	Consultant, Medical Virology and Infectious Diseases	catherine.houlihan@ukhsa.gov.uk
Dr Clare Warrell	Consultant Tropical Medicine and Infectious Diseases	clare.warrell@ukhsa.gov.uk
Dr Christina Petridou	Consultant, Microbiology and Infectious Diseases	christina.petridou@ukhsa.gov.uk
Dr Jane Osborne	Clinical Scientist	jane.osborne@ukhsa.gov.uk
Mr Barry Gibney	RIPL Laboratory Manager	barry.gibney@ukhsa.gov.uk
Dr Gillian Slack	Operations Manager	gillian.slack@ukhsa.gov.uk

To contact staff please use main RIPL telephone number 01980 612348.

Laboratory opening times

Normal working hours: 9am to 5pm Monday to Friday.

Note that in order to arrange urgent testing outside these normal working hours, you will have to discuss the clinical case with the RIPL on-call medical consultant via the Imported Fever Service.

Use of the laboratory

Diagnosing a rare or imported pathogen

The presentation of most imported diseases is very similar, and it can be difficult to distinguish between them clinically. Co-infections with more than one agent are also relatively common. For this reason, we provide panels of tests based upon the patient's symptoms and travel history that include the commonest differential diagnoses. The charge for this is more than for a single assay, but significantly less than 2 separate tests. Unless you have a specific reason for testing for a single agent, or are very familiar with current disease prevalence, we suggest that you provide as many clinical and travel details as possible and allow us to select the appropriate panel of tests. An appropriate geographical test panel will be run on all samples unless the opt out option is ticked on the request form.

Panels include both serology and PCR as required, with PCR tests being offered in addition to serology for acute cases. PCR tests are not normally performed for long-term conditions except Q fever, as they are highly unlikely to be positive and diagnosis relies on serology.

Arboviruses and rickettsiae are causes of febrile illness in travellers returning to the UK from many areas. Less frequently, illness caused by viral haemorrhagic fevers (VHFs) may have to be considered. Although not common, Q fever, anthrax, plague and other bacterial infections, derived either from within the UK or abroad, may also be considered as part of the differential diagnosis.

Common conditions such as malaria or enteric fever (typhoid) must not be forgotten and should be tested for, alongside more exotic diseases, as prompt treatment may be life-saving. Please note that testing for malaria and enteric fever is NOT provided by RIPL and must be arranged separately through local laboratories or specialised reference centres.

Additional tests may be available other than those listed, for special cases. If appropriate, please telephone to discuss (01980 612348 during working hours).

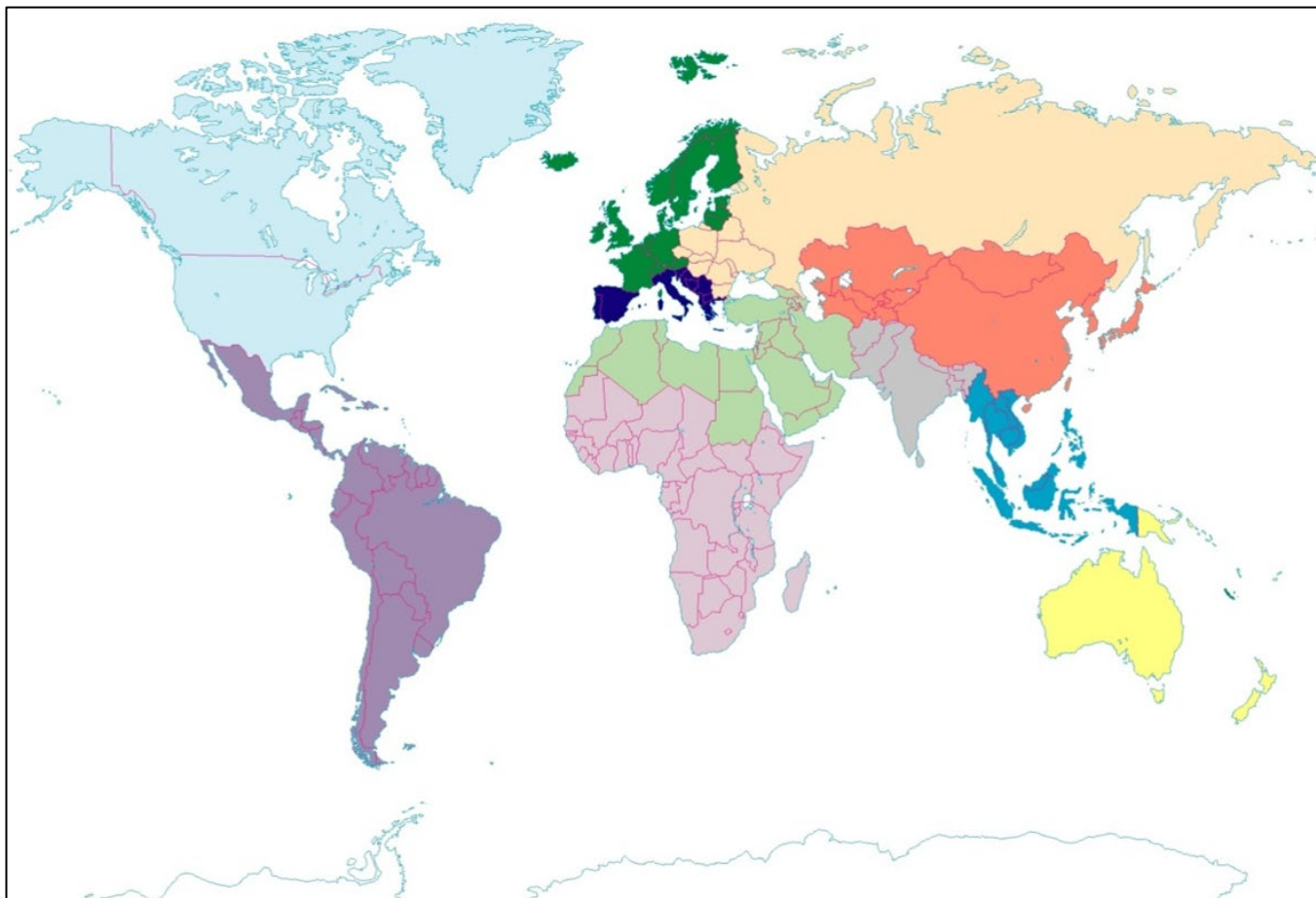
For Lyme disease testing, please see [Appendix 1: Lyme Disease](#).

For Leptospirosis testing, please see [Appendix 2: Leptospirosis](#).

Map of regions

Routine tests are run in geographic and symptomatic panels. Additional tests are added if the clinical details justify them, or by discussion with the referring physicians. The map below shows the main geographic groupings we use. However, the incidence of diseases is not constant across any given region and we welcome additional information that could help us offer a better service.

Figure 2. Map of regions



Map produced by PC Graphics (UK) Limited

Key to map

	Sub-Saharan Africa
	North Africa and western Africa
	Central and Eastern Asia
	Southern Asia
	South-Eastern Asia
	Australasia and Pacific Islands
	Northern and Western Europe
	Southern Europe
	Eastern Europe
	Northern America
	Latin America and Caribbean

Note that the tests included in each of the basic geographical panels may change over time but [Table 6](#) lists available assays. Please see [notes on viral haemorrhagic fevers](#), below, for additional information.

Typical incubation periods

In the following list [NP] indicates that testing is not provided by RIPL.

Short (less than 10 days)

Arboviruses

Enteric bacteria [NP]

Haemorrhagic fevers

Typhus and spotted fevers

Plague

Medium (10 to 21 days)

Malaria [NP]

Enteric fever (typhoid) [NP]

Scrub typhus

Brucellosis

Leptospirosis

Long (more than 21 days)

Viral hepatitis [NP]

Malaria [NP]

Tuberculosis [NP]

Filariasis [NP]

Risks of viral haemorrhagic fevers in different countries

Table 2. Risks of viral haemorrhagic fevers in different countries

	Countries where human outbreaks have occurred	Countries with evidence of endemicity, through sporadic cases or seroprevalence studies	Countries or areas with a theoretical risk based on geography but no reports of cases
Ebola and/or Marburg	Angola, Congo, DRC, Equatorial Guinea, Gabon, Guinea, Kenya, Liberia, Mali, Nigeria, Sierra Leone, South Sudan, Sudan, Uganda.	Ivory Coast, Tanzania, Zimbabwe,	Other Central and West African countries.
CCHF	Afghanistan, Albania, Bulgaria, China, Iraq, Iran, Kazakhstan, Kosovo, Mauritania, Pakistan, Russia, South Africa, Tajikistan, Turkey, UAE, Uganda, Uzbekistan.	Benin, Burkina Faso, DRC, Egypt, France, Georgia, Greece, Hungary, India, Kenya, Oman, Portugal, Spain (Avila region) Tanzania.	Africa, Balkans, Caucasus, Central Asia, Eastern Europe, Middle East.
Lassa	Benin, Guinea, Liberia, Nigeria, Sierra Leone, Togo.	Burkina Faso, Ghana, Ivory Coast, Mali.	Cameroon, Central African Republic, other West African countries.
Lujo		Zambia	

Note: The following viruses also have the potential to cause haemorrhagic features: hantaviruses, chikungunya virus, rift valley fever virus, dengue viruses and yellow fever virus.

For information on assessment of patients presenting with possible VHF, please refer to the UK Advisory Committee on Dangerous Pathogens (ACDP) Guidelines, 'Management of Hazard Group 4 viral haemorrhagic fevers and similar human infectious diseases of high consequence', and to the associated [ACDP viral haemorrhagic fevers risk assessment algorithm](#).

Requesting procedure (routine, urgent and out of hours)

All samples or routine

Use the [request form](#) available on the UKHSA RIPL website.

Urgent during working day

To discuss VHF testing or other urgent clinical enquiries regarding imported infections, please telephone the UK Imported Fever Service (0844 7788990). For other enquiries please telephone 01980 612348. Please ensure that you have all relevant clinical and travel or exposure history details.

Out-of-hours testing

This is based on discussions with the RIPL on-call medical consultant available via the UK Imported Fever Service number 0844 7788990. The back-up number to reach the on-call consultant is via UKHSA Porton Reception on 01980 612100.

Requesting additional tests and sample retention

Please telephone 01980 612348 during working hours to request additional tests and provide any additional information available. Please followup all verbal requests with email confirmation to RIPL@UKHSA.gov.uk. We will normally store samples for a limited time after initial testing, as shown in the table below.

Table 3. Sample type and time limit for requesting extra tests

Sample type	Retention period
CSF	6 months
Other fluids	6 months
Swabs	7 days
Dry tissue (skin, nail and so on)	28 days
Respiratory tract samples	28 days
Post-mortem samples	3 months

Sample type	Retention period
Wet tissue samples (ante-mortem)	6 months
Whole blood samples	Spun on receipt Plasma fraction kept for 6 months
Plasma	6 months
Serum	6 months
Medico-legal samples (plasma or sera)	30 years

Given the rare nature of many of the pathogens investigated by RIPL, samples which have reached the stated retention times above may be utilised for assay development and/or the manufacture of quality control material within UKHSA. All samples are discarded once either minimum retention is reached or potential downstream utility for quality or developmental purposes is exhausted.

Assay development may lead to identification of pathogens not previously considered by the requestor. In such cases, and providing patient management would be affected by this, contact will be made with the sender to discuss any implications.

Completing the request form

The [Rare and Imported Pathogens request form](#) (labelled P1) can be downloaded from the UKHSA RIPL website.

It is important to include a direct telephone number for the referring microbiology, virology or other specialty team on the request form so that any significant result can be communicated promptly by the RIPL team.

Requests forms must include complete patient identifying information as shown in Figure 3.

Figure 3. Patient demographics

PATIENT/SOURCE INFORMATION	
<input type="checkbox"/> Human <input type="checkbox"/> Animal* <input type="checkbox"/> Other*	*Please specify
<input type="checkbox"/> Inpatient <input type="checkbox"/> Outpatient <input type="checkbox"/> GP Patient <input type="checkbox"/> Other*	*Please specify
NHS number	Gender <input type="checkbox"/> male <input type="checkbox"/> female
Surname	Date of birth D D M M Y Y Y Y Age
Forename	Patient's postcode
Hospital number	Patient's HPT
Hospital name (if different from sender's name)	<input type="checkbox"/> ITU or Other ward/clinic
Have previous samples been sent to RIPL <input type="checkbox"/> Yes <input type="checkbox"/> No	Pregnant <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
	RIPL Lab ref. no P1 _ CO _ _ _ _ _

All unique samples sent must be clearly identified both on the request form and on the samples themselves. Collection time and date of sending to RIPL should also be recorded. Indicate sample reference numbers unambiguously and provide a description of all samples listed as 'other' in Figure 4.

Figure 4. Sample details

SAMPLE INFORMATION									
Sample type					Your reference				
<input type="checkbox"/> Serum \clotted blood									
<input type="checkbox"/> Plasma									
<input type="checkbox"/> EDTA whole blood									
<input type="checkbox"/> CSF									
<input type="checkbox"/> Other <i>(please specify)</i>									
Date of collection			D	D	M	M	Y	Y	Time
Date sent to RIPL			D	D	M	M	Y	Y	

To prevent delays in testing, it is extremely important that travel history and clinical details are provided to allow the correct set of tests for the region of travel to be chosen. If you have a specific reason for testing for a single agent, or are very familiar with current disease prevalence and wish to test **only** for specific infections, please check the box as shown in Figure 4. Otherwise, we recommend that you provide as many relevant details as possible (clinical syndrome, travel history including dates, onset of illness, relevant exposure history and so on) to allow us to select the appropriate panel of tests. Failure to provide sufficient information could result in a delay in testing while additional information or clarification of request is sought by a phone call or a report, and where this is not received, could lead to sample being rejected.

Please note that viral haemorrhagic fever (VHF) testing is not performed routinely and must be discussed prior to sending samples (see below).

Figure 5. Tests requested

TESTS REQUESTED	
RIPL will select the most appropriate panel of tests based on information provided below (i.e. travel and clinical details and suspected diagnosis). To opt out of this approach, tick the box and state test(s) required.	<input type="checkbox"/> Limit testing to the test(s) specified here ONLY

The request form should also include clinical and epidemiological information as shown in Figure 6.

Figure 6. Clinical and epidemiological information

CLINICAL/EPIDEMIOLOGICAL INFORMATION			
Foreign Travel within previous 21 days? <input type="checkbox"/> Yes <input type="checkbox"/> No		<input type="checkbox"/> Arthralgia	Other clinical details
Purpose of travel		<input type="checkbox"/> Encephalitis	
Date of travel (from UK)	D D M M Y Y	<input type="checkbox"/> Endocarditis	
Date returned (to UK)	D D M M Y Y	<input type="checkbox"/> Eschar	
Onset date	D D M M Y Y	<input type="checkbox"/> Fever	
Countries/areas visited	<input type="checkbox"/> Urban area	<input type="checkbox"/> Haemorrhage	
	<input type="checkbox"/> Rural area	<input type="checkbox"/> Leucopenia	
	<input type="checkbox"/> Open country	<input type="checkbox"/> LFTs raised	
	<input type="checkbox"/> Forests	<input type="checkbox"/> Lymphocytosis	
<input type="checkbox"/> Mosquito bite	<input type="checkbox"/> Tick bite	<input type="checkbox"/> Meningitis	
<input type="checkbox"/> Livestock exposure	<input type="checkbox"/> Other insect bite*	<input type="checkbox"/> Myalgia	
*Please specify		<input type="checkbox"/> Neutrophilia	Suspected Diagnosis?
Travel Vaccination History		<input type="checkbox"/> Rash	
Relevant Occupational History		<input type="checkbox"/> Respiratory symptoms	Antimicrobials given?
		<input type="checkbox"/> Retro-orbital pain	
		<input type="checkbox"/> Sore throat	
		<input type="checkbox"/> Thrombocytopenia	

Information on antimicrobial treatment should accompany requests for rickettsial and bacterial studies.

There are separate request forms for *Borrelia* (Lyme disease) testing and for Leptospirosis testing. Please see [Appendix 1: Lyme Disease](#) and [Appendix 2: Leptospirosis](#).

Leptospirosis testing will also be routinely added to samples from returning travellers where compatible travel and clinical details have been provided.

Please note that the completed request form constitutes a contract between the service user and RIPL and therefore acts as a de facto service agreement to perform diagnostic testing as outlined in this manual.

Specimens from patients who might have viral haemorrhagic fever

For patients presenting with suspected Viral Haemorrhagic Fever, testing **must** be discussed with the Imported Fever Service on 0844 7788990 prior to sending the sample. VHF testing will not be performed on samples that have not been discussed.

For other samples arriving in the laboratory where the clinical and travel details on the request form suggest that VHF should be considered (for example, fever on return from West Africa), the sample will only be processed if the form clearly states that VHF has been ruled out by the referring team (for example, because dates are not compatible, or symptoms are not in keeping with VHF). If the form does not state this, the samples will be held until further information is provided.

To avoid delays in processing we therefore strongly advise that forms are correctly completed with all relevant information and state that VHF testing is not required based on local risk assessment. If there is uncertainty, we advise discussion with a local microbiologist, virologist or Infectious Disease physician, who should contact the Imported Fever Service if uncertainty remains.

Detailed information on [assessment and testing for VHF](#) can be found online.

Specimen labelling

Use printed labels wherever possible. The specimen must be labelled with the same patient details as on the request form. Please ensure the full patient name and date of birth are legible. This is the minimum patient identification information required for sample processing. Multiples of sample types must be clearly distinguishable based on collection source/site or through use of unique reference numbers. ,

Please note that unlabelled or mismatched specimens will not be processed as the identity of the individual from which they have been taken cannot be guaranteed.

Types of specimens and specimen collection methods

Serum

One tube of serum for serology tests, ideally 1.5 millilitre (mL).

If this volume of sample is not available RIPL may be unable to perform all tests within a geographical panel.

Note that for VHF testing, a primary tube of clotted blood should be submitted rather than a separated serum aliquot.

Standalone Leptospirosis investigations require 1ml serum or plasma.

EDTA plasma

One tube of EDTA plasma for PCR assays, ideally 1.5mL.

Samples may not be suitable for testing if blood is lysed.

Note that for VHF testing, a tube of whole (unseparated) EDTA blood should be submitted; plasma will be separated on receipt.

Tissue samples

Tissue samples received for PCR testing should be un-homogenised and frozen. Samples received at room temperature may give rise to unreliable results, particularly for RNA viruses. Please note that fixed samples are likely to give inhibitory results and are not routinely processed.

Urine

Urine should be sent in a sterile, universal container without preservatives such as boric acid. A minimum of 1.5mL of urine is required.

CSF

For Lyme neuroborreliosis, CSF samples must be sent with a paired serum. A minimum of 600uL is required.

For other testing, a minimum of 250uL is required, and should be sent with any other relevant samples depending on the tests requested.

Viral swabs

Swabs for viral diagnosis should be sent in viral transport media (VTM). Charcoal or agar swabs are not suitable for viral or PCR testing and will be discarded.

Vesicle fluids

For poxvirus investigations please contact the laboratory on 01980 612348 for advice. Vesicle fluid or a swab in VTM are preferred.

Sample types such as heparinised blood or urine with preservatives that are inappropriate for RIPL tests will not be processed.

Specimens should be taken by experienced professionals using appropriate personal protective equipment and in accordance with local procedures and risk assessments. When obtaining bloods the use of a vacuum blood sampling system is strongly advised as this reduces the risk of sharps injuries.

Consent

Senders must obtain informed consent from patients for all samples referred to RIPL. RIPL will select an appropriate panel of tests based on the information provided and perform assays relevant to the best interest of the patient. RIPL does not require separate consent documentation to be sent, provided the sample is sent by a recognised service user.

Samples received directly from patients cannot be processed unless also requested by an appropriate medical professional.

Single pathogen-based diagnostic tests are performed when specifically requested (for example, dengue virus IgG and IgM; Lyme disease), but it is our evidenced experience that this may reduce the likelihood of obtaining a diagnostic answer. If the request for single pathogen testing is not specifically indicated on the request form, RIPL clinical staff will determine the appropriate Geographic Panel based testing according to the clinical details provided (either on the form or through discussion with the referring team).

Requests for further testing on samples received by RIPL can be made within the specified storage times for samples (see [Table 3](#)).

In all instances, RIPL may perform additional assays to confirm or clarify earlier assay results.

Submitting tissue samples from deceased people

Please contact the department on 01980 612348 to discuss testing of post mortem samples.

Packaging and transporting specimens

General recommendation

A triple packaging system is recommended by WHO. This should be used for all infectious substances and comprises 3 layers:

Primary receptacle

A primary watertight, leak-proof receptacle containing the specimen. The receptacle is packaged with enough absorbent material to absorb all fluid in case of breakage.

Secondary packaging

A second durable, watertight, leak-proof packaging to enclose and protect the primary receptacles. Several cushioned primary receptacles may be placed in one secondary packaging, but sufficient additional absorbent material shall be used to absorb all fluid in case of breakage.

Outer packaging

Secondary packagings are placed in outer shipping packagings with suitable cushioning material. Outer packagings protect their contents from outside influences, such as physical damage, while in transit. The smallest overall external dimension shall be 10cm x 10cm.

Additional requirements will depend on whether the infection risk posed by the specimen falls into category A or B.

Category A

An infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease in otherwise healthy humans or animals. Infectious substances meeting these criteria which cause disease in humans or both in humans and animals shall be assigned to United Nations number UN 2814 and packed according to Packing Instructions P620 for transport by road or rail. Samples known or reasonably expected to contain viral haemorrhagic fever viruses fall into Category A.

Further information on packaging requirements necessary for Category A substances, and examples of these, can be found in the [WHO Guidance on regulations for the Transport of Infectious Substances](#).

Category B

An infectious substance that does not meet the criteria for inclusion in Category A. Infectious substances in Category B shall be assigned to UN 3373 and must be packed to Packing Instructions P650. The vast majority of samples sent to RIPL will be Category B infectious substances.

Courier and postal deliveries

It is the responsibility of the sender to ensure that arrangements are in place in their contracts with courier companies to ensure that transport arrangements comply with current UK law, and to prevent delay the transport of urgent samples to RIPL.

Samples can generally be sent without the requirement for refrigeration (the exception is tissues which should, if possible, be frozen). There is, however, a maximum transport time before the potential for significant sample degradation becomes problematic. This is indicated as follows:

- blood/sera/plasma/CSF/urine – 7 days
- unfixed tissue – 48 hours
- swabs in VTM - 3 days
- dry swabs – 48 hours
- semen – 24 hours

Samples which have exceeded these transport times will still be processed but caveats will be added to any result interpretation given on reports.

Specimen limitations potentially affecting assay results

Factors that can affect assay performance are as follows:

- acquired factors (passively acquired antibody, immune response to vaccination, immunosuppression)
- biological factors (lipaemic, haemolysed, high bilirubin content)
- collection factors (use of correct blood collection tubes)

Specimen rejection criteria

Samples may be rejected if:

- there is insufficient patient identifiable information on either the sample or accompanying paperwork – some specimens are difficult to repeat (CSF, biopsies and so on) and these are discussed by the RIPL clinical team with the referring medical team. In exceptional circumstances, these may be processed
- the sample type is inappropriate for the investigation requested (for example, urine sample with a request for serology, charcoal swabs for PCR and so on)
- the sample has leaked in transit with little or no residual fluid in the original container
- multiple liquid samples have leaked in transit within a larger container leading to potential cross-contamination of samples
- the sample container is inappropriate for safe processing (for example, broken glass, syringe needles and so on)

The sending laboratory will be informed of any rejected samples through standard reporting procedure. Samples received in a manner that compromises the safety of RIPL laboratory staff will be telephoned in addition.

Note that RIPL does not routinely return samples back to the original referring laboratory. Under exceptional circumstances, for example if a sample is unrepeatable, returning a rejected sample may be possible, but we strongly recommend that referring laboratories always retain aliquots of all samples submitted other than those from suspected VHF cases.

Results and reports

Reports

Printed results are no longer routinely sent unless the referring laboratory is not registered to E-lab.

[E-lab details](#) can be found online.

Missing reports and archived reports can be posted if requested.

Telephoned results

All on-call (urgent) results and routine significant results are telephoned out to the referring laboratories or clinical teams as relevant.

Biological reference values

Biological reference values do not usually apply to pathogen based diagnostics. In general:

- IgG positive suggests exposure to an associated antigen at some time – IgM positive suggests recent exposure to an associated antigen
- indeterminate IgG or IgM implies that we are unable to clarify the presence of these serological markers
- an RNA or DNA positive result is diagnostic for that specific pathogen
- inhibitory RNA or DNA result implies that we are unable to assess the presence of the target nucleic acid because of inhibitors present in the sample

Clinical decision making, treatment of infection and medical advice

Clinical interpretation, decision making, diagnostic, treatment and infection control advice is provided using evidence-based laboratory algorithms and standardised interpretative comments. These have evolved over time with input from published literature, UK and international guidelines and input from leading UK-based and international microbiologists, virologists, infectious diseases physicians, veterinarians, histopathologists and epidemiologists. By the very nature of the work performed in the laboratory, quite often the clinical decision making is complex, and comments are intended to communicate effectively with microbiologists, virologists and infectious disease physicians within UK.

Specimen referrals

Rarely, samples may be sent to other UK or international laboratories to clarify a result. However, RIPL does not routinely refer samples to other laboratories or return samples back to the original referring laboratory.

Cost of testing

Please note that listed prices are for 1 April 2024 to 31 March 2025 and are adjusted annually.

NHS hospital laboratories

From 1 April 2024 to 31 March 2025, the cost for running an initial panel of serological and molecular tests is £192.39.

All these prices are subject to inflationary fluctuations.

Laboratories requesting specific individual tests **only** will be charged per test as follows:

Table 4. Test prices

Test	Price
Immunofluorescence	£108.24
Serology	£113.68
Real-time polymerase chain reaction (PCR)	£123.70
Lyme disease	See Appendix 1
Leptospirosis	See Appendix 2

Exceptions to this are tests for *Coxiella* serology (£102.26 for ELISA screen, £192.39 for those requiring immunofluorescence and/or PCR in addition) and *Rickettsia* spp. immunofluorescence (£115.72).

Borrelia tests are not covered by the screen charge and are charged separately.

Leptospira tests may be charged differently depending on mode of submission (see [Appendix 2](#)).

A disposal or handling fee will be made for specimens that are not tested (see below).

Private hospital laboratories

The cost for running a panel of serological and molecular tests based on the clinical history and epidemiology provided will be £288.57

Laboratories requesting specific individual tests **only** will be charged as follows:

Table 5. Test prices

Test	Price
Immunofluorescence	£162.36
Serology	£170.52
Real-time PCR	£185.56
Lyme disease	See Appendix 1
Leptospirosis	See Appendix 2

Exceptions to this are tests for *Coxiella* serology and *Rickettsia* spp. immunofluorescence for which separate charges apply. *Borrelia* tests are not covered by the screen charge and are charged separately.

Leptospira tests may be charged differently depending on mode of submission (see [Appendix 2](#)).

Non-UK international hospital laboratories

Pricing on request and similar to private hospital laboratories as indicated in [Table 5](#). Please note that rejected or inappropriate specimens due to inappropriate packaging, incorrect referrals and so on incur a disposal or handling fee (£20.88 NHS, £31.33 for other customers).

Available assays and turnaround times (TAT)

The assays used in RIPL are as follows:

- IgG and IgM enzyme immunoassays
- IgG and IgM indirect immunofluorescent assays
- RNA and DNA – block-based PCRs
- RNA and DNA – real-time PCRS
- RNA and DNA – sequencing
- pathogen culture

Assays obtained from commercial manufacturers are performed according to the manufacturer's instructions. Assays developed within RIPL are developed according to in vitro diagnostic assay development guidelines. Quality of examination procedures are ensured by having appropriate assay controls relevant to each pathogen. In addition, RIPL participates in multiple national and international External Quality Assurance schemes.

The standard turnaround times (TAT) in the following table indicate the time taken from receipt of the sample at RIPL to the test result being reported, and are given in working days (that is, excluding weekends and public holidays). Any significant results (for example, PCR positive) are telephoned within 3 days. In the case of retrospective testing, TAT is measured from the time of the addition of the test code. TATs for non-standard sample types may exceed those stated in this manual.

Out of hours testing is predominantly provided for suspected viral haemorrhagic fevers (VHFs) only, but other assays may be performed for exclusion purposes at the discretion of the RIPL consultant. Out of hours turnaround is generally between 8 to 12 hours from receipt depending on the panel of tests being performed. VHF samples arriving within routine working hours are processed on the day of receipt. All VHF test results are telephoned once available.

All assays are performed and technically validated either by, or under direct supervision of, HCPC registered biomedical scientists who have been deemed competent to undertake these investigations. Results are medically authorised by appropriately trained and registered clinicians.

Table 6. Summary of available tests

Numbers in square brackets – [n1], [n2] and [n3] – refer to notes at the end of the table.

A Y indicates a validated blood type but absence of it doesn't exclude testing

Investigation and method	Plasma	Serum	Non-blood samples	Standard turnaround time
<i>Anaplasma phagocytophilum</i> IgG by immunofluorescence (IF)		Y		10 working days
<i>Anaplasma phagocytophilum</i> DNA by RT-PCR [n1]	Y	Y		Developmental assay
<i>Bacillus anthracis</i> (anthrax) DNA by real-time PCR (RT-PCR)	Y	Y Note that serology is not useful for acute diagnosis	Tissue biopsy [n3], post-mortem tissue [n3], culture, eschar [n3], lesion washings [n3], suspect colonies [n3], urine	3 working days
<i>Borrelia burgdorferi</i> ELISA		Y		7 working days
<i>Borrelia burgdorferi</i> IgG/IgM Immunoblot		Y	CSF [n3]	7 working days (CSF service has a 4 week turnaround)
<i>Pan Borrelia</i> RT-PCR	Y	Y	Joint fluid [n3], tissue biopsy, CSF,	7 working days
<i>Brucella</i> spp. RT-PCR [n1]	Y		Suspect colonies [n3]	Developmental assay
<i>Burkholderia mallei</i> RT-PCR [n1]	Y		Tissue biopsy [n3], pus or discharge [n3] Suspect colonies [n3]	Developmental assay

Investigation and method	Plasma	Serum	Non-blood samples	Standard turnaround time
<p><i>Burkholderia pseudomallei</i> (melioidosis) RT-PCR [n1]</p> <p>Please note that, other than for suspected <i>B. mallei</i>, all other <i>Burkholderia spp.</i> colonies from culture should be sent to BRD, Colindale, for species identification and antimicrobial susceptibility testing. For direct <i>B. pseudomallei</i> PCR testing on tissues, pus or blood, samples should be sent to RIPL.</p>	Y		Tissue [n3], pus or discharge [n3] Suspect colonies [n3]	Developmental assay
Chikungunya IgG and IgM ELISA		Y		7 working days
Chikungunya RT-PCR	Y	Y		5 working days
<p><i>Coxiella burnetii</i> (Q-fever) Serology (ELISA screen for IgG and IgM. Positives titrated to end point by IF)</p>		Y		10 working days
<i>Coxiella burnetii</i> RT-PCR	Y	Y	Tissue [n3], heart valve [n3], urine [n3]	7 working days
Crimean-Congo haemorrhagic fever (CCHF) virus RT-PCR	Y	Y	Urine [n3]	Contact Imported Fever Service in advance. Result phoned directly to referring clinician.
Dengue IgG and IgM by ELISA		Y		7 working days

Investigation and method	Plasma	Serum	Non-blood samples	Standard turnaround time
Dengue virus RT-PCR	Y	Y		5 working days
Ebola group viruses RT-PCR	Y	Y	Urine [n3] Semen [n3]	Contact Imported Fever Service in advance. Result phoned directly to referring clinician.
Western, Eastern and Venezuelan equine encephalitis viruses RT-PCR [n1]	Y	Y	CSF [n3]	Developmental assay
Venezuelan equine encephalitis viruses IgG by IF [n1]		Y	CSF [n3]	Developmental assay
<i>Francisella tularensis</i> spp. IgG and IgM by ELISA		Y		7 working days
<i>Francisella tularensis</i> spp. RT-PCR	Y	Y	Tissue [n3], wound swab [n3], suspect colonies [n3], Urine [n3]	5 working days
Hendra virus or Nipah virus RT-PCR [n1]	Y	Y	CSF [n3]	Developmental assay. Contact Imported Fever Service in advance. Result phoned directly to referring clinician.
Hantaviruses IgG by IF	Y	Y		7 working days
Hantaviruses RT-PCR [n1]	Y		Urine [n3]	Developmental assay
Japanese encephalitis virus IgG by IF	Y	Y	CSF [n3] (accompanied by serum)	7 working days
Japanese encephalitis virus RT-PCR [n1]	Y	Y	CSF [n3] (accompanied by serum)	5 working days

Investigation and method	Plasma	Serum	Non-blood samples	Standard turnaround time
Lassa virus RT-PCR	Y	Y	Urine, throat swab [n3]	Contact Imported Fever Service in advance. Result phoned directly to referring clinician.
<i>Leptospira</i> spp. IgM by ELISA		Y		7 working days
<i>Leptospira</i> spp. RT-PCR	Y	Y	Urine CSF [n3]	5 working days
Marburg virus RT-PCR	Y	Y		Contact Imported Fever Service in advance. Result phoned directly to referring clinician.
Murray Valley encephalitis virus IgG by IF [n1]	Y	Y	CSF [n3] (accompanied by serum)	Developmental assay
<i>Orientia tsutsugamushi</i> (scrub typhus) IgG and IgM by ELISA [n2]		Y		7 working days
<i>Orientia tsutsugamushi</i> RT-PCR	Y	Y	Eschar biopsy [n3] or CSF [n3]	5 working days
Orthopoxviruses RT-PCR [n1]			Vesicle fluid [n3], crusts or swab [n3]	Developmental assay. Contact Imported Fever Service in advance if potential HCID.
Parapoxviruses RT-PCR [n1]			Vesicle fluid [n3], crusts or swab [n3]	Developmental assay.
Rickettsia (spotted fever and epidemic typhus groups) IgG and IgM by IF		Y		7 working days
Rickettsia RT-PCR	Y	Y	Eschar biopsy [n3], CSF [n3] or swab [n3]	5 working days

Investigation and method	Plasma	Serum	Non-blood samples	Standard turnaround time
Rift Valley fever virus IgG by IF [n1]	Y	Y	CSF [n3]	Developmental assay
Rift Valley fever virus RT-PCR [n1]	Y	Y	CSF [n3], urine [n3]	Developmental assay
Ross River virus IgG by IF [n1]	Y	Y		Developmental assay
Sandfly fever viruses (incl. Toscana virus) IgG by IF	Y	Y	CSF [n3] (accompanied by serum)	7 working days
Sindbis virus IgG by IF [n2]	Y	Y		7 working days
Tick-borne encephalitis group viruses IgG by IF	Y	Y	CSF [n3] (accompanied by serum)	7 working days
Tick-borne encephalitis RT-PCR	Y	Y	CSF [n3] (accompanied by serum)	5 working days
West Nile virus IgM and IgG by ELISA		Y	CSF [n3] (accompanied by serum)	7 working days
West Nile virus RT-PCR	Y	Y	CSF [n3] (accompanied by serum), urine [n3]	5 working days
Yellow fever virus IgG by IF	Y	Y	CSF [n3] (accompanied by serum)	7 working days
Yellow fever RT-PCR	Y	Y	CSF [n3] (accompanied by serum), tissue [n3]	5 working days
<i>Yersinia pestis</i> (plague) RT-PCR [n1]	Y			Developmental assay. Contact Imported Fever Service in advance. Result phoned directly to referring clinician.
Zika virus IgG and IgM by ELISA		Y		7 working days
Zika virus RT-PCR	Y	Y	Urine, semen	5 working days

Notes to Table 6

[n1] indicates developmental assays which are not included in the laboratory's UKAS scope. These are assay for which there has been limited technical validation data and which may not be performed routinely or regularly. Despite this, every effort is made to provide testing for these assays within a clinically relevant timeframe. Please contact the laboratory to discuss individual cases.

[n2] indicates assays which are fully validated but do not currently form part of the laboratory's UKAS scope.

[n3] indicates secondary sample types for which the assay is not fully validated. Turnaround times for these samples may be longer than those indicated for validated sample types.

For additional tests please discuss with the clinical team on 01980 612348.

UK Imported Fever Service

Urgent clinical advice on management and diagnosis of imported diseases can be obtained through the UK Imported Fever Service telephone line 0844 7788990. The Imported Fever Service is a partnership between RIPL, the Tropical and Infectious Diseases Unit at the Royal Liverpool Hospital, and the Hospital for Tropical Diseases, London. The service details are available through local consultant microbiologists, virologists and infectious disease physicians who should be contacted in the first instance.

Services to the public

RIPL serves the UK public by providing reference service to medical and public health teams across UK and the world.

RIPL does not offer diagnostic services or health advisory service or email-based communication directly to members of the public or patients. We discourage patients and relatives from contacting us directly.

All our communications are with a registered medical practitioner or accredited laboratory personnel. RIPL does not run a clinic or a hospital ward.

Results can only be issued to the requesting physician or medical unit and will not be given to patients directly. We reserve the right to check the authenticity of callers in order to protect the privacy of patients' personal data.

Education services

RIPL can provide occasional support for educational activities for groups or individuals. School and professional groups are invited to write to us with their requirements. Professional

scientists and medical staff may visit for familiarisation with our work or for research attachments subject to approval from RIPL staff, their own management and if relevant, national authorities. Such visits require prior approval by the management regarding date, duration and content and are subject to the availability of RIPL staff to provide suitable input.

Protection of personal information

RIPL staff are trained to treat all personal details in the strictest confidence, in compliance with the Data Protection Act 2018 and NHS Caldicott Guidelines. Surveillance reports about individual patients are shared only with the healthcare professionals caring for that patient and those who are investigating the source of an infection or outbreak. Competency is regularly reassessed through mandatory training exercises provided through Civil Service Learning.

Results over the telephone

RIPL staff will only give results to an appropriate healthcare professional.

Results will not be given to a patient, patient relative or associate under any circumstances. When preliminary results are provided over the telephone, the enquirer will be made aware that 'unvalidated results' could be subject to change when the final results become available.

Emailing patient information

Emails generally cannot be relied on to guarantee security of patients' data because it can be intercepted by a third party en route. NHSmail is an exception, allowing staff working in different NHS trusts to exchange confidential emails via nhs.net accounts.

Public health

Where appropriate, information is shared with relevant Health Protection Unit teams in order to determine the cause and extent of an outbreak in a community (institution, family group or the wider community) or to see whether an observed cluster of cases is related and constitutes an outbreak.

Any further pathogen culturing or sequencing of pathogens for public health benefit are performed in such a way that patient identity is not compromised.

Terms and conditions

RIPL services are provided in accordance with UKHSA terms and conditions of business. The [current version of UKHSA's terms and conditions](#) can be found on the UKHSA website.

RIPL complaints procedure

A complaint may be defined as any contact by a customer, in writing, by telephone or direct communication, where a customer is dissatisfied with the service provided. Complaints can be made in writing to:

Rare and Imported Pathogens Laboratory (RIPL)
UK Health Security Agency
Porton Down, Salisbury
Wiltshire SP4 OJG
United Kingdom

Complaints can be made by telephone to 01980 612348 or email to ripl@ukhsa.gov.uk

All complaints will be acknowledged in writing within 3 working days and are taken seriously, even if it is suspected that the problems may be caused by factors other than a fault with the service concerned. All complaints are investigated and uncomplicated cases will be resolved within 20 working days. If significant investigative work is required on our part, we will contact the complainant within 20 working days to outline an appropriate timeframe for resolution.

If local resolution of the complaint is not satisfactory or unsuccessful, the complainant has the right to request an independent review of the complaint. For details of the escalation process, see [the UKHSA complaints procedure](#) on the UKHSA website.

Accreditation

RIPL is accredited by the United Kingdom Accreditation Service (UKAS) to ISO 15189:2012 for the test repertoire stated on [the Schedule of Accreditation](#) which can be accessed online.

Summary of revisions

- clarification of *Burkholderia spp.* testing provision between RIPL and BRD Colindale
- increase in minimum volume requirements for Lyme CSF testing from 600 to 700 microlitres (µl)
- expansion of information provided to Users regarding complaints procedure
- updates to prices for financial year April 2024 to March 2025
- inclusion of details regarding samples which experience delays in delivery to the laboratory
- UKAS logo size reformatted

Appendix 1. Lyme Disease

Tests offered

Antibody testing on serum is the primary test for Lyme disease. RIPL uses a 2-tier testing methodology. The screening test is a sensitive, commercial, CE marked VisE1/pepC10 ELISA (combined IgG and IgM). Positive results are confirmed by a more specific immunoblot (separate IgG and IgM line blots).

Laboratory confirmation of neuroborreliosis is based on demonstrating intrathecal synthesis of borrelia-specific antibodies. RIPL has developed a CSF serology service using the ViraChip assay. This service is not currently included in the UKAS scope for the department.

Serological testing of CSF samples requires simultaneous testing of a contemporary serum in order for the CSF results to be interpretable. It also requires measurement of albumin, IgM and IgG levels in both the CSF and the serum.

In addition to serology, PCR is also available and may be useful in testing joint fluid, biopsy tissue and CSF. PCR is not usually performed on blood but please contact us to discuss if this test may be required.

We also have capacity to perform further testing for diseases that share some common features with Lyme. Medical personnel are invited to contact us to discuss the most suitable tests we can offer for their patient.

Sample type

Please send serum (600µl minimum volume) for routine Lyme testing.

If CSF serology testing is required, please submit at least 700µl CSF as well as at least 700µl of serum taken on the same day. If albumin, IgM and IgG levels on the CSF and serum are available, these should be provided on the request form. If the values are not provided by the referring laboratory, RIPL will arrange for these to be measured at University Hospital Southampton Immunology Department. Please note the CSF testing service has a turnaround of 4 weeks.

For PCR, the following sample types are accepted:

Joint fluid, tissue, CSF and EDTA plasma (after discussion with RIPL clinician). A minimum volume of 350µl will be required (or 0.1g of tissue).

Please refer samples with as much clinical data as possible including clinical presentation, date of symptom onset, history of tick bite, and UK location or country of exposure. Please also provide the results of any Lyme screening tests you or other laboratories have performed.

The [Lyme disease test request form](#) is available online.

Prices

Listed prices are for 1 April 2024 to 31 March 2025 and are adjusted annually.

Table 7. Price list

	NHS	Commercial
Lyme EIA	£32.95	£67.82
Lyme immunoblot (IgG+IgM) and EIA	£125.35	£188.02
Albumin, IgM and IgG on serum and CSF	£32.72	£49.42
Lyme PCR	£53.43	£114.64
Anaplasma IFA	£108.24	£162.36

Please note: an out-of-hours testing service is not provided.

Contact details

In case of queries, medical professionals should contact +44 (0)1980 612348 (9am to 5pm Monday to Friday) or email lyme.RIPL@ukhsa.gov.uk

There is no clinic at UKHSA Porton and we are unable to see patients or give telephone medical advice directly to members of the public. Please note that we may verify the authenticity of callers before giving results to ensure that we meet the requirements of patient confidentiality and good medical practice.

[Further information about Lyme disease](#) can be found online.

Appendix 2. Leptospirosis

Testing for Leptospirosis

The *Leptospira* Reference service was transferred from Hereford to UKHSA laboratories at Porton on 1 April 2015.

Tests offered

A full diagnostic service is provided 5 days a week (Monday to Friday). Clinical advice is available 24 hours, 7 days a week and should be accessed through RIPL or the Imported Fever Service where clinically appropriate (01980 612348 weekdays or 0844 77 88 990 weekends).

Requests for *Leptospira*-only testing (both primary and follow-up samples) should be submitted to RIPL at Porton Down using the [Leptospirosis request form](#).

Leptospirosis testing will also be routinely added to samples from returning travellers where compatible travel and clinical details have been provided.

Serology is the primary investigation for *Leptospirosis* diagnosis. The primary serological test performed will be an IgM ELISA.

PCR has shown improved detection on samples taken within 7 days of onset and will be performed on all samples collected within this period. Validation of the PCR for urine samples is under development as evidence suggests that urine may be PCR positive early in infection and for a longer period than in serum or plasma. Urine samples for PCR should be sent with a corresponding serum sample.

An environmental water testing service is not offered.

Sample type

Serology

1mL serum, plasma or clotted blood.

PCR

250µl Serum, EDTA blood, plasma.

Urine, CSF, bronchoalveolar lavage and tissue may be tested if supplied with corresponding blood sample.

Post-mortem tissue specimens

Unfixed.

Cerebral spinal fluid (CSF)

250µl (minimum volume).

Please refer samples with as much clinical data as possible including clinical presentation, date of symptom onset, UK location or country of exposure, occupation.

A [Leptospirosis request form](#) is available online.

Prices

Leptospirosis diagnosis frequently requires multiple samples. The service costs a flat fee of £116.60 (NHS) or £178.42 (private or commercial) per patient for leptospirosis testing. This charge includes:

- clinical advice
- any leptospira-specific diagnostic testing (multiple tests) that clinical information suggests is appropriate
- convalescent sample testing, which is essential for confirmation of diagnosis
- testing of multiple sample types, and follow-up samples

If clinically appropriate, testing for hantavirus may also be undertaken at RIPL, in which case the combined cost for leptospirosis and hantavirus testing per patient will be £144.65 (NHS), £216.98 (private or commercial).

Samples tested for leptospirosis as part of the initial panel of serological and molecular tests on a returning traveller will incur the standard RIPL panel charge. Listed prices are for 1 April 2024 to 31 March 2025 and are adjusted annually.

Contact details

In case of queries, medical professionals should contact +44 (0)1980 612348 (9am to 5pm Monday to Friday) or email RIPL@ukhsa.gov.uk (checked on weekdays only).

There is no clinic at UKHSA Porton and we are unable to see patients or give telephone medical advice directly to members of the public. Please note that we may verify the authenticity of callers before giving results to ensure that we meet the requirements of patient confidentiality and good medical practice.

Further information on Leptospirosis infections can be found at:

- [Leptospirosis](#)
- [Leptospirosis \(Weil's disease\)](#)

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 health secure.

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For queries or to request this document in other formats, please email ripl@ukhsa.gov.uk or call 01980 612348.

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