

Biological threats:

A Health Response for Ireland

**Produced by the Expert Committee – Contingency Planning
for Biological Threats**

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Note: These are interim guidelines which may be subject to changes as comments are received. Comments are welcome and should be sent to comments@health.irlgov.ie.

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List of Abbreviations

CAMR: Centre for Applied Microbiology Research

CDC: Centers for Disease Control and Prevention

CL-3: Containment level 3 laboratory

DOHC: Department of Health and Children

DPH: Director of Public Health

EOD: Explosives Ordnance Division

HEPA filtered: High Efficiency Particulate Air filtered

IMB: Irish Medicines Board

NDSC: National Disease Surveillance Centre

NIOSH: National Institute for Occupational Safety and Health

PCR: Polymerase chain reaction

PEP: Post exposure prophylaxis

PHLS: Public Health Laboratory Service

WHO: World Health Organisation.

Introduction

In the light of recent worldwide events it is clear that there is a need in this and every country for **preparedness** for dealing with people who have been exposed to or infected with agents associated with bioterrorism. It seems unlikely that a country such as Ireland would be the target of a primary bioterrorist attack. It is more likely that those who have been covertly exposed to bioterrorist agents abroad could enter this country before they develop signs of illness and could have their illness diagnosed in this country. Due to the high infectivity of many of the diseases associated with these bioterrorist agents it is necessary to have protocols in place to deal with all contingencies.

This protocol is a short-term plan which has been devised by the Expert Committee – Contingency Planning for Biological Threats set up by the Minister for Health and Children. It deals with the Category A agents: namely anthrax, smallpox, botulism, plague and tularaemia. These organisms pose a particular risk to public health because they can be easily disseminated or transmitted from person to person, they cause high mortality and morbidity or they require special action for public health preparedness. A separate set of guidelines for the management of cases of viral haemorrhagic fever has been produced by the National Disease Surveillance Centre and is available on their website at www.ndsc.ie.

The key strategic issues are preparedness and prevention, detection and surveillance, diagnosis and characterisation of biological agents, providing a prompt response and communication. This protocol stresses the importance of regular and timely communication with health care providers and the general public. It is a working document, which will be updated as comments are received. Comments are welcome and should be addressed to comments@health.gov.ie.

The translation of this protocol into action will require a concerted interagency and interdepartmental response. The Expert Committee – Contingency Planning for Biological Threats has worked with the army, the gardai and many government departments in the production of this protocol.

In the short term there is a need to

- Organise on-call rosters to ensure that appropriately trained individuals are available on a 24-hour basis should an emergency arise. *These should be arranged at health board level.*
- Stockpile appropriate antibiotics, antivirals, antitoxins, vaccines and arrange for appropriate storage. *This is being organised by the Expert Committee.*
- Designate hospitals as centres for reception of patients with smallpox or quarantine units for those who may have been exposed to smallpox and their contacts. *This is being organised by the Expert Committee.*
- Arrange the procurement and distribution of adequate quantities of personal protective clothing and equipment. *This is being organised by the Expert Committee.*

- Consider vaccination of staff in designated smallpox units and frontline emergency personnel. *Decisions regarding vaccine administration will be made by the Expert Committee in consultation with the Task Force.*
- Prepare information materials on the various biological agents for key health professionals. *This is being organised by the National Disease Surveillance Centre for the Expert Committee.*

Early detection is essential for ensuring a prompt response to biological attacks. The National Disease Surveillance Centre will integrate surveillance for illness resulting from biological agents into existing surveillance systems. New mechanisms for detecting, evaluating, and reporting suspicious symptoms or diseases will include changes in regulations to make diseases such as tularaemia and airborne botulism notifiable. The roles of the National Disease Surveillance Centre and other agencies are discussed later in this document.

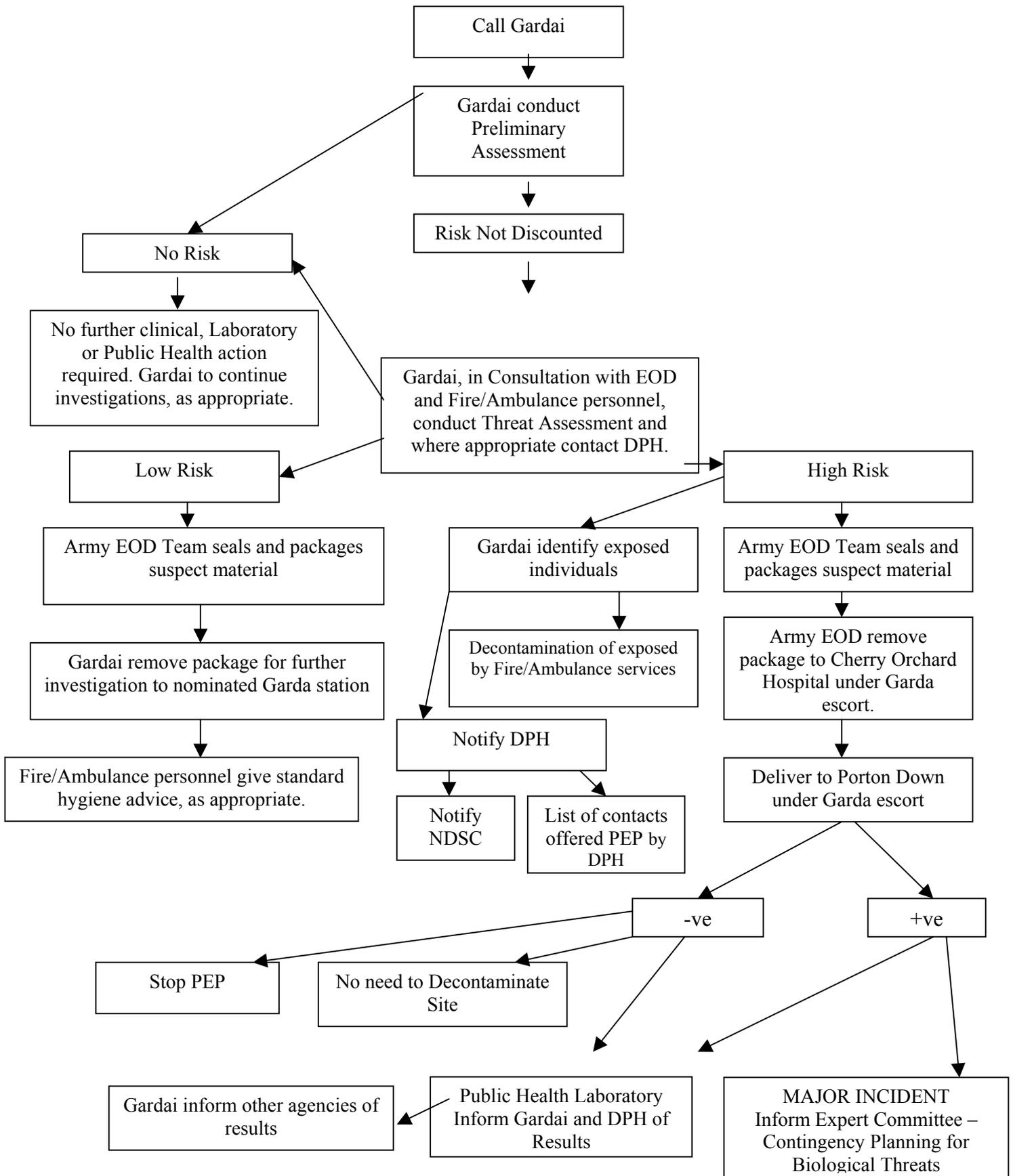
This protocol draws significantly on evidence and guidelines from other countries such as the UK and USA who have been preparing protocols for bioterrorist attacks for many years. It has been adapted for use in an Irish setting.

Immediate steps to be taken in the event of the discovery of a package suspected of containing anthrax*

- Call Gardaí (999 or 112).
- Gardaí to tightly seal off site and carry out preliminary investigation and determine risk categorisation (i.e.) no risk, low risk or high risk.
- If **no risk**, no further clinical, laboratory or public health action need be taken
- If risk is not discounted Gardaí, in consultation with the army and fire/ambulance personnel, conduct threat assessment and, where appropriate, contact Director of Public Health.
- If **low risk**, no further clinical, laboratory or public health action need be taken
- If **high risk** (package opened or unopened)
 - Fire and ambulance services (decontamination units) to carry out decontamination of exposed individuals on site using mobile units.
 - Director of Public Health to get a list of exposed individuals and to make local arrangements to ensure that appropriate advice and chemoprophylaxis are given. The administration of chemoprophylaxis may be done on site, in a hospital or in a healthcare setting. This will depend on locally agreed arrangements.
 - Army will arrange transport of all environmental specimens to Public Health Laboratory in Cherry Orchard Hospital.
 - Exposed persons to be contacted by Director of Public Health with the result of environmental sampling.
 - If anthrax is confirmed, this is a major incident and the Expert Committee – Contingency Planning for Biological Threats must be informed. They will advise on further medical action.
 - Army to carry out decontamination of environment **only in the case of an environmental sample that tests positive for anthrax**. If anthrax is confirmed, the exposed room/area must remain sealed off, as it is officially a crime scene. Heating or air conditioning must stay off.

* Some adaptations to these steps will be required if a package is suspected of containing biological agents other than anthrax. If a package is suspected of containing smallpox, for example, it should be taken to the Virus Reference Laboratory rather than to Cherry Orchard Hospital. If smallpox is confirmed, those exposed will be vaccinated and quarantined rather than given chemoprophylaxis (See section on smallpox for further details).

Figure 1: Steps to be taken on finding a suspicious package*



* This flow chart has been designed to deal with suspected anthrax cases. It can however be modified to deal with other agents as appropriate.

Critical Biological Agents

Category A

The Irish public health system and primary health-care providers must be prepared to address varied biological agents, including pathogens that are rarely seen in Ireland. High-priority agents include organisms that pose a risk to public health because they

- can be easily disseminated or transmitted person-to-person;
- cause high mortality, with potential for major public health impact;
- might cause public panic and social disruption; and
- require special action for public health preparedness

Category A agents include

- *Variola major* (smallpox);
- *Bacillus anthracis* (anthrax);
- *Yersinia pestis* (plague);
- *Clostridium botulinum* toxin (botulism);
- *Francisella tularensis* (tularemia);
- Viral haemorrhagic fevers,
 - Ebola hemorrhagic fever,
 - Marburg hemorrhagic fever
 - Lassa (Lassa fever),
 - Junin (Argentine hemorrhagic fever) and related viruses.

Category B

Second highest priority agents include those that

- are moderately easy to disseminate;
- cause moderate morbidity and low mortality; and
- require enhanced disease surveillance.

Category B agents include

- *Coxiella burnetti* (Q fever);
- *Brucella* species (brucellosis);
- *Burkholderia mallei* (glanders);
- alphaviruses,
 - Venezuelan encephalomyelitis,
 - eastern and western equine encephalomyelitis;
- ricin toxin from *Ricinus communis* (castor beans);
- epsilon toxin of *Clostridium perfringens*; and
- *Staphylococcus* enterotoxin B.

A subset of List B agents includes pathogens that are food- or waterborne.

These pathogens include but are not limited to

- *Salmonella* species,
- *Shigella dysenteriae*,
- *Escherichia coli* O157:H7,
- *Vibrio cholerae*, and
- *Cryptosporidium parvum*.

Category C

Third highest priority agents include emerging pathogens that could be engineered for mass dissemination in the future because of

- availability;
- ease of production and dissemination; and
- potential for high morbidity and mortality and major health impact.

Category C agents include

- Nipah virus,
- Hantaviruses,
- Tickborne hemorrhagic fever viruses,
- Tickborne encephalitis viruses,
- Yellow fever, and
- Multidrug-resistant tuberculosis.

Preparedness for List C agents requires ongoing research to improve disease detection, diagnosis, treatment, and prevention. Knowing in advance which newly emergent pathogens terrorists might employ is not possible; therefore, linking bioterrorism preparedness efforts with ongoing disease surveillance and outbreak response activities is imperative.

Proposed scenarios

The following scenarios outline the steps to be taken in the event of the covert or overt release of a biological agent in Ireland or the arrival of a secondary case from another jurisdiction.

Scenario One

Covert release of a biological agent in Ireland*

Accident and Emergency Physicians, general practitioners, occupational health physicians or other clinicians may become aware of

- Unusual presentations of illness
- A cluster of cases with similar symptoms
- A syndrome suggestive of bioterrorism

Preliminary response

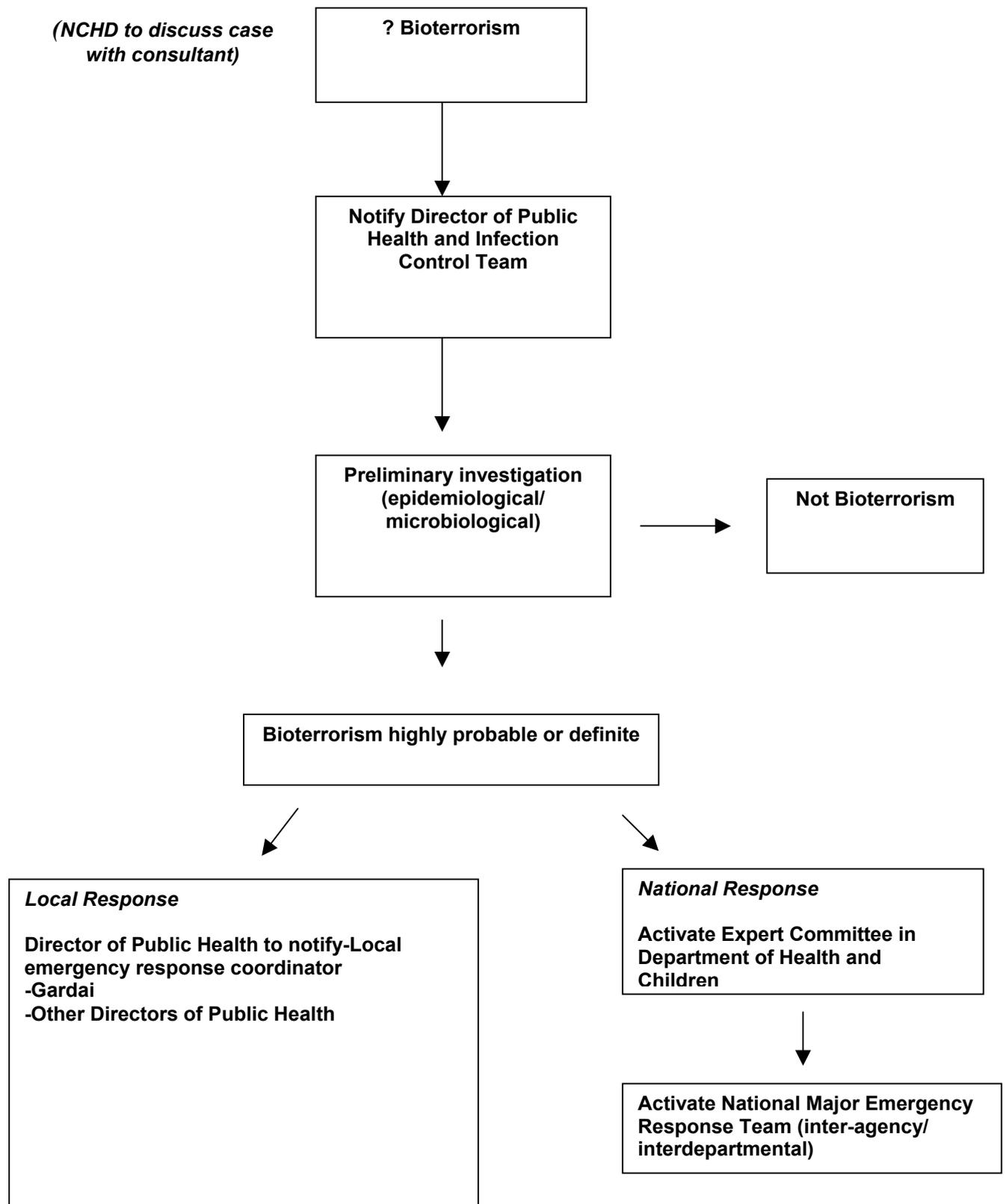
In this scenario the doctor consulted should have a high index of suspicion that any unusual presentations of illness or clusters of cases with similar symptoms may be associated with the release of a biological agent. The decision to contact the Director of Public Health or his /her representative should be taken after a non-consultant hospital doctor has discussed the case or cases with a consultant. A general practitioner or occupational physician who suspects disease caused by bioterrorist agents should also contact the Director of Public Health directly and without delay. In a hospital setting, the hospital infection control team and infectious disease consultant or other appropriate general physician should also be called.

The Director of Public Health or his/ her representative will set up a local team with an infectious disease consultant or other appropriate general physician and with microbiological, public health and environmental representation to commence an epidemiological investigation. If bioterrorism is deemed to be highly probable or definite at this stage the Expert Committee – Contingency Planning for Biological Threats will be convened along with the National Major Emergency Response Team and the Office for Emergency Planning will be informed. At a local level the Director of Public Health will also contact the Gardai, the local emergency response co-ordinator and the other Directors of Public Health. The Gardai will contact the army if required.

¹*Epidemiological principles must be used to assess whether a patient's presentation is typical of an endemic disease or is an unusual event that should raise concern. Features that should alert healthcare providers to the possibility of a bioterrorism related outbreak include

- A rapidly increasing disease incidence in a normally healthy population
- An epidemic curve that rises and falls during a short period of time
- An unusual increase in the number of people seeking care, particularly with fever, respiratory or gastrointestinal complaints
- An endemic disease rapidly emerging at an uncharacteristic time or in an unusual pattern (e.g. an increase in what appears to be chickenpox-like illness among adult patients, but which might be smallpox)
- Lower attack rates among people who have been indoors
- Clusters of patients arriving from a single locale
- Large numbers of potentially fatal cases (e.g. a large number of cases of acute flaccid paralysis with prominent bulbar palsies, suggestive of a release of botulinum toxin)
- Any one patient presenting with a disease that is relatively uncommon and has bioterrorism potential

Figure 2: Steps to be taken following the covert release of a bioterrorist agent in Ireland



Scenario Two

Overt release of a biological agent in Ireland

In the event of the overt release of a biological agent in Ireland the Expert Committee Planning for Biological Threats will be convened. **The relevant Health Board Emergency Plan will also be activated.** The Gardai, defence forces, emergency services and Director of Public Health will also be called.

Many of the principles described in this document with regard to designation of the exposed zone, decontamination of humans and the environment, administration of chemoprophylaxis/ treatment and laboratory investigations/ procedures apply regardless of whether the release is overt or covert.

Immediate steps to be taken in the event of the deliberate release or suspected release of any Category A biological agent

- Call Gardai (999 or 112).
- Gardai to tightly seal off exposed zone. **Exposed zone represents a high risk of infection. Anyone entering it must wear appropriate protective clothing.**
- Gardai to contact
 - Army
 - Fire and Ambulance Services
 - Directors of Public Health and
 - Expert Group – Contingency Planning for Biological Threats
- Fire and ambulance services to carry out decontamination of exposed individuals on site using mobile units.
- Environmental samples (e.g. suspect package) to be taken by army to Cherry Orchard Hospital (or Virus Reference Laboratory, UCD if smallpox virus is suspected).
- The area surrounding the site will remain designated as an exposed zone until sufficient time has elapsed. Environmental decontamination will be carried out by the army if required.
- Exposed persons will be given chemoprophylaxis if anthrax, plague or tularaemia is suspected. If high index of suspicion of smallpox, exposed persons will be vaccinated and moved to a sealed place of safety for medical observation. These individuals should be quarantined for 18 days with daily health and temperature checks.
- The Director of Public Health or his/ her representative will ensure that lists of exposed individuals are taken and that all exposed individuals are given chemoprophylaxis or immunised and quarantined as appropriate.

Scenario Three

Arrival of infected individuals in Ireland (secondary attack)

In the event of a secondary case of an infectious disease associated with a bioterrorist attack in another jurisdiction arriving in Ireland the management will depend on the disease in question.

Anthrax, for example, is not spread from person to person. The arrival of a person with smallpox, on the other hand, due to its high infectivity will necessitate immunisation of all health care workers likely to come in contact with all smallpox cases, hospitalisation of the case in a designated smallpox hospital unit and quarantine of contacts for up to 18 days as described in earlier scenarios. The Expert Committee – Contingency Planning for Biological Threats and the National Major Response Teams will be activated.

The confirmed use of bioterrorist agents in other countries must lead clinicians to have a high index of suspicion when patients present with symptoms which could be associated with the disease in question. Timely surveillance would be vital in those scenarios. **Information sheets will be circulated to medical practitioners outlining the cardinal signs for case detection of disease caused by the category A agents.**

In the event of an outbreak of smallpox in another country such as the United States of America or the United Kingdom the Department of Health and Children and the National Disease Surveillance Centre will be rapidly notified via the EU infectious disease surveillance network. Consideration will be given to restricting access to this country for those originating from the country in question or enforcing quarantine for 18 days for unvaccinated individuals travelling from those countries. Consideration would also be given to closing all routes into the country in extreme circumstances. The Expert Committee – Contingency Planning for Biological Threats will provide medical advice to inform these decisions.

Anthrax

A. Description of Agent/ Syndrome

(a) Aetiology/ epidemiology

Anthrax is a zoonotic disease caused by *Bacillus anthracis*, a spore-forming gram-positive bacillus. The disease occurs primarily in large domestic and wild herbivores which acquire spores through ingestion of contaminated soil. The reservoir of *B anthracis* is the soil and spores can remain viable for decades. Human infection usually follows contact with infected animals or contaminated animal products. Infection occurs usually through the skin and less commonly through the respiratory or gastrointestinal systems.

A previously undescribed form of anthrax, inhalational anthrax, appeared during the latter half of the 19th century, in wool sorters in England. This form of the disease was caused by aerosolisation of anthrax spores generated during the industrial processing of animal hides. Inhalational anthrax carries a much higher mortality rate than the cutaneous form of the disease. **Person-to-person transmission of inhalational disease does not occur. Direct exposure to vesicle secretions of cutaneous anthrax lesions may result in secondary cutaneous infection.**

About 2000 cases of cutaneous anthrax are reported globally each year. There are about 5 cases each year in the US and fewer than 1 case a year in the UK. There have been no human or animal anthrax notifications in Ireland during the last 25 years.

(b) Clinical features

Human anthrax infection can occur in three forms: pulmonary, cutaneous, or gastrointestinal, depending on the route of exposure. **Of these forms, pulmonary anthrax is associated with bioterrorism exposure to aerosolised spores.** Clinical features for each form of anthrax include:

Pulmonary

- Non-specific prodrome of **flu-like symptoms** follows inhalation of infectious spores.
- Possible brief interim improvement.
- Two to four days after initial symptoms, **abrupt onset of respiratory failure** and hemodynamic collapse, possibly accompanied by thoracic edema and a **widened mediastinum on chest radiograph** suggestive of mediastinal lymphadenopathy and hemorrhagic mediastinitis.
- Gram-positive bacilli on blood culture, usually after the first two or three days of illness.
- Treatable in early prodromal stage. Mortality remains extremely high despite antibiotic treatment if it is initiated after onset of respiratory symptoms.

Cutaneous

- Local skin involvement after direct contact with spores or bacilli.
- Commonly seen on the head, forearms or hands.
- Localized itching, followed by a papular lesion that turns vesicular, and within 2-6 days develops into a depressed black eschar.
- Usually non-fatal if treated with antibiotics.

Gastro-intestinal

- Abdominal pain, nausea, vomiting, and fever following ingestion of contaminated food, usually meat.
- Bloody diarrhoea, hematemesis.

- Gram-positive bacilli on blood culture, usually after the first two or three days of illness.
- Usually fatal after progression to toxemia and sepsis.

(c) Modes of transmission

The spore form of *B. anthracis* is durable. As a bioterrorism agent, it could be delivered as an aerosol. The modes of transmission for anthrax include:

- Inhalation of spores.
- Cutaneous contact with spores or spore-contaminated materials.
- Ingestion of contaminated food.

(d) Incubation period

The incubation period following exposure to *B. anthracis* ranges from 1 day to 8 weeks (average 5 days), depending on the exposure route and dose:

- **2-60 days following pulmonary exposure.**
- 1-7 days following cutaneous exposure.
- 1-7 days following ingestion.

(e) Period of communicability

Transmission of anthrax infections from person to person is unlikely. Airborne transmission does not occur, but direct contact with skin lesions may result in cutaneous infection.

(f) Preventive measures

Vaccination against anthrax is not recommended for the general public to prevent disease.

B. Infection control practices

Standard precautions are used for the care of patients with anthrax (see appendix 1).

Patient placement

Private room placement for patients with anthrax is not necessary. Airborne transmission of anthrax does not occur. Skin lesions may be infectious, but this requires direct skin contact.

Patient transport

Standard precautions should be used for transport and movement of patients with *B. anthracis* infections.

Cleaning, disinfection, and sterilisation of equipment and environment

Principles of standard precautions should be generally applied for the management of patient-care equipment and for environmental control.

Post-mortem care

Standard precautions should be used for post-mortem care. Full post mortems, however, are not recommended in cases of anthrax.

C. Post Exposure Management

Action in the event of opening a package/envelope that contains suspicious material, finding an already opened package or receipt of a suspicious package.

(a) Risk Assessment

Risk assessment by the Gardaí, in consultation with the army EOD and fire brigade/ ambulance personnel, is the key to managing these incidents. A proper description of the package is essential. This is the basis on which all subsequent action is taken.

Risk assessment is carried out by the Gardaí, on the basis of the story from the recipient of the package and their own observation. It will enable the package to be put into one of 2 categories:

- No risk
- Risk not discounted

which will determine further action.

- **Risk not discounted**

If some element of risk cannot be discounted, the Gardai in association with the army, and with the help of the emergency services will carry out a more detailed threat assessment. The advice of the Director of Public Health may also be sought at this stage.

- (i) Low risk**

This is where further assessment of the letter or package provides reassurance that it is a false alarm, or is an obvious hoax.

- (ii) High risk**

These are packages felt to have features that warrant deployment of the full range of specialist support.

(b) Medical management

If the Garda assessment declares “low risk”

The package will be moved to a central Garda location and maintained as forensic evidence. No clinical, laboratory or public health action should be taken. There is no need for environmental specimens to be taken. The people who might have been exposed must be reassured.

If the Garda assessment declares “high risk”

Once the Gardaí have completed their assessment, the package (whether opened or not) and any material from it, will be taken by the army and sent to Cherry Orchard Hospital, and from there to the Centre for Applied Microbiology Research (CAMR) in Porton Down in the UK for testing of environmental samples.

The Gardaí will determine who has potentially been exposed. This will include all those who have been in the room with the open package and people who moved through any contaminated area.

(c) Decontamination of patients

To be carried out by the fire brigade and ambulance services

The risk for re-aerosolisation of *B. anthracis* spores appears to be extremely low in settings where spores were released intentionally. In situations where the threat of gross exposure to *B. anthracis* spores exists, cleansing of skin and potentially contaminated fomites (e.g. clothing or environmental surfaces) may be considered to reduce the risk for cutaneous and gastrointestinal forms of disease. The plan for decontaminating patients exposed to anthrax may include the following:

- Instructing patients to remove contaminated clothing and possessions and store in labeled, plastic bags.
- Handling clothing minimally to avoid agitation.
- Instructing patients to shower thoroughly with soap and water (and providing assistance if necessary).
- Instructing attending personnel regarding Standard Precautions and wearing appropriate barriers (e.g. gloves, gown and surgical masks) when handling contaminated clothing or other contaminated fomites.
- Decontaminating environmental surfaces using an approved sporicidal/ germicidal agent or 0.5% hypochlorite solution (one part household bleach added to nine parts water).

The emergency services (fire brigade and ambulance services) will provide mobile decontamination units. Emergency staff should avoid close contact with exposed persons until they have been decontaminated.

(d) Prophylaxis

A list of those exposed must be made by the public health professional. Names, addresses, telephone numbers, and GP details (name and telephone number) should be recorded.

All persons with suspected anthrax exposure should be commenced immediately on chemoprophylaxis. The taking of nose swabs or blood samples is not recommended. Prophylaxis should continue until *B. anthracis* exposure has been excluded. Reassurance should be given that they have been given full treatment and pose no risk to their family and friends. They should be told that they will be contacted as soon as the results become available. They should then go home.

If *B. anthracis* exposure is confirmed, prophylaxis should continue for 8 weeks.

All patients on chemoprophylaxis should be referred to an infectious disease consultant or other appropriate general physician for investigation and follow-up. They should receive an anthrax information sheet and be instructed to seek medical attention immediately in the event of any suspicious symptoms developing.

Table 1. Recommended post-exposure prophylaxis after exposure to *Bacillus anthracis*

Antimicrobial agent	Adults	Children
Oral fluoroquinolones Ciprofloxacin	500mg bd	20-30mg per kg of body mass daily, divided into two doses – as a guide 10kg: 125mg bd 20kg: 250mg bd 30kg: 375mg bd 40kg: as for adult
If fluoroquinolones are not available or are contraindicated Doxycycline	100mg bd	5mg per kg body mass per day divided into two doses

**Ciprofloxacin is not licensed for use in children or pregnant women.*

Paediatric use of fluoroquinolones and tetracyclines can be associated with adverse effects that must be weighed against the risk of developing a lethal disease.

Note that cephalosporins are **ineffective** for the treatment of anthrax.

If the results confirm anthrax was present in the sample this is now a major incident and the Expert Committee – Contingency Planning for Biological Threats must be informed and will advise on further medical action.

If *B.anthraxis* exposure is confirmed the organism must be tested for penicillin susceptibility. If susceptible, exposed children may be treated with oral amoxycillin 40mg per kg of body mass per day divided with doses 8 hourly (not to exceed 500mg, three times daily).

(e) Treatment

The treatment for anthrax is shown below in Table 2.

Table 2: Recommended treatment for inhalation and ingestion anthrax

	Initial Therapy	Optional therapy if strain is proven susceptible	Duration
Adults	Ciprofloxacin 400mg iv every 12hr (change to oral 500 mg bd when appropriate)	Penicillin G. 4 million iU iv every 4hr (change to oral therapy when appropriate)	8 weeks
Children*	Ciprofloxacin 20-30mg/kg per day iv divided into 2 daily doses, not to exceed 1g per day	Age <12y: penicillin G 50,000 iu/kg iv every 6hr Age 12y: penicillin G 4million iu iv every 4hr (change to oral therapy when appropriate)	8 weeks
Pregnancy		Same as for non pregnant adult	

**Ciprofloxacin is not licensed for use in children or pregnant women.*

Change to oral therapy when considered appropriate.

*Note that cephalosporins are **ineffective** for the treatment of anthrax.*

Treatment of cutaneous anthrax is with oral Ciprofloxacin 500mg bd for 7 days. This can be changed to penicillin if the organism is found to be sensitive. Treatment may need to be continued for up to 60 days if there is a suspicion of deliberate release in order to provide cover for inhalation anthrax, which may have been acquired concurrently.

Note: Ciprofloxacin is recommended because of the risk of genetic engineering of anthrax which is penicillin resistant.

Contacts of cases

There is no need to provide antibiotic prophylaxis to contacts of patients with anthrax unless there is concern that they were also exposed to the initial release.

(f) Environmental decontamination

To be carried out by the army

The greatest risk to human health following a release of anthrax spores occurs during the period in which anthrax spores remain airborne, called *primary aerosolisation*. The duration and scale of the infectious risk depends on the duration for which spores remain airborne and the distance they travel before they fall to the ground. This depends on meteorological conditions and aerobiological properties of the dispersed aerosol. The aerosol is likely to be fully dispersed within hours to 1 day at most, well before the first symptomatic cases would be seen.

An **exposed zone** will be defined according to the time and place of release in order to identify all persons exposed to primary aerosolisation. The area surrounding the site of release will remain designated as an exposed zone until sufficient time has elapsed and the risk of infection has subsided. Once the spores have settled, although they remain infectious for long periods, the risk to human health is much lower.

Decontamination of small areas may be achieved with 0.5% hypochlorite solution (one part household bleach added to nine parts water).

The room in which the package and other areas of the building deemed to be contaminated should remain tightly sealed until results from the suspicious substance are known. Heating or air conditioning should remain off. If they are positive further advice in decontamination will be provided. If this advice is not deemed feasible, decontamination of the exposed zone may be achieved as described above.

Protection of frontline workers

This includes all emergency staff involved in management at the scene of a release, as well as those involved in treating patients with anthrax.

Protective clothing

The **exposed zone** presents a high risk of infection, and anyone entering it should wear full protective equipment including high-efficacy air filter masks conferring full biological protection. Healthcare workers will not normally be asked to enter this zone. It is possible, however, that they may be called to treat casualties, for example if an explosive device has accompanied the release of biological agent. In this case the appropriate protective clothing should be worn.

Exposed persons will normally be moved from the exposed zone, through decontamination, and into a holding area for medical assessment and administration of prophylactic treatment. Those involved in decontamination, and others who have any contact with contaminated clothing and fomites should observe standard precautions - gloves, masks, gowns, eye protection and hand washing. Emergency staff who attend exposed persons after decontamination has been completed do not need to take any special precautions.

For healthcare workers involved in the management of hospitalised patients with all forms of anthrax, standard precautions provide sufficient protection, and mortuary staff should use similar barrier protection. More sophisticated countermeasures for airborne protection such as high-efficacy air filter masks airborne protection are **not** required.

Antibiotic prophylaxis

Healthcare workers entering the **exposed zone** should be offered antibiotic prophylaxis as in Table 1. Prophylactic treatment may also be considered for frontline workers involved in other activities including:

- Decontamination of exposed persons.
- Handling exposed persons.
- Management of patients or disposal of bodies infected with anthrax.

Decisions about who should receive prophylaxis should be taken on an individual basis according to duration and degree of potential exposure, and taking into account the availability and side effects of prophylactic treatments.

D. Laboratory Support and Confirmation

B anthracis is a hazard group 3 pathogen. All laboratory procedures should be performed in a Containment Level 3 laboratory using a Class 1 microbiology safety cabinet by experienced medical laboratory scientists. Diagnosis of anthrax is confirmed by aerobic culture performed in a CL-3 laboratory. Use of standard precautions (gloves, masks, gowns, eye protection and hand washing) in the laboratory reduces the risk of cutaneous anthrax to zero.

Samples to be taken from humans

- Nasal swabs should be taken **only** if environmental samples test positive for anthrax.
- Swabs from cutaneous lesions.
- If a patient is acutely ill with clinical signs of anthrax then blood (approx 10ml) should be taken. (If they have received antibiotics, culture may be negative).

Clinical microbiology laboratories should take care not to regard all isolates of *Bacillus species* as contaminants, especially if isolated from sterile sites (blood, CSF) and /or multiple cultures are positive from the same patient. All sterile site *Bacillus* isolates should be further evaluated, and if non-motile or non-haemolytic (particularly if they form short chains) and /or if the clinical syndrome is suggestive of anthrax, the isolates should be immediately referred to reference laboratory via Cherry Orchard laboratory.

ALL HUMAN CLINICAL SAMPLES SHOULD BE SENT TO THE PUBLIC HEALTH LABORATORY IN CHERRY ORCHARD HOSPITAL.

Samples to be taken from the environment

Samples should be taken from any material (soil, dust, clothing, swabbing etc) present in the environmental area thought to have been exposed to the release of anthrax spores, or soiled by exudates from humans.

ALL ENVIRONMENTAL SAMPLES SHOULD BE SENT TO THE PUBLIC HEALTH LABORATORY IN CHERRY ORCHARD HOSPITAL WHO WILL SEND THEM ON TO CAMR IN THE UK.

Post mortem specimens

Samples may be taken from dead humans to assist diagnosis, including:

- Blood (approx 10ml) from a vein.
- Nasal swabs.
- Swabs of haemorrhagic exudate from orifices.
- Swabs or sample of other body fluids if appropriate.

However full post-mortems are discouraged if anthrax is suspected because of the risk of releasing anthrax spores present in body fluids, drips etc.

Procedure

- Phone laboratory to inform them that samples are on their way

(01)6206175 office hours/ (01)6264702 out of hours

- To accompany sample
 - Put code on sample (BAB/number of sample)
 - Brief details of incident
 - Name of doctor in charge
 - Contact telephone number of doctor in charge

Smallpox

A. Description of Agent/ Syndrome

(a) Aetiology/ epidemiology

Smallpox is a severe viral disease caused by variola virus that no longer exists naturally, having been declared eradicated in 1980. The last community-acquired case was in Somalia in 1977. A fatal laboratory-acquired case occurred in the United Kingdom in 1978. The global eradication of smallpox was certified in December 1979 and endorsed by the World Health Assembly in 1980. Smallpox was an endemic disease that affected both adults and children. Nowadays it would be classed as a viral haemorrhagic fever, because haemorrhage was a major feature of severe and terminal infection.

The variola virus exists legitimately in two laboratories in the world: one in the CDC in Atlanta, USA, and the other in Koltsovo in the former USSR.

(b) Clinical features

Smallpox infection can produce illnesses with a wide range of severity. Smallpox had two main forms: variola major and variola minor. The two forms showed similar lesions. The disease followed a milder course in variola minor.

In the event of a deliberate release of smallpox in Ireland, it is unlikely that single, mild cases of feverish, pox-like illnesses would occur. It is more likely that clusters of moderate to severe disease would be seen. In the event of a deliberate release of smallpox in another country then single cases of feverish, pox-like illness may present and should be thoroughly evaluated.

Malignant presentations of smallpox

This is the common type of disease occurring in non-immunised populations. They are characterised by the following features:

- Abrupt onset with moderate fever (up to 39C), extreme prostration, severe headache, intense, ill-defined pain in the back, chest or loins and intense anxiety. Fever may abate slightly on the second to third day, but this improvement does not persist beyond the third day.
- On the second to third day, an intense, blotchy erythematous rash resembling measles or rubella appears on the face, backs of hands, upper chest and back.
- The maculopapular rash does not appear until the fourth to sixth day. They appear first on the face, and are tiny and superficial, hot and tender, giving the impression of intense sunburn.
- This slowly evolves into a vesicular rash between the eighth to the 13th or 14th day, with new and enlarging vesicles appearing in the first few days, and coalescence of vesicles to form soft, flaccid bullae covered by macerated skin, which easily rubs off.
- By the 13th or 14th day of illness, the soft, moist skin exfoliates, leaving extensive, painful, denuded areas
- Death may occur in the first 48 hours before any feature of smallpox has appeared. Most fulminating cases die by the fourth or fifth day; many other malignant cases die between the eighth and fifteenth day.

Smallpox must be distinguished from other illnesses such as chicken pox.

Figure 3: Differentiation between Smallpox and Chickenpox

	Variola	Varicella
Incubation	7-19 days	14-21 days
Prodrome	Fever malaise for 2-4 days before rash	Minimal
Pock distribution	Centrifugal: greater on face and limbs than trunk, usually palm and soles	Centripetal: greater on trunk than face and limbs, seldom on palms and soles
Pock appearance	Deeply embedded lesions: vesicular→pustular→umbilicated→scab	Superficial lesions: vesicular on erythematous base→pustular→scab
Evolution of pocks	Synchronous: crops in same stage of evolution	Asynchronous: crops in different stage of evolution in same area
Scab formation	10-14 days after onset of rash	4-7 days after onset of rash
Scab separation	14-18 days after onset of rash	Within 14 days after onset of rash
Infectivity	From onset of fever until all scabs separate	From 1 day before onset of rash until all vesicles scab (usually 1 week)

(c) Modes of transmission

Smallpox is most often contracted via the airborne route, but can also be transmitted by direct transfer of vesicle fluid, saliva or respiratory secretions. **Patients are not infectious during the asymptomatic incubation period.** Viruses are excreted from the throat of patients from the beginning of their feverish illness. Patients are most infectious on the second and third day of fever, but remain infectious either until death or until all scabs have been shed following recovery. Vesicle fluid and scabs from the drying skin lesions contain viable virus, and contaminated clothing has been implicated as the source of new outbreaks of infection. Close contact has been demonstrated to result in efficient transmission of smallpox; household contact produces the highest secondary attack rate, and contact in an open ward has also caused verified outbreaks. Although casual contact, such as working in the same building, is much less likely to result in transmission, airborne spread of virus in air conditioning has been implicated as a cause of smallpox outbreaks. In smallpox outbreaks in Asia and Africa, the secondary attack rate in households varied from 37% to 96%. **Some WHO experts have estimated today's rate of transmission to be 10 new infections per infected person.** There is no animal reservoir. Insects play no role in transmission.

(d) Incubation period

The range is 7-19 days, with a median of 12 days. The time between exposure and onset of feverish illness and infectiousness is generally regarded to be 10-14 days.

(e) Period of communicability

Patients are infectious from the onset of fever. Infectivity peaks on the second and third day of fever. Infectivity falls gradually as scabs cover skin lesions.

(f) Mortality

Estimates of mortality are complicated by the fact that documented epidemics were always modified either by the presence of some immune individuals in a population or by interventional immunisation. Also, some strains of variola were highly virulent and others much less so. Mortality in natural epidemics was reported as 15-50% for variola major and nearer to 1% for variola minor. Importation into naïve populations (e.g. Shetland islands or among native Americans), was reported to cause 50-90% mortality. The highest mortality was seen in children aged less than 1 year and in the elderly.

(g) Organism survival

Depending on the conditions, viruses can survive for long periods of time in dry scabs (13 years has been documented), and in refrigerated cultures (up to 39 years has been documented). **However, in normal environmental conditions, the virus is highly unlikely to survive for more than 48 hours.**

B. Infection control practices

Immune personnel should ideally carry out patient care. Personal protective equipment should include

- disposable gloves
- an impermeable gown and cap or overall
- a dust-mist mask and
- eye protection (e.g., disposable visor or ‘all-round’ spectacles).

Patient placement

All **suspected** cases of smallpox in the community should be immediately isolated at the point of diagnosis (at home, in a separate room in the GP’s surgery or in a hospital A+E department) until they can be transferred to an isolation unit in a hospital.

Designated ambulances will be used for patient transport. An Infectious Diseases Consultant or other appropriate general physician, as well as the Director of Public Health should be called urgently. **Patients with smallpox will be admitted to designated hospitals with negative pressure isolation rooms and consultant infectious disease input.**

Suspected and confirmed cases should preferably be cared for in a **negative-pressure isolation room with HEPA-filtered extract ventilation** if available. **The best option for several cases occurring simultaneously would be cohort-isolation, preferably in a separate hospital or building.** This would make the best use of available infection-control nursing skills, and facilitate the management of highly infectious clinical waste.

Patients should remain **in isolation** until all crusts have been shed from the skin lesions, usually a period of about three weeks. Monitoring and support should take place within the isolation area, or in a dedicated high-dependency or intensive care unit from which other types of patients are excluded. Patients with smallpox should be asked to wear surgical masks in order to minimise the generation of infectious respiratory droplets.

Cleaning, disinfection, and sterilisation of equipment and environment

All contaminated instruments, excretions, fluids and other materials should be decontaminated chemically or by heat or incineration. The disposal of clinical waste should be secure. It is advisable that all waste should be decontaminated before disposal. This can be achieved by autoclaving in a disposal-cycle autoclave. Laundry is hazardous, as body fluids, vesicle fluid and scabs from the lesions render the patient’s bedding infectious. Contaminated clothing and bedding, if not incinerated, should be autoclaved or washed in hot water containing hypochlorite bleach. Therefore procedures within the laundry must be agreed before sending any laundry. Sheets and blankets should be removed from the bed with minimum shaking, and placed into alginate-stitched bags within secondary plastic bags. Bags should be transferred direct to the laundry, where the alginate-stitched bags should be immediately placed into the washing machine, and the outer bags should be discarded into a secure clinical waste system. Fumigation of premises may be done with formaldehyde.

Post mortem specimens

If the diagnosis is known, post-mortem examinations should be kept to a minimum. Cremation is the preferred method for disposal of the deceased. Cadavers should be cremated as quickly as possible in a properly designed facility, whenever possible and **all persons coming in contact with them should be vaccinated** or at least placed on daily fever watch. Body bags treated with hypochlorite bleach can also be used.

C. Post Exposure Management

The basis of control of smallpox in a non-immune community is early recognition and diagnosis, so that immediate action can be taken to contain the virus and prevent further transmission. A deliberate release may be overt with an announcement and/or confirmation by environmental sampling. However, it is also possible that a deliberate release may be covert and will not be identified until the first cases of disease arise. Since smallpox no longer occurs naturally, any **confirmed** cases indicate a deliberate release. Ireland may at risk of receiving persons who have been exposed as a result of deliberate releases in other countries.

(a) Decontamination of patients

To be carried out by the fire brigade and ambulance services

Decontamination of exposed persons is important, since although variola virus is **rapidly inactivated** in normal environmental conditions, there may be a risk of **secondary aerosolisation** from contaminated clothing and other fomites. At the first opportunity, exposed individuals should remove all clothing and deposit it in safe laundry bags (e.g. alginate-stitched and contained within outer plastic bags) for later disinfection or destruction. They should then shower and wash their hair, then put on clean clothing before proceeding for medical assessment, vaccination and observation (this will be a clinical area just outside the exposed zone and within the cordon that will be established at the scene of the incident).

The emergency services (fire brigade and ambulance services) will provide mobile decontamination units. Emergency staff should avoid close contact with exposed persons until they have been decontaminated.

(b) Prophylaxis and post-exposure immunisation

The most effective countermeasure against smallpox is vaccination before exposure. The natural history of a successful vaccine 'take' is the development of one or more pocks over six to eight days, then progressive crusting in the following eight to 10 days. After this process has been documented, the patient may be declared immunised. Vaccination after exposure is also effective in reducing the attack rate, and the severity of those cases that occur despite early immunisation. **In the event of any suspicion of smallpox the Expert Committee – Contingency Planning for Biological Threats will provide detailed advice on who should receive vaccination.**

Targeted vaccination of close contacts is the mainstay of smallpox outbreak control as it assures the administration of vaccine to those with the greatest risk of developing smallpox (and thus the greatest need for vaccination) and limits the number of unnecessary vaccinations in those individuals with little risk of disease (least need for vaccination). Although smallpox vaccine is safe and effective, vaccine adverse events can occur in a small number of vaccine recipients, especially those with immune system deficiencies (*see section f below*).

Smallpox vaccination strategies in an outbreak will be based on:

1. Quickly identifying and isolating smallpox cases
2. Identifying and vaccinating their close contacts
3. Monitoring the vaccinated contacts and isolating the contacts if fever develops

4. Vaccinating household members of contacts without contraindications to vaccination in order to protect them if the contact develops smallpox.
5. Vaccinating health-care and public health workers who will be directly involved in evaluating, treating, transporting, or interviewing potential smallpox cases
6. Vaccinating other response personnel who have a reasonable probability of contact with smallpox patients or infectious materials (e.g. selected law enforcement, emergency response or military personnel).

Supervision and follow up of persons at risk of smallpox

Individuals who have been present in the exposed zone, and close contacts of symptomatic cases of smallpox are at risk of developing the disease. **While post-exposure vaccination does not guarantee immunity, or even reduction in severity of the disease it should be undertaken as quickly as possible.**

Following vaccination, all people at risk of infection either from exposure to primary aerosolisation or close contact with symptomatic smallpox cases must be put in quarantine for up to 18 days and followed up with daily health and temperature checks until it has been confirmed that they are free of infection. **At present the Expert Committee – Contingency Planning for Biological Threats recommends that these contacts be quarantined in a designated hospital. This recommendation will remain under review. Other options for quarantine include (a) the use of other facilities such as former military installations or hotels or (b) confining contacts to their homes with daily temperature checks.**

(c) Treatment

There is no specific treatment for smallpox. Management of cases is expectant and supportive. **Vaccination in the first four days of the incubation period can modify the course of the disease, and reduces the mortality by about 50%.**

A number of treatments are, however, under investigation as chemotherapeutic agents. One of these, Cidofovir, has produced promising results in laboratory studies. Cidofovir is an antiviral agent that selectively inhibits the viral DNA polymerase. In vitro tests have shown that it inhibits both vaccinia virus and 35 different isolates of variola virus. Work is currently in progress to improve the formulation of Cidofovir so that it can be delivered orally. Aerosol delivery has already demonstrated that the drug is effective at lower concentrations than that used in systemic treatments.

When the patient has survived the infection and all scabs have separated, there is no indication for infectious diseases follow-up.

(d) Environmental decontamination

The initial risk to human health following a release of smallpox occurs during the period in which the virions remains airborne, called **primary aerosolisation**. The duration and scale of infectious risk depends on the duration for which virions remain airborne and the distance they travel before they fall to the ground. This depends on meteorological conditions and aerobiological properties of the dispersed aerosol.

An **exposed zone** will be defined according to the time and place of release in order to identify all persons exposed to primary aerosolisation. The area surrounding the site of release will remain designated as an exposed zone until sufficient time has elapsed and the risk of infection has subsided. **Following primary aerosolisation, variola**

virus is destroyed rapidly by UV light, and therefore environmental decontamination is unlikely to be necessary. If necessary fumigation of premises may be done with formaldehyde.

Protection of frontline workers

Protective clothing

In the event of release of smallpox the **exposed zone** presents a high risk of infection, and anyone entering it should wear **full protective equipment** such as Type 3 respirators in conjunction with Class A suits conferring full biological protection.

Exposed persons will normally be moved from the exposed zone, through decontamination, and into a place of safety for medical assessment, vaccination and subsequent observation. Those involved in decontamination, and others who have who have any contact with contaminated clothing and fomites should observe **standard precautions** and in addition should wear high efficacy masks and eye protection. For frontline workers who attend exposed persons after decontamination has been completed, standard precautions will provide sufficient protection – **even those who have been infected are not infectious to others until the incubation period has elapsed and symptoms start to develop.**

Cases of clinical smallpox in the community should be isolated as quickly as possible and cared for by the absolute minimum number of people, who should observe standard precautions, and in addition wear high efficacy masks and eye protection as soon as these are available. In hospital, staff will be involved in patient care and handling of contaminated clothing, bed linen and fomites. If these staff have not been immunised, they should wear full protective clothing including disposable gloves, impermeable gown or apron (or preferably an impermeable one-piece coverall, if available) and waterproof boots; head-cover (or integral hood); dust-mist respirator mask (or cowl-type respiratory protection, such as ‘Easibreathe 5’); and eye protection. After immunisation, these precautions may be modified to standard precautions. Similar precautions should apply to mortuary workers involved in the disposal of bodies.

(e) Management of an outbreak of smallpox

Emphasis must be placed on preventing epidemic spread. Smallpox patients are not infectious during the early stage of the disease but become so from the first appearance of fever and remain so until all scabs have separated. **In the presence of a strong surveillance system sensitive to smallpox cases and backed by an adequate infrastructure, rapid and thorough containment actions can break the transmission chain and halt a smallpox outbreak within a relatively short time.** Containment involves efficient detection of cases and identification of cases and identification and vaccination of contacts.

Patients diagnosed with smallpox should be physically isolated. All persons who have or will come into close contact with them should be vaccinated. As hospitals have proven to be sites of epidemic magnification during smallpox outbreaks, patient isolation at home is advisable where hospitals do not have isolation facilities. Whatever the policy, isolation is essential to break the chain of transmission.

Patients who developed rash before their isolation should be asked to recount all recent contacts. Contacts and family members should be vaccinated. If it is not feasible to vaccinate contacts, they should be placed on daily fever watch, which should continue up to 18 days from the last day of contact with the case. If these contacts have two consecutive readings of 38 degrees centigrade or above they should be isolated. **Information sheets will be produced for all contacts of smallpox cases.** All specimen collectors, care givers and attendants coming into close contact with

patients should be vaccinated as soon as smallpox is diagnosed as the cause of an outbreak. In the case of a widespread outbreak, people should be advised to avoid crowded places and follow public health advice on precautions for personal precaution.

Patients with smallpox who require transport to hospital will be transported in designated ambulances.

(f) Vaccines

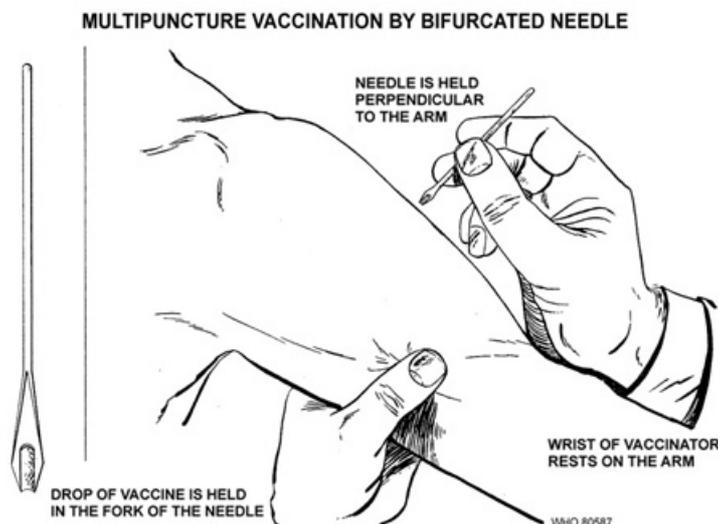
Smallpox vaccine contains live vaccinia virus, a virus in the orthopoxvirus family, which is closely related to variola virus. It does not contain smallpox virus and cannot transmit smallpox. Vaccination is likely to offer significant protection against disease and death if administered up to 4 days after exposure. If symptoms appear, they are milder and mortality is less in vaccinated than in non-vaccinated persons. Even when immunity has waned, vaccinated persons shed less virus and are less likely to transmit the disease. A single dose vaccine usually prevents smallpox infection for at least 10 years.

The vaccine is freeze-dried and sealed in ampoules for later re-suspension in sterile buffer and subsequent intradermal inoculation by multiple puncture with a bifurcated needle. A certified clinical 'take' of vaccinia vaccine is the development of one or more pocks over 6-8 days, then progressive crusting in the following 8-10 days. Smallpox vaccination should be undertaken by those who have completed training in the procedure.

Existing vaccines have proven efficacy but also have a high incidence of adverse side-effects. The risk of adverse events is sufficiently high that vaccination is not warranted if there is no or little real risk of exposure. Vaccine is contraindicated for certain groups. These include:

- Pregnant women
- Persons with immune disorders or experiencing therapeutically- induced immunosuppression
- Persons with HIV infection, and
- Persons with a history of eczema.

Figure 4: Smallpox vaccination technique



WHO instructions for vaccine administration using the bifurcated needle (multipuncture technique)

1. **Site of vaccination.** Outer aspect of upper arm over the insertion of deltoid muscle.
2. **Preparation of skin.** None. If site is obviously dirty, a cloth moistened with water may be used to wipe the site. Use of a disinfectant can kill the vaccine virus.
3. **Withdrawal of vaccine from ampoule.** A sterile bifurcated needle (which must be cool) is inserted into the ampoule of reconstituted vaccine. On withdrawal, a droplet of vaccine, sufficient for vaccination, is contained within the fork of the needle.
4. **Application of vaccine to the skin.** The needle is held at a 90-degree angle (perpendicular) to the skin. The needle then touches the skin to release the droplet of vaccine. For both primary and revaccination, 15 up and down (perpendicular) strokes of the needle are rapidly made in the area of about 5mm in diameter (through the drop of vaccine deposited on the skin). The strokes should be sufficiently vigorous so that a trace of blood appears at the vaccination site. If a trace of blood does not appear, the strokes have not been sufficiently vigorous and the procedure should be repeated. Although it is desirable not to induce frank bleeding, the proportion of successful takes is not reduced if bleeding does occur.
5. **Dressing.** No dressing should be used after vaccination
6. **Sterilization.** WHO strongly recommends the use of disposable needles.
7. **Unused vaccine.** Unused, reconstituted freeze-dried vaccine should be discarded at the end of each working day.

Complications of vaccination

Four main complications are associated with vaccination, three of which involve abnormal skin eruption.

- **Eczema vaccinatum** occurred in vaccinated persons or unvaccinated contacts who were suffering from or had a history of eczema. In these cases, an eruption occurred at sites on the body that were at the time affected by eczema or had previously been so. These eruptions became intensely inflamed and sometimes spread to healthy skin. Symptoms were severe. The prognosis was especially grave in infants having large areas of affected skin.
- **Progressive vaccinia** (vaccinia necrosum) occurred only in persons who suffered from an immune deficiency. In these cases the local lesions at the vaccination site failed to heal, secondary lesions sometimes appeared elsewhere on the body, and all lesions spread progressively until – as was likely- the patient died, usually 2-5 months later. As vaccination ceased in most countries prior to the emergence of HIV/AIDS, the consequences of the currently much larger pool of persons suffering from immunodeficiency were not reflected in recorded cases of progressive vaccinia.
- **Generalized vaccinia** occurred in otherwise healthy individuals and was characterized by the development, from 6-9 days after vaccination, of a generalized rash, sometimes covering the whole body. The prognosis was good.
- **Postvaccinial encephalitis**, the most serious complication, occurred in two main forms. The first, seen most often in infants under 2 years of age, had a violent onset, characterized by convulsions. Recovery was often incomplete, leaving the patient with cerebral impairment and paralysis. The second form, seen most often in children older than 2 years, had an abrupt onset, with fever,

vomiting, headache, and malaise, followed by such symptoms as loss of consciousness, amnesia, confusion, restlessness, convulsions and coma. The fatality rate was about 35%, with death usually occurring within a week.

- The best estimates of the frequency of these complications come from a 1968 study by the United States involving over 14 million vaccinated persons. Altogether nine deaths occurred.
 - Progressive vaccinia occurred in 11 persons, with 4 deaths.
 - Eczema vaccinatum was more common, with 74 cases and no deaths. Sixty additional cases of eczema vaccinatum occurred in contacts of vaccinated persons, with one death.
 - Generalize vaccinia occurred in 143 cases, with no deaths.
 - Encephalitis was observed in 16 persons, with 4 deaths.

On the basis of this study, it was estimated that approximately one death per million resulted from complications following primary vaccination and one death per four million following revaccination.

D. Laboratory Support and Confirmation

Smallpox is a Hazard Group 4 pathogen and must be handled in high containment facilities. These are available at the Centre for Applied Microbiology and Research (CAMR) laboratory where environmental specimens will be sent for diagnosis.

In the event of a covert deliberate release of smallpox, specimens from vesicular lesions of the first unsuspected cases will be examined in the National Virus Reference Laboratory before the diagnosis is known. However pox viruses cannot be readily distinguished from one another except by the polymerase chain reaction (PCR) assay. Specimen handling and examination should take place in **at least a Containment Level 3 laboratory** using a Class 3 protective safety cabinet..

If there is any suspicion of smallpox on the basis of either clinical symptoms or from the laboratory examination, then clinical samples from patients in designated hospitals should be inactivated on site and sent to the Virus Reference Laboratory, UCD for a rapid diagnosis using PCR. Clinical samples from patients in non-designated hospitals should be sent to the Virus Reference Laboratory, UCD who will then forward the samples to Special Pathogens Reference Unit, CAMR, Salisbury, Wiltshire, UK.

Samples to be taken from acutely ill humans

Clinical specimens useful for making a diagnosis include:

- Whole blood for viral culture, PCR and antigen detection.
- Vesicle fluid for electron microscopy, PCR and viral culture.
- Scrapings or impression smears from the base of lesions.
- Scabs from developed lesions.

The use of sharps should be minimised, and all sharps, slides and specimen bottles should be discarded into a sharps disposal system immediately after use. Blood and tissue samples must be recorded, and “tracked” through the transport and laboratory system.

Post mortem specimens

If the diagnosis is known, post-mortem examinations should be kept to a minimum. Skin biopsies, even of apparently unaffected skin before the vesicular rash develops, can show the presence of smallpox virus. Post-mortem blood specimens, obtained by cardiac puncture, are useful for diagnostic tests. **Only immunised staff should handle bodies.**

Transport of samples

Strict procedures should be followed for the transport of samples of suspected smallpox, both from the clinical environment to the laboratory, and from local laboratories onto the reference laboratory.

Summary:

Steps to be taken in the event of the diagnosis of a case of smallpox in Ireland

- The patient should be isolated in a negative pressure isolation room in a designated smallpox unit.
- The best option for several cases arising simultaneously is cohort isolation, preferably in a separate hospital or building. **Hospitals will be designated for this purpose.**
- **Patient care should ideally be carried out by immune personnel.**
- Personal protective equipment should include disposable gloves, an impermeable gown or overall, a dust-mist mask and eye-protection.
- Patients should be kept in isolation until all crusts have been shed from the skin lesions, usually a period of about three weeks.
- All contacts (household contacts and face-to-face contacts) should be vaccinated and quarantined for 18 days with daily temperature checks

Immediate steps to be taken in the event of the deliberate release or suspected release of smallpox virus

- Call Gardai (999 or 112).
- Gardai to tightly seal off exposed zone. **Exposed zone represents a high risk of infection. Anyone entering it must wear full protective clothing.**
- Gardai to contact
 - Army
 - Fire and Ambulance Services
 - Directors of Public Health and
 - Expert Committee – Contingency Planning for Biological Threats
- Fire and ambulance services (decontamination units) to carry out decontamination of exposed individuals on site using mobile units.
- Environmental samples (e.g. suspect package) to be taken by army to Virus Reference Laboratory to identify or outrule smallpox virus.
- If high index of suspicion of smallpox, exposed persons will be vaccinated and moved to a sealed place of safety for medical observation. These individuals should be quarantined for 18 days with daily health and temperature checks. **Staff working in this unit should be immunised against smallpox.**
- The area surrounding the site will remain designated as an exposed zone until sufficient time has elapsed. **Following primary aerosolisation, variola virus is destroyed rapidly by ultra-violet light and therefore environmental decontamination is unlikely to be necessary.**
- The Director of Public Health or his/ her representative will ensure that exposed individuals are immunised. Vaccination will also be offered to:

- Frontline workers who enter the exposed zone or are involved in the decontamination of exposed persons or handling of exposed clothing and fomites*
- Laboratory staff who handle specimens from smallpox patients, and
- Mortuary workers.
- Vaccination will be considered for families of healthcare workers who are involved in clinical management of smallpox patients.

* A fomite is defined as an inanimate object or substance that serves to transfer infectious organisms from one individual to another

Botulism

A. Description of Agent/ Syndrome

(a) Aetiology/ epidemiology

Botulism is most commonly produced as a result of ingesting botulinum neurotoxin, produced by *Clostridium botulinum*, which is recognised as being one of the most toxic compounds on earth. Improperly prepared food or canned products usually cause botulism. Wound botulism occurs following penetrating injuries complicated by soil contamination. The injection of illegal drugs can also cause wound botulism.

A deliberate release may involve contamination of food and water supplies, but would most likely involve airborne dissemination of toxin, producing botulism through inhalation.

(b) Clinical Features

Botulinum toxin is a neurotoxin, which acts by blocking neurotransmission. The typical clinical picture involves bulbar palsy and skeletal muscle weakness. The onset of signs is dose dependent. Both foodborne and inhalational botulism have the same set of symptoms; in addition, abdominal cramps, nausea, vomiting, and diarrhoea generally precede foodborne poisoning. Progressive muscular paralysis leads to pharyngeal and diaphragmatic paralysis and if untreated, generally death. Aggressive treatment has reduced the mortality rate to about 5%.

1. Inhalational:

- 3rd day after exposure: mucus in throat, difficulty swallowing, dizziness
- 4th day after exposure: difficulty moving eyes, dysarthria, unsteady gait, extreme weakness.

2. Foodborne:

- *Symptoms*: diplopia, dysarthria, dysphagia, dry mouth, fatigue, dizziness, nausea, vomiting, leg and arm weakness.

Botulism must be differentiated from other neurological conditions such as Guillain Barre Syndrome, myasthenia gravis and stroke.

Figure 5: Selected Possible Mimics and Misdiagnoses of Botulism

Condition	Distinguishing Features
Guillain-Barré Syndrome and variants (Miller-Fisher syndrome)	History of antecedent infection; paresthesias; often ascending paralysis; early areflexia; eventual CSF protein increase; EMG findings
Myasthenia Gravis	Recurrent paralysis; EMG findings; sustained response to anticholinesterase therapy
Stroke CNS Depressants (e.g., acute alcohol intoxication, organophosphates, carbon monoxide, or nerve gas)	Paralysis often asymmetric; abnormal CNS image History of exposure; excessive drug levels detected in body fluids
Lambert-Eaton Syndrome	Increased strength with sustained muscle contraction; evidence of lung carcinoma; EMG findings similar to botulism
Tick Paralysis	Paresthesiae; ascending paralysis; tick attached to skin

Any presentation of a previously healthy patient with sudden onset of afebrile descending flaccid paralysis should be notified immediately to the Director of Public Health.

(c) Modes of transmission

Foodborne botulism is acquired by the ingestion of contaminated food. Inhalational botulism is acquired by the inhalation of botulism toxin.

(d) Incubation period

The onset of symptoms in naturally occurring cases occurs between 2 hours and 8 days after ingestion, depending on the type and dose of toxin. **Following aerosol exposure onset of symptoms may be more rapid, possibly occurring less than one hour after exposure.**

(e) Period of communicability

Person to person transmission does **not** occur. Toxin can be detected in the faeces of cases, but normal infection control precautions will prevent ingestion.

(f) Mortality

Without treatment mortality can reach 100%, but this can be considerably reduced with supportive treatment and the use of antitoxin. The lethal dose of *Cl. botulinum* toxin for an adult can be less than 1 microgram.

(g) Organism survival

Cl. botulinum is a spore-forming organism. Spores survive well in the environment, and may also survive heat and cooking. The toxin undergoes natural inactivation in surface and drinking water over several days. It is destroyed by chlorine. The toxin can be more stable in some foods and drinks, but is inactivated by heat and normal cooking.

(h) Antimicrobial susceptibilities

In cases of botulism which result from ingestion or inhalation of toxin, antibiotic therapy is not appropriate. Intravenous administration of anti-toxin is recommended.

B. Infection control practices

Patient placement:

Patient-to-patient transmission of botulism does not occur. Patient room selection should be consistent with availability, but single room placement is not necessary. Standard precautions are sufficient for the nursing of patients.

Patient transport

Standard precautions should be used for transport and movement of patients with botulism.

Cleaning, disinfection and sterilisation of equipment and environment

Principles of standard precautions should be generally applied to the management of patient-care equipment and environmental control

Immunisation of contacts:

None

Treatment:

Supportive care and passive immunisation with equine antitoxin. Antitoxin should be given as soon as the diagnosis is suspected. Antitoxin is available from Cherry Orchard Hospital.

Post-mortem care

Standard precautions should be used for post-mortem care.

C. Post Exposure Management

The post exposure management for botulism is similar to that described for anthrax.

(a). Decontamination of patients

To be carried out by the fire brigade and ambulance services

Botulinum toxin naturally loses activity over a few days, and the risk of infection from contaminated clothing is low. However, in the event of release of large amounts of toxin, clothing and other fomites may be sufficiently contaminated to pose a risk from hand to mouth ingestion. In such situations, decontamination may require:

- Removal of contaminated clothing and possessions. They should be stored in labelled double plastic bags until they can be washed with soap and water.
- Minimal handling of clothing and fomites to avoid agitation.
- Instructing exposed persons to shower thoroughly with soap and water.
- Instructing attending personnel to wear appropriate barrier protection and to use standard precautions when handling contaminated clothing and other fomites.

(b). Prophylaxis and post-exposure immunisation

The use of antibiotics post-exposure is **not** indicated. Although a toxoid vaccine is available, it has no effect in post-exposure treatment. Certain individuals who work with the organism or toxin (such as laboratory staff) can be given pre-exposure immunisation. However, following exposure, people must be observed for symptoms for the first few hours after release. Instructions will be given to seek immediate medical attention should symptoms develop later.

(c). Treatment

Specific treatment of botulism is with trivalent equine antitoxin. It must be given as early as possible after a clinical diagnosis has been made, and not delayed for the results of confirmatory laboratory tests. A test dose is necessary in view of the risk of serum sickness or anaphylaxis. Detailed instructions on administration are provided with each dose. Antimicrobial therapy is appropriate only in cases of wound botulism; use penicillin and metronidazole according to standard dosing regimens.

(d). Environmental decontamination

Following a known release, re-aerosolisation of toxin is not thought to pose a serious risk, and the toxin naturally loses activity over a few days. The contaminated area will remain out of bounds for at least this period, and subsequently environmental decontamination is not necessary. In situations where surfaces have been grossly contaminated and cannot be avoided for these few days, they should be cleaned with a 0.5% solution (5,000ppm) of hypochlorite.

Protection of frontline workers

Protective clothing

The release of a Botulinum toxin aerosol will create an **exposed zone** that presents a high risk of inhaling toxin. Anyone entering this zone should wear full protective equipment such as Type 3 high efficacy air filter masks with Class A suits, conferring full biological protection. Exposed persons will normally be moved from the exposed zone, through decontamination if necessary, and into a place of safety for medical

assessment. Frontline workers involved in decontamination, and others who have who have any contact with contaminated clothing and fomites need only observe standard precautions (gloves, gowns and hand washing) for adequate protection.

(e). Antibiotic prophylaxis

Antibiotic prophylaxis is not indicated.

D. Laboratory Support and Confirmation

Cl. botulinum is a Hazard Group 2 organism and normal laboratory precautions are sufficient to provide protection. The specimens can be handled in a Containment Level 2 laboratory on the open bench to prepare and package them for onward transportation to a reference laboratory.

Samples to be taken from acutely ill humans

- Serum. At least 10ml. Serum samples must be collected before antitoxin is administered.
- Faeces. At least 10g in a sterile container.
- Vomitus, gastric washings or gut contents. At least 10g in a sterile container
- Bronchiolar lavage or similar in a sterile container.
- Wound: Pus, surgical debridement biopsy tissues into a sterile container.

Confirmation of the clinical diagnosis is by identifying botulinum toxin or the organism itself in the patients' faeces, stomach contents, or specimens from wounds, and the demonstration of toxin in blood samples. Routine laboratory tests are not helpful and **specimens should therefore be sent immediately to a reference laboratory**

Post mortem specimens

Heart blood (10ml), if not haemolysed, should be sent for serum for serum collection. Specimens of faeces, stomach contents and from infected wounds may also be useful.

Transport of samples

All samples must be kept **refrigerated** after collection. (See Appendix 3 for further details on packaging and transport).

Plague

A. Description of Agent/ Syndrome

(a) Aetiology/ epidemiology

Plague is an acute infection caused by *Yersinia pestis*, a gram-negative coccobacillus. It is a zoonosis, but human-to-human transmission can occur, principally through infectious respiratory droplets.

Isolated cases and outbreaks of plague are still reported regularly from several countries in Africa, Asia, South America and the USA. During the 1980s approximately 1000 cases/ year were reported to the World Health Organisation. This increased during the 1990s to a peak of over 5,000 in 1997.

Although the creation of an infectious plague aerosol is not easy, threat of a deliberate release of plague may be from the release of large quantities of *Y. pestis* in an aerosol.

(b) Clinical features

Clinicians should be aware of the possibility of plague pneumonia. **The diagnosis of plague should be considered if cases of the following clinical presentations occur in previously healthy patients, especially if two or more cases arise that are linked in time and place:**

- Sudden onset of severe, unexplained respiratory illness.
- Unexplained death following a short febrile illness.
- Sepsis with Gram-negative coccobacilli identified from clinical specimens.

Other forms of plague include bubonic plague and septicaemic plague.

- **Pneumonic plague**

Although uncommon in naturally occurring plague, it is the expected presentation following the deliberate release of aerosolised *Y. pestis*. The illness usually begins after an incubation period of 1-3 days with intense headache and malaise, fever, vomiting and marked prostration. Cough and dyspnoea develop with the production of watery, bloodstained sputum. Physical signs in the lungs are often minimal but chest X-rays show evidence of multilobar consolidation or bronchopneumonia. Respiratory failure develops quickly and mortality is high. **Appropriate antibiotic treatment must be given within 24 hours of onset if mortality is to be reduced.** The high mortality from plague has fallen dramatically with the advent of effective antibiotic therapy. In cases reported to WHO during 1983-1997 the overall fatality rate was 8%.

Pneumonic plague may result in human-to-human transmission via infectious droplets from patients with a productive cough. It is also a potential risk in laboratory workers handling cultures of *Y. pestis*.

- **Bubonic Plague:**

This normally accounts for 90% of cases of plague. The incubation period is 1-8 days. The onset of illness is sudden with fever, rigors, headache, confusion with nausea and vomiting. Buboes (extremely painful, enlarged, inflamed lymph nodes) appear 6-8 hours after onset of symptoms. Up to 15% of patients will develop pneumonic plague and become potentially infectious. The associated mortality rate is about 12%.

- **Septicaemic Plague:**

This form of plague which accounts for 10% of plague cases may be primary or secondary to the bubonic form. The presentation is as for any gram-negative

septicaemia with fever, rigors, nausea, vomiting, diarrhoea and abdominal pain. Purpura, disseminated intravascular coagulopathy (DIC), peripheral cyanosis and necrosis can then develop. The associated mortality rate is about 30%.

(c) Mode of transmission

Naturally occurring infection is transmitted by the bites of infected fleas. Human to human transmission can occur through infectious respiratory droplets from cases of plague pneumonia. This usually requires close contact with symptomatic cases. The infectious dose, by aerosol, is approximately 100-500 organisms.

(d) Incubation period

With primary pneumonia the incubation period is short, only 1-3 days.

(e) Period of communicability

Pneumonic plague is transmissible to other people as long as there are viable organisms in the sputum. **In practice this would be for 72 hours after starting effective antibiotic treatment.**

(f) Mortality

The high mortality from plague has fallen dramatically with the advent of effective antibiotic therapy. **In cases reported to WHO during 1983-1997, the overall fatality rate was 8%.**

(g) Antimicrobial susceptibilities

Y. pestis is generally very susceptible to a large number of antibiotics including aminoglycosides, b-lactams, trimethoprim, fluoroquinolones, cephalosporins, tetracyclines, chloramphenicol and sulphonamides. In mouse experiments ciprofloxacin was superior to doxycycline for prophylaxis against *Y. pestis* infection. Ciprofloxacin has the added advantage that it may also be used in the treatment of other diseases associated with bioterrorist agents such as anthrax and tularaemia.

B. Infection control practices

For pneumonic plague, *droplet precautions* should be used in addition to standard precautions (see appendix 1). All persons entering the room should wear high efficiency masks and eye protection.

Patient placement

Patients should be placed in private rooms where possible and droplet precautions used. **Cases of suspected and confirmed pneumonic plague should be nursed in standard isolation in a single room, with the door closed wherever possible, for the first 72 hours of treatment.** In the event of a large outbreak, patients may be cohorted together in a designated ward.

Patient transport

The movement and transport of patients on droplet precautions should be limited to essential medical purposes only. In order to minimise dispersal of droplets the patient should wear a surgical-type mask when transport is necessary.

Cleaning, disinfection, and sterilisation of equipment and environment

Principles of standard precautions should be generally applied to the management of patient-care equipment and for environmental control

Post-mortem care

Post-mortem examinations should not be undertaken unless absolutely necessary. However, if they are undertaken, the pathologist should be warned of the suspected/known diagnosis. Universal precautions should be observed with the use of additional personal protective clothing (masks and eye protection). Instruments should be autoclaved. **Antibiotic prophylaxis should be offered to mortuary staff if the deceased has not completed a 72-hour course of appropriate antibiotics.** Cremation is the preferred method for disposal of the deceased.

C. Post Exposure Management

(a). Decontamination of patients

To be carried out by the fire brigade and ambulance services

The risk of acquiring infection from the contaminated clothing of exposed persons is low. Heavily exposed persons should be instructed to remove outer clothing, which should be placed in sealed plastic bags prior to washing according to local infection control policies. They should then be instructed to shower thoroughly with soap and water.

(b). Post-exposure prophylaxis

In the event of exposure to a deliberate release of *Y. pestis*, or after contact with a case of pneumonic disease, antibiotic prophylaxis should be initiated as soon as possible. On the basis of clinical experience with tetracyclines and in vivo experiments with fluoroquinolones, the regimens outlined in Table 3 are recommended. Antibiotic prophylaxis should be continued for a period of 7 days.

Table 3: Recommended prophylaxis for those at risk from *Y. pestis*

Antimicrobial agent	Adults	Children
Oral fluoroquinolones Ciprofloxacin	500mg bd	20-30mg per kg of body mass daily, divided into two doses – as a guide 10kg: 125mg bd 20kg: 250mg bd 30kg: 375mg bd 40kg: as for adult
If fluoroquinolones are not available or are contraindicated Doxycycline	100mg bd	5mg per kg body mass per day divided into two doses

Paediatric use of fluoroquinolones and tetracyclines can be associated with adverse effects that must be weighed against the risk of developing a lethal disease.

In healthcare and laboratory staff who have had continuing exposure, prophylaxis should be extended to 7 days after the last contact with a patient or sample considered to be infectious.

The inactivated vaccine, consisting of formalin-killed bacteria, is **no longer available**. This vaccine had uncertain efficacy in protecting humans, particularly from plague pneumonia, and the long time interval to produce antibodies means that it would be ineffective in the event of a deliberate release of the organism.

All contacts of cases of **symptomatic pneumonic plague** should receive antibiotic prophylaxis as described above. The infection is not contagious until symptoms develop and patients are producing sputum. Other forms of plague are not generally contagious. Contacts will include those who have had short periods of intimate contact at less than 2 metres and those with longer periods of household or work contact when the case was symptomatic.

(c) Treatment

Streptomycin, tetracycline and chloramphenicol are the antibiotics traditionally used in the treatment of plague. Streptomycin has been the treatment of choice, particularly for severe infections, but is no longer widely available in Ireland. There have never been any clinical studies with other aminoglycosides, but there are reports of successful treatment with gentamicin and kanamycin. There is no clinical experience with fluoroquinolones for the treatment of human infection, although in vitro susceptibilities and animal experiments suggest that they would be effective. Recommended treatments are outlined in Table 4.

Table 4: Recommended treatment for plague.

<p>First line therapy</p>	<p>Gentamicin At standard doses for severe sepsis, according to local protocols; (preferred for pregnant women). or Streptomycin Adults: 1g intramuscularly, twice daily. Children: 15mg/kg/day intramuscularly, twice daily. Renal function should be monitored and blood taken for gentamicin or streptomycin levels.</p>
<p>Optional therapy if first line unsuitable</p>	<p>Ciprofloxacin Adults: 400 mg intravenously twice daily; or 500-750 mg orally twice daily. Children: 15 mg/kg intravenously twice daily; or 20 mg/kg orally twice daily. Should avoid giving ciprofloxacin or doxycycline to pregnant women or children under 8 years.</p>
<p>Preferred therapy for milder cases when an oral drug is preferred</p>	<p>Ciprofloxacin (orally as above) Or Doxycycline * Adult dose: 100 mg orally, twice daily. Children: (if 8yr and <45 kg) 50 mg orally, bd Should avoid giving ciprofloxacin or doxycycline to pregnant women or children under 8 years.</p>
<p>Preferred therapy for plague meningitis</p>	<p>Chloramphenicol Dose of 25mg/kg/day iv,QID. (achieves good concentrations in CSF)</p>

(d). Environmental decontamination

The initial risk to human health following a release of plague occurs during the period in which the bacteria remain airborne, called primary aerosolisation. The organisms are killed rapidly by drying and exposure to sunlight. In the event of a known release, an exposed zone will be defined according to the time and place of release in order to identify all persons exposed to primary aerosolisation. The area surrounding the site of release will remain designated as an exposed zone until sufficient time has elapsed and the risk of infection has subsided. Once this time has elapsed, the organisms can

be considered dead and non-infectious, therefore environmental decontamination is not required.

Protection of frontline workers

This includes all emergency staff involved in management at the scene of a release, and healthcare staff involved in the care of patients.

Protective clothing

In the event of release of *Y. pestis* the **exposed zone** presents a high risk of infection, and anyone entering it should wear full protective equipment such as Type 3 air filter masks with Class A suits, conferring full biological protection. Frontline workers involved in decontamination, and others who have any contact with contaminated clothing and fomites should observe standard universal precautions - gloves, gowns, eye protection and hand washing, and in addition should wear high efficacy masks and eye protection. Healthcare workers who attend exposed persons after decontamination has been completed need observe universal precautions only.

(e). Antibiotic prophylaxis

Post exposure prophylaxis should be given to all frontline workers who are called into the exposed zone, and those who are subsequently involved in the decontamination of exposed persons. In addition healthcare workers attending patients with suspected or confirmed pneumonic plague (who are within 72 hours of starting treatment), and mortuary staff who handle the deceased (who have not received a full 72 hour course of treatment) should also receive prophylactic antibiotics. In addition to antibiotic prophylaxis, frontline workers involved at the scene of a release, and healthcare workers and mortuary staff involved in the management of plague cases should be advised to seek urgent medical attention should they develop a febrile illness.

(f) Follow up for persons at risk of plague infection

This includes all those present in the exposed zone, as well as contacts of plague cases. Those at risk should receive post-exposure prophylaxis , and in addition all exposed persons should monitor themselves for the development of fever and/or respiratory symptoms for a period of seven days and report to the appropriate medical authorities if necessary. Anyone at risk who develops fever above 38.5°C (or infants who develop tachypnoea) should be immediately hospitalised, isolated, and started on treatment for plague, pending microbiological diagnosis of the illness.

D. Laboratory Support and Confirmation

Y. pestis is a Hazard Group 3 pathogen and should thus be covered by existing risk assessments for handling such organisms in diagnostic laboratories. All laboratory procedures should be performed, by experienced medical laboratory scientists, in a Containment Level 3 facility using a Class 1 protective cabinet. **All samples should be sent to the Public Health Laboratory in Cherry Orchard Hospital.**

Samples to be taken from acutely ill humans

- Blood for culture.
- Sputum.
- CSF aspirate should be taken if clinically relevant.
- Acute and convalescent sera should be sent to the reference laboratory – serological diagnosis is possible and useful in culture-negative cases. However antibodies may not be detectable when the patient first presents.

Post mortem specimens

Samples may be taken from dead humans to assist diagnosis, including:

- Blood (approx 10ml) from a vein if possible.
- CSF, if clinically relevant.

However full post-mortems are discouraged if plague is suspected because of the risk of aerosolising organisms present in body fluids, drips etc. If postmortem is carried out, swabs or samples of lung, spleen or lymph node should be sent.

Isolation and Identification

Smears may be stained with Gram, Giemsa or Wayson's (if available) stains to demonstrate bipolar staining coccobacilli. Rapid presumptive identification can be made by immunofluorescence staining of smears using specific F1 antibodies labelled with fluorescein – smears should be heat fixed and sent to the Reference laboratory.

Culture

Y. pestis is a small Gram negative coccobacillus, which commonly exhibits bipolar staining and pleomorphism, particularly in clinical specimens. The diagnosis of plague must be confirmed by culture. Specimens for culture should be inoculated onto blood agar and MacConkey agar, and incubated aerobically both at 28^o C for optimal growth and 37^oC for detection of the F1 antigen. Aspirates and CSF should also be plated into an enrichment broth with subculture after 24-48 hours. The addition of *Yersinia* CIN agar may be useful for culture of “contaminated” specimens, ie. Sputum.

On blood agar the organisms forms tiny, translucent colonies after 24 hours, after 48 hrs incubation colonies range between 1-2 mm in diameter and grey-white to slightly yellow in colour; there is no haemolysis. On MacConkey agar it appears as pinpoint non-lactose fermenting colonies, which disappear after 2-3 days, presumably due to autolysis. *Y. pestis* is catalase positive and oxidase negative.

All suspect isolates must be sent to the reference laboratory for PCR etc.

Transport of samples

Strict procedures should be followed for the transport of samples of suspected *Y. pestis* to the laboratory. (See Appendix 3).

Tularaemia

A. Description of Agent/ Syndrome

(a) Aetiology/ epidemiology

Tularaemia is an acute infectious disease caused by *Francisella tularensis*, a gram-negative coccobacillus. It is distributed world-wide, particularly in North America, many parts of continental Europe, the former Soviet Union, China and Japan. *F. tularensis* is one of the most infectious pathogenic bacteria known, requiring inoculation or inhalation of as few as 10 organisms to produce recognisable clinical disease. Tularaemia (also known as rabbit, or deer fly fever) is acquired under natural conditions by inoculation of the organism (taken from animal blood or tissue fluids) in the bites of deerfly, mosquitoes or ticks. Less commonly, inhaling contaminated dusts or ingesting contaminated food or water can also produce clinical disease. People of all ages and both sexes appear to be equally susceptible to tularaemia. Human-to human transmission does not occur.

Although *F tularensis* could be used as a weapon in a number of ways, an aerosol release would have the greatest adverse medical and public health consequences

(b) Clinical features

The clinical manifestation of the disease is related to the route of exposure. Onset is usually sudden with fever and flu-like symptoms (headache, chills and rigors, generalised myalgia, coryza and sore throat).

- **Typhoidal:** a primary septicaemic syndrome may follow inhalation of infectious material. This form tends to present with features of systemic disease; fever and collapse. Gastrointestinal symptoms can be prominent, hence the confusing name.
- **Pleuropulmonary:** inhalation of infected material may also be followed by pneumonic involvement. Sudden onset of acute febrile illness, progressing to pharyngitis, bronchiolitis, pneumonitis, pleuritis, hilar lymphadenitis.
- **Ulceroglandular:** an ulcer appears at the site of introduction of the organism with swelling of the regional lymph nodes.
- **Oropharyngeal:** ingestion of organisms in food or water may produce painful pharyngitis, abdominal pains, diarrhoea and vomiting.

Radiology may show peribronchial infiltrates leading to bronchopneumonia in 1 or more lobes, often accompanied by pleural effusion and enlarged hilar nodes. Signs may be absent or minimal, with only 1 or several small, discrete pulmonary infiltrates, or scattered granulomatous lesions of lung parenchyma or pleura. The diagnosis is usually made clinically and confirmed by a rise in antibodies that appears in the second week of disease. The diagnosis of tularaemia can be very difficult, however, given the non-specificity of symptoms

(c) Mode of transmission

The disease may occur from the inhalation of dust from contaminated soil, from arthropod bites or by ingestion of contaminated food or water.

(d) Incubation period

The range is 1-14 days (usually 3-5days).

(e) Period of communicability

Tularaemia is not directly transmitted from person to person. Unless treated, the infectious agent may be found in the blood during the first 2 weeks of disease.

(f) Mortality

The typhoidal form of tularaemia has a 30-60% case fatality rate if left untreated.

(g) Antimicrobial susceptibilities

The treatment of tularaemia is generally streptomycin or gentamycin for 7 to 14 days.

B. Infection control practices

Patient placement

Tularaemia is not directly transmitted from person to person. Private rooms are not required.

Patient transport

Standard precautions should be used for transport and movement of patients with tularaemia.

Cleaning, disinfection, and sterilisation of equipment and environment

Principles of standard precautions should be generally applied to the management of patient-care equipment and environmental control.

Immunisation of contacts

Current vaccines offer incomplete protection and are not currently recommended.

Post-mortem care

Post-mortem examinations are not recommended if tularaemia is suspected. However if they are undertaken, standard universal precautions should be observed. Cremation is the preferred method of disposal for the deceased. Embalming of bodies is strongly discouraged.

C. Post Exposure Management

(a). Decontamination of patients

To be carried out by the fire brigade and ambulance services

The number of viable organisms that are re-aerosolised following the handling of contaminated clothing of exposed individuals is probably low. Clothing from exposed individuals should be placed, with minimum agitation, in sealed plastic bags prior to laundering using a hot cycle (i.e. >70°C). In view of the fact that the identity of any biological agent is unlikely to be known at the time of release, exposed individuals should be instructed to shower thoroughly using soap and water. People exposed to powder or liquid aerosols containing *F. tularensis* should wash themselves and their clothes with hot soapy water.

(b) Post exposure prophylaxis

Given the short incubation period of tularaemia and incomplete protection of current vaccines against inhalational tularaemia, vaccination is not recommended for postexposure prophylaxis. The working group recommends use of the live vaccine strain only for laboratory personnel routinely working with *F tularensis*.

In the unlikely event that authorities quickly become aware that an *F tularensis* biological weapon has been used and are able to identify and reach exposed persons during the early incubation period, exposed persons should be prophylactically treated with 14 days of oral doxycycline or ciprofloxacin

(c) Treatment:

Treatment will vary depending on whether the incident is small and contained and capable of being managed in hospital or whether the incident requires mass casualty treatment.

Table 5: Contained casualty treatment of tularaemia*

Adults	<ul style="list-style-type: none">• Gentamicin, 5 mg/kg IM or IV daily• Streptomycin, 1G IM bd (If available) <p>Alternative choices</p> <ul style="list-style-type: none">• Doxycycline, 100 mg IV bd• Chloramphenicol, 15 mg/kg IV qd• Ciprofloxacin, 400 mg IV bd
Children	<ul style="list-style-type: none">• Gentamicin, 2.5 mg/kg IM or IV tds• Streptomycin, 15 mg/kg IM twice daily (should not exceed 2 g/d) (If available) <p>Alternative choices</p> <ul style="list-style-type: none">• Doxycycline; if weight ≥ 45 kg, 100 mg IV twice daily; if weight <45 kg, give 2.2 mg/kg IV bd• Chloramphenicol, 15 mg/kg IV qd• Ciprofloxacin, 10-15 mg/kg IV bd‡
Pregnant Women	<ul style="list-style-type: none">• Gentamicin, 5 mg/kg IM or IV daily• Streptomycin 1G IM bd

Alternative choices

- *Doxycycline*, 100 mg IV bd
 - *Ciprofloxacin*, 400 mg IV bd
-

Gentamicin, for 10 days, is effective in the treatment of tularaemia. It is given intravenously up to 7mg/kg per day. Antibiotic levels should be taken 6 to 14 hours later. At 6 hours the gentamicin level should be ≤ 6.5 mg/litre. At 14 hours ≤ 2 mg/litre. For all stages in between the Hartford nomogram can be used. Streptomycin up to 15mg/kg twice daily by intramuscular injection was regarded as the drug of choice for the treatment of non-meningeal tularaemia in both adults and children but it is no longer widely available in Ireland. A minimum of 10 days should be given and subsequent dosing adjusted in accordance with renal function and serum levels. It is recognised that these agents are not routinely used as monotherapy in the treatment of acute febrile illnesses including pneumonia. When tularaemia is suspected but not confirmed microbiologically or serologically, an aminoglycoside should be added to an appropriate antibiotic regimen and **not used** as a single agent. Other antibiotics can be stopped when the identity of *F. tularensis* is confirmed and antibiotic susceptibility data available. Ciprofloxacin is active in vitro and in animal studies and has been used successfully to treat a number of **cases** in both children and adults. Tetracycline and chloramphenicol are bacteriostatic against *F. tularensis* and if they are used in treatment at least 21 days therapy is required to reduce the chance of relapse. Due to the poor penetration of aminoglycosides into CSF chloramphenicol may be added to streptomycin in the treatment of patients with clinical features of meningitis.

(d) Environmental decontamination

Under natural conditions, *F. tularensis* may survive for extended periods in a cold, moist environment. Experts currently lack information on survival of intentionally dispersed particles but would expect a short half-life due to desiccation, solar radiation, oxidation and other environmental factors, and a very limited risk from secondary dispersal. In circumstances of a laboratory spill or intentional use in which authorities are concerned about an environmental risk (eg, inanimate surfaces wet with material thought to contain *F. tularensis*), decontamination can be achieved by spraying the suspected contaminant with a 10% bleach solution (1 part household bleach and 9 parts water). After 10 minutes, a 70% solution of alcohol can be used to further clean the area and reduce the corrosive action of the bleach. Soap water can be used to flush away less hazardous contaminations. Persons with direct exposure to powder or liquid aerosols containing *F. tularensis* should wash body surfaces and clothing with soap and water. Standard levels of chlorine in municipal water sources should protect against waterborne infection.

Protection of healthcare workers

This involves all emergency staff involved in management at the scene of a release as well as those involved in treating patients with tularaemia.

Protective clothing

Following an overt release of *F. tularensis* the area affected by primary aerosolisation will depend on the time and place of release. This exposed zone presents a high risk of infection, and anyone entering it should wear full protective equipment including

high-efficiency air filter masks conferring full biological protection. Exposed persons will normally be moved from the exposed zone, through decontamination and into a holding area for clinical assessment and the administration of prophylaxis.

Professionals involved in the decontamination of exposed individuals and handling of contaminated clothing and fomites should observe standard universal precautions—gloves, plastic aprons along with face masks (as described in Appendix 1) and eye protection if splashing is likely. Hands should always be washed after the removal of gloves. Those handling individuals who have been decontaminated do not need to take special precautions.

(e) Antibiotic prophylaxis and immunisation

Healthcare workers entering the exposed zone should be offered antibiotic prophylaxis. Prophylactic antibiotics may also be considered for frontline workers involved in other activities including:

- Decontamination of exposed persons
- Handling of exposed persons
- Management of patients or disposal of bodies of patients dying of tularaemia

Decisions about to whom prophylaxis should be offered, should be taken on an individual basis according to duration and degree of exposure and taking into account the availability and side effects of prophylactic treatments available.

Persons beginning treatment with streptomycin, gentamycin, doxycycline, or ciprofloxacin in the incubation period of tularaemia and continuing treatment daily for 14 days might be protected against symptomatic infection.

Given the short incubation period of tularaemia and incomplete protection of current vaccines against inhalational tularaemia, vaccination is not recommended for postexposure prophylaxis.

Table 6: Suggested mass casualty treatment and post exposure prophylaxis for tularaemia*

Adults	<ul style="list-style-type: none"> • <i>Doxycycline</i>, 100 mg orally twice daily • <i>Ciprofloxacin</i>, 500 mg orally twice daily
Children	<ul style="list-style-type: none"> • <i>Doxycycline</i>; if ≥ 45 kg, give 100 mg orally bd; if < 45 kg, give 2.2 mg/kg orally bd • <i>Ciprofloxacin</i>, 15 mg/kg orally twice daily‡
Pregnant Women	<ul style="list-style-type: none"> • <i>Ciprofloxacin</i>, 500 mg orally twice daily • <i>Doxycycline</i>, 100 mg orally twice daily

*One antibiotic, appropriate for patient age, should be chosen from among alternatives. The duration of all recommended therapies is 14 days.

‡Ciprofloxacin dosage should not exceed 1 g/d in children.

Postexposure prophylactic antibiotic treatment of close contacts of tularaemia patients is not generally recommended since human-to-human transmission of *F tularensis* is not known to occur.

D. Laboratory Support and Confirmation

F. tularensis is a Hazard Group 3 pathogen and should thus be covered by existing risk assessments for handling such organisms in diagnostic laboratories. Specimen handling and examination should take place in at least a Containment Level 3 laboratory by experienced medical laboratory scientists using a Class 1 protective safety cabinet.

Samples to be taken from acutely ill humans

- Blood. Typically, serum antibody titres do not attain diagnostic levels until 10 or more days after onset of illness, and serology would provide minimal useful information for managing an outbreak.
- Respiratory secretions: sputum, tracheobronchial secretions and blood should be cultured using cysteine- enriched medium. PCR and antigen detection procedures at reference laboratories may also provide rapid identification.
-

Pathology

- Histological findings of acute suppurative necrosis followed by granulomatous reactions
- Target organs include lungs, lymph nodes, spleen, liver and kidney

Transport of samples

Strict procedures should be followed for the transport of samples of suspected *F. Tularensis* to the laboratory. (See appendix 3)

Risk communication

In the event of illness occurring in Ireland as a result of bioterrorism at home or abroad there will be a need for an organised national and local communications response to allay widespread public fear and anxiety and to prevent panic.

The development of informational materials and resources that can be quickly and broadly disseminated to health care providers, the public and other key partners is critical before any cases of illness associated with bioterrorist agents occur. The public will immediately need to be given information that will help people minimise their risk of contracting disease.

Pre-Event Communication Objectives (i.e. before cases of disease associated with bioterrorist agents are confirmed)

- Increase public, health care provider, policy maker, media and key partner knowledge and understanding of the diseases associated with bioterrorist agents and the general approaches/ concepts that would be used should there be a confirmed outbreak (such as isolation or quarantine in the case of smallpox). Educational materials will be designed for this purpose.

Event/Post-Event Activities (i.e. after a likely or confirmed case)

- Once illness associated with bioterrorism has been verified, a National Communications Centre will be established in the Department of Health and Children.
- A national cascade system for communicating rapidly with health professionals will be initiated by the Department of Health and Children. Local partners at health board level will be contacted and provided with information and materials that will enable them to respond to local media, public and health care provider inquiries.
- A national telephone hotline will be established to immediately provide information to the public.
- Websites will be used to quickly provide information, updates, fact sheets and frequently-asked question documents to health care providers, the public and the media. All media and public materials will be posted to the Department of Health and Children and National Disease Surveillance Centre websites and to other governmental websites.
- Daily routines will be implemented for informing and responding to the media, health care providers, partner and public enquiries.
- Key personnel will provide advice and information on the national radio and television stations.
- Fact sheets on the diseases in question will be distributed widely.

At health board level

- Health boards will organise telephone helplines which will be manned by health board staff

- Key personnel will provide advice and information on local radio stations
- Information will be circulated in local newspapers
- Health Board websites will provide access to relevant and timely information.

Summary of roles of different agencies in the event of a case of disease associated with bioterrorism

Laboratories (All laboratories need input from a consultant microbiologist)

In the case of suspected anthrax, plague or tularaemia

- All human samples will be analysed in the Public Health Laboratory, Cherry Orchard Hospital
- All environmental samples will be analysed in CAMR, Southampton until Cherry Orchard Hospital is in a position to analyse the environmental samples
- The Public Health Laboratory will receive and package the environmental samples to be sent to CAMR.

In the case of suspected smallpox

- All human and environmental samples will be sent to the VRL.
- Human clinical samples will be inactivated on site where possible and analysed by the VRL.
- Environmental samples will be analysed in CAMR. Advice on packaging and transport will be supplied by the Expert Committee – Contingency Planning for Biological Threats

In the case of suspected botulism

- All human and environmental samples will be analysed in Colindale. Advice on packaging and transport will be supplied by the Expert Committee – Contingency Planning for Biological Threats.

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Health Boards/ Departments of Public Health

- Director of Public Health to establish local group with public health, environmental health, infectious disease consultant (or other appropriate general physician) and microbiological representation to oversee epidemiological investigation. Commence epidemiological investigation. (Health Board CEOs to make arrangements for appropriate 24 hour cover).
- Director of Public Health to contact Department of Health and Children and National Disease Surveillance Centre immediately bioterrorist attack is suspected.
- Notify Directors of Public Health in other health board areas.
- Allocate extra public health staff to affected area.
- Provide information to A&E departments, laboratories, GPs and other clinicians.
- Liaise with communication director.
- Provide regular information to public via media, telephone helplines, website etc
- Circulate information leaflet should be circulated to all exposed persons with advice on actions to be taken in the event of developing suspicious symptoms.
- Bioterrorism plan should be integrated with local emergency planning

Role of National Disease Surveillance Centre

- Coordinating national surveillance. Development of surveillance databases. Dissemination of timely information to health care professionals, other agencies and general public.
- Collation and interpretation of national epidemiological information
- Providing 24 hour advice to health professionals, media, other agencies involved and general public.
- Coordinating national response. Providing national outbreak team
- Mapping epidemiological information to small area level.
- Liaison with counterparts in UK, USA, Europe

Role of Department of Health and Children

- Representation on Expert Committee and National Major Emergency Response Team
- Liaison with other government departments: Justice, Defence, Environment, Dept of Taoiseach
- Liaison with Directors of Public Health
- National media briefing
- Provision of 24 hour advice to other agencies
- Liaison with NDSC
- Liaise with IMB regarding antibiotics/ vaccines

Role of Expert Committee – Contingency Planning for Biological Threats

- Source of expert advice to government and Minister for Health and Children in the event of a bioterrorist attack
- Preparation and updating of protocols

Role of Irish Medicines Board

- Procuring of adequate supplies of antibiotics, antitoxin, vaccines
- Advice regarding administration of vaccines and antibiotics and monitoring of adverse effects
- Liaison with Department of Health and Children

Appendices

Appendix 1: Summary of treatment and infection control practices for specific diseases associated with bioterrorism

Table 7: Mode of treatment for specific diseases associated with bioterrorism

<i>Disease</i>	<i>Treatment</i>	<i>Chemoprophylaxis</i>	<i>Immunisation</i>
Anthrax	Antibiotics	Yes	Not indicated
Smallpox	Antibiotics for skin infections	No	Yes
Botulism	Antitoxin	No	Antitoxin
Plague	Antibiotics	Yes	Not indicated for pneumonic plague
Tularaemia	Antibiotics	Yes	Not indicated
Viral haemorrhagic fevers Lassa Ebola/Marburg	Antivirals	Antivirals (Crimean-Congo Fever and Lassa Fever)	Not indicated

Table 8: Summary of infection control practices

Agent	Single room	Precautions	Immunisation of staff
<i>Anthrax</i>	No	Standard	No
<i>Smallpox</i>	Negative pressure isolation room	Airborne	Yes
<i>Botulism</i>	No	Standard	No
<i>Plague</i>	For 72 hours	Droplet	No
<i>Tularaemia</i>	No	Standard	No

Definition of standard, airborne and droplet precautions

Definitions

Standard precautions

All patients in healthcare facilities, including symptomatic patients with suspected or confirmed bioterrorism-related illnesses, should be managed utilising standard precautions. Standard precautions are designed to reduce transmission from both recognised and unrecognised sources of infection in healthcare facilities, and are recommended for all patients receiving care, regardless of their diagnosis or presumed infection status. Standard precautions prevent direct contact with all body fluids (including blood), secretions, excretions, nonintact skin (including rashes), and mucous membranes. Standard precautions routinely practiced by healthcare providers include:

Handwashing

Hands are washed after touching blood, body fluids, excretions, secretions, or items contaminated with such body fluids, whether or not gloves are worn. Hands are washed immediately after gloves are removed, between patient contacts, and as appropriate to avoid transfer of microorganisms to other patients and the environment. Either plain or antimicrobial-containing soaps may be used.

Gloves

Clean, non-sterile gloves are worn when touching blood, body fluids, excretions, secretions, or items contaminated with such body fluids. Clean gloves are put on just before touching mucous membranes and nonintact skin. Gloves are changed between tasks and between procedures on the same patient if contact occurs with contaminated material. Hands are washed promptly after removing gloves and before leaving a patient care area.

Masks/Eye Protection or Face Shields

A mask and eye protection (or face shield) are worn to protect mucous membranes of the eyes, nose, and mouth while performing procedures and patient care activities that may cause splashes of blood, body fluids, excretions, or secretions.

Gowns

A gown is worn to protect skin and prevent soiling of clothing during procedures and patient-care activities that are likely to generate splashes or sprays of blood, body fluids, excretions, or secretions. Selection of gowns and gown materials must be suitable for the activity and amount of body fluid likely to be encountered. Soiled gowns are removed promptly and hands are washed to avoid transfer of microorganisms to other patients and environments.

Droplet precautions

Droplet precautions are used for patients known or suspected to be infected with microorganisms transmitted by large particle droplets, generally larger than 5 μ in size that can be generated by the infected patient during coughing, sneezing, talking, or during respiratory-care procedures. Droplet precautions require healthcare providers and others to wear a surgical-type mask when within 3 feet of the infected patient. Based on local policy, some healthcare facilities require a mask be worn to enter the room of a patient on droplet precautions. Droplet precautions should be maintained until the patient has completed 72 hours of antimicrobial therapy.

Patient placement recommendations for droplet precautions include:

- Placing infected patient in a private room.
- If private rooms are not available a cohort of symptomatic patients with similar symptoms and the same presumptive diagnosis can be placed in a room together
- Spatial separation of at least 3 feet between infected patients and others should be maintained when cohorting is not achievable.
- Patients requiring droplet precautions must not be placed in the same room as an immunocompromised patient.
- Special air handling is not necessary and doors may remain open.

Airborne precautions

Airborne precautions are used for patients known or suspected to be infected with microorganisms transmitted by airborne droplet nuclei (small particle residue, 5 μ or smaller in size) of evaporated droplets containing microorganisms that can remain suspended in air and can be widely dispersed by air currents. Airborne precautions require healthcare providers and others to wear respiratory protection when entering the patient room. (Appropriate respiratory protection is based on facility selection policy; must meet the minimal NIOSH standard for particulate respirators).

Patients suspected or confirmed with smallpox require placement in rooms that meet the ventilation and engineering requirements for Airborne Precautions, which include:

- Monitored negative air pressure in relation to the corridor and surrounding areas.
- 6 – 12 air exchanges per hour,
- Appropriate discharge of air to the outdoors, or monitored high efficiency filtration of air prior to circulation to other areas in the healthcare facility.
- A door that must remain closed.
- In the event of a large outbreak, patients who have active infections with the same disease (i.e., smallpox) may be cohorted in rooms that meet appropriate ventilation and airflow requirements for Airborne Precautions.

Appendix 2: How to handle anthrax and other biological agent threats

Adapted from CDC Health Advisory document and PHLS guidelines

Many facilities in the USA have received anthrax threat letters. Most were empty envelopes; some have contained powdery substances. The purpose of these guidelines is to recommend procedures for handling such incidents.

DO NOT PANIC

1. Anthrax organisms can cause infection in the skin, gastrointestinal system, or the lungs. To do, so the organism must be rubbed into abraded skin, swallowed, or inhaled as a fine, aerosolized mist. Disease can be prevented after exposure to the anthrax spores by early treatment with the appropriate antibiotics. Anthrax is not spread from one person to another person.
2. For anthrax to be effective as a covert agent, it must be aerosolized into very small particles. This is difficult to do, and requires a great deal of technical skill and special equipment. If these small particles are inhaled, life-threatening lung infection can occur, but prompt recognition and treatment are effective.

GENERAL

Every business and organisation should assess and review their protocols for handling mail. Good sense and care should be used in inspecting and opening mail or packages.

- Examine (feel) unopened envelopes for foreign bodies or powder.
- Do not open letters with your hands: use a letter opener.
- Open letters and packages with a minimum of movement to avoid spilling any contents.
- Each organisation should assess whether it is a possible target threats. Based on this assessment, you may wish to consider additional precautions such as wearing gloves and restricting the opening of mail to a limited number of trained individuals.

SUSPICIOUS UNOPENED LETTER OR PACKAGE MARKED WITH THREATENING MESSAGE SUCH AS “ANTHRAX”:

1. Do not shake or empty the contents of any suspicious envelope or package.
2. PLACE the envelope or package in a plastic bag or some other type of container to prevent leakage of contents.
3. If you do not have any container, then COVER the envelope or package with anything (e.g., clothing, paper, trash can, etc.) and do not remove this cover.
4. Then LEAVE the room and CLOSE the door, or section off the area to prevent others from entering (i.e., keep others away).
5. WASH your hands with **soap and water** to prevent spreading any powder to your face.
6. What to do next...
 - If you are at **HOME**, then report the incident to the Gardai.

- If you are at **WORK**, then report the incident to the Gardai, **and** notify your building security official or an available supervisor.

ENVELOPE WITH POWDER AND POWDER SPILLS OUT ONTO SURFACE:

1. DO NOT try to CLEAN UP the powder. COVER the spilled contents immediately with anything (e.g., clothing, paper, trash can, etc.) and do not remove this cover!
2. Then LEAVE the room and CLOSE the door, or section off the area to prevent others from entering (i.e., keep others away).
3. WASH your hands with **soap and water** to prevent spreading any powder to your face.
4. What to do next...
 - If you are at **HOME**, then report the incident to the Gardai.
 - If you are at **WORK**, then report the incident to the Gardai, **and** notify your building security official or an available supervisor.
5. REMOVE heavily contaminated clothing as soon as possible and place in a plastic bag, or some other container that can be sealed. This clothing bag should be given to the emergency responders for proper handling.
6. SHOWER with **soap and water** as soon as possible. *Do Not Use Bleach Or Other Disinfectant On Your Skin.*
7. If possible, list all people who were in the room or area, especially those who had actual contact with the powder. Give this list to both the local public health authorities so that proper instructions can be given for medical follow-up, and to the Gardai for further investigation.

QUESTION OF ROOM CONTAMINATION BY AEROSOLIZATION:

For example: small device triggered, warning that air handling system is contaminated, or warning that a biological agent released in a public space.

1. Turn off local fans or ventilation units in the area.
2. LEAVE area immediately.
3. CLOSE the door, or section off the area to prevent others from entering (i.e., keep others away).
4. What to do next...
 - If you are at **HOME**, then **dial 999 or 112** to report the incident to Gardai.
 - If you are at **WORK**, then **dial 999 or 112** to report the incident to Gardai **and** notify your building security official or an available supervisor.
5. SHUT down air handling system in the building, if possible.

6. If possible, list all people who were in the room or area. Give this list to both the local public health authorities so that proper instructions can be given for medical follow-up, and to law enforcement officials for further investigation.

HOW TO IDENTIFY SUSPICIOUS PACKAGES AND LETTERS

Some characteristics of suspicious packages and letters include the following...

- Excessive postage
- Handwritten or poorly typed addresses
- Incorrect titles
- Title, but no name
- Misspellings of common words
- Oily stains, discolorations or odour
- No return address
- Excessive weight
- Lopsided or uneven envelope
- Protruding wires or aluminum foil
- Excessive security material such as masking tape, string, etc.
- Visual distractions
- Ticking sound
- Marked with restrictive endorsements, such as “Personal” or “Confidential”
- Shows a city or state in the postmark that does not match the return address

Appendix 3: Transportation of samples

(a) Transportation of samples with suspicion of agents associated with bioterrorism

The following procedures should be adopted for the transport of all specimens, and also all cultures for confirmation. These apply within hospitals and laboratories as well as for specimens sent to the reference laboratory. All health boards should have contracts with suitably approved courier companies.

- Every effort should be made to avoid external contamination of specimen containers during specimen collection.
- The primary container (bijoux or similar) should be screwed tight, labelled and placed in an intact plastic bag.
- A 'High Risk' label should be affixed to both specimen and request form. The latter should include any other relevant information and include adequate clinical details to indicate level of suspicion.
- Under no circumstances should the request form be placed in the same bag as the specimen.
- The bag should be sealed, using tape or heat sealer. Pins, staples and metal clips should not be used. A separate bag should be used for each specimen.
- Each specimen must then be placed in a leak-proof secondary container with sufficient absorbent material to absorb all the contents should leakage occur.
- Each specimen must be packaged individually – ie three specimens, three separate packages.
- The secondary container should be externally disinfected – e.g. by wiping with 0.1% hypochlorite (1,000ppm).

Samples sent to the reference laboratory

- Secondary containers should be placed within a final outer tertiary packaging.
- This packaging **must** comply to the UN 602 standard packaging for the transport of infectious substances by air, road or rail
- The package should be certified to this standard and carry the appropriate UN certification numbers on the tertiary packaging along with the following information:
 1. BIOHAZARD – danger of infection symbol Class UN 6.2.
 2. Instructions not to open if found.
 3. Telephone number of a responsible person – e.g. Consultant Microbiologist, Laboratory Manager.
- The container should be transported by an approved courier, without delay, directly to the reference laboratory.

Samples sent within hospitals and laboratories

- Secondary containers should be placed in a good quality box, which is well taped up and clearly labelled 'Pathological Specimen – Open only in Laboratory'
- Specimens should be transported by hand by a responsible person using the above packaging. Vacuum-tube systems should **not** be used for transportation of specimens within hospitals or laboratories.
- Extra care should be taken to ensure that laboratory records are kept to a high standard.

(b) Transport of samples collected from individuals suspected as being infected with smallpox.

1. Non designated hospital handling smallpox patients

Before the sample is collected, the case should be discussed with an infectious disease consultant or another appropriate general physician to confirm that the index of suspicion for smallpox is high enough to merit investigation

- Avoid external contamination of specimen containers during specimen collection.
- The primary container should be screwed tight, **clearly** labelled with patient details and placed in an intact plastic bag.
- A “**high risk**” label should be affixed to both specimen and request form. It is important that all relevant clinical details are included.
- **Under no circumstances should the request form be placed in the same bag as the sample**
- The bag should be sealed, using tape or heat sealer and a separate bag should be used for each sample. **Staples and metal clips should not be used to seal the bag.**
- Each bagged specimen should be placed in a leak-proof secondary container with sufficient absorbent material to absorb all the contents of the specimen should leakage occur.
- Each specimen should be packaged individually.
- Wiping with 0.1% hypochlorite should externally disinfect the secondary container.
- Secondary packages should be placed within a final outer tertiary package, which **must conform to UN 602 standard packaging** for the transport of infectious substances.
- The package should carry the appropriate UN certification and the following information;
 - **BIOHAZARD – danger of infection symbol Class UN 6.2**
 - **Instructions not to open if found**
 - **Telephone number of a responsible person – i.e. Consultant Microbiologist**
- The container should be transported by a suitably approved courier company to the Virus Reference Laboratory, University College Dublin, who will arrange transport to the Special Pathogens Reference Unit, CAMR, Salisbury, Wiltshire, UK.

2. Designated hospital handling smallpox patients

- The sample will be added to a primary container supplied by the Virus Reference Laboratory containing a liquid (such as guanidinium thiocyanate lysis buffer) which inactivates the virus and prepares the specimen for molecular investigation.
- The primary container should be screwed tight, **clearly** labelled with patient details and placed in an intact plastic bag.

- A “**high risk**” label should be affixed to both specimen and request form. It is important that all relevant clinical details are included.
- **Under no circumstances should the request form be placed in the same bag as the sample**
- The bag should be sealed
- Each bagged specimen should be placed in a leak-proof secondary container with sufficient absorbent material to absorb all the contents of the specimen should leakage occur.
- Each specimen should be packaged individually.
- Wiping with 0.1% hypochlorite should externally disinfect the secondary container.
- Secondary containers should be placed in a good quality box which is well taped up and clearly labelled “pathological specimen”.
- This container should be transported by a suitably approved courier company to the Virus Reference Laboratory, University College Dublin, where molecular investigations will be performed.

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