5. Guidance for General Practitioners

5.1 Action to take on recognising cases of unusual illness

Prepare in advance by taking a look at your surgery and consider how you would control access and segregate patients. At the initial clinical assessment a case may appear to be of unusual illness by virtue of its type, severity and/or symptoms. Summary of actions on recognising such a case:

- Think about it – see algorithm figure 1
- Refer for advice to usual local sources raising concerns about unusual presentations as necessary
- Discuss with local HPU

The GPs direct involvement with cases will differ according to the category of incident. In an acute incident (most likely to be due to a chemical agent) the most seriously affected casualties will be taken to hospital. However, there may be some people with more minor symptoms who leave the scene and see their GP's. It is possible that some of these may be unaware that they have been exposed to any risk. In a delayed incident (more likely to be due to an infectious agent) GP's may well be pivotal in first recognising the unusual nature of the illness. Once again the patient may be unaware that they have been exposed to any risk. **A high index of suspicion is vital**, and the importance of a thorough history cannot be overstated in determining the cause.

Where an incident of unusual illness has been recognised in another setting but might affect other patients, the local HPU or incident control team should ensure that GP's are given all the information they require in order to safely manage patients and protect themselves and their staff. Very early on in an incident however there may not have been enough time for this to occur. This guidance is intended to help GP's through the early stages of decision-making under these circumstances. The HPA-RCGP clinical action cards entitled *New diseases, New threats* may also provide helpful information.

5.2 Personal safety and patient containment

If you suspect that a patient has an unusual illness - consider the safety of yourself, your staff and other people in the environment where you are seeing the patient. It is not possible to outline appropriate measures for all possible scenarios in this document. You should **call for expert advice immediately;** they will advise not only on personal safety but also on the further management of the patient(s) and of any exposed but not ill people (including yourself and your staff).

5.3 Further management of case(s)

The local HPU will advise on the further management of the case(s). Patients may be sent home with advice or perhaps prophylaxis depending on the likely agent involved. In many cases however the likely further management will be transfer to a hospital for further investigation and care. Always ask at what level of risk patients should be transported, so that this information can be passed on to the ambulance service. Sometimes decontamination of the patient may be required prior to transfer to hospital; this will usually be done by ambulance professionals at the scene.

Do not perform any investigations on the patient - these should only be done in the hospital environment or other appropriate facility.

Where a decision to transfer to hospital has been made the GP should:

- call the hospital to which the patient is to be taken; local HPU may advise on which hospital to use
- speak to the relevant clinician at the receiving hospital, if possible, to ensure that any special requirements of the case are known before the patient arrives there
- arrange for an ambulance - tell ambulance control if the patient is infected or potentially contaminated and whether decontamination has been recommended

5.4 Further health protection for other exposed people

The local HPU will advise you if any decontamination, prophylaxis or other follow-up is required for other exposed people. The GP should make a list of all those believed to have been exposed. This should contain the name, address, age, GP details, contact details and likely level of exposure. Advice about environmental decontamination, which may be necessary, and how this should be arranged, will be provided from the appropriate expert advice provider (appendix 1).

5.5 Record keeping

The importance of comprehensive record keeping cannot be over emphasised. In addition to the usual clinical records, include details of the advice received, actions taken to protect self and others, and who else has been informed.

GUIDANCE FOR OCCUPATIONAL HEALTH SERVICES

6. Guidance for Occupational Health services

6.1 Action to take on recognising cases of unusual illness

An employee/ client of an organisation may turn to their OHS for advice if they are suffering with unusual symptoms or they feel they have been exposed to someone who has an unusual illness. These clients may have been exposed through the course of their work, if NHS or emergency service employees, or they may have been exposed during an acute incident. If a client presents to the OHS with an unusual illness it is crucial that they are identified as early as possible (see checklist 1).

A detailed clinical history is essential and full and concise written records should be maintained. This should include their name, age, address, GP details, 24-hour contact details, their level of contact with the case and any adverse health effects reported. Refer to section 2.4 and appendix 3 for detailed information which should be sought.

6.2 Personal safety and patient containment

If it is suspected that a client has an unusual illness - consider the safety of yourself, your staff and other people in the environment where you are seeing the client. It is not possible to outline appropriate measures for all possible scenarios in this document. You should **call for expert advice immediately** (see appendix 1); they will advise not only on personal safety but also on the further management of the client(s) and of any exposed but not ill people (including yourself and your staff).

6.3 Further management of case(s)

The local HPU will advise on further management of the case. The client may be sent home with advice or perhaps prophylaxis depending on the likely agent involved. In many cases the likely further management of the case will be transfer to hospital for further investigation/ care. Ensure you inform the ambulance service and the hospital as to the level of risk which has been advised by the HPU.

All tests and investigations will be performed by the treating hospital. However, OHS in the NHS may be asked to take samples from clients/ employees of their own organisation for investigation, dependant on resources available to them. Early decontamination may be vital to minimise harm and OHS may be asked to assist if the resources are available to them, e.g. shower/ washing facilities.

OHS should ensure they inform the line manager if the employee is not returning to the workplace, in line with organisational absence policies. Return to work programmes for employees exposed to an unusual illness should incorporate the relevant advice from the local HPU and in liaison with relevant specialists and GP.

6.4 Further health protection for other exposed people

There may be staff who have had unprotected contact with a patient or colleague prior to realisation that special precautions should be taken. They are considered to be exposed until otherwise proven and expert advice (appendix 1) sought as to further management. Depending upon the nature of the incident full decontamination, prophylaxis, or some other measure(s) may be required.

6.5 Record keeping

The importance of comprehensive record keeping cannot be over emphasised. In addition to the usual clinical records, include details of the advice received, actions taken to protect self and others, and who else has been informed.

6.6. Participation in occupational health registers

The HPA will establish a register of all those people who are exposed to the effects of an incident where unusual symptoms occur and the emergency response which follows. The OHS will be asked to assist with these registers. The register will have a number of functions, including to:

- ensure that anyone who was exposed has full information about the support services available
- monitor peoples health for longer-term effects

The management of the register will be overseen by a steering committee, which could include representatives from DH, NHS, HPA, emergency services and London transport.

This multi-agency approach to OH follow-up is important because in many disasters, the number of individuals occupationally deployed from any single agency is typically small and subtle health problems related to the deployment may not be detected.

GUIDANCE FOR HISTOPATHOLOGISTS AND ANATOMICAL PATHOLOGY TECHNOLOGISTS

7. Guidance for histopathologist and Anatomical Pathology Technologists

As a histopathologist or an Anatomical Pathology Technologist (APT) you may become involved with investigating cases of unusual illness in several ways, you may:

- recognise similar unusual pathology at post-mortem examination of patients who may have died in different settings and with no connections having been previously made between them
- receive laboratory results from a previously performed post-mortem examination, which indicate an unusual illness
- be informed about an unusual illness which has already been recognised as such and asked to perform a post-mortem examination
- the case may arise either from a death in hospital, the community or in a deceased that has been repatriated to the UK from abroad

The following sections give you guidance on what to do in each of these situations. It is likely that the autopsy will have been commanded by a coroner or the procurator fiscal in Scotland[2]. The coroner needs to be informed if the case involves an unusual illness that had not been appreciated at the time of initial inquiries. If the deceased should be moved to another mortuary for safety reasons, the coroner will need to be informed before further arrangements are enacted.

Health and safety issues should be considered as a priority in every incident, and should be discussed with the local health and safety or OHS with appropriate speed. It is reasonable to consider developing contingency plans in advance of any such incident in order to safe guard staff. Information such as age, address, GP details and contact details, could be gathered in advance as part of contingency plans providing it is regularly updated and securely held.

It should be remembered that strict adherence to procedures for the prevention of infection as outlined in the HSE *Safe working and the prevention of infection in the mortuary and post-mortem room* (2003) and Royal College of Pathologists *Guidelines on autopsy practice* (2002) documents will minimise the risk of transmission of most pathogens. If there is a risk of an HG4 organism then specific advice must be followed.

If the circumstances are such that the body has already been embalmed, further laboratory investigations (whether chemical, microbiological or radiological) are likely to be significantly compromised. There are no formally validated tests for work on embalmed tissues and therefore it may not be possible to produce a definitive result. However, tissue preservation may be excellent and immuno-cytochemical analysis can be as good as in surgical or rapid autopsy material and a number of agents, including VHFs, anthrax and smallpox can be identified in such fixed material.

Advice may need to be given to funeral directors and the bereaved in terms of specific procedures for handling, viewing and/ or disposal of the deceases, as outlined in the HSE *Controlling the risks of infection at work from human remains – A guide for those involved in the funeral services (including embalmers) and those involved in exhumation* (2005).

7.1 Unusual illness recognised during post-mortem examination

On recognising pathology consistent with an unusual illness during autopsy:

- do not proceed any further with the procedure
- contact the OHS for advice concerning personal safety - it is generally safer to continue with the autopsy procedure, once the body cavities have been opened, than to transfer an opened high-risk deceased patient to another mortuary. Seek specific HPA advice on what samples of tissues and body fluids should be taken and how they should be handled – see also section 7.4
- liaise with the coroner and/ or the senior clinician in charge of the case and between you ensure that you have informed infection control, the local HPU and CFI/ CHaPD/ RPD as appropriate
- make a list of all those pathology staff (i.e. pathologist, anatomical pathology technologists) that had direct contact with the deceased - this list should include name, age, address, GP details, contact details, the nature of their contact and any adverse health effects reported

[2] From here on, if in Scotland, substitute the procurator fiscal for the coroner

7.2 Unusual illness recognised after laboratory results from post-mortem examination
Where the laboratory investigation from a post-mortem examination indicates an unusual illness:
- liaise with the coroner and/ or the senior clinician in charge of the case and between you ensure that you have informed infection control, the local HPU, and CFI/ CHaPD/ RPD as appropriate
- contact the OHS for advice concerning management of any potentially exposed pathology staff
- make a list of all potentially exposed staff (i.e. pathologist, APTs) with their name, age, address, contact details, GP details and level of exposure

7.3 Unusual illness recognised clinically and a request for post-mortem examination made
The most important guidance here is:
DO NOT PERFORM A POST-MORTEM EXAMINATION ON ANY PATIENT RECOGNISED AS HAVING AN UNUSUAL ILLNESS UNTIL EXPERT ADVICE HAS BEEN SOUGHT FROM THE HPA
Where experts have advised that an autopsy could be done, this should only be performed where the facilities and available equipment are appropriate to the level of risk and staff have received adequate training. The autopsy may be performed locally, in which case the extent of tissue and body fluid sampling is critical – see below. Or it may be advised that the deceased be removed to another unit with higher standards of containment and staff with more experience of the range of conditions known or suspected. If the unusual illness is recognised before the deceased has been opened in a public mortuary, it may be advisable to have the case removed to a hospital mortuary with appropriate experience; the coroner will need to be consulted first.

7.4 Sampling
If after discussion a post-mortem examination is felt to be appropriate, the suggested samples to take are:

7.4.1 Toxicological
The Toxi-box or ChEAKs (see section 4.5) can be used for sampling at post-mortem:
- bladder contents can be collected in the universal container for urine **(without preservative)**
- **peripheral** venous blood specimens can be collected - toxicological blood samples should be filled in the same order of priority as for sampling from an acutely ill patient

In addition other samples may be useful in a toxicological investigation since the concentration of chemical agents can be much higher in certain body sites than in blood or urine. The following should be collected in universal urine containers **without preservative**:

- gastric contents
- bowel content at different levels through the gut
- liver tissue
- kidney tissue
- muscle tissue (skeletal and cardiac)
- fat
- brain
- cerebrospinal fluid (CSF)
- lung tissue
- vitreous

Toxicological sample handling procedures:
- Toxi-Box/ ChEAKs samples should be handled in exactly the same way as for sampling from acutely ill patients. However, **tissue samples in universal containers should be put in individual plastic bags** within a cardboard container to keep them separate from each other and from blood and urine specimens. This is to prevent cross contamination. A second cardboard container may be necessary depending on the number of samples taken.
- An analysis request form for **toxicological investigation** (appendix 2) should accompany the sample and should be marked **high risk**.
- All samples should be transported as high risk according to local protocols.
- Where deliberate release is suspected or there are other forensic considerations, chain of evidence documentation should accompany the samples (appendix 2).
- Samples for toxicological analysis in Toxi-Boxes/ ChEAKs should be sent to the local clinical chemistry laboratory. The **laboratory should be telephoned in advance** to expect the samples.

7.4.2 Microbiological

Due to the high risk of post-mortem microbial contamination and autolysis, it is preferable that any autopsies that are deemed to be appropriate should be performed within 24 hours of the patient's death, if possible. In cases suspected to be of an unusual illness only at the time of autopsy, the time from death will almost always be >1 day. It is still important to take all the appropriate samples as indicated in this document. To increase the validity of culture and PCR results, emphasis MUST be placed on aseptic technique for specimen collection. Possible samples to be taken are shown below. Samples should be collected with appropriate precautions.

Stained smears and tissues on glass microscope slides

Collect all stained and unstained slides and send these with the clinical material. Secondary testing such as immunofluorescence and molecular biology can be performed on this material.

Microbiological sample handling procedures:

- Use standard request forms marked **high risk** for the transfer of clinical material to the laboratory – indicate on request form the time elapsed since death
- All samples should be transported as high risk according to local protocols.
- Where deliberate release is suspected, or there are other forensic considerations, chain of evidence documentation should accompany the samples (appendix 2).
- Samples for microbiological analysis should be sent to the local microbiology laboratory. This **laboratory should be telephoned in advance** to inform them about the samples and any specific cause that may be suspected.

Possible post-mortem samples for microbiological and histological examination

Sample	Requirements
Serum if possible or whole blood without anticoagulant. If the mortuary does not have a safe centrifuge, the sample should be sent to an appropriate microbiology department for centrifugation and serum separation	• 2 x 5-10ml minimum • store in a container suitable for freezing at -70°C
Whole blood (EDTA)	• 2 x 5-10ml minimum • store in a container suitable for freezing at -70°C
Blood cultures (from peripheral venous blood)	One set (aerobic and anaerobic bottles)
Tissues e.g.: • local inflammatory lesions or abscess material • liver • spleen • lung • kidney • heart • enlarged lymph nodes • bone marrow • other organs with gross pathologic changes • vitreous	• collect samples using aseptic technique • collect samples at least **in duplicate** • tissue fragments should measure 1cc • place one of duplicate samples into sterile universal container for microbiological examination and storage at –70°C • fix second of duplicate samples with 10% buffered formalin for subsequent paraffin embedding after 24 hours of fixation (since antigenicity decreases for immunohistochemical assays with prolonged formalin fixation)
Urine	• Collected aseptically in sterile container suitable for freezing and storage at -70°C
Faeces/ gut contents	• Collected in sterile container suitable for freezing and storage at -70°C
CSF, pleural fluid, pericardial fluid, vesicular fluid	• Collected aseptically in sterile container suitable for freezing and storage at -70°C

7.4.3 Radiological

A post-mortem examination hazard will only be present where it is suspected that there is incorporated radioactivity.

Where incorporated radioactivity is present then careful consideration needs to be given (in concert with police, coroner and other properly interested parties) as to whether the need to perform a post-mortem examination is outweighed by the risks of performing a post-mortem examination. If a decision is taken to perform a post-mortem examination then careful planning will be required to ensure that an appropriate safe system of working is designed (including physical adaptation of the chosen mortuary facility); that the extent of the examination needed is carefully planned; that all the wastes generated are carefully collected and disposed of appropriately; and that thought has been given to the safe processing of any toxicological, microbiological or histological tests that may be required. The potential hazards of such an examination may be better identified by the analysis of clinical specimens obtained ante-mortem and specimens, such as muscle blocks, obtained by minimally invasive means post-mortem for radiological activity.

The design and supervision of the safe systems of working for such a post-mortem examination should be jointly managed by an approved Radiation Protection Adviser on behalf of the institution providing the post-mortem facilities and an appropriate person appointed by the HPA.

Samples will be radiochemically analysed at specialist institutes. The HPA can advise on where these analyses can be made and on the requirements for transporting samples.

The choice of tissues and organs, and the amounts of each required for analysis, will depend on the radionuclide(s) involved and this should be known and discussed prior to the post-mortem examination. However, as a default the range of tissues listed above for toxicological and microbiological analyses, plus a limb long bone or a rib could be collected and where possible at least 50g of solid materials and 20ml of fluids.

GUIDANCE FOR LOCAL LABORATORIES

8. GUIDANCE FOR LOCAL LABORATORIES

Health and safety issues should be considered as a priority in every incident, and should be referred to the local health and safety or OHS with appropriate speed.

It is reasonable to consider developing contingency plans in advance of any such incident in order to safe guard staff. Information such as age, address, GP details and contact details, could be gathered in advance as part of contingency plans providing it is regularly updated and securely held.

8.1 Safe handling of specimens in laboratories

In practice, most of the laboratory hazard involved in samples from a patient with unknown illness will be microbiological rather than toxicological or radiological. It is unlikely that chemicals or radionuclides in specimens will be at high enough concentration to pose a threat to the health of those analysing them. However, all samples could potentially pose an infectious risk. Furthermore, where deliberate release is suspected it is always possible that the exposure may have been to a mixture of chemical, biological or radiological agents. Therefore:

All laboratories should handle specimens as if potentially high risk
Always seek expert advice

Decontamination and waste disposal should be performed as per standard guidelines for laboratory practice e.g. hypochlorite (5,000ppm available chlorine) disinfection for decontaminating surfaces that may have been exposed. All waste should be autoclaved or incinerated.

Prophylaxis for laboratory staff will not normally be required, especially if the specimens have been handled correctly. If there are particular concerns, or if there has been a spillage, then please seek expert advice.

Procedures for managing accidents within the laboratory should already be in place. Where appropriate, decontamination of personnel may be necessary. Full written records of all accidents should be kept. A list should be maintained of all staff handling specimens. This should include name, age, address, GP details, contact details, and the nature of their contact with specimens.

The Advisory Committee on Dangerous Pathogens has advised that high risk samples can be safely processed using closed system automatic analysers for routine patient support tests.

The Toxi-Box or ChEAKs samples will be used to analyse for all possible chemical agents and will not normally be examined in local clinical chemistry laboratories.

Local microbiology laboratories will potentially constitute the most hazardous laboratory environment because of the way in which samples are processed. All clinical samples received from potential cases and cultures/material derived from those samples should therefore be processed by experienced Biomedical Scientists. A Class 1 protective cabinet in a Containment Level 3 (CL3) facility should be used for all handling until further evidence and advice allows alternatives. If a deliberate release is suspected all material should be held in a secure facility within a CL3 room.

If there is any suspicion that a Hazard Group 4 (HG4) pathogen is involved then specimens must only be processed in facilities appropriate for such pathogens and expert advice should be sought immediately. Such facilities are located at HPA Cfl, HPA CEPR, and at DSTL. Some clinical material may have been received in pathology departments and been processed to some extent prior to the recognition of an incident. If this situation arises, remaining material should be retrieved and moved to the appropriate containment facility immediately.

8.2 Sample processing and referral

Particular care should be taken to ensure that laboratory records are kept to a high standard and that chain of evidence documentation is maintained where deliberate release is suspected or there are other forensic considerations. Please ensure that **as a minimum,** patient surname, forename, date of birth and specimen laboratory number, are completed on all referral forms.

To assist in the tracking of sample progress and results of investigations, laboratories (either diagnostic or specialist/ reference) which receive clinical diagnostic material from such cases should

inform the microbiology or toxicology coordinator as soon as possible after receipt, and provide sufficient information to enable tracking of what material has been sent where. If there is any suspicion that a case is unusual, all the excess samples must be kept pending further notice so that they are available for further diagnostic tests as necessary.

8.2.1 Routine haematology and biochemistry
Samples can be processed in the local laboratory but should be treated as **high risk**.

8.2.2 Toxicology
Samples for toxicological analysis (Toxi-Boxes or ChEAKs) should be temporarily stored in the local laboratory (**without opening or centrifuging them**) at 4°C. From here they should be rapidly transferred (at least within 24 hours) to the appropriate medical toxicology laboratory since some toxins degrade or absorb onto sample tubes with prolonged storage. The medical toxicology laboratory should be telephoned to inform them that samples will be sent to them.

Details of suitable analytical toxicology laboratories and advice should be sought from CHaPD (contact details in appendix 1).

Guidance on safe transfer of samples to the medical toxicology laboratory is given in section 8.7. Care should be taken to ensure that all laboratory records are complete and that chain of evidence documentation (appendix 2) is maintained, particularly where deliberate release is suspected or there are other forensic considerations.

8.2.3 Radionuclides
Analysis for levels of radionuclides in tissue samples and body fluids requires specialised facilities not normally present in the local laboratory. Specimens should therefore be referred to centres advised by HPA. Samples must be frozen, not in formalin.

If the laboratory has processed samples that are later known or suspected to have contained radionuclides expert assistance should be sought to monitor work surfaces, laboratory waste, apparatus and, if necessary, the staff themselves. Initially this assistance would be provided by the radiological protection advisor and local medical physics department.

8.2.4 Microbiology
The first point of contact for reporting the existence of a patient(s) who has presented with an unexplained illness of suspected infectious aetiology is the Emerging Infections and Zoonoses (EIZ) department at HPA Cfl on 020 8327 7483. Specific microbiological and public health advice will then be obtained from the relevant experts, together with advice on appropriate samples and handling. **Seek advice and refer specimens as appropriate.**

Local clinical microbiology laboratories with CL3 facilities will receive specimens from cases of unusual illness and their diagnostic investigations will be supported by a range of reference laboratories (CL3 or CL4) including those at HPA Cfl and HPA CEPR (see appendix 1). These reference laboratories have the capability for the investigation of clinical samples for unusual pathogens, particularly those which could be associated with a deliberate release. They are also able to subsequently confirm, identify, and perform further analyses on, potentially significant isolates, using a range of techniques including sophisticated molecular technologies.

8.3 Receipt of clinical samples by local microbiology laboratories
As part of the blind screen, hospital clinicians and pathologists have been asked to take at least two sets of blood cultures, 4 x 5ml clotted blood, and 4 x 5ml EDTA blood along with any other clinically relevant samples, and to send these to their local microbiology laboratory. Samples should have been labelled as high risk by submitting staff, and should be handled according to local protocols for such samples.

Local laboratories should immediately discuss with Cfl if the cause is unknown or with the appropriate reference laboratory if a specific pathogen is suspected. Refer to *Protocol for the investigation of microbiologically unexplained serious illness and death*:
http://www.hpa.org.uk/infections/topics_az/deliberate_release/Unknown/Unknown_Agent_Protocols.pdf

Depending on the clinical signs and the samples available further material may also need to be sent to other reference laboratory(s). Instructions for the safe transport of specimens to national reference laboratories are given in section 8.7.

Expert advice should always be sought but it is anticipated that in most cases clinical specimens will, if practical, be aliquoted on receipt, or soon thereafter. A portion would then be used for preliminary investigations locally, and the rest placed in several containers suitable for freezing (at –70°C or at the lowest freezer temperature available) for archiving or possible transfer to reference facilities at a later date. Where an illness is recognised as unusual retrospectively, any remaining samples should be retrieved and transferred to the laboratory's CL3 area.

If the local laboratory does not have operational CL3 facilities then the remaining samples should be forwarded directly to either a nearby laboratory with such facilities (depending on local arrangements), or to the appropriate national reference laboratory.

8.4 Sample investigations and storage

All samples should be handled using appropriate containment facilities. Keep all samples. Given the unknown nature of the agent involved laboratory techniques to maximise the potential of identifying any infective agent are advised. It is likely that this may involve prolonged enrichment and selective aerobic and anaerobic culture, nucleic acid amplification techniques, electron microscopy, and viral culture. The following investigations may be clinically indicated:

- **Blood cultures**
  Automated systems should detect most, if not all, bacterial agents. However, if negative after your standard interval, consider extending incubation. Please retain negative bottles for possible subsequent examination by PCR or other testing methods. Negative blood culture bottles should be aliquoted into 3x1ml containers and stored at –70°C or lowest temperature available.
- **Respiratory secretions**
  Sputum, broncho-alveolar lavage or similar for standard cultures and virology; consider extending incubation if no significant isolates after standard interval. Please retain portions of sample at –70°C or lowest temperature available.
- **Nose and throat swabs**
  If a deliberate release is suspected, culturing nose swabs for *Bacillus anthracis* may be useful for epidemiological purposes.
- **Pus or tissue, or swab of local lesion/vesicular fluid**
  Pus and tissue samples for microbiology:
  - Plate directly for aerobic and anaerobic cultures, and include enrichment cultures
  - Consider extending incubation if no significant isolates after standard interval
  - Where practical a portion of the sample should be retained at –70°C or lowest temperature available

  Samples for **virological investigations** should be referred if necessary for investigation by EM, immunofluorescence, culture, and PCR as appropriate
- **Serum to be retained for possible subsequent examination or refer for possible toxin assay**
  - Acute sample (taken near time of admission) and convalescent sample
  - Store at –70°C or lowest temperature available
- **Whole blood in EDTA to be retained for possible subsequent molecular examination**
  - Acute sample (taken near time of admission) and convalescent sample
  - Store at –70°C or lowest temperature available
- **Urine for standard tests and to be retained for possible subsequent examination**
  - Store at –70°C or lowest temperature available
- **Faeces/ stools**
  - Routine culture and potential microbial toxin detection
  - Store at –70°C or lowest temperature available
- **Other samples**
  If cerebrospinal fluid, pleural fluid, pericardial fluid, or any other specimens are taken as part of the clinical workup, consider extending incubation if negative after your standard interval. Retain any isolates obtained. Reserve a portion of the sample at –70°C or lowest temperature available.

Collect all **stained and unstained** slides. Secondary testing such as immunofluorescence and molecular biology may be performed on this material.

- **Isolates**
  Identification should be attempted. If it is not possible to confidently identify the organism as a known non-pathogen, susceptibility tests should be set up and the isolate referred on to the appropriate national reference laboratory. **Interpreting any isolate as 'not significant', particularly those from sterile sites, in the context of a suspected deliberate release should only be done with extreme caution.**
  All bacterial isolates cultured from these patients should be retained locally for possible subsequent examination.

8.5 General guidance for local laboratories on prioritisation and transfer of samples

- **Expert advice should be sought** from CfI on which national reference laboratory to send samples to. Laboratories are listed in appendix 1.
- National reference laboratories must be informed of any samples which are being sent
- Information on packaging and transportation are given in section 8.7. **All specimens should be labelled and handled as high risk**
- The speed with which specimens/ isolates are referred will depend on the context of the investigation
- Depending on the scale of the incident and other factors, prioritisation of material for referral according to clinical manifestations and other available information may be necessary. Specialist microbiological investigations may be focussed on patients conforming fully to the working case definition to avoid swamping the laboratory investigation system(s) with potentially less relevant/irrelevant diagnostic material
- **Please ensure that any remaining samples are retained and stored** at the local laboratory. It is possible that for certain incidents a designated laboratory may act as a sample repository.
- Laboratories should complete their standard documentation and if necessary a chain of evidence form (appendix 2) on referral of samples to the national reference laboratories

8.6 Specific guidance for local laboratories on storage and referral of samples
Isolates:

- Retain *all* bacterial isolates cultured from these patients
- Refer all potentially significant isolates for confirmation and further work e.g. sub-typing or bio-toxin analysis (after antimicrobial susceptibility tests have been set up locally)
- If it is not possible to confidently identify an isolate as a known non-pathogen, or if it is unidentifiable, it should be referred for formal identification (see 8.5)
- Information on classic deliberate release agents is available at:
  http://www.hpa.org.uk/infections/topics_az/deliberate_release/default.htm)

Clinical specimens:
Local laboratories should receive (for acute and/or pathological samples) as a minimum, a set of blood cultures, a clotted blood sample and an EDTA sample. Some of these routine clinical samples may be referred directly to specialist reference laboratory(s). Depending on the specifics of the patient, and on the nature of the incident, and following expert advice, it may also be appropriate to refer some or all of the following additional specimens:

Specimen	Requirements
Respiratory samples	• A portion of BAL or other respiratory sample, stored frozen at -70°C (or lowest available/achievable temperature)
Pus/ tissue samples	• Pus or *non-fixed* tissue to be stored at -70°C or lowest available / achievable temperature • If only *fixed* tissue samples are available these may be examined using molecular approaches
Urine	• 5mls for further investigation, which may include toxin assay
Faeces/ stools	• Store at –70°C (or lowest temperature available/achievable) for culture/microbial toxin detection
Other body fluids	• Including cerebrospinal fluid, pleural fluid, pericardial fluid and other sterile site specimen • Please retain any sample remaining after routine examination at –70°C for possible subsequent examination

8.7 Safe transport of specimens from local to other laboratories
Both Toxi-Box/ ChEAKs and microbiological samples should be handled similarly with respect to packaging and transport. NOTE: The ChEAKs comply with transport regulations for Cat B UN3373 and no further packaging is required. The kits may also be used for the transport of radiological or microbiological Cat B samples.

Most clinical samples, **EXCEPT** those from suspected smallpox or viral haemorrhagic fever patients, are generally classified as Category B and assigned to UN3373 (Biological Substance, Category B) and should be packaged in accordance with PI650. Clinical samples and cultures assigned to UN3373 may be posted. Cultures of organisms are also usually Category B, except those included in the deliberate release group.

All cultures of *deliberate release* organisms and some clinical samples, including those taken from smallpox or VHF patients, fall into Category A - Infectious substances capable of causing disease in humans or animals (see ACDPs Appendix 1.2, Table A2 ☎).

Category A infectious substances are assigned to UN 2814 and must be packaged in accordance with UN Packaging Instructions PI620 (road/ rail) or PI602 (air). P620 and P602 are identical specifications but given different codes in ADR and ICAO regulations respectively (for a full description of PI see unece). Category A transfers should be individually requested through an approved courier. The service will be a next day tracked door-to-door delivery, which must be signed for at collection and receipt.

Packaging for any category of sample must meet with UN performance requirements i.e. UN-type approved packaging for Division 6.2 substances. The packaging should consist of an inner package (watertight receptacle, watertight secondary packaging, an absorbent material in sufficient quantity to absorb the entire contents placed between the receptacle and the secondary packaging) and a rigid outer package of adequate strength for capacity, mass and intended use. Packages should be marked with the proper shipping name i.e. *Infectious substance affecting humans*, the appropriate UN number (e.g. UN 2814) and the appropriate warning label (i.e. the danger sign for infectious substances).

In the event of suspected deliberate release, local support services e.g. police and armed services should be asked to transfer/ deliver materials to reference facilities as appropriate.

8.8 Recognising cases of unusual illness
Up to this point this guidance has assumed that the laboratory has become involved in investigating cases of unusual illness **after** those cases have been recognised clinically as unusual. It is however possible that it is the laboratory that first recognises cases of unusual illness. Under these circumstances you should do the following:

- Liaise with the senior clinician in charge of the case and between you ensure that you have informed infection control, the local HPU, and HPA CfI, CHaPD/ NPIS or RPD as appropriate
- Seek expert advice concerning management of any potentially exposed laboratory staff
- Make a list of staff that may have been exposed with their name, age, address, contact details, GP details and level of exposure.

GUIDANCE FOR PUBLIC HEALTH PROFESSIONALS

9. Guidance for public health professionals

Investigating outbreaks and incidents of disease is a core function of public health. For public health professionals specifically involved in health protection much of the guidance that follows will be standard practice. However, those not routinely involved in health protection might be called upon to take the initial public health role during an incident (e.g. out of hours) and this guidance should assist them in that function. If local plans are available, they should be followed. **Comprehensive record keeping is essential.** All information received, advice given and actions taken should be logged, signed, dated and timed. Your local generic log should be used.

9.1 Action when an incident is first reported

Section 2 outlined how outbreaks or incidents might come to light and suggested a classification for further management based on this and the basic epidemiology. This guidance recommends to all health professionals who might first recognise cases of unusual illness that they should inform the CCDC at the local HPU or their deputy immediately. Checklist 3 details useful information to obtain and record when an incident or outbreak is first reported to you.

Note that **if deliberate release is a possibility you should immediately discuss this with the police** (figure 3). This may then trigger the guidance that has already been produced for deliberate release: http://www.dh.gov.uk/assetRoot/04/07/17/86/04071786.pdf

If a specific agent is strongly suspected from the beginning it may be more appropriate to use the specific guidance. The public health management of acute chemical incidents and biological agents is comprehensively described on the DH and HPA websites:
http://www.dh.gov.uk/PolicyAndGuidance/EmergencyPlanning/DeliberateRelease/fs/en
http://www.hpa.org.uk/infections/topics_az/deliberate_release/defaultDAR.htm

For incidents which are believed to be due to radiation exposure, clinical information is readily available from your local oncology centre or contact the HPA (see appendix 1) for advice on management. The *Safety Reports Series No.2 Diagnosis and treatment of radiation* produced by the International Atomic Energy Agency is also available as a pdf at: http://www-pub.iaea.org/MTCD/publications/PDF/P040_scr.pdf .

9.2 Management of an outbreak or incident according to presentation

The first step in management of an outbreak/incident of unusual illness is to decide whether this is an acute incident i.e. requiring an immediate urgent response or whether there is more of a delay in the presentation of patients. Radiation outbreaks/ incidents may present acutely or after a delay depending on the dose incurred. Delayed presentation may have been preceded by self-medication for flu-like symptoms.
The same overall objectives apply to the management of both types of outbreaks/ incidents, to:

- care for the sick
- control the source
- determine the extent of the possible incident/exposure
- prevent others being affected
- monitor the effectiveness of the measures taken
- prevent a recurrence
- consider whether the cluster may be the result of deliberate action

It is also important to consider the needs of staff and other patients.

For both categories it is likely that broadly similar tasks will need to be carried out to manage the outbreak/incident. The difference between them lays in the speed with which things happen and hence the priorities given to different tasks. Acute outbreaks/incidents are much less likely to be due to infectious causes because of the variations that occur in the natural history of these diseases (e.g. range of incubation period).

The algorithm (figure 1) illustrates the management of acute outbreaks or incidents which is further explained in section 9.3. Here the acute nature of presentation of cases makes speed of identification of the likely agent imperative to best inform management of known cases and prevent further developing. The speed of response is particularly crucial for acute incidents. It is vital to seek expert advice immediately. Figure 3 illustrates the management of outbreaks/ incidents where patients present over a longer period of time, which is further explained in section 9.4.

Checklist 3: Information for public health professionals to obtain and record on receiving reports of an outbreak/ incident of unusual illness

- Who reported the outbreak/ incident?
  - Name
  - Position
  - Organisation
  - Contact details
- How has the outbreak/incident come to light?
- Where have cases occurred? Are there any common exposures recognised at this stage?
- Over what time period have cases been detected?
- Who are the cases? Are they from a particular social group or setting?
- How many cases are recognised at the moment?
- What are the symptoms experienced by the cases? (as much detail as possible)
- Have any of the cases been seen by a specialist clinician? If so what is their working diagnosis and clinical findings?
- Have specimens been taken and where have they gone for analysis? When will results be available?
- Have there been any deaths?
- Have the ambulance service and local hospitals/ GPs been warned?
- Where are the cases being managed?
- What is being done to manage cases at the moment?
  - Has decontamination of cases taken place? How?
  - What treatment if any has been instituted?
- Who else has possibly been exposed and might be at risk of developing this illness? Has a list of these been made?
- Are there any conditions occurring which might increase the risks to others e.g. health care workers exposed, ongoing incident, weather forecasts?
- What is being done to prevent the development of new cases at the moment? e.g.:
  - Protection of emergency and health care staff
  - Evacuation/sheltering
  - Quarantine
  - Prophylactic treatment
- What agencies are involved at the moment? Get contact details. Has any agency declared a major incident? Who else has been informed?
- Is there any information available about the likely cause of the illnesses at the moment?
- Is there any evidence of deliberate action in causation of the illnesses e.g. threats received?
- Are other public health units involved?

9.3 Managing acute outbreaks or incidents

For an acute outbreak/ incident, speed is necessary to ascertain the likely aetiological agent and hence ensure appropriate treatment of cases and protection of others. These episodes are most likely to be due to chemical agents, though biological toxins may also produce outbreaks of acutely ill people. Exposures to radiation are a less likely cause, but could occur for example where an abandoned source has been accidentally or deliberately disturbed. Occasionally an outbreak might be due to epidemic hysteria. Although the features of the illness, the way it has presented and the group affected may indicate this as a diagnosis early on, it is mainly a diagnosis of exclusion where no organic cause has been identified.

The urgent priority for an acute incident is to get as much information as possible about the clinical features of the illnesses and the circumstances that may have produced exposure. This should assist in identifying the likely aetiological agent and will advise on the management of casualties and on measures to be taken to protect health care and other professionals who may have been involved in managing the incident, including decontamination. Checklist 4 summarises the actions to be taken in the immediate management of acute outbreaks/ incidents.

Checklist 4: Actions for immediate public health management of an acute outbreak or incident

GATHER INITIAL INFORMATION LISTED IN CHECKLIST 1

IF YOU SEE ANY OF THE FOLLOWING:

- Single case of disease due to uncommon, non-indigenous agent in patients with no history suggesting an explanation for illness
- New or unusual clusters of infections with a number of ill people presenting around the same time
- Cluster of patients with a similar syndrome with unusual characteristics or unusually high morbidity or mortality
- Unexplained increase in the incidence of a common syndrome above seasonally expected levels occurring in an unusual setting or key sector of the community

SEEK EXPERT ADVICE in order to advise accordingly:

- Identification of likely causative agent(s)
- Likely clinical effects of agent
- Decontamination and treatment of cases
- Ensure appropriate measures to protect others and prevent other cases occurring
- Ensure appropriate investigations are conducted on cases
- Decide whether a major incident should be declared (number of casualties, use of resources)
- Assess whether more cases are likely to occur e.g. continuing exposure, weather conditions
- Establish a list of those exposed but not ill who may need follow up with contact details
- Assess whether the cases may be the result of deliberate action

ALERT OTHERS who may need to know or be involved, for example these may include:

- PCT and SHA colleagues
- Regional colleagues (neighbouring PCTs, Regional Director, regional HEPA, Resilience Groups)
- Health care providers (hospitals, EDs, GPs)
- HPA national centres of expertise (CfI, CEPR, CHaPD,RPD)
- Emergency services
- Local Environmental Health Department
- Local Authorities
- County / local multi-agency emergency planning forums (which may include many of those on this list)
- Local utilities
- Other relevant agencies e.g. EA, HSE, FSA, DWI
- Emergency Planning Coordination Unit at DH
- Devolved Administrations, including their public health service
- Media

➢ Consider convening an **ICT** (see section 9.5)
➢ Consider lines of **communication**
➢ Consider alerting and advising affected population
➢ Consider a site visit (but address personal safety issues) - note this is not usually helpful for acute incidents
➢ Formulate case definition and establish a database on cases
➢ Arrange follow-up

9.4 Managing outbreaks or incidents with delayed presentation (see figure 3)

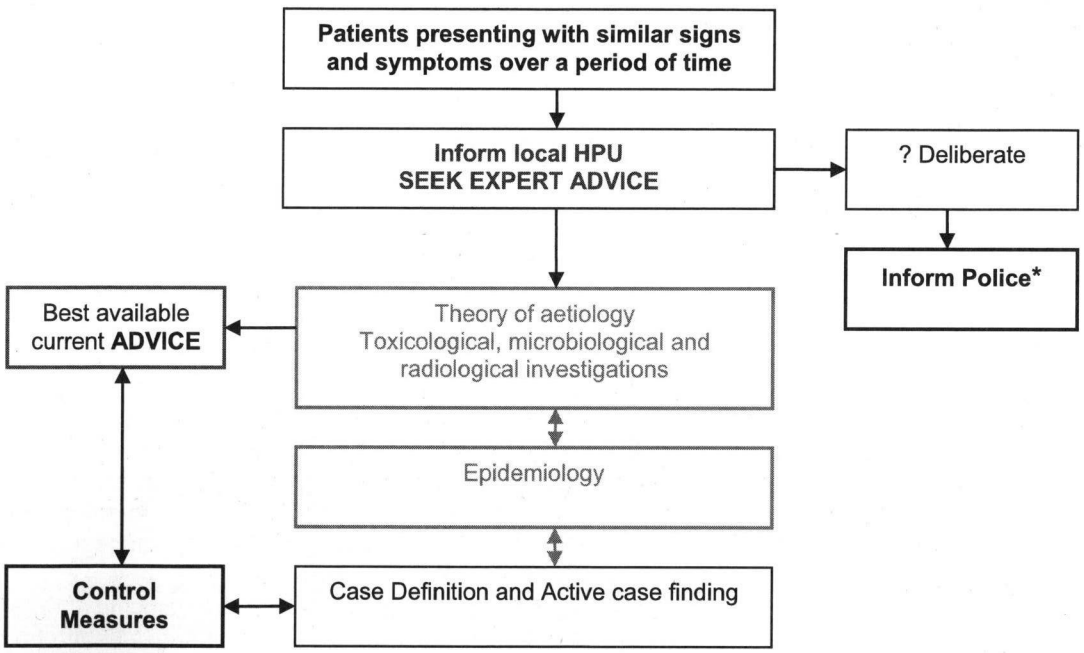
The cause of delayed onset outbreaks/incidents will usually be more uncertain than for acute outbreaks. Here an ICT should be set up at an early stage to ensure rapid investigation (see section 9.5). The important elements to be included in management are to **seek expert advice** and involvement to ensure:

- appropriate investigation of cases
- formulation of case definitions
- active case finding
- data collection on cases
- data collection on exposed but not ill people

- producing best available current advice on management of symptomatic cases
- producing and enacting best available current advice for public health protection including prophylaxis of persons who may have shared a common exposure
- assessment of risk to others e.g. contacts, health care worker, etc
- assessment of whether cases may be the result of deliberate action
- communication with all those who need to know

Management will essentially be an iterative process with constant refinement of the theory of aetiology and consequent advice. In the absence of a confirmed diagnosis e.g. an unknown agent, the precautionary principal should be employed until an agent is diagnosed or likely routes of transmission become known. It is important to try to ascertain the aetiological agent as soon as possible. There should be early liaison with laboratory colleagues to ensure appropriate collection and referral of samples (see section 8). It is suggested that during the management of these incidents, individuals are delegated to fulfil particular key functions and tasks which are summarised on page 48. Roles and responsibilities at local, regional and national level should be established early on in the incident.

Figure 3: Initial public health management of outbreaks or incidents with delayed presentation



*If a specific memorandum of understanding/ protocol is not in place between the local HPU/ Regional HPA Office and their local police force for dealing with such incidents, then advice on contacting the appropriate unit within the police service can be obtained from the ERD duty officer (01980 612100).

9.5 Investigation of the outbreak or incident

9.5.1 Case definitions

- A broad initial case definition should be used to avoid missing potential cases
- Subcategories of possible, probable and confirmed cases can be defined for the purpose of focusing investigative efforts
- Where cases are occurring in several districts, regions or countries it is important to ensure that standard definitions are agreed between the teams managing the incidents in different localities
- As more information becomes available the case definition may be refined

9.5.2 Active case finding

- A system may need to be instituted to actively find additional cases, and decisions will need to be taken about whether this should be done at local, regional, national or international level
- The case definitions should be supplemented with additional information to allow clinicians and pathologists to assess whether they might have cases. The contact number of a nominated medically trained individual(s) (e.g. the incident clinical adviser) should be provided in case they require additional information.

- A system should be developed for reporting of cases to a central information collection site - whether this is at a local, regional and national level depends on the extent of the outbreak or incident

Specific functions or tasks to be delegated to individuals

Function title	Function encompasses
Incident clinical adviser (e.g. Medical Director of receiving hospital)	• Advising clinicians and others reporting possible cases • Examination of clinical notes of cases where necessary • Development of proforma for collection of clinical information on cases • Collation of clinical information on cases
Incident information officers (e.g. senior clerical staff)	• Compilation and dissemination of list of essential contact details to ICT members • Receipt of case reports • Maintenance of the line-listing of cases • Regular construction and updating of epicurve • Distribution of regular epidemiological update bulletins to all who need to know • Compilation of a list of people who may have been exposed but are not as yet ill • Distribution of additional information to those who need to know e.g. changes to case definitions, clinical advice, investigative protocols etc
Microbiology and toxicology coordinators (e.g. laboratory staff of relevant specialty)	• Record and track what samples have gone to which laboratories • Chase results • Maintain database of results • Report results to incident team and local public health

9.5.3 Appropriate investigation of cases

- An initial theory of possible cause can be developed on the basis of initial clinical and epidemiological evidence
- Protocols for blind screening for toxicological and microbiological agents have been developed (see section 4.5) - expert laboratory advice should therefore be sought early in the investigation
- Decisions will need to be made with expert service providers about which national toxicology, microbiology or radiological reference laboratories to send samples to
- Nominated individuals should be assigned responsibility for chasing and compiling laboratory results and ensuring that these results are passed on to the ICT and the local public health team if this is different. Depending on the scale of the incident it may be appropriate for results to be collated at a local, regional or national level.

9.5.4 Reporting results

It is anticipated that delegated individuals within the HPA will be responsible for collating results on human and environmental samples. **All results should be reported to the relevant coordinator by laboratories processing samples**. The overall public health managerial lead for the incident will be able to direct laboratories to the relevant coordinator. This lead may be taken for example by the local HPU, a Regional Director, the chair of an ICT or STAC, or a national agency. The coordinators should be in close and continuing communication with those leading the incident.

The coordinator has responsibility to track samples and results between local and reference laboratories as well as to the HPU or ICT. Reference laboratories will communicate individual patient results to referring laboratories who should then liaise with the clinical team with responsibility for patient care. Subject to overall security considerations, it is hoped that patient name, date of birth etc will be used as identifiers for individual patients for all communications between the parties involved.

In the event of a suspected deliberate release it is possible that other bodies will need to be informed of results, for example law enforcement agencies. However, **reporting results to outside agencies should only be done by the ICT**.