INITIAL INVESTIGATION AND MANAGEMENT OF OUTBREAKS AND INCIDENTS OF UNUSUAL ILLNESSES

With Particular Reference To Events That May Be Due To Chemical Or Biological Causes, Including Deliberate Releases

A Guide for NHS Staff

Produced by the Public Health Laboratory Service and the Chemical Incident Response Service

These are interim guidelines and will be revised once the Health Protection Agency becomes functional

Comments to: DRcomments@phls.org.uk

CONTENTS

ABBREVIATIONS USED

A & E	Accident and Emergency
CAMR	Centre for Applied Microbiological Research
CCDC	Consultant in Communicable Disease Control
CDSC	Communicable Disease Surveillance Centre
CIPU	Chemical Incident Provider Unit
CPHL	Central Public Health Laboratory
CPHM	Consultant in Public Health Medicine
DH	Department of Health
DWI	Drinking Water Inspectorate
EA	Environmental Agency
EPCU	Emergency Planning Coordination unit
FSA	Food Standards Agency
HSE	Health and Safety Executive
JHAC	Joint Health Advisory Cell
NPIS	National Poisons Information Service
NRPB	National Radiological Protection Board
PCR	Polymerase Chain Reaction
PCT	Primary Care Trust
PHLS	Public Health Laboratory Service
PMBS	Police Main Base Station
PPE	Personal protective equipment
SHA	Strategic Health Authority
SpR	Specialist Registrar

FLOWCHARTS, TABLES & CHECKLISTS

1. Introduction

1.1 Purpose and scope

Outbreaks and incidents of unusual illnesses might have any one of a number of causes: infectious[1], chemical[2], nutritional[3], radiological[4] or even hysterical[5]. In a few instances, chemical or biological agents have been released deliberately[6].

This document is intended as an aid to decision making for those working in the NHS in England who may be involved in the initial investigation, management and response to outbreaks of unusual illness where the cause is not immediately apparent. It also aims to assist health personnel in making a judgement about whether an outbreak is due to natural or accidental cause or deliberate release.

The document cannot cover all possible eventualities, nor is it intended to be a comprehensive guide. However, prompt appropriate actions are likely to be crucial and this guidance aims to ensure that all NHS and other health protection personnel involved are confident about initial decisions and actions.

1.2 Intended audience

This document is aimed at clinicians who might be the first to detect cases of unusual illness, as well as laboratory personnel and other NHS staff responsible for health protection e.g. public health personnel. It is set out so that users from different fields can readily identify the guidance that specifically pertains to them, but can also appreciate the larger context within which that specific guidance operates.

1.3 How to use this document

All users are recommended to read the General Guidance section first. This section deals with information which is pertinent to all sections of the NHS, but which is not duplicated in specific guidance for different groups of professionals. Readers from different specialties will then find specific guidance for their role in the relevant dedicated section.

GENERAL GUIDANCE
FOR ALL USERS

2. General guidance for all users

2.1 Definitions

Unusual illness may be of:

(a) unknown aetiology, or
(b) known aetiology but not usually expected to occur in the UK or setting where it has been observed, or
(c) known aetiology that does not behave as expected e.g. failure to respond to standard therapy.

An **outbreak** is said to occur where:

- the number of cases observed is greater than the number expected over a given time period;
- two or more cases are linked by epidemiological, microbiological, or toxicological features.

Clearly one case of a serious unusual illness (e.g. inhalational anthrax) is of concern for public health but since this cannot be technically termed an outbreak it is instead referred to as an **incident.**

Although an outbreak or incident of unusual illness may be the result of natural or accidental processes, the possibility that it may be due to a **deliberate release** of a harmful agent must always be remembered. Deliberate release may be **overt**, where it is immediately apparent that a release has occurred, although the precise content of the release may not be clear. A deliberate release may however be **covert**, with the first indication of a release being the presentation of people with unusual illness. Health professionals have a crucial role to play in identification of such covert releases.

2.2 Critical factors in the initial response

The critical factors in responding to outbreaks or incidents of unusual illness are:

- A high level of awareness of the possible occurrence of such outbreaks/incidents, including those due to deliberate release.
- Immediate attention to issues of patient decontamination and containment and staff safety when cases occur.
- Early expert clinical assessment of patients to consider the most likely cause before epidemiological and tests results become available and institute rapid relevant investigations and management.
- Effective communication between different sectors of the health service and between the NHS and other relevant agencies (e.g. PHLS-CDSC/CPHL).
- Effective co-ordination of the response by an overall incident management lead.

2.3 Summary of the roles of different health professionals in the initial investigation and management of outbreaks or incidents of unusual illness

Flowchart 1 summarises the roles of health professionals in the initial investigation and management of outbreaks or incidents of unusual illness. These roles are further clarified in the relevant sections for each field. **Contact numbers for health professionals to seek expert advice are given in Appendix 1.**

2.4 Initial analysis of outbreaks and incidents of unusual illness

Although definitive diagnosis of an unusual illness will usually require laboratory confirmation, initial clues as to its causes come from three main pieces of information:

- The way in which cases came to light
- The basic epidemiology (when, where, who)
- The clinical features

These can be used to classify the outbreak or incident of illness into two basic categories for further management (see Flowchart 2).

Case detection

An outbreak/incident of unusual illness may be detected in several different ways and the means of detection may itself give clues as to likely aetiology as shown in Table 1.

Flowchart 1: Summary of initial steps investigation and management of outbreaks or incidents of unusual illness

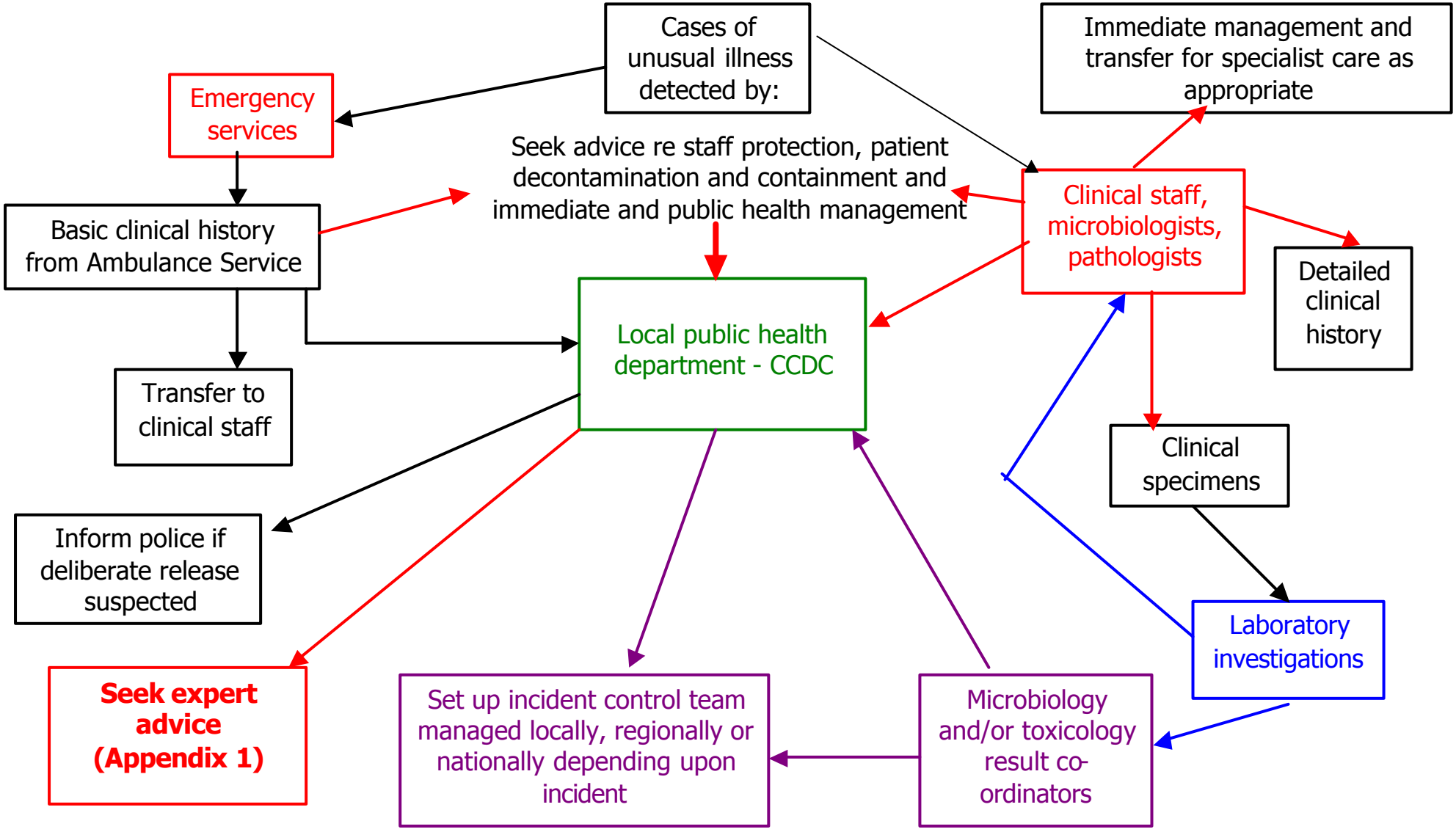


Table 1: Detection of outbreaks of unusual illnesses

Most likely means of detection of unusual illness:		
Acute chemical incident	**Unusual but recognised infectious disease**	**Unknown**
• Emergency services e.g police/ambulance • Accident and Emergency departments • General public • Chemical Incident Provider Unit (CIPU) • National Poisons Information Service (NPIS) • Declared releases • Media	• Vigilance of healthcare professionals: Consultants in Communicable Disease Control (CsCDC), medical microbiologists, A & E departments, clinicians, ID physicians • Routine surveillance e.g. referral of cases to Communicable Disease Surveillance Centre (CDSC) • National Reference Laboratory • The general public • The media • Declared releases • NHS Direct	• Vigilance of healthcare professionals • Exceptional reporting • General public • Media • NHS Direct

Epidemiology

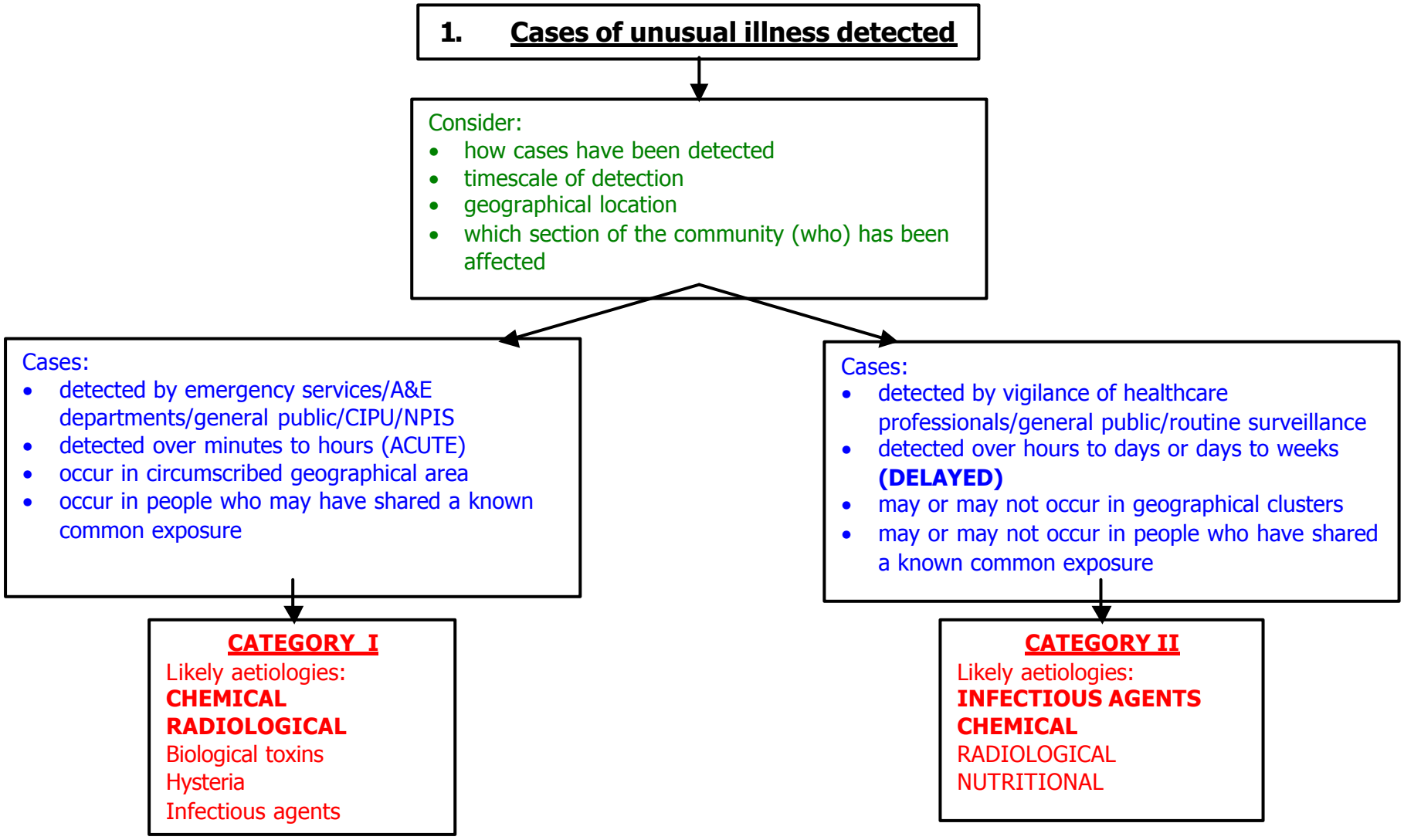
Time: In particular, timescale of case presentation. Have cases presented over minutes, hours, days or weeks?

Place: Is the geographical location of the cases confined to a small area (cluster) or are they more diffuse?

Person: Are all sections of the community affected or has the illness occurred in a subset of the population that may have shared common exposures?

Flowchart 2 shows an initial classification of unusual illnesses into two broad categories of possible aetiology on the basis of means of detection and basic epidemiology.

Flowchart 2: Initial classification of possible aetiology of an outbreak/incident of unusual illness for further investigation and management



Clinical features

As always in medicine, a good history is key in diagnosing the cause of an illness. As much information as possible should therefore be gathered about the clinical features and clinical course of the illness as well as about potential risks/exposures. This is particularly important in the case of acute presentations of outbreaks where speed of diagnosis may be crucial to save the lives of cases, and for the protection of others.

Many biological and chemical agents could potentially be used in a deliberate release, including agents that clinicians will often see in the course of routine work as well as more exotic agents. It is not possible to give a comprehensive guide to the presenting features of all the agents that might be used. **The key is to maintain a high index of suspicion**.

Table 2 shows the presenting features of some unusual biological and chemical agents that might be used. Please note that **this table is only a very brief guide** and that comprehensive guidance on these agents is available on the PHLS website at **http://www.phls.org.uk/topics_az/deliberate_release/menu.htm**

Table 3 shows the presenting features and management of exposure to **radiation**.

Table 4 shows the features and management of **epidemic hysteria (mass psychogenic illness)**. Note that mass psychogenic illness may also complicate an outbreak/incident of unusual illness with an organic basis, where people are frightened. It is a diagnosis of exclusion.

(Tables 2, 3 and 4 are found on pages 28-31 in the 'Guide for hospital clinicians' section)

Although nutritional deficiencies have been described as possible causes of outbreaks of disease in countries with malnutrition, this should be unlikely in this country. This should be considered if those affected are from a section of the community that may have experienced general food shortages or a particular dietary lack.

2.5 Important notes for laboratory investigations

ALL SAMPLING FOR LABORATORY INVESTIGATIONS SHOULD BE CONDUCTED IN A HOSPITAL SETTING

- All samples should be regarded as **high risk** and labelled and handled as such until further information is available.

- The guidance primarily covers the toxicological and microbiological investigation of symptomatic individuals. It does not attempt to cover the investigation of "exposed" but asymptomatic people. The investigation of such people will depend in a large part on the nature of the 'incident' and results of investigations on symptomatic individuals.

- The guidance on investigation primarily addresses the issue of the "blind screen" for possible biological/chemical agents. However, it is important to remember that the investigations undertaken will to a large extent be guided by the clinical picture. Furthermore, by the time cases have been recognised as being unusual some investigations will already have been performed. It will always be important to seek expert guidance from the **Emergency Advisory Services** (Appendix 1).

- It is envisaged that in most circumstances, initial microbiological investigations on clinical samples will be performed locally in laboratories with operational containment level 3 facilities

- In an overt deliberate release there may be information available about the agent used. This will guide the investigations of choice. However it should be remembered that information may be misleading and that substances released may be mixtures of different agents. It may still therefore be appropriate to conduct a blind screen.

- If a particular agent is suspected, or as information evolves, it may be appropriate to change to specific investigations as outlined in Chapter 7.

- Where there are large numbers of similar cases, although samples may be taken from all, it may be more practical to concentrate investigative efforts on highly representative cases in the first instance.

- In the event of a suspected deliberate release chain of evidence (or chain of custody) documentation should also accompany all specimens (Appendix 3). In larger incidents this would only be required for several of the initial cases. Urgent clinical investigations should not be delayed significantly by chain of evidence issues. The police will take the leading role if deliberate release is suspected.

- Clinical and epidemiological features of suspected cases should always be recorded to allow development of a "working case definition".

- **The investigative guidance is not appropriate for category 4 biological agents (see Appendix 2 for a list of category 4 agents). If there is any suspicion of a category 4 agent, expert guidance should be sought immediately.**

2.6 Personal protective equipment and decontamination

Personal safety considerations should always be paramount for NHS staff dealing with cases of unusual illness.

The provision of Personal Protective Equipment (PPE) is important in protecting staff from contaminated casualties and material in the event of an accidental or overt deliberate release (or possible release) of biological or chemical agents.

NB An incident site will be cordoned into hot, warm and cold zones. The hot zone describes the area in which gross biological/chemical contamination levels might occur. **Health care staff should not enter the hot zone**. Operations in this zone will be undertaken by the Fire Service who have the training and equipment for this. Health care staff may work in the warm zone decontaminating and treating casualties. In the warm zone staff may be exposed to some liquid chemical and vapours in a chemical release, and there may be low level contamination in a biological release**. It is therefore essential that health care staff use PPE to protect them while working in the warm zone**.

In the past PPE provision in the Health Service has been patchy, but over the last two years a specification for national PPE for health service staff has been drawn up after much research and has been funded. From April 2002, PPE will be provided for all Ambulance and Acute Trusts and will include portable decontamination units. Many Acute and Ambulance Trusts have protocols for decontamination of casualties. The Department of Health has issued a protocol for hospital Trusts to follow if they do not have their own policy[7].

2.7 Infection control

This document does not cover details of infection control in any health care settings. Advice should always be sought from the hospital infection control team, or in community settings from the local CCDC. **Expert advice can be obtained from the appropriate units listed in Appendix 1.**

2.8 Communication issues

1. Close liaison between clinicians, laboratories, public health officials and expert advice centres is essential in facilitating effective investigation and management.

2. Overall management may be taken by local, regional or national public health professionals depending on the nature of the incident. These professionals will convene an incident control team assigning specific roles to individuals including for communication. **Any press enquiries should be directed to those responsible for overall management of the incident who will have a delegated press officer. On no account should press enquiries be fielded by anyone else.**

3. Microbiology and toxicology co-ordinators will be designated within the incident control team during an incident to collect and collate all investigation results. All results should be reported to these individuals, who have the responsibility to report back results to the incident control team.

4. Where there are large numbers of similar cases in multiple sites, unique identifiers across all the sites and not just one site will be needed. In emergency circumstances the use of patient name, date of birth etc as identifiers would avoid possible confusion and would be compatible with Caldicott principles and the Data Protection Act 1998.

5. All NHS staff involved in investigating and managing outbreaks/incidents of unusual illness should be sure to maintain comprehensive records of information they have received and actions they have taken. These should always be signed, time and dated.

GUIDE FOR THE AMBULANCE SERVICE

3. A guide for the ambulance service

As an ambulance service professional you may become involved with outbreaks/incident of unusual illness in several ways:

- You may be the first responder in category I incidents (see below) where there may be a large number of casualties involved simultaneously.
- You may be called to an individual or small groups of cases involved in category II incidents, either by the patients themselves or by other health professionals.

Much of the advice which follows re-iterates what will usually be standard practice.

3.1 Category I incidents

These are most likely to be chemical incidents for which the ambulance service already has established procedures. However, where the aetiology is not yet shown to be chemical, it is important to remember that biological agents may be involved. This is particularly the case where deliberate release is suspected since mixed agents could potentially be used. The key issues in response are summarised in Checklist 1.

The crucial points are:

- Ensure personal safety
- Tell and seek advice from the Chemical Incident Service Providers
- Decontaminate cases
- Communicate with other health professionals
- Keep comprehensive records

3.2 Category II incidents

Category II incidents are more likely to have an infectious aetiology.

You may be called out to assess the patient at an early stage and the unusual nature of the illness may not be recognised until after your involvement ends. You may then later be contacted by the local public health department, or someone from the incident control team, to provide you with information about any likely exposure that you may have had and what, if any, prophylactic treatment will be offered to you.

If you are called out by a patient and you suspect an unusual illness from your initial assessment, you should:

- Contact your local CCDC (or on-call support if out of hours) for immediate advice concerning personal safety, patient containment and decontamination as appropriate whether the police need to be contacted.
- Alert the hospital to which you are taking the patient of your suspicions.

Expert advice for the CCDC will be provided from CDSC.

Once again keep comprehensive records of the incident and ensure that a full list is made of personnel involved, their roles and 24 hour contact details.

Where you are asked to transfer a patient where unusual illness has already been suspected or recognised by another health professional, standard procedures should apply for the transfer of patients according to risk category. If you are in doubt, seek expert advice (Appendix 1).

3.3 Equipment decontamination

Standard operating procedures will exist for decontamination of equipment after an incident. Please **contact the CCDC for further advice** if necessary and to determine whether any further measures are necessary for ambulance personnel protection.

Checklist 1: Actions to be taken by ambulance professionals in responding to a category I incident

1. **Full personal protective equipment** should be used by all personnel entering the warm zone and dealing with casualties.

2. **Brief assessment** of presenting features of cases and history of incident.

3. **Contact chemical experts** (Appendix 1) for further advice concerning personal safety and decontamination of cases.

4. **Decontaminate** cases according to advice received and the standard protocol.

5. **Contact the hospital** (A&E Consultant) to alert them to the arrival of cases (number, clinical state, incident history, decontamination status).

6. **Contact local CCDC** (or on-call public health support if out of hours) to inform them:
    - Nature of the incident: where, when, what
    - Number of casualties
    - Clinical state
    - Containment and decontamination activities in place
    - Anyone else at risk? (Make a list in case follow up is required)
    - Any conditions which might increase the risk to others?
    - Other agencies involved
    - Has a major incident been declared by any agency?
    - Is deliberate release suspected?
    - Where cases are being managed
    - To discuss with the **police** if deliberate release is suspected

7. **Keep comprehensive records** of all information received and action taken.

8. **Record details of all ambulance professionals** involved, with role taken and 24 hour contact details in case clinical follow up of staff is required.

GUIDE FOR
HOSPITAL CLINICIANS

4. A guide for hospital clinicians

This guidance starts from the premise that patients have presented to hospital with an unusual illness and takes you through the acute process of their management. Personal safety and patient containment are vital.

4.1 Personal safety

See Flowchart 3.

Personal safety considerations are paramount for the response of front line clinical staff to cases of unusual illness.

- Wherever cases of unusual illness present, irrespective of the suspected aetiology, clinical samples must be taken from patients using Universal Precautions and with the utmost care to avoid inoculation injuries. It may also be appropriate to use high efficiency masks and eye protection available from the hospital infection control team.
- Always consider whether decontamination of patients is required.

Always seek expert advice (Appendix 1).

Always contact your infection control team.

4.2 Summary of actions to be taken by hospital clinicians dealing with cases of unusual illness

Your role as a clinician in the investigation and management of cases of unusual illness can be summarised into the following components:

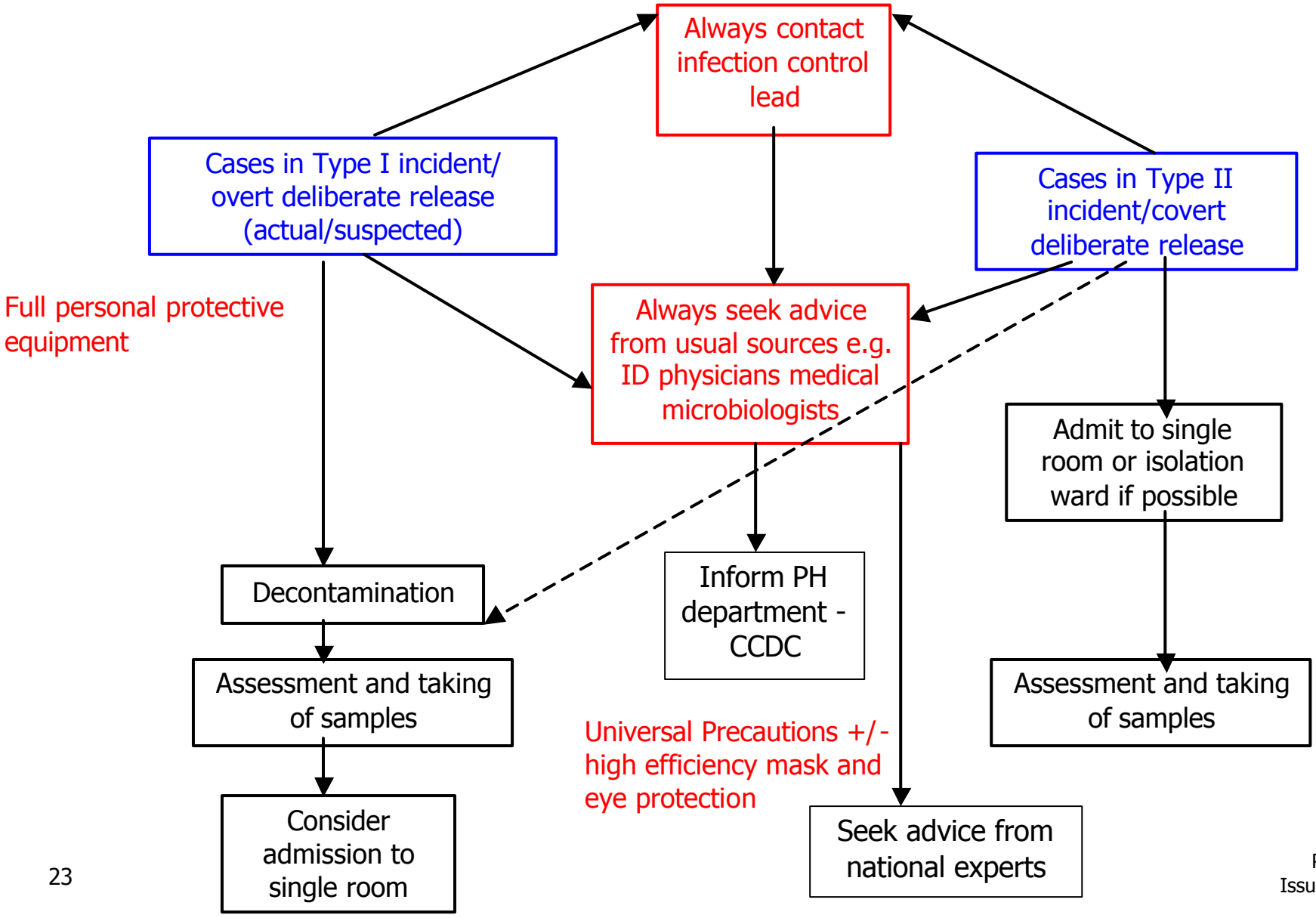
- Protection of self and others exposed to the patient [sections 4.1 and 4.3].
- Detailed clinical assessment and appropriate investigations of the patient [section 4.6] and appropriate treatment of cases [section 4.7].
- Communication with other NHS staff [section 4.8].
- Samples to be taken [section 4.9]

Flowchart 4 summarises the actions you should take when dealing with cases of unusual illness.
Checklist 3 and Checklist 4 provide tools for you to use in an acute situation
Checklist 5 summarises the advice you receive.

The importance of comprehensive record keeping cannot be over emphasised. This should cover not only the usual clinical records but also details of the advice that has been received, actions taken to protect self and others, and who else has been informed. Be sure to date, time and sign all entries.

It may be that the fact that this is an unusual illness is identified only when the results of investigations are available. The same fundamental elements of management as described here will also apply to this situation. However there will inevitably be issues about potential risks to others before the illness was recognised as unusual. Under these circumstances it is important to promptly inform the infection control doctor, the local CCDC and to discuss the case(s) with the appropriate expert advice services.

Flowchart 3: Personal safety of hospital staff and general management of patient



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

A full written record should be maintained of all staff who have been directly involved with the care of the case. This should include their name, age, address, GP details, 24 hour contact details and their level of contact with the case.

CATEGORY I INCIDENTS/SUSPECTED OVERT DELIBERATE RELEASE

In a **category I incident** (where the presentation is acute and a chemical/toxic aetiology is most likely) **decontamination is crucial** in preventing secondary contamination. This will also be important in suspected overt deliberate release of biological agent and where cases may have been exposed to, for example, unidentified powders or gases. It is anticipated that healthcare workers will not normally enter the hot zone and that medical assessment will be performed after decontamination in a place of safety. Anyone entering the 'exposed zone' should wear full personal protective equipment (PPE).

Decontamination

There is likely to be some prior warning that casualties will arrive in an Accident and Emergency department, and cases should have been decontaminated prior to transfer to hospital. If this has not been performed then it should be done immediately on arrival at hospital. Guidance has been produced on appropriate decontamination methods for Trusts which do not have their own policies[7]. **Health care workers involved in basic life support of casualties before they have been decontaminated must wear full PPE.**

Where the aetiological agent is chemical and the patient has been appropriately decontaminated, it is unlikely that human body fluids will constitute a significant risk to health care staff during either assessment or the taking of samples. However, it must be remembered that in a potential deliberate release scenario, exposure may have been to both chemical and biological agents and therefore even after decontamination Universal Precautions should be taken to protect against biological agents. It may also be appropriate to use high efficiency masks as used for patients with MDR-TB (dust/mite masks meeting the 1992 Personal Protection Equipment (EC Directive) regulations[8]), and eye protection whilst in close contact with the patient. Always seek expert advice.

CATEGORY II INCIDENTS

For a category II incident (where presentations may be more delayed and biological agents are rather more likely) the situation is more complicated because of the manner in which patients might present. Although health care staff may be pre-warned of the arrival of cases of unusual illness, it is also possible that the healthcare staff will be the ones recognising the unusual nature of the presentation. As soon as there is any suspicion of an unusual aetiology all staff should take precautions to protect themselves, primarily from biological agents, although decontamination might once again be appropriate if the clinical picture is suggestive of chemical exposure. Expert advice should be sought immediately but given the unknown nature of the agent involved it would certainly be appropriate to wear high efficiency masks as used for patients with MDR-TB (as above[8]), and eye protection whilst in close contact with the patient, in addition to standard universal precautions of gowns and gloves.

4.3 Patient containment issues

Where illness is due to an unknown aetiological agent patients should wherever possible, be nursed in a single isolation room, preferably on an in-patient ward. Cohort nursing may be necessary depending on the numbers involved. Where there are grounds for believing that the illness may have a chemical aetiology, transfer to a ward should not be done until decontamination of the patient has occurred. Universal Precautio ns should be implemented as for all infectious hospital patients. It may be appropriate for all persons entering the room to wear high efficiency masks (dust/mite masks meeting the 1992 Personal Protection Equipment (EC Directive) regulations[8]), and eye protection in addition to standard Universal Precautions until further information is available. It may also be advisable to limit the transport of patients to essential medical investigations only and for patients to wear high efficiency masks during transport. **(Note however that to ensure high quality diagnosis, especially for the first cases detected, X-rays should be performed in the X-ray Department rather than by mobile machine wherever possible).** Cleaning, disinfection and waste disposal as for standard isolation procedures should be appropriate e.g. clean contaminated environmental surfaces with 0.5% hypochlorite solution (5,000ppm). This guidance does not provide definitive advice on infection control issues. Therefore cases should always be discussed with the infection control team. Expert advice should always be sought about patient containment and infection control issues and about how to manage other patients or staff who may have been potentially exposed.

ALWAYS CONTACT YOUR INFECTION CONTROL TEAM

Flowchart 4: Actions to be taken by hospital clinicians dealing with cases of unusual illness

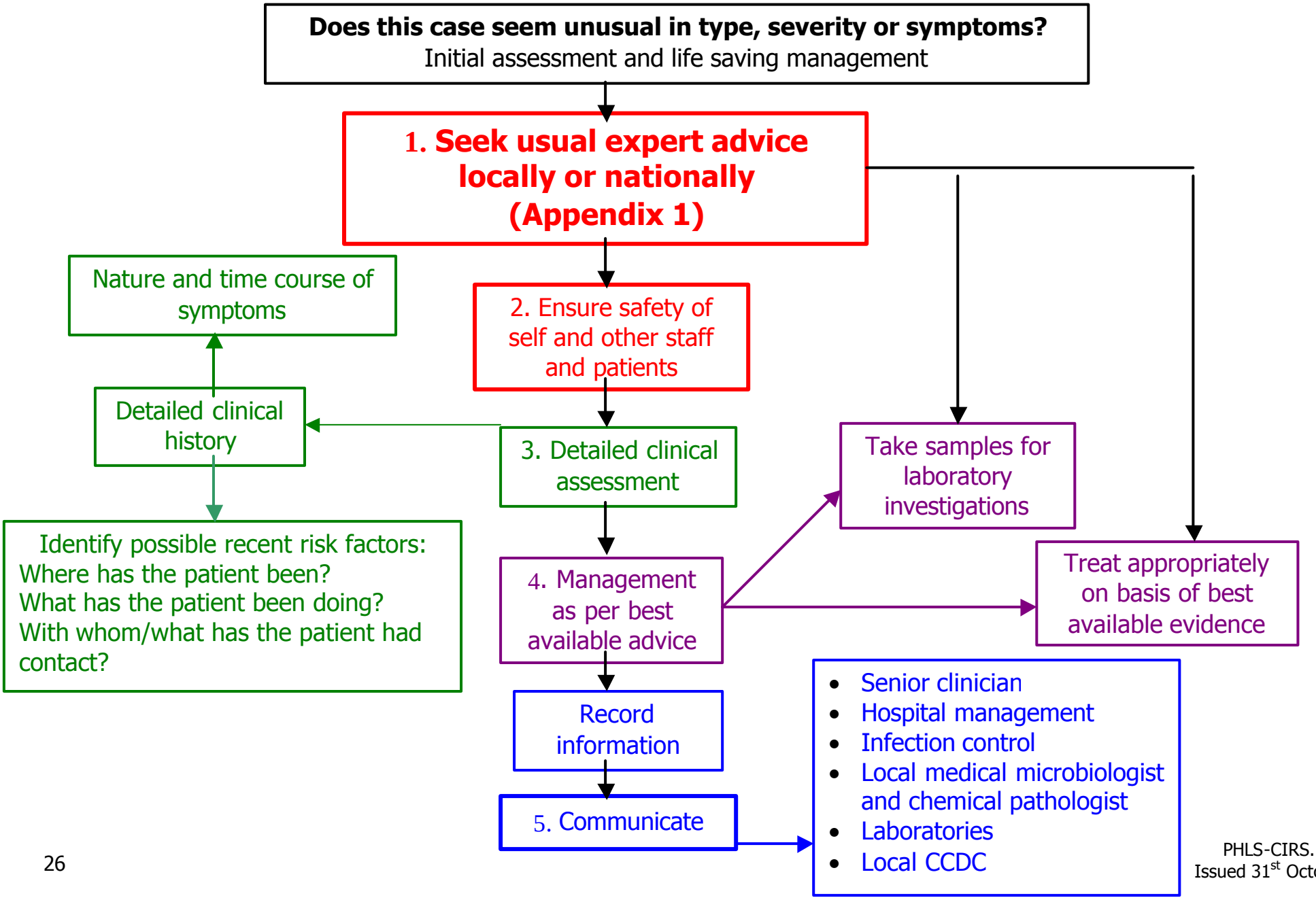


Table 2: Presenting features of biological and chemical agents which might be used in a deliberate release

A) Biological Agents

Agent	Presenting features
Anthrax	**See guidelines at http://www.phls.org.uk/topics_az/anthrax/guidelines.pdf** Inhalational: Non-specific flu-like prodrome* followed 2-4 days later by respiratory failure. Widened mediastinum on chest X-ray. Cutaneous: Raised itchy inflamed pimple which over 2-6 days progresses to a papule then a **painless** vesicle surrounded by extensive oedema, culminating classically in a black eschar. Gastrointestinal: Severe abdominal pain, nausea, vomiting, watery/bloody diarrhoea. *Note: may also present as bacteraemia/meningitis.*
Plague	**See guidelines at http://www.phls.org.uk/topics_az/plague/plague_guidelines.pdf** Pneumonic: Intense headache, malaise, fever, vomiting, prostration, cough and dyspnoea, watery blood stained sputum. Multilobar consolidation/bronchopneumonia on chest X-ray. Bubonic: Swollen, painful, tender lymph nodes with associated oedema and erythema. *Note: may also present in septicaemic/meningitic/pneumonic/pharyngeal forms.*
Smallpox	**See guidelines at http://www.phls.org.uk/topics_az/smallpox/smallpox_guidelines.pdf** Fever, severe prostration, severe headache, intense ill-defined pain in back/chest/loins. 2-3 days later blotchy erythema may develop usually on face, back, hands, upper chest and back, which may become haemorrhagic/purpuric. In the more typical presentation, a maculopapular rash begins on days 3-4 mainly on the face/extremities. This progresses to classical vesicular and then pustular lesions that may go on to coalesce to form bullae covered by macerated skin.
Botulinum Toxin	**See guidelines at http://www.phls.org.uk/topics_az/botulism/botulism_guidelines.pdf** Acute onset of bilateral cranial nerve involvement. Descending weakness or paralysis that may extend to complete flaccid paralysis. The patient remains alert with no loss of sensation and no fever.
Tularaemia	**See guidelines at http://www.phls.org.uk/topics_az/deliberate_release/pdf/tularemia_guidelines.pdf** Many different forms depending on mode of transmission: Pneumonic (acute flu-like +/- clinical pnemonitis/pneumonia), ulceroglandular (local pruritic papule develops into pustule and then into an indolent ulcer +/- eschar, plus lymph node enlargement and rupture to release caseous material), typhoidal (flu-like plus diarrhoea and vomiting), septicaemic, pharyngeal, oculoglandular (corneal ulceration plus lymph node enlargement).

* Influenza and seasonal respiratory disease differ from anthrax in having a prodrome associated with rhinorrhoea and sore throat.

A) Biological agents continued.

5. Agent	Presenting features
Haemorrhagic fever viruses:	**See guidelines at http://www.phls.org.uk/topics_az/deliberate_release/pdf/VHF_guidelines.pdf**
a) Lassa	a) insidious onset; fever, shivers, malaise, headache and general aches. Sore throat is common and may have tonsillar/pharyngeal exudate. In severe attacks, lethargy and prostration disproportionate to fever. May progress to oedema, encephalopathy, pleural effusion and ascites.
b) Crimean-Congo	b) abrupt onset fever, chills, malaise, irritability, headache, severe limb and loin pain. Followed by anorexia, nausea and vomiting. Face and neck flushed and oedematous, and conjunctival/pharyngeal injection. Petechial rash begins on trunk and spreads to whole body; bleeding manifestations appear on 4th or 5th day.
c) Ebola and Marburg	c) acute fever, diarrhoea which may be bloody, and vomiting. Headache, nausea and abdominal pain are common. May progress to conjunctival injection, dysphagia, hiccups, and haemorrhagic symptoms such as epistaxis, haematemesis, melaena and purpura may develop. Some patients at 3-8 days have a maculopapular rash over the trunk which then desquamates.
Glanders and melioidosis	**See guidance at http://www.phls.org.uk/topics_az/deliberate_release/pdf/glandersmelioidosis_guidelines.pdf** Clinical features of both diseases are very variable. For each infection, one form of disease may progress to another and infections may present acutely with rapid progression and death, or run a chronic or relapsing course. The three main clinical syndromes are: a) overwhelming sepsis with metastatic foci of infection b) pyrexia of unknown origin with high and swinging fever c) localised infection, most commonly of the lung, but also of visceral abscesses, or skin and soft tissues

B) Chemical Agents

Note that clinical presentation will depend on the route of exposure and the dose received, and that symptoms may evolve over some time.

Agent	Presenting features
Nerve Agents	Parasympathetic effects: copious secretions, bronchospasm, bradycardia, abdominal cramps, diarrhoea, miosis. Nicotinic effects: muscle fasciculation, weakness, respiratory paralysis, tachycardia, hypertension. Central nervous system effects: confusion, ataxia, emotional lability, convulsions, coma, central respiratory depression. **See guidelines at http://www.phls.org.uk/topics_az/deliberate_release/pdf/chemical_nerve_agents.pdf**
Mustard	Eyes: painful, inflamed, blepharospasm, photophobia, watering. Skin: erythema, blistering (particularly where clothes are tight), pigmentation. Systemic: nausea, vomiting, headache, rhinorrhoea, sore throat, hoarse/lost voice, tachycardia, hyperventilation, cough. **See guidelines at http://www.phls.org.uk/topics_az/deliberate_release/pdf/chemical_mustard_gas.pdf**
Chlorine	Eye, nose and throat irritation, cough wheeze and dyspnoea, sputum, bronchospasm and chest pain, chemical pneumonitis and/or pulmonary oedema, nausea and vomiting, metabolic abnormalities. **See guidelines at http://www.phls.org.uk/topics_az/deliberate_release/pdf/chlorine.pdf**
Hydrogen Cyanide	Low concentrations: dyspnoea, headache, dizziness, anxiety, tachycardia, nausea, drowsiness, metallic taste. High concentrations: hyperventilation, loss of consciousness, convulsions, fixed and dilated pupils, death from respiratory/cardiac arrest in minutes, skin remains pink despite tissue hypoxia. **See guidelines at http://www.phls.org.uk/topics_az/deliberate_release/pdf/cyanide.pdf**
Phosgene	3 different phases: 1. Early: irritation to eyes, lacrimation, blepharospasm, nausea and vomiting, tight chest, retrosternal discomfort and bronchoconstriction, hypotension, bradycardia/tachycardia. In severe exposure, haemolysis and rapid death. 2. Latent: may appear well, symptoms precipitated by exercise. 3. Oedematous phase: (non cardiogenic) pulmonary oedema. **See guidelines at http://www.phls.org.uk/topics_az/deliberate_release/pdf/phosgene.pdf**

Table 3: Presenting features and management of exposure to radiation

Types of radiation exposure that might arise from an accident/deliberate release	• External to body; involving part or whole of the body. • Internal radioactive materials ingested, inhaled or deposited in wounds.
Recognising radiation injuries by their clinical manifestations:	Following a high level exposure, injuries evolve over time in distinct phases. The length and timing of these phases depends on the dose received. Low doses do not produce observable effects.
Whole body exposure	• Initial prodromal phase with nausea, vomiting, fatigue and possibly fever and diarrhoea. • Latent period of varying lengths. • Period of illness characterised by infection, bleeding and gastrointestinal symptoms caused by deficiencies of cells of the haematopoietic system and, at higher doses by loss of cells lining the gastrointestinal tract.
Local exposure	• Depending on dose can produce in the exposed area: erythema, oedema, dry and wet desquamation, blistering, pain, necrosis, gangrene or epilation. • Local skin injuries evolve **slowly over time**, usually weeks to months. • Local skin lesions may be **very painful** and **difficult to treat by usual methods**.
Partial body exposure	• A combination of varying symptoms as above. • Type and severity of symptoms depends on dose to and volume of the exposed part of the body.
Internal contamination	• Usually no symptoms unless the intake has been very high, which is extremely rare.
Differential diagnosis of radiation injury	Consider radiation injury in a differential diagnosis if the patient presents with: • A description of circumstances that might have led to a radiation exposure (e.g. work with scrap metal). • Nausea and vomiting, especially if accompanied by erythema, fatigue, diarrhoea or other symptoms and gastro intestinal infections and/or allergy excluded. • Skin lesions without knowledge of a chemical or thermal burn, or insect bite, or history of skin disease or allergy, but with desquamation and epilation in the exposed area further to erythema having occurred 2 to 4 weeks earlier. • Epilation or bleeding problems (such as petechiae, gingival or nose bleeds) with a history of nausea and vomiting 2 to 4 weeks previously.

Table 4: Features and management of epidemic hysteria (mass psychogenic illness)

Definition	Epidemic hysteria (mass psychogenic illness) is characterised by symptoms, occurring among a group of persons with shared beliefs regarding those symptoms, that suggest organic illness but have no identifiable environmental cause and little clinical or laboratory evidence of illness[5]. This is essentially a diagnosis of exclusion but prompt identification of the outbreak is important to limit cases.
Symptoms	The range of symptoms may be very wide and inconsistent, but commonly include nausea, vomiting and/or dizziness. Relapses can occur in the same person over multiple days of the outbreak.
Group affected	Typically: • Adolescents or children • Groups under stress • Females disproportionately more than males
Setting	The most common settings for outbreaks are schools and factories and while most are short lived some outbreaks can extend over a month or more.
Triggers	• An environmental trigger, e.g. seeing something suspicious • Illness in an index case
Spread	Symptoms usually: • Follow awareness of illness in others • Spread rapidly by apparent 'visual transmission' • Are aggravated by a prominent emergency or media response • Resolve after patients are separated from each other and removed from the environment in which the outbreak began
Management	Recommended treatment involves: • Separating those who are ill from those who are not • Providing reassurance • Observing those who are ill while using a calm and authoritative approach

4.4 Determining whether cases of illness have occurred naturally/accidentally or as a result of deliberate action.

Whenever an outbreak/incident of unusual illness occurs, consideration should always be given to whether it is a natural or accidental phenomenon or whether it might be the result of deliberate action. The setting and nature of the outbreak/incident may give some indication of a deliberate release and Checklist 2 contains a list of pointers to the possibility of a deliberate release. It is adapted from a document produced by the Centers for Disease Control and Prevention in the USA[9], and from reference 10.

None of the features in Checklist 2 are specific for outbreaks/incidents by deliberate release. However, with any of these features, the possibility of a deliberate release should be considered. Note that for infectious agents, the presentation of illness due to deliberate release may be more sudden, more severe and involve larger numbers than in natural outbreaks. The time course may show a more rapid rise than is characteristic in a natural outbreak. This might be particularly the case where there has been aerosol dispersion of the agent. Most infectious agents considered likely to be used in deliberate releases are not normally transmitted person to person the main exception being smallpox and pneumonic plague.

Checklist 2: Pointers that an outbreak/incident of unusual illness may have been caused by a deliberate release

- Prior warning received of malevolent intent
- A number of ill people with similar disease or syndrome presenting around the same time
- A number of cases of unexplained disease, syndrome or death
- Single case of disease caused by an uncommon agent
- Unusual illness in a population
- Recognised illness occurring in an unusual setting within a community
- Illness affecting a key sector of the community
- Higher morbidity and mortality than expected with a common disease or syndrome
- Failure of a common disease to respond to usual therapy
- Multiple unusual or unexplained disease entities coexisting in the same patient without other explanation
- Disease with an unusual geographic or seasonal distribution
- Multiple atypical presentations of disease agents
- Similar typing of agents isolated from temporally or spatially distinct sources
- Unusual, atypical, genetically engineered, or antiquated strain of agent
- Simultaneous outbreaks of similar illness in non-contiguous areas
- Atypical transmission routes e.g. by aerosol, food or water
- Deaths or illness among animals that precedes or accompanies illness or death in humans
- Illness only among people in proximity to common ventilation systems
- Suspected or known deliberate/inadvertent release in another country

4.5 What to do if deliberate release is suspected

The local consultant in communicable disease control (CCDC) or their deputy should be notified whenever health professionals are involved with cases of an unusual illness. **Where a deliberate explanation for the outbreak/incident is suspected, the CCDC should immediately discuss this with the police. The local police have to then liase with the anti-terrorist unit of the Metropolitan Police who co-ordinate National responses.** It should be noted that alerting the police does not mean that forensic consideration will prevail as ***it is accepted that care of affected and exposed persons has the highest priority except in the most exceptional circumstances***.

The police will establish a Police Main Base Station (PMBS) to accommodate a major incident room and the various agencies involved. A Police Incident Commander will lead on the incident from this point forward and will:

- Establish and chair a coordinating group which will include a Director of Public Health or nominated representative;

- Ask the local or Regional Director of Public Health to establish and chair a Joint Health Advisory Cell (JHAC).

An incident control team (see section 8.5) will be convened and this should liase closely with the JHAC as outlined in the guidance produced by the DH[10].

4.6 Detailed clinical assessment and appropriate investigations

A detailed clinical history is essential in establishing the cause of an unusual illness. The more information gathered in the early stages, the easier the investigation, as common features emerge. Basic epidemiological data includes:

- Where:
  - has the patient been recently?
  - do they live?
  - do they work?
- Have they travelled anywhere?
- How did they travel?
- Have they attended any special events?

- What has the patient been doing recently? What is their job? What do they do as hobbies/for recreation? Have they had any particular exposures e.g. to particular foods/drink/drugs, to unidentified substances? Have they done anything new/strange recently?

- Who or what has the patient been mixing with recently? Have they had contact with animals/other ill people?

- Ask the patient what they think has caused the illness. This may reveal "unusual" events or experiences which may give clues.

Where junior doctors are alerted by the history or examination to the possibility of an unusual illness they should immediately involve their senior colleagues, and wherever possible request an expert clinical assessment.

Routine and specific laboratory investigations are discussed in section 4.9 (but see section 4.3 for patient containment issues). Please ensure that the necessary routine and special request forms are completed for investigations as per this section. Where deliberate release is suspected (or there are other forensic considerations) it is also very important to complete a chain of evidence form (Appendix 3).

4.7 Appropriate treatment of cases

Appropriate life saving treatment should be instituted as required with due regard to personal safety. Expert advice concerning specific treatment of cases should be sought. Until the results of laboratory investigations are available it may be necessary to treat on the basis of "best available current advice" given the state of knowledge. Where a specific agent is strongly suspected it may be more appropriate to switch to specific guidance.

4.8 Communication with other NHS staff

As soon as you suspect that you may be dealing with an outbreak or incident of unusual illness (which may involve just one case), you should inform:

- the senior consultant responsible for the care of the patient, and through them the hospital management.
- the infection control team in the Trust.
- and seek expert advice concerning safety of personnel and patient containment as well as investigations and treatment.
- the laboratories that "high risk" specimens will be sent to them.
- the local medical microbiologist and chemical pathologist.
- the local consultant in communicable disease control.

Always remember to pass on your suspicions to the local CCDC if you feel the incident/outbreak may be the result of deliberate release.

Checklist 3: Checklist of actions for hospital clinicians dealing with cases of unusual illness

Action	Date & time completed
Brief initial assessment of case(s)	
Institute measures to ensure personal safety of self and others	
Institute appropriate patient containment	
Inform infection control	
Contact appropriate expert service provider for advice	
Involve senior/expert clinician or seek expert advice	
Detailed clinical assessment of case(s)	
Take samples for investigation (treat as "high risk"), and complete routine and special request forms as well as chain of evidence form* where deliberate release is suspected or there are other forensic considerations	
Discuss with local medical microbiologist	
Discuss with local chemical pathologist	
Send specimens to local laboratories as "high risk" according to local protocol	
Treat case(s) according to best available current advice	
Record all information and actions taken in notes	
Record contact details of all staff who have been involved in direct patient care	
Inform local laboratories of "high risk" specimens	
Inform local CCDC	
Inform hospital management	

*obtainable from Appendix 3

Checklist 4: Information for hospital clinician to record about case(s) of unusual illness

Name of clinician recording information with contact details

Hospital

Number of cases

Is deliberate release suspected?

Is there any information available about others who might be exposed/at risk (including staff)?

For each case:

- Name
- Address
- Sex
- Age
- Occupation
- GP details
- Date and time of presentation
- Mode of presentation (Walk-in, ambulance, GP referral etc.)
- Name of senior clinician in charge
- Ward
- Date/time of onset of symptoms
- Nature of symptoms/severity of illness
- Has there been an expert clinical assessment? By whom?
- Clinical findings (who performed assessment?)
- Any risk factors/exposures identified?
- Relevant past medical history/drug history?
- Samples taken
- Investigation available
- Working diagnosis
- Management: decontamination, treatment
- Outcome

What is being done to prevent the development of further cases e.g. patient containment/staff protection?

Record all staff in contact with patient with their personal contact details.

Checklist 5: Record of Advice Received

Query	Advice	Source (name and telephone)
Staff protection		
Patient containment		
Patient investigation		
Patient treatment		
Who else to inform		
Other		

4.9 Investigation of patient(s): samples to be taken

Introduction

For an unusual illness where the aetiology is strongly suspected it may be more appropriate to switch to specific guidance.

For an unusual illness where the aetiology is not certain, it is preferable to take samples for a "blind screen" for both toxicological and microbiological investigations, as well as for routine haematology and biochemistry. Some chemicals cannot be directly assayed but their presence can be inferred and their effect measured from the results of routine tests.

Although this guidance tells you what samples to take for a "blind screen", always discuss investigations with the relevant expert.

Always consider taking samples for toxicology. It may not be necessary to analyse all samples taken once the clinical picture becomes clear, but without appropriate specimens taken at the appropriate time identification of an agent retrospectively may not be possible. Special kits called "toxi-boxes" have been produced for use in such circumstances and are available in Accident and Emergency departments. Toxi-boxes should always be used where available because the special bottles used avoid chemical contamination of the specimens.

With respect to microbiological investigation it is very important that appropriate good quality samples are obtained and referred to National reference laboratories for a number of investigations, including prolonged enrichment culture and molecular detection techniques. For virological investigations, this will also include electron microscopy, PCR and viral culture. Thus, normally sterile site samples (with no commensal flora to complicate interpretation) in sterile containers are preferred wherever possible, provided they are clinically relevant.

Collect samples as early as possible, preferably before specific treatments are given. However provision of potentially life saving treatment should not be delayed by sampling procedures.

Toxicological "blind screen"

"Toxi Boxes" consist of:

- 1 x 10ml plastic lithium heparin tube
- 1 x 5ml glass lithium heparin tube
- 1 x 4ml EDTA tube
- 1 x 60ml universal container for urine (the top is wide enough for males and females to urinate into directly, thereby minimising risk of cross contamination)
- Corrugated cardboard for wrapping samples
- 1 x form (this must be filled in for each patient see Appendix 3)
- 1 x double plastic bag for form and samples
- 1 x cardboard container

In order of importance, the samples for a **'blind' toxicological screen** should consist of:

Adults

- 10ml blood in plastic lithium heparin tube
- 5ml blood in glass lithium heparin tube
- 4ml blood in EDTA tube
- 30ml urine without preservative

Children

- 5ml blood in glass lithium heparin tube
- 5ml blood in EDTA tube
- 30ml urine without preservative

If toxi-boxes are not available use routine specimen bottles but also send an empty specimen bottle of the same type and from the same batch for every specimen to act as a control for "background" chemical contamination associated with the specimen container used.

Sample handling procedures for toxicological samples
• To pre-clean venepuncture site **do not use proprietary wipes** or swabs (e.g. Mediswabs) since these contain solvents and trace elements which could interfere with assays. **Sterile water (or dry cotton wool** if skin is reasonably clean) should be used for this purpose.
▪ Use only **blood bottles with plastic or lined metal tops** – chemicals can leach from blood tubes with gel separators, or those containing mucous heparin solutions. 'Vacutainers', soft plastic bottles, reusable containers and rubber bungs can contaminate specimens. Use the 'Toxi Box' toxicological analytical sampling kit wherever possible (see above).
• Every effort should be made to avoid external contamination of specimen containers during specimen collection.
▪ Each of the tubes should be filled. The 5ml glass heparinised blood tube should be filled so that there is a minimum air space in the tube. All tubes should be screwed tight. Do not centrifuge.
▪ Label the samples **"High Risk"**.
▪ Place the samples in the sealable section of the plastic bag.
▪ Complete a chemical incident analysis form (Appendix 3), marking it **"High Risk"** and place this in the other section of the plastic bag.
▪ Wrap the plastic bag tightly in the corrugated cardboard to avoid damage in transit and place in the cardboard container.
▪ Tape the cardboard container shut.
▪ Transport to the hospital chemical pathology laboratory as soon as possible according to local protocols for **high risk** samples.
▪ Telephone the laboratory in advance to inform them about the samples.
▪ In the event of suspected deliberate release, or where there are other forensic considerations, chain of evidence documentation should also accompany samples (Appendix 3).

Microbiological "blind screen"

The following samples are appropriate for a "blind" microbiological screen.

(Volumes quoted below relate to adult samples; smaller volumes appropriate from children)

Sample	For	Requirements
Blood cultures	**Extended aerobic and anaerobic culture**	**Two sets of blood cultures immediately (from one bleed) with another two if possible within the first hour (also from one bleed).** **Please inform if antibiotics have been given prior to sampling**
Sera	**Serology** **Biological toxin assays**	**2 x 10mls clotted blood, for both acute (admission) and convalescent phases.** **Acute may be used acutely for toxin assays. Excess to be frozen and saved**
Whole blood (EDTA tube)	**Molecular investigations e.g. PCR**	**2 x 10mls whole blood, acute phase**
Urine	**Standard testing and storage**	**Clean catch into sterile container – optimal volume >20mls.**

Other samples may also be appropriate for microbiological examination depending upon specific clinical features and other available information e.g.:

Respiratory tract samples e.g. sputum, bronchoalveolar lavage.
Nose and throat swabs.
Pus and vesicle fluid or swab of local lesions if present

Pus: As large a volume as feasible, placed in sterile containers for microscopy, aerobic and anaerobic culture, and susceptibility testing.
Local lesion (no pus): swab of lesion put immediately into transport medium for aerobic and anaerobic culture.
Vesicular fluid: should be swabbed and placed into viral transport medium and/or dried onto a microscope slide.

Biopsy tissues: collected aseptically from local inflammatory lesion, necrosis or abscess, or if surgical debridement is performed.

- As many samples as possible from multiple areas; quantity is important.
- Tissue:
  - Placed in sterile containers for direct culture (aerobic and anaerobic) and freezing.
  - Formalin-fixed (10% buffered formalin) or paraffin embedded.

Faeces/Stools.

Other Body fluids: e.g. cerebrospinal fluid, pleural fluid, pericardial fluid.

Sample handling procedures for microbiological samples
• The primary container should be screwed tight, labelled and placed in an intact plastic bag.
• Every effort should be made to avoid external contamination of specimen containers during specimen collection.
• A **"High Risk"** label should be affixed to the specimen.
• Each specimen must be packed individually, i.e. three specimens, three separate packages.
• The bags should be sealed. Pins, staples and metal clips should not be used.
• The request form should include any other relevant information and include adequate clinical details. It should be labelled **"High Risk"**.
• The request form must be placed in a different bag to the specimen.
• Specimen bags and request form bags should be attached to each other using tape.
• Specimens should be transported to the hospital laboratory as rapidly as possible according to local protocols for **high risk** specimens.
• In the event of suspected deliberate release, or other forensic considerations, chain of evidence documentation should also accompany samples (Appendix 3).
• Secondary containers should be disinfected by wiping with hypochlorite (1,000 ppm) solution or alcohol wipes.

Other routine investigations

- Routine samples for biochemistry and haematology should be sent as usual to the local laboratory for analysis. Where blood is required for transfusion, consider the use of O negative blood since cross-matching poses an infectious hazard in the laboratory.
- Please telephone the laboratory to expect the samples.
- **Routine specimens should be handled, labelled and transported as "High Risk".**
- Standard blood gas analysers should **not** be used since they pose an infection hazard. Only machines using a cassette system which minimises the infectious hazard should be used.

Checklist 6: Specimens to be taken from cases of unusual illness

- Cases should be decontaminated before samples are taken.
- Samples should be taken using **universal precautions** in all cases and personal protective equipment used where the hazard is high or uncertain.
- Specimens should be **collected and transported safely to the laboratories as rapidly as possible**.
- The receiving **laboratory should be contacted by telephone** to expect the samples.
- **Samples and request forms should be clearly labelled and note that special** investigations may be required.
- Samples should be identified as **"high risk"** according to local protocols.
- In the event of a suspected deliberate release, or where there are other forensic considerations, **chain of evidence documentation** should also accompany specimens

For toxicological examination

Use the specially prepared **"Toxi boxes"**. Use **sterile water (or dry cotton wool** if skin is reasonably clean) to pre-clean venepuncture site.

Adults	Children
• 10ml blood in plastic lithium heparin tube • 5ml blood in glass lithium heparin tube • 4ml blood in EDTA tube • 30ml urine without preservative	• 5ml blood in glass lithium heparin tube • 5ml blood in EDTA tube • 30ml urine without preservative

For microbiological examination

Volumes quoted refer to samples from adults.

Blood cultures	Ideally at least two sets immediately with another two within the first hour if possible.
Sera	2 x 10mls clotted sample for both acute (admission) and convalescent phases.
Whole blood (EDTA tube)	2 x 10mls whole blood for both acute (admission) and convalescent phases.
Urine	Clean catch collection into sterile container (> 20mls).
Other specimens as appropriate	Respiratory tract, nose and throat swabs, pus, vesicle fluid, swabs of local lesions, biopsy tissues, faeces, cerebrospinal fluid, pleural fluid, pericardial fluid etc.

Routine biochemistry and haematology samples should also be taken.

GUIDE FOR
GENERAL PRACTITIONERS

5. A guide for general practitioners

As a general practitioner you may become involved with cases of unusual illness in several ways:

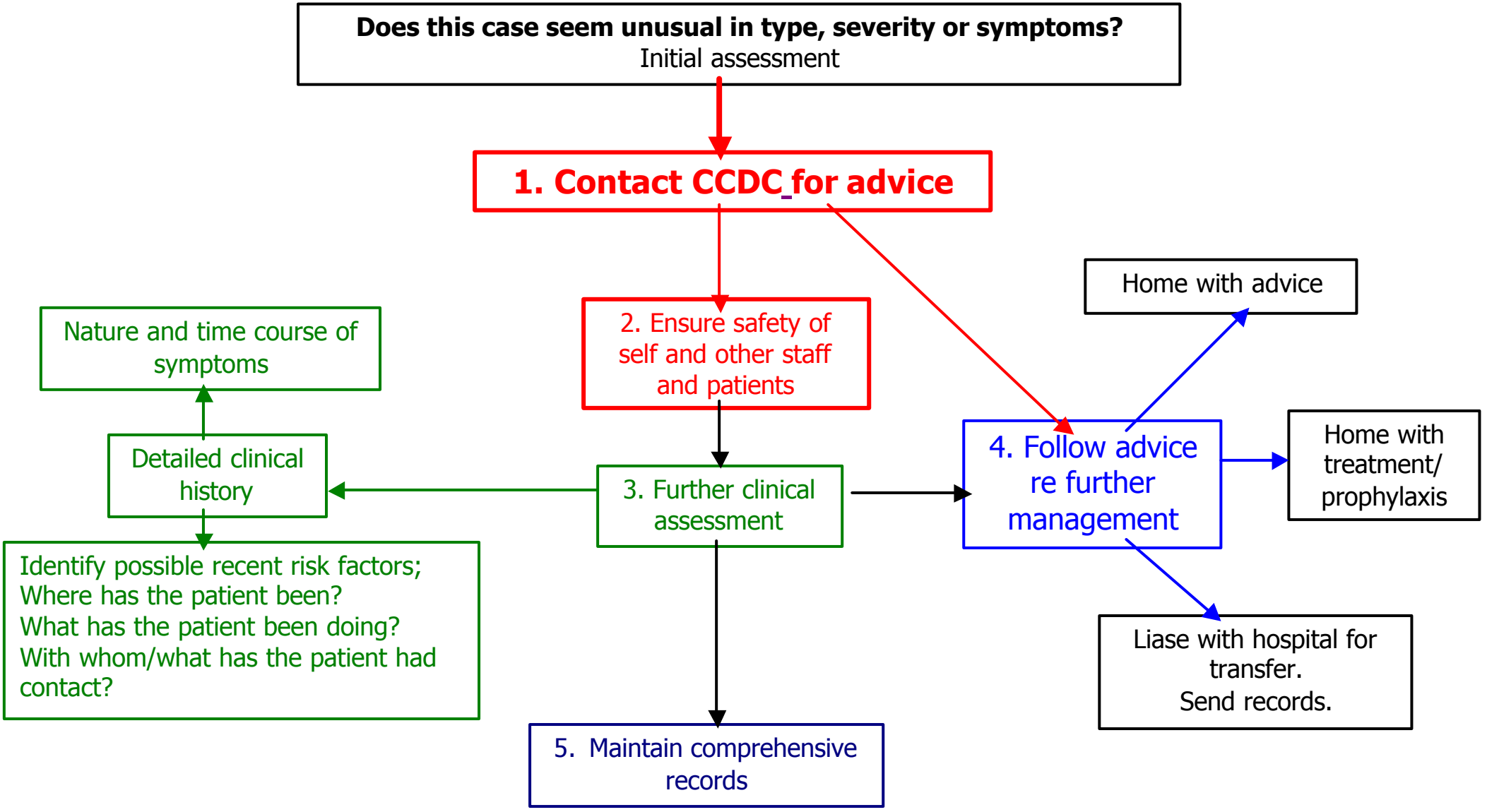
- You may be involved directly with ill cases.
- You may be involved with people who have been exposed to risk but are not currently ill and come to you for advice or seeking prophylaxis.
- You may be involved with the "worried well" who are not sure whether they have been exposed to risk and who come to you for reassurance/advice.
- You may be asked by the local public health department or the incident control team to assist if prophylaxis needs to be administered to exposed people on a large scale.

Where an incident of unusual illness has been recognised in another setting but might affect your patients, the local public health department or incident control team should ensure that you are given all the information you will require in order to safely manage patients and protect you and your staff. Very early on in an incident however there may not have been enough time for this to occur. It is hoped that this guidance will help you through the early stages of your decision making under these circumstances.

5.1 Action to take on recognising cases of unusual illness

Actions to be taken on recognising a case of unusual illness are summarised in Flowchart 5.

Flowchart 5: Action to be taken by General Practitioners on recognising unusual illness



Your direct involvement with cases will differ according to the category of incident. In a category I 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 GPs. It is possible that some of these may be unaware that they have been exposed to a risk. In a category II incident (more likely to be due to an infectious agent) you 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 risk. **A high index of suspicion is vital**, and the importance of a thorough history cannot be overstated in determining the aetiology.

The nature and time course of the symptoms is very important but also consider in particular any potential risk factors. For example:

- Where has the patient been recently? Where do they live? Where do they work? Have they travelled anywhere? How did they travel? Have they attended any special events?

- What has the patient been doing recently? What is their job? What do they do as hobbies/for recreation? Have they had any particular exposures e.g. to particular foods/drink/drugs, to unidentified substances? Have they done anything new/strange recently?

- Who or what has the patient been mixing with recently? Have they had contact with animals/other ill people?

- Ask the patient what they think has caused the illness. This may reveal "unusual" events or experiences that may give clues.

Always think about whether or not the case(s) could have arisen as the result of deliberate release.

5.2 Call CCDC for advice – CCDC may obtain advice from experts (Appendix 1)

Personal safety and patient containment

As soon as you suspect that a patient may have an unusual illness you should think first and foremost about 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 expert for advice immediately** and 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 the case(s)

Your local CCDC will advise you on the further management of the case(s). It is not possible to cover here all likely scenarios but it is possible that in some cases patients may be able to 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 what level of risk patients should be transported as so that you can pass this information on to the ambulance service. Sometimes decontamination of the patient may be required prior to transfer to the hospital and this would usually be done by ambulance professionals at the scene.

Do not perform any invasive investigations on the patient yourself. These should only be done in the hospital environment.

Where a decision to transfer to hospital has been made you should:

- Call the hospital to which the patient is to be taken. The local CCDC may have a view on which hospital should be used.
- Arrange for an ambulance, telling ambulance control what level of risk the patient should be transferred as, and whether decontamination has been recommended.

5.4 Further health protection for other exposed people

Your local CCDC will advise you if any decontamination, prophylaxis or other follow up is required for other exposed people including yourself and your staff. You should make a list of all those you believe 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 will be provided from the appropriate expert advice provider (Appendix 1) and how this should be arranged.

5.5 Record keeping

The importance of comprehensive record keeping cannot be over emphasised. This should cover not only the usual clinical records but also details of the advice that has been received, actions taken to protect self and others, and who else has been informed. Be sure to date, time and sign all entries.

GUIDE FOR PATHOLOGISTS

6. A guide for pathologists

As a pathologist you may become involved with investigating cases of unusual illness in several ways:

- You may recognise similar unusual pathology at postmortem of patients who may have died in different settings and with no connections having been previously made between them.
- You may receive laboratory results from a previously performed post mortem which indicate an unusual illness.
- You may be informed about unusual illness which has already been recognised as such and asked to perform post mortems.

The following sections give you guidance on what to do in each of these situations.

6.1 Unusual illness recognised by you at post-mortem

On recognising pathology consistent with an unusual illness at post mortem you should do the following:

- Do not precede any further with the procedure.
- Contact CCDC for advice concerning personal safety and whether to proceed with the post-mortem
- Liase with the senior clinician in charge of the case and between you ensure that you have informed infection control and the local CCDC.
- Make a list of all those pathology staff who have had direct contact with the body. This list should include name, age, address, GP details, contact details and the nature of their contact.

6.2 Unusual illness recognised from laboratory results from post-mortem

Where the laboratory investigation from a post-mortem indicate an unusual illness you should do the following:

- Liase with the senior clinician in charge of the case and between you ensure that you have informed infection control and the local CCDC.
- Contact CCDC for advice concerning management of any potentially exposed pathology staff.
- Make a list of all potentially exposed staff with their name, age, address, contact details, GP details and level of exposure.

6.3 Unusual illness recognised clinically and a request for post-mortem made to you

The most important guidance here is:

DO NOT PERFORM A POST MORTEM ON ANY PATIENT RECOGNISED AS HAVING AN UNUSUAL ILLNESS UNTIL EXPERT ADVICE HAS BEEN SOUGHT.

Where experts have advised that a post-mortem could be done, this should only be done where the facilities and available equipment are appropriate to the level of infectious risk and the staff have received adequate training.

If after discussion a postmortem is felt to be appropriate, suggested samples to take are as follows.

Toxicological

The "Toxi-box" (see section 4.9) can be used for sampling at post-mortem.

- Bladder contents can be collected in the universal container for urine **(without preservative).**
- **Peripheral** 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 (see section 4.9).

In addition other samples may be useful in 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 content
- Liver tissue
- Kidney tissue
- Muscle tissue (skeletal and cardiac)
- Fat
- Brain
- Lung tissue

Toxicological sample handling procedures
"Toxi-box" samples should be handled in exactly the same way as for sampling from acutely ill patients (section 4.9). However, **tissue samples in universal urine 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** can be found at Appendix 3. This form 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 3).
Samples for toxicological analysis in "Toxi boxes" should be sent to the local clinical chemistry laboratory. This laboratory should be telephoned in advance to inform them about the samples.

Microbiological

Due to the high risk of post mortem microbial contamination, it is preferable that any autopsies that are deemed to be appropriate should be performed within 24 hours of the patient's death. 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.

Microbiological sample handling procedures
Please use standard request forms for the transfer of clinical material to the laboratory. These forms 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 3).
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.

Possible post-mortem samples to be taken for microbiological examination to determine aetiology

Sample	Requirements
Serum	• 2 x 5-10mls minimum • store in a container suitable for freezing at –70°C
Whole blood (EDTA)	• 2 x 5-10mls minimum • store in a container suitable for freezing at -70°C
Blood cultures	3 sets
Tissues e.g.: • local inflammatory lesion/abscess • liver • spleen • lung • kidney • heart • enlarged lymph nodes • bone marrow • other organs with gross pathologic changes	• 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

Note: Stained smears and tissues on glass microscope slides.

Please 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.

GUIDE FOR
LOCAL LABORATORIES

7. A guide for local laboratories

7.1 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. It is unlikely that chemicals 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 both chemical and biological. 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. in the laboratory 0.5% hypochlorite (5,000ppm) 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 concerns or if there has been a spillage then please seek expert advice.
Procedures for managing accidents with in the laboratory should 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 who have handled 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[11].

The toxi-box samples will be used to analyse for all possible agents and will not normally be examined in local clinical chemistry laboratories.

Local **microbiological** laboratories will potentially constitute the most hazardous laboratory environment because of the way in which samples are processed. All clinical samples received from potential case patients and cultures/material derived from those samples should therefore be processed by **experienced MLSOs or scientists, using a Class 1 protective cabinet in a Containment Level 3 facility** until further evidence and advice allows alternatives. If a deliberate release is suspected all material should be held in a secure facility within a containment level 3 room. If there is any suspicion that a **hazard group 4 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 CPHL, CAMR and at Dstl, Porton Down). Some clinical material may have arrived in pathology departments and been processed to some extent prior to the recognition of an incident. If this situation arises, remaining material should be moved to the appropriate containment facility immediately.

7.2 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 completed 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. These identifiers are more meaningful than individual case series numbers.
To assist the tracking of specimen progress and results investigations, recipients (diagnostic and specialist/reference laboratories) of clinical diagnostic material from such cases should inform the **microbiology or toxicology coordinator,** providing sufficient information to enable tracking of what material has been sent where. Please use the forms provided (Appendix 3).

Routine haematology and biochemistry

Samples can be processed in the local laboratory but should be treated as **"high risk".**

Toxicology

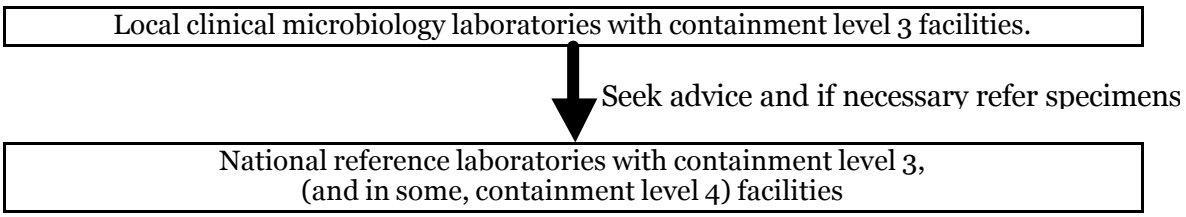
Samples for **toxicological** analysis (Toxi-boxes) should be temporarily stored in the local laboratory **(without opening or centrifuging them)** at 4°C. From here they should be transferred as quickly as possible to the appropriate medical toxicology laboratory (at least within 24 hours) since some 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.

Liase with whoever is leading the overall public health management of the incident to determine to which medical toxicology laboratory samples should be sent.

Guidance on safe transfer of samples to the medical toxicology laboratory is given in section 7.7. Care should be taken to ensure that all laboratory records are well maintained and to ensure that chain of evidence documentation (Appendix 3) is completed, particularly where deliberate release is suspected or there are other forensic considerations.

Microbiology

Local laboratories will receive specimens from cases of unusual illness and will be supported by two National reference laboratories (CPHL and CAMR). These are capable of providing a generic response capability in the investigation of **clinical samples** and also confirmation, identification and further work up of **potentially significant isolates** (e.g. sub-typing and bio-toxin analysis of isolates) using a range of techniques including sophisticated molecular technologies.



7.3 Receipt of clinical samples by local microbiology laboratories

Samples should have been labelled as "high risk" by submitting staff, and should be handled according to local protocols for such samples.

Hospital clinicians and pathologists have both been asked to take at least two sets of blood cultures, two bottles of clotted blood and two bottles of EDTA blood and to send these to their local microbiology laboratory along with other clinically relevant samples, all of which should be labelled "high risk".

Providing sufficient material is available for local testing of the above specimens, local laboratories should immediately send the following to the National reference laboratory advised by CPHL or CAMR. Of both acute and pathology samples:

- One set of blood cultures (If there are samples pre and post antibiotic administration the "pre" samples should be retained for local culture).
- One bottle of clotted blood.
- One bottle of EDTA blood.

Depending on the clinical signs and the samples available further material may also need to be sent to the National reference laboratory.

Instructions for the safe transport of specimens to National reference laboratories are given in section 7.7.

Expert advice should always be sought but it is anticipated that in most cases **remaining** clinical specimens will, if practical, be aliquoted on receipt. A **portion** would then undergo **basic examination locally** (including culture and antimicrobial susceptibility testing on "suspicious" isolates). and **the rest placed in several containers suitable for freezing** (at −70°C or alternatively at the lowest freezer temperature available) for archiving or possible transfer to reference facilities at a later date.

If the local laboratory does not have operational containment level 3 facilities then the remaining samples should be forwarded directly to either a nearby laboratory with appropriate facilities (depending on local arrangements) or to the appropriate National reference laboratory
Where an illness is recognised as unusual retrospectively, any remaining samples should be transferred to containment level 3 facilities. After reviewing current results and available samples, transfer of material to National reference laboratories may be indicated.

7.4 Sample investigations and storage in local laboratories

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 on selected specimens. 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 or below –20°C.

- **Respiratory secretions**
  Sputum/BALs 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 *B. anthracis* may be useful for epidemiological purposes.

- **Pus or tissues at operation or swab of local lesion/vesicular fluid**
  - **Pus, and tissue samples for microbiology:**
    - Plate directly for standard aerobic and anaerobic cultures -subject to enrichment culture.
    - 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 investigation** should be referred for investigation by EM, immunofluorescence, culture and PCR as appropriate.

- **Serum (spun) to be retained for possible subsequent examination or refer for possible toxin assay**
  - Acute sample (near time of admission) and convalescent.
  - Store at –70°C or lowest temperature available.

- **Whole blood in EDTA to be retained for possible subsequent molecular examination**
  - Acute, preferably admission 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, culture as routine, consider extending incubation if negative after your standard interval and 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**
  Simple tests to determine the likely identity of the isolates may be carried out. If it is not possible to confidently identify the organism as a known 'non pathogen' antimicrobial 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.

7.5 General guidance for local laboratories on prioritisation and transfer of clinical samples to specialised facilities (National Reference Laboratories) for investigation

General considerations

- Expert advice should be sought from CPHL or CDSC on which National reference laboratory to send samples to.
- National reference laboratories **should be informed of any samples which are to be sent to them.**
- Information on packaging and transportation are given in section 7.7. **All specimens should be labelled and handled as "High Risk".**
- The speed with which specimen/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.
- In addition to specimens referred, **please ensure that archival specimens are retained and stored** at the local laboratory or designated central site.
- A **microbiology summary submission form** for samples forwarded for reference testing from local laboratories can be found at Appendix 3. Laboratories should complete this form in addition to their standard documentation and a chain of evidence form on referral of samples to the National reference laboratories.

7.6 Specific guidance for local laboratories on storage/referral of clinical specimens and isolates to National reference laboratories

Isolates:

- Please retain all bacterial isolates cultured from these patients**.**
- Please refer all potentially significant isolates to CPHL/CAMR (or other PHLS Reference facility where relevant) for confirmation and potential further work up e.g. sub-typing and bio-toxin analysis (after antimicrobial susceptibility tests have been set up locally).
- If a particular agent is suspected it might be appropriate to switch to specific guidance.
- If it is not possible to confidently identify any isolate as a known 'non pathogen' they should be referred to CPHL/CAMR for formal identification (see 8.5 point 1).

Clinical specimens:

Local laboratories should routinely be sending (for acute and/or pathological samples) a set of blood cultures, a clotted blood sample and an EDTA sample to the National reference laboratory. Following expert advice ŧ may also be appropriate to refer the following specimens to CPHL or CAMR.

Specimens for possible referral to National reference laboratories

Specimen	Requirements
Respiratory samples	• A portion of BAL or other respiratory sample, stored frozen at -70°C (or lowest available/achievable temperature).
Pus and tissue samples	• Pus/non-fixed tissue -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 specimens. • Please retain any sample remaining after routine examination at –70°C for possible subsequent examination.

7.7 Safe transport of specimens from local to other laboratories e.g. National reference laboratories/medical toxicology laboratories

Microbiological samples should be placed within a leak proof secondary container containing enough absorbent material to mop up the entire contents in the event of spillage. The toxi-box for toxicological specimens should similarly be placed in such a secondary container[#]. The secondary containers should then be placed within a final outer tertiary packaging. This packaging must comply with the UN 602 standard packaging for the transport of infectious substances by air, road or rail. It will be important to ensure that sufficient stocks of UN602 compliant packaging and appropriately trained staff are readily available.

The package should be certified to this standard and carry the appropriate UN certification numbers on the tertiary packaging along with the following information:

- Biohazard danger of infection symbol Class UN 6.2.
- Instructions not to open if found.
- Telephone number of a responsible person e.g. consultant microbiologist or laboratory manager.

Adequately packaged materials should be sent by an approved courier to the National reference laboratory. 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. The latter course of action will need to be ratified/approved by the Joint Health Advisory Cell.

7.8 Reporting results

It is anticipated that delegated individuals will be responsible for collating toxicology and microbiology results on human and environmental samples. These individuals would be termed the **toxicology co-ordinator** and the **microbiology co-ordinator** respectively. These co-ordinators would be expected to liase with each other and one may take overall responsibility for collating all results. For example this may be done by the microbiology co-ordinator in a category II incident or the toxicology co-ordinator in a category I incident. **All results should be reported to the relevant co-ordinator by all laboratories processing samples.** Whoever has overall public health managerial lead for the incident will be able to direct laboratories to the relevant co-ordinator. This lead may be taken for example by the local CCDC, a Regional Epidemiologist, the Chair of an Incident Control team or JHAC, or a National Agency. The co-ordinators should be in close continuing communication with those leading the incident.

[#] **NB/ The standard toxi-box was unavailable when the recent batch was made up and distributed (personal communication Virginia Murray). The one currently in circulation therefore is of a slightly different size to the standard box. This has implications for secondary and UN 602 packaging which need to be resolved.**

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.

The co-ordinator has responsibility to track samples and results between local and reference laboratories as well as to the CCDC or incident control team. Reference laboratories will communicate individual patient results to referring laboratories who should then liase with the clinical team with responsibility for patient care.

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 agencies outside the NHS should only be done by the incident control team**.

7.9 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. This is perhaps most likely for microbiology laboratories. Under these circumstances you should do the following:

- Liase with the senior clinician in charge of the case and between you ensure that you have informed infection control and the local CCDC.
- Seek expert advice concerning management of any potentially exposed laboratory staff.
- Make a list of staff who may have been exposed with their name, age, address, contact details, GP details and level of exposure.

A GUIDE FOR
PUBLIC HEALTH PROFESSIONALS

8. A guide for public health professionals

Investigating outbreaks and incidents of disease is one of the routine aspects of public health business. For public health professionals specifically involved in health protection much of the guidance which follows will be standard practice. However, junior staff and 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 will particularly assist them in that function.

Comprehensive record keeping is essential. All information received advice given and actions taken should be logged, signed, dated and timed.

8.1 Action when an incident is first reported

Chapter 2 outlined how outbreaks/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 local CCDC (or their deputy) immediately.

Checklist 7 details the information which it is useful to obtain and record when an incident/outbreak is first reported to you.

Note that **if deliberate release is a possibility you should immediately discuss this with the police.** This may then trigger the guidance which has already been produced for deliberate release[10].

If specific agent is strongly suspected from the outset it may be more appropriate to switch to the specific guidance. The public health management of acute chemical incidents is comprehensively described elsewhere[12]. For incidents which are believed to be due to radiation exposure, the NRPB will advise on management[13] and clinical advice obtained locally from health physics and radiotherapy departments in the NHS will be an important first call for advice.

Checklist 7: Information for public health professionals to obtain and record on discovering 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 recognized 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 recognized 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 healthcare staff
- Evacuation/sheltering
- Quarantine
- Prophylactic treatment

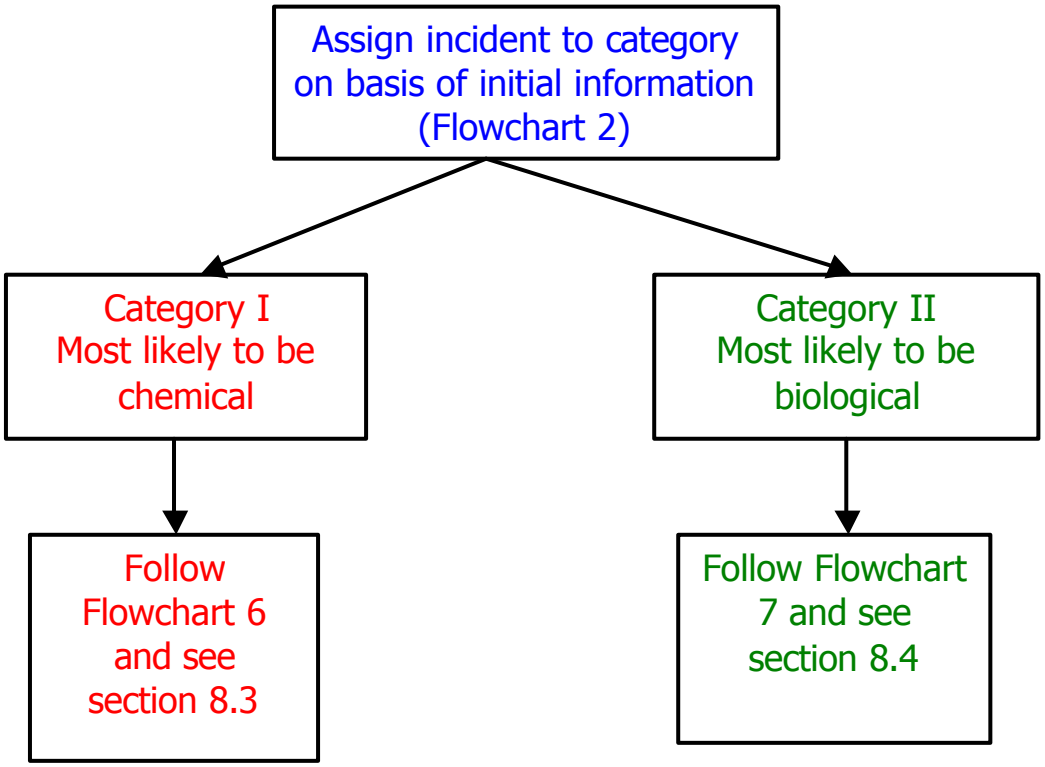
What agencies are involved at the moment? Get contact details. Has any agency declared a major incident? Who else has been informed?

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?

8.2 Management of an outbreak/incident according to category classification

The first step in management of an outbreak/incident of unusual illness is to assign an incident to either category I or II.



The same overall objectives apply to the management of both category I and category II outbreaks/incidents. These are:

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

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 lies in the speed with which the overall objectives must be achieved, and hence the priorities given to different tasks.

Flowchart 6 illustrates the management of Category I outbreaks/incidents which is further explained in section 8.3. 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 crucial task is therefore to seek expert advice immediately.**

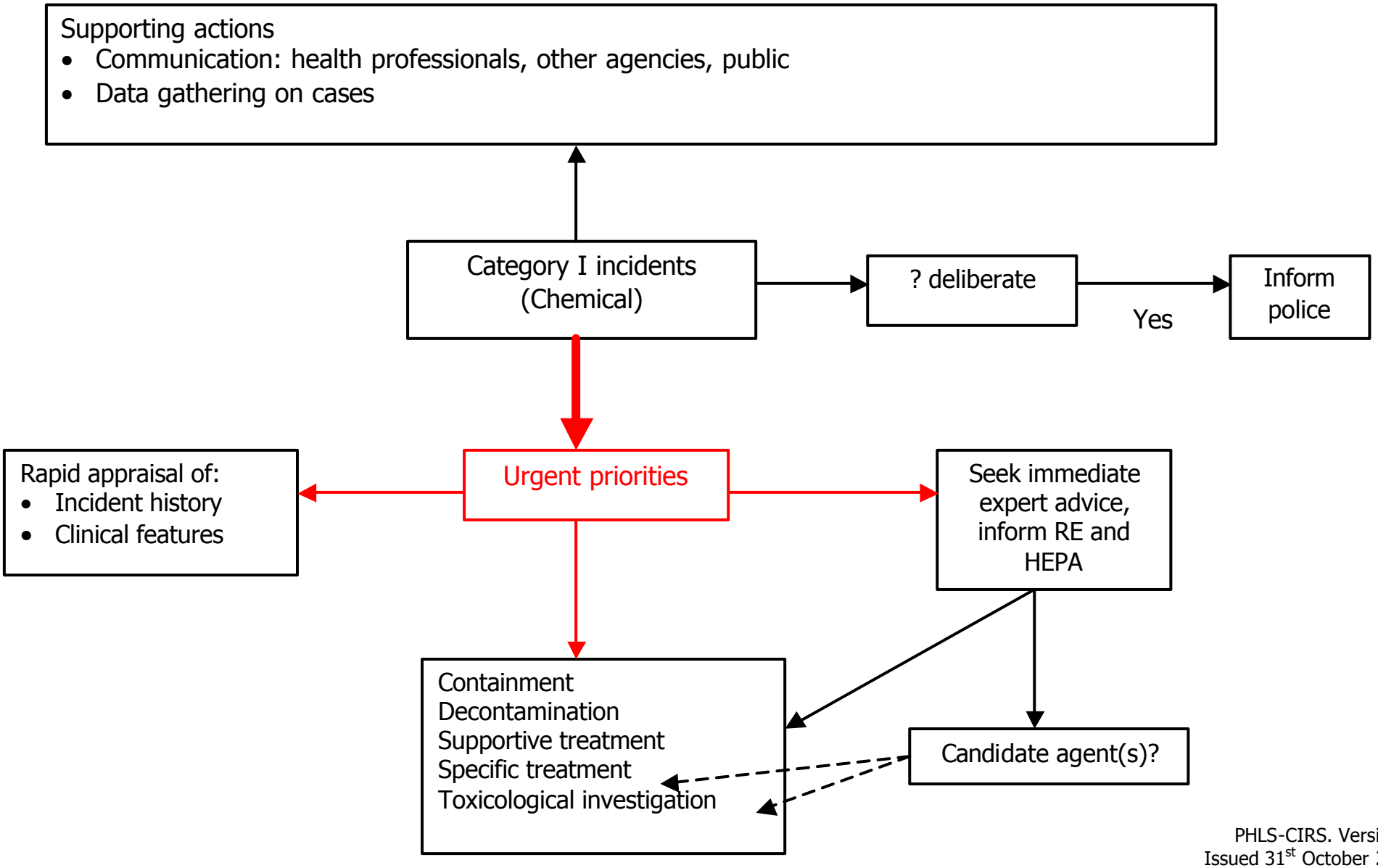
Flowchart 7 illustrates the management of Category II outbreaks/incidents, which is further explained in section 8.4.

8.3 Managing Category I outbreaks/incidents

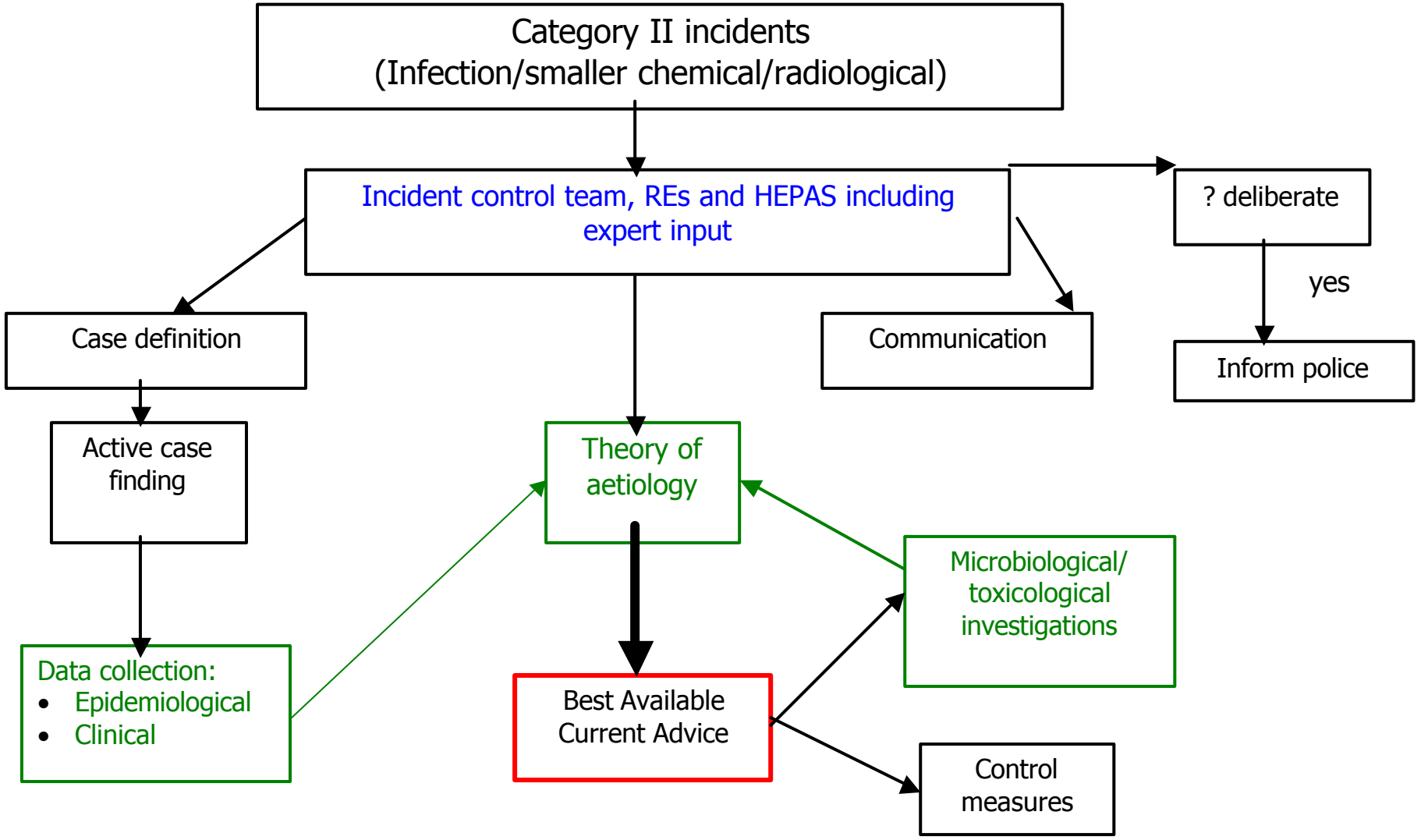
For a category I outbreak/incident speed is necessary to ascertain the likely aetiological agent and hence ensure appropriate treatment of cases and protection of others. These episodes are most likely to be due to chemical agents, though biological toxins may also produce outbreaks of acutely ill people. 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 (see Table 4). Category I outbreaks/incidents are much less likely to be due to infectious causes because of the variations which occur in the natural history of these diseases (e.g. range of incubation period).

The urgent priority for a category I incident is to get as much information as possible about the clinical features of the illnesses and the circumstances that may have produced exposure. From the clinical features seen they will be able to assist in identifying the likely aetiological agent and will advise on the management of casualties and on measures to be taken to protect others including health care professionals and others who may have been involved in managing the incident. Checklist 8 summarises the actions to be taken in the immediate management of category I outbreaks/incidents.

Flowchart 6: Initial public health management of category I outbreaks/incidents



Flowchart 7: Initial public health management of category II outbreaks/incidents



Checklist 8: Summary of actions for immediate public health management of category I outbreak/incident

Gather initial information listed in checklist one

Seek expert advice

Identify likely causative agent(s)

Determine likely clinical effects of agent

Ensure appropriate 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 Strategic Health Authority colleagues
- Regional colleagues (neighbouring PCTs, regional epidemiologist, regional Health Emergency Planning Advisor (HEPA))
- Healthcare providers (hospitals, A&E, GPs)
- Emergency services
- Local Environmental Health Department
- Local utilities
- Enforcement agencies e.g. Environment Agency (EA), Health and Safety Executive (HSE), Food Standards Agency (FSA), Drinking Water Inspectorate (DWI)
- National Focus for chemical incidents
- Emergency Planning Co-ordination Unit at Department of Health
- Media

Consider convening an incident control team (see section 8.5)

Alert and advise affected population

Consider a "site" visit but personal safety paramount

Formulate case definition and establish a database on cases

8.4 Managing Category II outbreaks/incidents

The aetiology of category II outbreaks/incidents will usually be more uncertain than for category I outbreaks. Here an incident control team should be set up at an early stage to ensure rapid investigation (see section 8.5 for membership and suggested agenda for first meeting). The important elements to be included in management are as follows:

- Seek expert advice
- Formulating case definitions
- Active case finding
- Appropriate investigation of cases
- Data collection on cases
- Data collection on "exposed but not ill" people
- Producing "best available current advice" on management of individual cases
- Producing and enacting "best available current advice" for public health protection
- Assessment of whether cases may be the result of deliberate action
- Communication with all those who need to know

The management of a type II outbreak will essentially be an iterative process with constant refinement of the theory of aetiology and consequent advice. It is suggested that during the management of these incidents, named individuals are delegated to fulfil particular key functions. These functions are summarised in Table 5 and referred to in the notes which follow. The individuals assigned to these key functions may or may not be part of the formal incident control team. Note that it may be necessary to divert staff from normal duties to fulfil these functions.

Table 5: Specific functions to be delegated to individuals

Function title	Function encompasses	Required individual
Incident clinical adviser	• Advising those reporting on the clinical features associated with "case" • Examination of clinical notes of cases where necessary • Development of proforma for collection of clinical information on cases. • Collation of clinical information on cases	Medically qualified e.g. CCDC, CPHM. Public Health SpR
Incident information officers	• Compilation and dissemination of list of essential contact details to incident team members • Receipt of case reports • Maintenance of a linelist 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 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.	Information officer/scientist
Microbiology and toxicology coordinators	• Record what samples have gone to which laboratories • Chase results • Maintain database of results • Report results to incident team, and local public health	Medical microbiologist and toxicologist

Case definitions

- A broad initial case definition should be used to avoid missing potential cases.
- Subcategories of "possible", "probable" and "definite" 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.

Active case finding

- A system may need to be instituted to actively find additional cases.
- 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 judge "caseness", and the contact number of a nominated medically trained individual/individuals ("incident clinical adviser") should be provided for additional information where required.
- A system should be developed for reporting of cases to a nominated individual(s) ("Incident information officer"). The incident information officer should liase closely with the incident clinical adviser.

Appropriate investigation of cases

- An initial theory of possible aetiology 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 4.9). Further expert input may add to this protocol according to the circumstances and as the incident evolves. Such additions must be promptly communicated to clinicians, pathologists and other users.
- Decisions will have to be made about what degree of "caseness" to further investigate (e.g. just definites, or definites and probables etc).
- Decisions will need to be made in conjunction with expert service providers about which toxicology and National microbiology reference laboratories to send samples to.
- Nominated individuals should be assigned responsibility for chasing and compiling toxicological and microbiological results on cases as appropriate. These individuals would be termed the microbiology and toxicology co-ordinators respectively. One of these may take overall responsibility for collating results. Depending on the scale of the incident it may be appropriate for results to be collated at a local, regional or national level.
- All results from all laboratories should be returned to the co-ordinators. They then have the responsibility of ensuring that clinicians in charge of cases have received the results and that the results are passed on to the incident control team and the local public health team if this is different.
- Reference laboratories will communicate test results directly to the referring laboratory who will have the responsibility of informing the clinicians in charge of the case(s) and the incident team.

Data collection on cases

- The incident information officer should be responsible for maintaining and updating a linelisting of all possible, probable or definite cases.
- This should include as a minimum dataset: case identification, assessment of "caseness", date of presentation, location, contact details for clinician in charge of case, whether or not further investigation has been conducted, outcome of case (recovery, death etc).
- An epicurve of cases should be constructed and updated regularly by the incident information officer. The shape of the epicurve can give important clues as to the aetiology; point source versus continuing source versus propagated source.
- A proforma should be developed to gather additional epidemiological and clinical information about cases whose "caseness" justifies further investigation. Decisions will need to be taken about whether this should be done at the district, regional or national level but would also be a function of the incident clinical adviser within the team.
- By agreement, the proforma should be completed by the clinician in charge of the case from the case notes and where appropriate by further interview of the patient.
- Consideration should also be given to direct examination of medical records or interview of cases by the incident clinical adviser to spot similarities between cases which might not be evident to clinicians dealing with individual cases.
- The incident clinical adviser should be responsible for collating all the more detailed information.

Data collection on "exposed but not ill" people

Decisions will need to be made about how to define exposure. A list should be compiled as far as possible of those who have been potentially exposed but who are not as yet ill (incident information officer). This should include not only the general public at risk but also consideration of the healthcare workers and professionals from other agencies who may have been involved with the incident. The list should include name, address, date of birth, contact details and GP details along with a classification of exposure risk.

Producing "best available current advice" on management of individual cases

- Guidance on appropriate individual management will initially be based on the working theory of aetiology.
- Advice sheets should be produced for clinicians who may encounter cases. This task would be best done by the expert advisors to the incident team.
- As more evidence is obtained advice sheets should be updated.
- Consideration should be given to the use of websites to disseminate advice.

Producing and enacting "best available current advice" for public health protection

- Guidance on appropriate public health management will initially be based on the working theory of aetiology.
- Decisions will need to be taken about how to manage exposed but not ill people.
- Responsibility for enactment of public health protection activities will need to be clarified and resource requirements identified.

Assessment of whether cases may be the result of deliberate action

- On the basis of the clinical and epidemiological evidence as it evolves, repeated assessments should be made of whether cases may be the result of deliberate action.
- Where deliberate action is a possibility the matter should be discussed with the police.

Communication

- A focal point for contact about the incident should be identified.
- Effective communication with all those who need to know is crucial to the management of any outbreak/incident.
- Systems need to be set up from the outset to ensure that regular updates and communications are built into investigation and management.
- A full list of all essential contact details should be compiled and disseminated to all parties involved by a nominated individual (e.g. incident information officer). This should be updated regularly.
- The incident information officer should disseminate regular updates of summary data and developments to all parties involved in management.
- Those who need to know might include:
    - Strategic Health Authority and PCT colleagues
    - Regional colleagues (neighbouring PCTs/SHAs, regional epidemiologist, regional HEPA)
    - Healthcare providers (hospitals, A&E, GPs)
    - Expert agencies (CDSC, CPHL, CIPUs, NRPB)
    - Emergency services
    - Local Environmental Health Department
    - Local utilities
    - Enforcement agencies e.g. Environment Agency (EA), Health and Safety Executive (HSE), Food Standards Agency (FSA), Drinking Water Inspectorate (DWI)
    - Emergency Planning Co-ordination Unit at DH
    - Media
- **A nominated press office should handle all media enquiries for the incident.**

8.5 Incident control team

It may be necessary to consider convening an incident control team for either category I or II outbreaks. This would usually be chaired by the CCDC, regional epidemiologist or national epidemiologist, depending upon the circumstances of the incident. It should include representatives from key organisations involved in the management of the incident with the necessary seniority and expertise to be able to take decisions. For example:

- A representative of the Chief Executive of the PCT/Regional Office
- A representative from the Environmental Health Department of the Local Authority
- Representatives from the emergency services (fire, police, ambulance)
- Representatives from local utilities
- Representative from the enforcement agencies (FSA, EA, DWI, HSE)
- Expert advisers from the relevant agencies (CIPU, NRPB, CDSC, CPHL)
- Representatives from laboratory investigative services
- A press officer
- Secretarial support

A suggested agenda for the first meeting is given in Checklist 9.

It is not possible in this document to provide guidance beyond these initial stages of incident investigation and management, however throughout the incident the team will need to re-appraise:

- Evidence re aetiology
- Investigations required
- Measures to manage individual cases and for public health protection
- Risk assessment for public health
- Likelihood of deliberate action
- Resource requirements
- Communications

It will also need to consider:

- Criteria for declaring the outbreak/incident over
- Closure information dissemination
- Post incident report writing

Post incident health monitoring, particularly where was the causative agent was chemical/radiological

Checklist 9: Suggested agenda for first incident control team meeting.

- Agree a case definition
- Determine whether active case finding is necessary and how this will be done
- Examine available evidence re aetiology and consider whether the incident may be the result of deliberate action
- Assess risks to public health given current knowledge of aetiology
- Ensure that care of cases is appropriate given current knowledge of aetiology
- Consider who else is at risk, including health professionals and other agencies who may have been involved in managing the incident
- Decide how others should be protected given current knowledge of aetiology, who will be responsible for this and how it will be resourced
- Define measures necessary to identify the cause of the illnesses, including environmental sampling as appropriate
- Identify additional expert assistance which may be required for investigation or management of the illnesses
- Define mechanisms for data collection and collation
- Define measures necessary to monitor the effectiveness of containment
- Identify personnel and other resources necessary to manage the outbreak/incident
- Identify who needs to know
- Define measures for communication to the public, press and other organisations and individuals
- Assign functions both within and outside the incident control team
- Decide the necessary frequency of meetings

9. Appendix 1

Contact numbers for expert support agencies for the management of outbreaks of unusual illness

FOR HEALTH PROFESSIONALS ONLY

Agency	Regions Covered	Phone	Fax (9am to 5pm)
Infectious diseases			
PHLS, CDSC	England, Wales, Northern Ireland	0208 200 6868 (24 hour)	0208 200 7868
PHLS, CPHL	England, Wales, Northern Ireland	0208 200 4400 (24 hour)	0208 200 7874
CDSC Wales	Wales	02920 521 997	02920 521 987
CDSC Northern Ireland	Northern Ireland	02890 263 765	02890 263 511
SCIEH	Scotland	0141 300 1100	0141 300 1170 (general) 0141 211 3600 (on call)
Chemical hazards			
CIRS	London, South East, South West, Eastern, Trent, North, West	0207 771 5383 (routine) 0207 358 9165 (emergency for HAs) 0207 6359191 (24hrs)	0207 771 5382 (routine) 0207 6359191 (24hrs)
SCIEH	Scotland	0141 300 1100	0141 300 1170 (general) 0141 211 3600 (on call)
Chemical Hazard Management and Research Centre	West Midlands	0121 414 3985 0121 414 6547 0207 394 5112 (emergency)	0121 414 3630
CIMSU	Wales	02920 716 738 02920 715 278 (emergency)	02920 070990
CIS-Newcastle	Northern and Yorkshire	0191 222 7195 0836 774 367 (24 hr)	0191 222 6442
Radiological hazards			
National Radiological Protection Board	Leeds, Oxfordshire (Head office)	01235 834 590 (24 hr) 0113 267 9041 (Leeds)	0113 261 3190 (Leeds)

* Note that this appendix has been included pro-tem until the formation of a central unusual incident advisory service with a single one number point of contact.

10. Appendix 2

Advisory Committee on Dangerous Pathogens Categorisation of Biological Agents

Biological agents have been categorized into four Hazard Groups based on their pathogenicity, potential hazard to employees, transmissibility to the community and availability of effective prophylaxis or treatment.

Definitions

Biological agent
'Any micro-organism, cell culture or human endoparasite, including any which may have been genetically modified, which may cause any infection, allergy, toxicity or other wise create a hazard to human health.'

Hazard Group 4
'A biological agent that causes severe human disease and is a serious hazard to employees; it is likely to spread to the community and there is usually no effective prophylaxis or treatment available.'

List of Hazard Group 4 agents - all are viruses	
Arenaviridae Old world -Lassa fever New World -Guanarito -Junin -Machupo -Sabia **Bunyaviridae** Nairoviruses -Crimean/Congo haemorrhagic fever **Filoviridae** Ebola Reston Ebola Siena Ebola Sudan Ebola Zaire Marburg	**Flaviviridae** Kyasanur forest disease Omsk Russian spring summer encephalitis **Herpesviridae** Herpesvirus simiae (B virus) **Paramyxoviridae** Nipah **Poxviridae*** Variola (major and minor) **Unclassified viruses** Equine morbilliv irus

* Note that smallpox would be re-designated as level 3 once a case appears.

11. Appendix 3

The following analysis request forms are included at the end of this document and may be copied for use as needed:

- "Toxi-boxes" Chemical Incident Analysis Request Form
- Summary Submission Form for Clinical Samples Forwarded for Microbiology Reference Testing from Cases of 'Unusual Diseases'
- Chain of Evidence Form

'Toxi boxes' Chemical Incident Analysis Request Form

Referring Laboratory **Medical toxicology laboratory**

Please complete in block capitals
Unless you are certain as to the sample required please check with your Regional Chemical Provider Unit

Patient Surname and Christian names (Surname First)	D.O.B.	Age	Sex	Hospital No.

Ward/Unit	Hospital/Institution
Analysis Requested by:	Consultant

Sample Date	Sample Time	Sample Type	Req.Lab. No	MT Lab No
		Heparinised Blood (10ml)		
		Heparinised Blood (5ml)		
		EDTA Blood		
		Urine		

Name and address for report

Telephone No:-

Telephone No for Urgent results:-

Place of Exposure (if known)

Exposed to (Generic/Chemical names if known).

Length of Exposure (if known)

Clinical features

Name and address for invoice.

Telephone number

Please send a photocopy of this form to the toxicology co-ordinator

Summary Submission Form for Clinical Samples Forwarded for Microbiology Reference Testing from Cases of 'Unusual Diseases'

In addition to your standard documentation, including where available laboratory-specific request forms please complete this form summarizing all samples to be forwarded and send a photocopy of it with all referrals to the different reference laboratories, highlighting the actual specimen types included in each package. This will facilitate appropriate testing and archiving at the central laboratories. (If material from any one case has previously been referred please indicate at 3*.)

1. Case information:

Patient name _____Patient's Hospital number_____a__,❒ Male ❒ Female

Patient address……Post Code……..

Date of birth **___/___/___,** Age…….. Suspected diagnosis:…… … Outcome (if known)……..

Date of onset of symptoms ____/____/____ Symptoms/signs…….. ……..

……..

Clinician's name ……..

Hospital name and post code……..

Originating laboratory: ……

Date referred to Reference Laboratory(s):____/____/____

2. Contact information for microbiologist referring samples:

Name……Telephone…….

Out of hours contact phone……..Fax……E-mail……..

Full postal address: ……..

……

3. Previous material referred? YES/NO, if Yes where to?……

Please list material to be referred overleaf highlighting (using the tick boxes) those actually enclosed

4. Clinical specimens to be referred

	Specimen type and description e.g. EDTA whole blood, swab-lesion	Your lab number	Ante/ Post-mortem	Specimen Date	**Reference Laboratory name**	**Ref. lab Accession number***	**Date received at Ref. lab.***	**Specimen type***
? 1								
? 2								
? 3								
? 4								
? 5								
? 6								

5. Isolates

Isolate	Presumptive I.D.	Your lab number	Original specimen type e.g. swab, fluid	Specimen description e.g. pleural fluid	Ante/ Post-mortem	Specimen Date	**Reference Laboratory name**	**Ref. lab Accession number***	**Date received at Ref. lab.***
? 1									
? 2									
? 3									
? 4									
? 5									

THANK YOU FOR COMPLETING THIS FORM

*__**FOR THE ATTENTION OF RECEIVING REFERENCE LABORATORY**__.

__On receipt of this form please add in date received, your Lab accession number(s) and for clinical specimens please indicate the exact type of sample received if not already stated-blood-EDTA/serum/culture, urine, faeces, csf, respiratory-secrections/swab, tissue, pus, other fluid, swab or slide. Please send a photocopy of this form with your lab address stamp or other identification to:__

__Microbiology coordinator ,,__

__Address__

__Contact number -E-Mail Fax number__

Unusual illness chain of evidence form

To be used where deliberate release is suspected or other forensic considerations are important

Patient name	Sex	Date of Birth

Hospital number	Ward

Doctor	Bleep number	Consultant

Sample type	Sample date	Sample time	Laboratory number

Name of person handing over samples		Name of person receiving samples	
Grade		Grade	
Signature		Signature	
Date		Date	
Name of person authorising handover		Address	
Signature			
Date			

Please note that **a separate form must be filled in every time samples change hands**, starting from the doctor taking the samples. All forms should be kept together.

Verbal authorisation from the consultant in charge of the case should be obtained before sending the samples to the laboratory. However, samples should not be delayed to await their signature, which can be filled in later. Laboratories will have their own local protocols for who is sufficiently senior to authorise sample handover and these should be adhered to.

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