National Plague Control Guidelines





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PREFACE

It gives me great pleasure to introduce The Plague Control Guidelines. Human cases of plague have been notifiable in South Africa since 1919 with the first recorded case going as far back as 1899. The last reported case was in 1982 in Coega, Eastern Cape. However, countries surrounding South Africa continue to report human plague. Thus, it is extremely important that South Africa remains vigilant and establishes plague surveillance in high-risk areas.

The aim of this document is to provide a source of reference to the persons involved in the control of plague in South Africa. The outcome aimed for is a uniformed approach to plague surveillance nationally, appropriate treatment of plague cases and prompt and efficient outbreak response in the event of a plague outbreak.

These guidelines are based on the Plague Manual: Epidemiology, distribution, surveillance and control compiled by the World Health Organisation, findings from research conducted in South Africa and experience gained from plague surveillance programmes in the country.

The development of these guidelines was initiated by the National Department of Health and they were compiled in collaboration with the National Plague Working Group and other experts in the field.

Three different aspects of plague are dealt with in the document. The first section deals with the epidemiological aspects of plague, while the second section is concerned with the clinical side of plague and the last is more for personnel involved in prevention and control of plague.

It is hoped these guidelines will be used by all role players to provide effective plague control and management in South Africa.

Mabalala

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1. EPIDEMIOLOGY OF PLAGUE

Plague is an acute bacterial infection caused by *Yersinia pestis*, which mainly affects rodents. Wild plague exists independent of human populations and their activities in natural foci of the disease in wild rodent colonies. These natural foci require constant surveillance, since plague has a high potential for spread into susceptible areas. Conditions in each natural focus may be expected to vary and require monitoring to determine the extent and characteristics of the disease in a given area. Such studies define the importance and magnitude of the plague problem in particular foci and provide baseline data for surveillance and integrated control programmes.

Transmission between rodents is by their flea ectoparasites. Domestic plague is closely associated with rodents living with humans and can cause epidemics in both human and animal populations. Transmission from rodents to humans is by their flea ectoparasites under appropriate conditions. The ecology of plague is highly variable as there is a complex interaction between the hosts, vectors and the plague bacilli that is influenced by factors such as host susceptibility, season, temperature, humidity, and availability of food and the transmission efficiency of fleas.

The World Health Organization in 2003 reported 2 651 plague cases and 175 deaths globally. Of these reports, 80% were from 12 countries in Africa and the countries in southern Africa included Namibia, Angola, the DRC, Malawi, Tanzania, Mozambique, Zimbabwe and Madagascar.

Plague was first introduced to South Africa through its harbours during the third pandemic, which began its worldwide spread from Hong Kong in 1894. The disease spread inland with several outbreaks occurring, following which it spread to wild rodents in remote areas. These wild rodents are at present the most important potential sources of plague. Between 1899 and 1926, 2 568 cases with 1505 deaths were collected by the South African Institute for Medical Research; formal notifications began in 1921 (see Apnnexure 1). Although the incidence of plague decreased from the 1950s it remains a threat, since susceptible wild rodent foci exist in several parts of South Africa, namely Eastern Cape, Northern Cape, Free State, Mpumalanga and Gauteng Provinces.

In South Africa the last reported outbreak of plague occurred in Coega, Eastern Cape in 1982, with 13 cases and 1 death. Many years may lapse between the occurrences of isolated cases or epidemics; therefore continuous surveillance of rodents and their vector populations are important even during periods when no human cases are reported. Plague is subject to the International Health Regulations and every case must be notified to the World Health Organization and the health authorities of a country.

2. ETIOLOGY OF PLAGUE

2.1. Transmission and plague pathways

Transmission of plague from animal to humans is usually via the bite of an infected flea (Figure 1). When a flea feeds, blood is taken into the stomach. If plague bacilli are present in the blood meal they are taken into the flea's midgut, multiply and form an obstruction at the flea's proventriculus. As the flea repeatedly attempts to feed, the ingested blood prevented from reaching its stomach due to this obstruction, mixes with the plague bacilli and is regurgitated into the wound. The time until infectivity of a flea that has ingested plague bacilli varies with their species and external temperature and humidity, as does the survival time of fleas, which is also influenced by whether or not they are fed.

Yersinia pestis is a Gram-negative coccobacillus, a member of the Enterobacteriaceae. At the DNA level it is very closely related to Yersinia pseudotuberculosis but for reasons of safety its status as a separate species has been maintained. Yersinia pestis is an obligatory parasite; it can not exist in the environment on its own.

Box 1 Important animal hosts in the transmission of plague in South Africa

1. Gerbils

The primary reservoirs of sylvatic plague in Southern Africa are the rodents of the sub-family Gerbilinae and include: Namaqua gerbil - *Desmodilus auricularis* (Karoo and parts of the Kalahari), highveld gerbil – *Tatera brantsii* (highveld and Kalahari), bushveld gerbil – *Tatera leucogaster*.

Associated fleas:

Xenopsylla pirei (Namaqua gerbil) X. philoxera (Tatera spp)

2. Commensal rodents

Domestic rodents are closely associated with humans on farms, villages and in cities. Black rat – *Rattus rattus* House mouse – *Mus musculus* Norway rat – *Rattus norvegicus*

Associated fleas: *X. brasiliensis, X. cheopis, Echidnophagea gallinacea*

3. Mastomys coucha

The multimammate mouse is the important link between sylvatic plague foci and the domestic environment. *M. coucha* is known to enter deserted gerbil burrows where it can become infected with plague and transfer it to rodents in the domestic environment.

4. Other rodents

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Many rodent species have been found infected with plague in southern Africa e.g:

Striped mouse - Rhabdomys pumilio

Vlei rat - Otomys irroratus

Springhare – Pedetes capensis

The springhare is found in close association with gerbils. This rodent is hunted extensively for food by many rural people and plague cases have resulted from handling or eating infected animals.

Associated fleas include: Dinopsyllus ellobius and Chiastopsylla rossi

Under the right circumstances any flea may be a vector. However, the oriental rat flea, *Xenopsylla cheopis* is one of the most effective vectors whilst the cat, dog and human fleas (*Ctenocephalides felis*, *C. canis*, *Pulex irritans*) are poor vectors.



3. HUMAN PLAGUE

Humans may acquire plague from direct contact with infected wild rodents or other animals and their predators, usually in the course of hunting, trapping, skinning or meat cutting. Person to person spread of plague is almost invariably airborne, but flea-borne inter-human plague transmission, usually involving the human flea *Pulex irritans*, can occur.

3.1. Clinical manifestations of plague

Three forms of the plague exist: bubonic plague, pneumonic plague, and septicaemic plague. Plague is readily treatable but a high index of suspicion is required to recognise the disease when transmission to humans is rare, when it appears after long periods of dormancy in endemic areas, and when patients present outside endemic areas.

3.1.1. Bubonic plague

The most characteristic and common presentation of plague, it results from a flea bite or direct contamination of an open skin lesion by plagueinfected material. The incubation period is between 2 and 8 days (rarely up to 15 days); it is characterised by sudden onset of fever, chills, headache and weakness followed shortly by intensely tender enlargement of regional lymph nodes usually in the groin, armpit or neck. Bubonic plague may present with gastrointestinal symptoms such as abdominal pain, nausea, vomiting and diarrhoea. Clinical severity varies from case to case and from focus to focus with appropriate treatment in uncomplicated cases fever and general clinical symptoms resolve over 3-5 days. Septicaemic and pneumonic plague can complicate bubonic plague.

3.1.2. Septicaemic plague

This form is the bloodstream infection with *Y. pestis* and is characterised by the absence of peripheral buboes. Bloodstream dissemination to diverse parts of the body including meninges may occur. Mortality is high if not treated.

3.1.3. Pneumonic plague

Pneumonic plague results from haematogenous spread of *Y. pestis* to the lungs. Bacterial multiplication accompanied by a marked inflammatory response occurs in pulmonary tissue and the alveolar spaces from where bacteria are released during coughing episodes.

Y. pestis can also spread to contacts by the respiratory droplet route and can initiate an epidemic of primary pneumonic plague. Person-to-person transmission requires face-to-face exposure within 2 meters of a coughing patient i.e. droplet spread. The organism does not permeate room air where the patient is housed and is not carried through air ducts or vents. Pneumonic plague is highly contagious and close contacts may develop disease within 1 to 3 days. Disease onset is characterised by chills, fever, headache, body pains, and weakness and chest discomfort, later followed by cough, bloodstained sputum production, increasing chest pain, difficulty in breathing, hypoxia, and haemoptysis. Respiratory failure and death follow. Pneumonic plague is frequently fatal unless treated within 18 to 24 hours of onset.

3.1.4. Others

Plague meningitis, (cutaneous) plague and plague pharyngitis are other rare presentations of the disease.

3.2. Diagnosis of plague

3.2.1. Case definitions of human plague

- A. Suspected plague should be considered when one or both of the following conditions are presented:
 - 1. Clinical symptoms that are compatible with plague, e.g. fever, sepsis syndrome, lymphadenopathy and / or acute pneumonitis in a person who resides in, or who has recently travelled to a plague-endemic area.
 - 2. If Gram-negative and / or bipolar-staining coccobacilli are seen on a smear taken from affected tissues, e.g.:
 - Bubo (bubonic plague)
 - Blood (septicemic plague)
 - Tracheal / lung aspirate (pneumonic plague)
- B. Presumptive plague should be considered when one or both of the following conditions are presented:
 - 1. Smear or tissue material is positive for the presence of Yersinia pestis F1 antigen by immunofluorescence, by enzyme-linked immunoassay (ELISA), or other validated antigen detection systems e.g. rapid dipstick assay.
 - 2. Only a single serum specimen is tested and the anti-F1 antibody titre is positive by ELISA.
- C. Confirmed plague is diagnosed when one of the following conditions is met:
 - 1. A culture isolate is lysed by Y. pestis-specific bacteriophage.
 - 2. Two sequential serum specimens demonstrate a four-fold anti-F1 antibody titre difference by ELISA.

3.2.2. Laboratory diagnosis of plague

A definitive laboratory diagnosis of *Y. pestis* infection is based on the isolation and identification of the organism from clinical specimens or by demonstrating a diagnostic change in antibody titre in paired serum specimens.

Routine diagnostic specimens for smear and culture include the following: whole blood; aspirates from suspected buboes; pharyngeal swabs, sputum samples or tracheal washes from those with suspected plague pharyngitis or pneumonia; and cerebrospinal fluid from those with suspected meningitis. Materials for culture should be sent to the laboratory either fresh or frozen on dry ice.

3.3. Management of plague and prevention of spread

When a diagnosis of human plague is suspected on clinical and epidemiological grounds, appropriate specimens for diagnosis should be obtained immediately and the patient should be started on specific antimicrobial therapy without waiting for a definitive answer from the laboratory. Suspected plague patients with evidence of pneumonia should be placed in isolation, and managed under respiratory droplet precautions.

3.3.1. Specific therapy

Different classes of drugs are being used in the treatment of plague; most drugs used have not been approved for this purpose because of lack of evidence from controlled drug trial studies. These drugs have however proved to be highly effective in the treatment of plague. Some classes of antibiotics in this section are not registered for use in South Africa but have been included for information purposes. The full treatment guide for plague in South Africa is outlined in Annexure 2 of this document.

Aminoglycosides (streptomycin and gentamicin)

Streptomycin is the most effective antibiotic against *Y. pestis* and the drug of choice for treatment of plague, particularly the pneumonic form. Gentamicin has been found to be effective in animal studies, and is also used to treat human plague. Although not approved by the Food and Drug Administration (FDA) for treatment of plague, gentamicin is more readily available than streptomycin and has been used successfully.

Chloramphenicol

Chloramphenicol is a suitable alternative to aminoglycosides in the treatment of bubonic or septicaemic plague and is the drug of choice for treatment of patients with *Y. pestis* invasion of tissue spaces into which other drugs pass poorly or not at all (such as plague meningitis, pleuritis, or endophthalmitis). Chloramphenicol may be used adjunctively with aminoglycosides.

Tetracyclines (doxycycline)

This group of antibiotics is bacteriostatic but effective in the primary treatment of patients with uncomplicated plague, and as post-exposure prophylaxis. Tetracyclines may also be used adjunctively with other antibiotics.

Sulfonamides

Sulfonamides have been used extensively in plague treatment and prevention; however, some studies have shown higher mortality, increased complications, and longer duration of fever as compared with the use of streptomycin, chloramphenicol or tetracycline antibiotics. The combination trimethoprim-sulfamethoxazole has been used both in treatment and prevention of plague.

Fluoroquinolones

Fluoroquinolones, such as ciprofloxacin, have been shown to have good effect against *Y. pestis* in both *in vitro* and animal studies. Ciprofloxacin is bacteriocidal and has broad-spectrum activity against most Gram-negative aerobic bacteria, including Enterobacteriaceae and *Pseudomonas aeruginosa*, as well as against many Gram-positive bacteria. Although it has been used successfully to treat humans with *Francisella tularensis* infection, no controlled studies have been published on its use in treating human plague.

Fluoroquinolones are used empirically to treat critically ill patients and have demonstrated activity against Y. pestis but are not FDA approved for this indication.

Other classes of antibiotics (penicillins, cephalosporins, macrolides)

These classes of antibiotics have been shown not to be effective in the treatment of plague and they should not be used for this purpose.

3.3.2. Treatment of plague during pregnancy and in children

With correct and early therapy, complications of plague in pregnancy can be prevented. The choice of antibiotics during pregnancy is confounded by the potential adverse effects of three of the most effective drugs. Streptomycin may be ototoxic and nephrotoxic to the foetus. Tetracycline has an adverse effect on developing teeth and bones of the foetus. Chloramphenicol carries a risk of grey baby syndrome or bone-marrow suppression. Experience has shown that an aminoglycoside eg. gentamicin when judiciously administered, is effective and safe for both mother and foetus, and in children. Because of its safety, intravenous or intramuscular administration, and the ability to have blood concentrations monitored, gentamicin is the preferred antibiotic for treating plague in pregnancy and children

3.3.3. Supportive therapy

The clinician must prepare for intense supportive management of plague complications, utilizing the latest developments for dealing with Gramnegative sepsis. Aggressive monitoring and management of possible septic shock, multiple organ failure, acute respiratory distress syndrome (ARDS) and disseminated intravascular coagulopathy should be instituted.

3.3.4. Post exposure prophylactic therapy

Persons in close contact with pneumonic plague patients, or persons likely to have been exposed to *Y. pestis*-infected fleas, to have had direct contact with body fluids or tissues of a *Y. pestis*-infected mammal, or exposed during a laboratory accident to known infectious materials should receive antibiotic preventive therapy, if the exposure was in the previous six days. The preferred antimicrobials for preventive or abortive therapy are the tetracyclines, chloramphenicol, or one of the effective sulfonamides.

Primary prophylaxis, i.e. the administration of an antibiotic prior to exposure, may be indicated when persons must be present for short periods in plague-active areas under circumstances in which exposure to plague sources (fleas, pneumonic cases) is difficult or impossible to prevent.

3.3.5. Vaccination

A plaque vaccine is available for human use, but cannot be used routinely. The vaccine should be considered for high-risk proffesionals only. The vaccine is therefore indicated for persons whose work routinely brings them into close contact with *Y. pestis*, such as laboratory technicians in plague reference and research laboratories and persons studying infected rodent colonies

3.4. Prevention and control of human plague transmission

A multidisciplinary approach should be involved since one case constitutes an outbreak. The first consideration in control of human plague is direct attack on reported foci of infection. This involves diagnosis and recognition of the disease, which is essential to establish firmly the existence of plague and isolation of the patient and of the immediate contacts as well as focal attack on the area invaded by plague through disinfestation of premises and persons.

3.4.1. Notification

All suspected and confirmed cases should be reported immediately to the local health authority, Port Health authority, provincial health authority and National DoH by telephone. International Health Regulations require submission of a case report of both suspected and confirmed cases immediately to the WHO.

3.4.2. Samples

The local branch of the National Health Laboratory Service or the National Institute for Communicable Diseases (NICD) should be contacted immediately so that the necessary specimens can be safely collected for rapid confirmation of the diagnosis. Samples required are blood, sputum, bubo aspirate or tissue, but it is important to consult with the laboratory before collecting specimens.

3.4.3. Isolation

The patients' clothing and baggage should be cleared of fleas using an insecticide effective against local fleas and known to be safe for people; patients should be seen by a doctor, their condition evaluated and the patients hospitalised and barrier nursed. For patients with bubonic plague (if there is no cough and the chest x-ray is negative) drainage/secretion precautions are indicated for 48 hours after start of effective therapy. For patients with pneumonic plague, strict isolation with precautions against airborne spread is required until 48 hours of appropriate antibiotic therapy have been completed and there has been a favourable clinical response.

3.4.4. Concurrent disinfection

Disinfection of sputum and purulent discharges and articles soiled therewith, and terminal cleaning is required. Bodies of people and carcasses of animals that died of plague should be handled with strict aseptic precautions.

3.4.5. Quarantine

Those who have been in household or face-to-face contact with patients with pneumonic plague should be provided with chemoprophylaxis (Annexure 2) and placed under surveillance for 7 days; those who refuse chemoprophylaxis should be maintained in strict isolation with careful surveillance for 7 days.

3.4.6. Protection of contacts

In epidemic situations where human fleas are known to be involved, contacts of bubonic plague patients should be disinfested with an appropriate insecticide. All close contacts should be evaluated for chemoprophylaxis. Close contacts of confirmed or suspected plague pneumonia cases (including medical personnel) should be provided with chemoprophylaxis (see Annexure 2).

3.4.7. Investigation of contacts and source of infection

Search for people with face-to-face exposure to pneumonic plague patients, and for sick or dead rodents and their fleas. Flea control must precede or coincide with antirodent measures. Dust rodent runs and harborages in the vessel, containers or warehouses, or affected residential areas with an insecticide labelled for flea control and known to be effective against local fleas.

3.4.8. Education

In areas where plague affects animals, community education is the cornerstone of prevention of plague. Education should include:

- The importance of rat-proofing buildings, appropriate storage and disposal of food, garbage and refuse to prevent access to food and shelter by rodents;
- · Transmission of plague and methods of exposure;
- The importance of avoiding flea bites by using insecticides and repellents;
- · Rodent control, inexpensive rodent traps and about safety aspects of poisons;
- Communities should be encouraged to monitor their neighbourhoods for rodent die-offs and to report these and other rodent population fluctuations to local authorities for further investigation.

It is important to build capacity amongst the local community health workers, traditional healers, and medical practitioners to recognise, diagnose and treat the disease. They could play an instrumental role as regards giving information about the rodent populations, dogs or cats in the area.

3.5. Human surveillance

Plague is a notifiable condition in South Africa and is one of the infectious diseases the International Health Regulations (IHR) consider to be public health emergencies; IHR stipulate that all confirmed cases of human plague be investigated and reported through appropriate authorities to the World Health Organization.

3.5.1. Passive surveillance

Whenever clinical symptoms or laboratory results suggest that a patient is infected with *Y. pestis*, the suspected case should be reported immediately. This will allow public health authorities to:

- 1. Advise on treatment and management of human plague cases;
- 2. Initiate efforts to identify the source of infection;
- 3. Determine the extent of any epizootic activity;
- 4. Assess the potential for additional human cases;
- 5. Disseminate information on plague to health care personnel; and
- 6. Implement emergency prevention and control measures.

Prompt reporting is especially important for cases of pneumonic plague because this form of the disease can be transmitted directly from person to person via infectious aerosols. Emergency procedures as described below must be implemented immediately to prevent further human infections. Local doctors and other health care workers must be familiar with the symptoms of plague. If a patient's symptoms suggest human plague, samples should be collected for diagnostic confirmation at a laboratory.

3.5.2. Community surveillance

It should not be assumed that health care workers, laboratory personnel and other public health authorities in plague-endemic areas are familiar with plague diagnosis and treatment. It is important to ensure that members of the local health care community are aware of the possibility of cases of plague occurring. This can be accomplished through brief training courses, plague surveillance newsletters, brief notes in other health-related newsletters or periodic contact with other health personnel.

3.5.3. Active surveillance

Following identification of a suspect case of human plague, surveillance personnel should immediately determine whether other cases exist or have occurred recently in the same vicinity. Hospital and clinical records from areas near where the case occurred should be reviewed and local health care providers should be interviewed to identify other potential cases. If possible, blood and other appropriate samples should be obtained from survivors who are considered to be potential cases to determine whether these persons are infected with or have antibody against *Y. pestis*. If possible, blood samples should be obtained from other family members or likely contacts. Record reviews and interviews with health care personnel should also be done when plague is identified for the first time in a region's animal or flea populations. In such situations, human cases might have occurred recently but may have been misdiagnosed or gone unreported. While performing the above activities, surveillance personnel should brief local health workers on plague diagnosis, treatment, prevention and control and explain the activities of the plague surveillance programme.

3.6. Standardised report writing

Human case reports should be standardised so that whenever possible the same information is recorded for each case. This will result in a database that can be combined with rodent and vector surveillance data to design better plague prevention and control strategies. The reporting form should include core patient information, clinical observations and treatment, laboratory results and results from epidemiological and, environmental investigations.

3.6.1. Core information

The following core information should be collected for each patient: age; sex; occupation; residence, including country; place of exposure if known; source of exposure if known; date of onset; clinical presentation (bubonic, septicaemic, pneumonic); treatment; recovered or fatal; possible exposure of others in contact with the patient; and preliminary classification of the case as suspected, presumptive or confirmed.

3.6.2. Clinical observations and treatment

Whenever possible, additional information on the clinical course and treatment of the disease should be recorded, including: antibiotics administered; dosage given; duration of treatment; elapsed time between the onset of symptoms and initiation of antibiotic therapy; unusual observations or complications (such as the occurrence of skin ulcers, insect bites, disseminated intravascular coagulation, meningitis, other); presence of cough; productivity of cough; intensity and duration of fever; and location and size of buboes.

The last sign (location of buboes) can provide useful information on the likely modes of transmission. For example, the presence of an inguinal bubo is strong evidence that the patient was infected by fleabite.

3.6.3. Laboratory analyses

The report should document all relevant laboratory work including: types of samples analysed (blood, sputum, bubo aspirate, serum, other); dates of sample collection; light and fluorescence microscopy results; chest X-ray results; haematological findings; bacteriological results; results of serological tests; and autopsy results for fatal cases.

3.6.4. Additional epidemiological and environmental information

An epidemiological investigation should be performed for each human case to determine the source of infection and the risk of additional human cases. Reports of these investigations should include:

- 1. a complete history of the patients' activities and travel during the incubation period of the infection;
- 2. results of field studies to determine which animal and flea species are likely sources of infection or pose a continuing threat to humans proximity of infected rodents and fleas to human dwellings or workplaces;
- 3. estimated number of people involved in activities that place them at high risk of plague infection; and
- 4. Information on possible exposure to Y. pestis infection of patient contacts (especially important for pneumonic plague cases).

3.6.5. Epidemiologic follow-up of pneumonic plague cases

When there is clinical evidence of plague pneumonia, it is important to document the efforts that were made to isolate pneumonic plague patients and protect health care personnel. The length of time a patient remained in isolation should be recorded, along with the results of periodic sputum tests. These tests are done to determine whether *Y. pestis* is present in the patient's sputum (patients should remain in isolation until test results are negative). Attempts should be made to identify and prophylactically treat individuals who had contact with the patient during the incubation period of the infection. If possible, throat swabs or serum samples should be collected from known patient contacts. Probable contacts can be ascertained from interviews with the patient, family and friends.

A history of the patient's travel and activities will suggest possible contacts. Even in the absence of plague pneumonia, it should be determined whether other persons with similar exposure histories have contracted plague. The results of tests performed on samples from patient contacts should be recorded.

3.6.6. Ecological and environmental observations

A basic understanding of the area's landscape ecology is useful for predicting the future course of epizootics and identifying areas of high risk for humans. Information should be collected on predominant vegetation types and the amount of local land surface covered by each vegetation type, roads, railways, airports, and seaports, land use patterns (agricultural, residential, industrial, other), types of dwellings present and whether these dwellings and associated food storage areas or other man-made sites provide food and harbourage for rodents. Flea and rodent control programmes implemented as a result of human plague case investigations should be described with an evaluation of their success.

3.7. Outbreak measures

Actions to be taken if a plague case is suspected or confirmed.

- Report case-based information to the district outbreak control coordinator.
- Collect specimens for confirming the case.
- Investigate the case

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- After the blood samples and/or other samples have been sent, treat the patient and administer chemoprophylaxis of close contacts with doxycycline or tetracycline for seven days from time of last exposure.
- Determine the extent of any epizootic activity
- Disseminate information on plague to health care personnel and communities

Actions to be taken if a suspected case is confirmed

- Isolate patients and contacts of pneumonic plague with precautions against airborne spread (e.g. wear masks) until at least after 48 hours of appropriate antibiotic therapy.
- Mobilise community to enable rapid case detection and treatment and to recognize mass rodent die-off as a sign of possible impending epidemic.
- Identify high-risk population groups through person, place, and time analysis.

Box 2 Continued p	lague control measures following an outbreak
Surveillance of cases:	Active surveillance of possible new cases and passive surveillance i.e. reporting of suspected cases, should be continued once weekly for one month.
Flea control:	Dwellings must be treated with insecticides for flea control twice weekly during quarantine and afterwards once a month for one year.
Rodent control:	Active rodent control must continue for 6 months. All land owners and responsible authorities must be involved in this control.
Serological surveillance:	Serum samples must be taken from dogs and rodents every 3 months and seronegative dogs must be re-bled every 3 months.
Education:	Education must continue, especially to improve environmental conditions and to prevent future outbreaks.
Epidemiological report:	A complete epidemiological report including each case must be completed and forwarded to the Department of Health (National Office).

3.7.1. General safety precautions

Wear gloves when handling rats or wildlife during surveillance.

Medical and field personnel should wear protective clothing and chemoprophylaxis should be taken.

Surveillance personnel must protect themselves from infection with plague by reducing the risk of being bitten by fleas. Appropriate repellents are those containing N,N-diethyl-m-toluamide (DEET) as active ingredient.

Personnel using rodenticides must read the instructions on the insert and follow the safety measures outlined therein.

3.7.2. Communication network

A national plague communication network should be maintained and include all relevant stakeholders and plague experts. A review of plague control and relevant indicators should take place annually or earlier if required.

4. PLAGUE IN ANIMALS

4.1. Epidemiology of plague in animals

The important animal hosts for the maintenance of plague are primarily rodents although many other mammals are naturally infected. Urban and commensal rats, *Rattus rattus*, were important in early epidemics. However, their present importance is restricted to a few plague areas in the world and they do not generally play a role in maintaining plague in the wild.

Today, most human plague is acquired in rural settings with wild animals forming the reservoir. Epizootic rodent hosts are susceptible to plague and there is a high mortality in these populations. Wild rodent die offs are therefore characteristic of plague epizootics and a warning sign of possible spread of plague to commensal rodents and to humans and their pets. Related rodent species living in close association may respond differently to plague infection e.g. in South Africa, *Mastomys coucha* is highly susceptible whilst its morphologically identical sibling species, *M. natalensis* is highly resistant.

4.1.1. Rodent reservoirs

The main reservoir was long thought to be the gerbil, *Tatera brantsi*. The passage of plague infection in Free State Province, South Africa, has been traced from gerbils as the reservoir to other wild rodents, e.g. *Otomys irroratus* to *Mastomys natalensis* to *Rattus rattus* and to humans. *M. natalensis* is now understood to be a species complex: early studies separated it into species A and B. The distribution of human plague in southern Africa is apparently linked to the distribution of species B of the *Mastomys (sensu stricto) (Praomys) natalensis* species complex, now called *M. natalensis*.

Studies have been done to determine if the sibling species of *M. natalensis (Mastomys coucha)*, *Aethomys chrysophilus*, *Tatera leucogaster* and *A. namaquensis* differed in their potential as reservoirs of plague in southern Africa. *A. namaquensis* is extremely plague-sensitive, much more so than *A. chrysophilus*, and the two may therefore play different roles in the plague cycle. In an outbreak of plague in Coega in the Eastern Cape Province of South Africa in 1982, plague antibody was found in two rodent species: the four-striped mouse, *Rhabdomys pumilo*, and the vlei rat, *Otomys irroratus*. Sera from 3012 rodents of 24 species captured in South Africa were tested for antibody to the Fraction 1 antigen of *Y. pestis* by passive haemagglutination. Of 24 species investigated, antibodies were found in seven (0.23%) rodents of three species, Desmodillus auricularis and *Tatera brantsii* in the Northern Cape Province and in *R. pumilo* in the Eastern Cape Province. The gerbils *Tatera brantsii*, *T. leucogaster* and *T. afra* play an important role in southern African plague epidemiology.

4.1.2. Flea Vectors

The fleas most frequently found on the rodent reservoirs of plague are *X. philoxera*, *X. brasiliensis* and *Dinopsyllus ellobius*. However, in ports and coastal towns *X. cheopis* is the dominant flea species on *Rattus* species and is the dominant flea vector of plague.

T. leucogaster and *M. coucha* are highly susceptible to plague and die soon after infection, making it unlikely that they act as reservoir hosts. Because they are relatively resistant to plague, *Aethomys chrysophilus* and *M. natalensis* are the more likely reservoirs. *M. coucha* and *M. natalensis* are semi-domestic and probably act as a link between humans and the true sylvatic foci of plague.

4.2. Plague control in animals

Control of plague transmission is directed at regulating the rodent reservoirs and flea vectors of the disease. The objective of this is to reduce the density of the rodent–flea vectors as quickly and as completely as possible.

The key objectives of plague control are to:

- 1. Identify and enumerate potential mammalian hosts and flea vectors.
- 2. Highlight zoonotic plague infections in order to geographically map plague foci.
- 3. Detect or anticipate epizootics before they spill over into domestic rodent or human populations.
- 4. Detect and notify outbreaks of plague promptly.
- 5. Verify atiology of all suspected non-outbreak-related cases and the first 5 to 10 outbreak-related cases.

Effective plague control is based on preventive measures e.g. structured active surveillance, appropriate rodent and flea control methodology.

4.2.1. Surveillance

Effective plague prevention and control require up-to-date information on the incidence and distribution of the disease. The best way of gathering the information is through a surveillance programme that collects, analyses, interprets and disseminates clinical, epidemiological, and epizootiological data on plague.

Systematic collection of surveillance information over many years provides information that can be used to:

- · Predict where future human cases and rodent epizootics may occur.
- Identify the most common zoonotic sources of human infection.
- · Identify the most important rodent and flea species maintaining a given focus of Yersinia pestis.
- Develop flea indices.
- Identify the hosts and flea species that should be targets for control measures.
- Assess the effectiveness of plague prevention and control measures.
- · Identify local ecological factors or human activities that may result in increased plague exposure risks for humans and rodents.
- Detect trends in the epidemiology and epizootiology of plague in a given region.

In areas where natural susceptible foci occur e.g. Eastern and Northern Cape, Free State, Mpumalanga and Gauteng Provinces, surveillance, including monitoring and evaluation programmes should be developed, and surveillance teams, including representatives of veterinary services, should be established. Equipment required is listed in Annexure 3. Members of the surveillance team should be familiar with rodent ecology; rodent and ectoparasite collection and identification; methods for collecting, preserving and shipping blood, tissues, carcasses and ectoparasite samples; measures for safely handling rodents and collecting specimens; how to identify local rodent species, and methods of preparing voucher specimens to verify field identification of rodents.

An investigation of the area under surveillance should be carried out to gather information on predominant vegetation types and amount of local land surface covered by each vegetation type, roads, railways, airports, and seaports, land use patterns (agricultural, residential, industrial, other), types of dwellings present and whether these dwellings and associated food storage areas or other man-made sites provide food and harbourage for rodents. Available data should be plotted on maps for purposes of orientation and for locating suitable study sites. A basic understanding of the area's landscape ecology is useful for predicting the future course of epizootics and identifying areas of high risk for humans. A geographic information system (GIS) is very useful for these purposes.

4.2.1.1. Rodent Surveillance

Rodents are the primary vertebrate reservoirs of plague, and nearly all human cases are associated with rodent epizootics. Surveillance programmes that monitor plague activity in susceptible rodent populations alert public health authorities to increased human plague risks, thus allowing prevention and control programmes to be implemented before human plague cases occur. Identification of plague in rodent populations also serves as a warning that human cases may appear and require treatment and follow-up. Rodents from rodent die-offs should be collected and analysed for the presence of *Y. pestis* which can be detected in moist marrow samples taken from long bones such as the femur even when animals have been dead for several days or weeks.

If the surveillance team cannot identify rodent species, the dead rodents must be sent to an appropriate laboratory for expert identification. During a plague epizootic the transportation of rodents from one area to another should be avoided to prevent the possible spread of the disease.

All specimens must be clearly labelled and a data sheet should also accompany each specimen. Depending on the materials available, laboratory requirements and the time required to ship specimens to the laboratory, rodents that cannot be identified by the team should be sent to the NICD Special Bacterial Pathogens Reference Unit, 1 Modderfontein Road, Sandringham, Johannesburg.

4.2.1.2. Dog and carnivore surveillance

Dogs do not usually die from plague infection but produce a specific *Y. pestis* antibody in response to infection and serve as excellent sentinel animals for plague surveillance. These serum samples are particularly useful in detecting plague in the absence of overt rodent plague, to obtain data in areas where plague infection is widespread or in areas where plague is quiescent.

4.2.1.3. Flea surveillance

Fleas are the primary vectors of plague and knowledge of local flea species and their hosts is essential for estimating risks of human plague infection and designing specific control measures appropriate for local situations. The relative importance of local flea species as plague vectors can usually be determined by analysing relevant surveillance data, including the numbers of fleas per host, host preferences and *Y. pestis* infection rates for the species of fleas collected.

Flea collections are made from all rodents and other mammals that are found dead as well as from rodents trapped alive, rodent nests and burrows, domestic animals and dwellings, especially when infested with rodents. The procedures for flea collection are further outlined below. Fleas that cannot be identified by the team should be sent to Special Bacterial Pathogens Reference Unit.

4.2.2. Specific Control Measures (Annexure 4)

4.2.2.1. Dogs and cats

Dogs and cats in these areas should be treated periodically with appropriate insecticides. Domestic animals, like humans, may intrude into wild plague foci and acquire the infection via fleas or by eating infected rodents. Cats, in contrast to dogs, develop clinical plague and a number of cases of direct cat-to-human transmission have been described.

4.2.2.2. Rat control programmes

Control programmes for rats should be maintained in both urban and rural areas to facilitate basic sanitary conditions in these areas. Measures to control fleas should be conducted prior to rodent control activities

4.2.2.3. Environmental Health

Environmental Health officers should report fluctuations in rodent populations, i.e. increases, decreases or large-scale die offs to Department of Health authorities immediately.

5. PLAGUE LEGISLATION

5.1. International Health Regulations

The International Health Regulations (IHR, 2005) deals with measures applicable to the prevention and importation of plague and notification of the World Health Organization.

5.2. National Health Act, 2004

The National Health Act 2004 outlines the roles and responsibilities of national, provincial and local government. Designation of airports as sanitary airports is published under the Government Notice No 498 of 11 April 2003. The designation of ports as approved ports is published under Government Notice No 499 of 11 April 2003.

6. MONITORING AND EVALUATION

The interventions implemented to control plague should be monitored and evaluated regularly. The monitoring and evaluation should be done to assess the effectiveness of those interventions.

6.1 Data management

- Plague surveillance data should be collated, and analysed on a regular basis for monitoring and evaluation of plague transmission.
- All data should be centrally stored where it is accessible.
- Data should be analysed by person, place and time on a regular basis.
- Provincial, district indicators and databases should be developed for monitoring and evaluation.
- Regular feedback should be provided to relevant stakeholders nationally, provincially and by district.
- Geographical maps of 1:250 000 for a whole province should be used for survey planning. Maps of 1:50 000 for a health district and orthophotos with topography intervals are recommended.

6.2. Indicators

Impact indicators

- 1. Plague mortality rate (under fives, 5-14years olds, 15+, pregnant women) in past 24 months
- 2. Morbidity attributed to plague (under fives, 5-14years olds, 15+, pregnant women) in past 24 months.

Outcome indicators

- 1. Percentage of dogs serological positive tested in the past 6 months per municipality
- 2. Percentage rodents serological positive tested in past 6 months per municipality
- 3. Percentage flea-infested rodent nests sampled in past 6 months per municipality
- 4. Percentage fleas found on rodents captured in past 6 months per municipality
- 5. Presence of rodent die-offs in past month per municipality
- 6. Rodent trap success rate in past 6 months per municipality
- 7. Rodent flea index from trapping conducted in past 6 months per municipality

- 8. Nest flea index from past trappings conducted in 6 months per municipality
- 9. Percentage ships (local and international) inspected for rodents per port in last 12 months
- 10. Percentage ships complying with regulations (de-ratting certificate, free pratique) per port in last 12 months.
- 11. Percentage of airports conducting rodent control in past 12 months per province.
- 12. Percentage of harbours conducting rodent control in past 12 months per province.

Process indicators

- 1. Percentage health care professionals trained in case management in last 24 months per district
- 2. Percentage environmental practitioners trained in rodent control in last 24 months per district
- 3. Number of municipalities financing plague surveillance and control activities
- 4. Number of districts with outbreak response plans
- 5. Percentage of health promoters trained in plague surveillance and control
- 6. Percentage of municipalities conducting rodent control activities bi-weekly at the onset of the breeding season and last two months towards the end of the breeding season (Sept, Oct, Nov, March, April, May) in the past 12 months in plague enzootic areas.
- 7. Percentage of CDC co-ordinators trained in plague control per district in last 24 months.

7. REFERENCES

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8. GLOSSARY

Active surveillance: following identification of a suspect case of human plague, surveillance staff should determine whether other cases exist or have occurred recently in the same vicinity.

Antibody: an immune or protective protein evoked in man and other animals by an antigen.

Antigen: any substance that as a result of coming into contact with the appropriate cells induces a state of sensitivity and or resistance to infection.

Aspirate: to remove gas or fluid from body cavity by suction.

Bacteriophage: a virus with a specific affinity for bacteria; they have been found in association with all groups of bacteria.

Chitin: a polymer similar to the structure of cellulose comprising the horny substance in the exoskeleton of insects and other arthropods.

Commensal: animal living harmlessly with another and sharing its food.

Distribution (geographical): the natural arrangements of plants, animals and diseases within a particular region.

Ecology: the science of communities. The science of relationships of organisms to environment.

Ecological factors: immediate influences affecting organisms directly, in most instances biotic and abiotic forces. Factors that interact and can hardly be isolated in ecological work.

Epidemiology: the study of the prevalence and spread of disease in a community.

Epidemic: The occurrence in a community or region of cases of an illness (or an outbreak) with a frequency clearly in excess of normal expectancy. Applied to a disease or parasite, which becomes widespread and attacks more than expected numbers of humans at the same time.

Enzootic: temporal pattern of disease occurrence in an animal population in which disease occurs with predictable regularity. Disease of animals, which is indigenous to a certain locality.

Endemic: Indigenous or native disease in a restricted locality; a disease prevailing continually in a region.

Epizootic: denoting a disease attacking large numbers of animals; animal equivalent of human epidemics.

Focus: an ecosystem in which an infectious agent and/or animal reservoir normally persists in nature.

Haemoptysis: bronchial or pulmonary bleeding, resulting in coughing up of blood.

Hypoxia: decrease below normal levels of oxygen in inspired gases, arterial blood or tissue.

Immunofluorescence: the use of fluorescein-labelled antibodies to identify bacterial, viral or other antigenic material specific for the labelled antibody.

IM: intramuscularly, within the substance of the muscle.

Incidence: the number of new cases of a disease in a population over a period of time.

IV: intravenous, within a vein.

Lymphadenopathy: enlarged lymph glands.

Meningitis: inflammation of the membranes of the brain or spinal cord.

NHLS: National Health Laboratory Services

NICD: National Institute for Communicable Diseases

Pharyngitis: inflammation of the mucous membrane and underlying parts of the throat

Pneumonitis: inflammation of the lungs.

PO: per os, by mouth.

Proventriculus: part of the foregut of the flea near beginning of midgut, which is a modified organ, which can sieve, can be well-developed or just function as a valve.

Quiescence: being dormant or inactive.

Reservoir: living or non-living material in or on which an infectious agent multiplies and is dependent for its survival in nature.

Scats: faeces.

Sepsis syndrome: presence of various pus-forming or other pathogenic organism or their toxins in the blood or tissue.

Suppurative: forming pus.

Surveillance: an observational study that involves continuous monitoring of disease occurrence with in a population; may be active or passive.

Sylvatic: rural.

Vector: An arthropod actively or passively responsible for the dissemination of a disease-producing organism or parasite. An invertebrate animal (e.g. tick, mite, flea, mosquito) capable of transmitting an infectious agent among vertebrates.

Zoonosis: a disease of humans acquired from animal source. Infection shared in nature by human and other animals, which are the usual host.

Annexure 1:

Notified plague cases and deaths, 1921–1982.

Year	Case	Death
1921	33	-
1922	42	23
1923	2	1
1924	372	235
1925	112	68
1926	71	46
1927	75	56
1928	39	31
1929	65	42
1930	145	89
1931	71	44
1932	22	16
1933	31	16
1934	39	29
1935	290	184
1936	253	165
1937	52	17
1938	70	-
1939	77	-
1940	47	-
1941	90	-
1942	79	-
1943	77	-
1944	63	-
1945	39	24
1946	15	1
1947	9	3
1948	34	5
1949	32	10
1950	21	-
1951	-	9
1952	4	3
1953	12	0
1954	7	2
1955	8	0
1956	3	0
1957	5	0
1959	10	0
1961	1	0
1962	7	0
1964	1	0
1965	1	0
1966	1	1
1967	1	-
1968	4	0
1970	2	0
1972	1	0
1974	0	1
1982*	13	1
1002		

Source: National Department of Health (Epidemiological Comments 1982; 9: 2-16.) No cases reported between 1975 and 1981. The death in 1974 was only reported at death, data for the fields marked with – was not available.* National epidemiology and surveillance notification system.

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Plague treatment and prophylaxis guidelines

Severe plague, defined as bubonic plague with severe systemic symptoms and signs. Includes bubo-septicaemic plague, septicaemic plague, pneumonic plague, plague meningitis

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Drug	Treatment regimen Duration of treatment: 10 days	Pregnancy and lactation	Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen Duration of prophylaxis: 7 days
Gentamicin First line treatment 	Adults 5 mg/kg IV every 24 hours or 2.5 mg/kg IV 12 hourly	Given the severity of the condition the same product as in non-pregnant adults should be considered. It is recommended, when possible, to cease breast feeding.	Not used for prophylaxis
	Children 7.5 mg/kg IV 24 hourly		Not used for prophylaxis
 Streptomycin First line treatment 	Adults 1 g IM 12 hourly	Given the severity of the condition the same product as in non-pregnant adults should be considered. It is recommended, when possible, to cease breast feeding. Streptomycin may be ototoxic and nephrotoxic to the fetus	Not used for prophylaxis
	Children 15 mg/kg IM 12 hourly (max 2g)		Not used for prophylaxis
Chloramphenicol First line treatment 	Adults 25 mg/kg IV 6 hourly		Not used for prophylaxis
 mandatory if meningitis, pleuritis, endophthamitis or other tissue localisation occur, to be used alone or together with streptomycin and gentamycin Treatment up to 21 days in view of the risk of relapse 	Children 25 mg/kg IV 6 hourly		Not used for prophylaxis

Drug	Treatment regimen Duration of treatment: 10 days	Pregnancy and lactation	Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen Duration of prophylaxis: 7 days
Ciprofloxacinsecond line treatment	Adults 400 mg IV 12 hourly followed by 500 mg oral 12 hourly	Given the severity of the condition the same product as in non pregnant adults should be considered. It is recommended, when possible,	Adults first line prophylaxis 500 mg oral 12 hourly
	Children 10-15 mg/kg IV 12 hourly followed by 10- 15 mg/kg oral 12 hourly. The daily dose for children should not exceed that in adults.	to cease breast feeding.	Children 10-15 mg/kg oral 12 hourly
Doxycycline Second line treatment 	Adults 100 mg oral 12 hourly	Given the severity of the condition the same product as in non pregnant adults should be	Adults 100 mg oral 12 hourly
	Children >8 years and > 45 kg: adult dose >8 years and < 45 kg: 2 mg/kg oral 12 hourly daily	children less than 8 years old.	Children Second line prophylaxis Second line prophylaxis 8 years and > 45 kg: 2 mg/kg oral 12 hourly

Uncomplicated plague, defined as uncomplicated bubonic, pharyngeal or carbuncular plague.	mplicated bubonic, pharyngeal or carb	uncular plague.	
Drug	Treatment regimen	Contraindications	Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen
Ciprofloxacin	Adults 400 mg IV 12 hourly followed by 500 mg oral 12 hourly	Given the severity of the condition the same product as in non pregnant adults should be considered. It is recommended, when possible, to cease breast feeding.	Adults 500 mg oral 12 hourly
	Children 10-15 mg/kg IV 12 hourly followed by 10- 15 mg/kg oral 12 hourly The daily dose in children should not exceed that in adults.		Children 10-15 mg/kg oral 12 hourly
Doxycycline	Adults 100 mg oral 12 hourly	Given the severity of the condition the same product as in non pregnant adults should be considered. It is recommended, when possible, to cease breast feeding.	Adults 100 mg oral 12 hourly
	Children >8 years and > 45 kg: adult dose >8 years and < 45 kg: 2 mg/kg oral 12 hourly	Contraindicated in children less than 8 years old.	Children >8 years and > 45 kg: adult dose >8 years and < 45 kg: 2 mg/kg oral 12 hourly

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Annexure 3: Equipment required for the collection of dog/rodent specimens

- Transport, maps, camping equipment and rodent identification key.
- Boots, rubber gloves, overalls, masks, goggles, flea repellent for team member protection.
- Muzzles, dog chain and tourniquet for handling dogs.
- Traps, bait, trap bag, forceps, cotton wool for rodent capture
- White tray, plastic bags, ether, pen brush, tooth brush, flea tubes, alcohol, test tubes for dog/rodent flea capture.
- Syringes and needles, blood tubes, refuse bag, ether, cotton wool, tube ranks, labels, pens for blood collection from dogs and rodents.
- Electric or hand centrifuge, pipettes, rubber teats, serum tubes, orange sticks, labels, pens, fridge, and record book for processing bloods.
- Salt, insecticide to kill fleas, rodenticide, honey jars for rodent carcases
- Global Positioning System (GPS)

Annexure 4:

Pesticides registered for use in South Africa and recommended by WHO for the control of fleas

Pesticide	Formulation		Dosage	Application directions
	Туре	Grams per active	Per 10I water or as	
		ingredient	indicated	
Deltamethrin	EC	15g/l	100ml/5l water/100m ²	Coarse spray onto surfaces frequented by fleas
Permethrin*	AL	2.5g/l	-	Coarse spray onto surfaces frequented by fleas
	DP	5g/kg	-	Dust lightly
	FD	135g/kg	1 tin/120-1000m ³	Ignite and let smoulder
	WP	250g/kg	50-67.7g	Coarse spray onto surfaces. Use higher rate for longer residual action
Propoxur*	DP	10g/kg	-	Dust freely
	EC	200g/l	250-500ml	Coarse spray or brush onto surfaces
	WP	500g/kg	200g	Coarse spray or brush onto surfaces frequented by fleas
Gamma-BHC*	DP	6g/kg	-	Dust freely

AL=Other liquids to be applied -self defining. Products applied undiluted

CS=Capsule suspension - A stable suspension of capsules in a fluid (normally intended for dilution in water)

EC=Emulsifiable concentrate- A liquid, homogenous formulation to be applied as an emulsion after dilution in water

DP=Dusting powder - A free-flowing powder, suitable for dusting

FD=Smoke tin – special forms of smoke generators

WP=wettable powder – A powder formulation to be applied as a suspension after dispersion in water.

Pesticides registered for use in South Africa and recommended by WHO for the control of rodents

Pesticide	Formulation		Dosage	Application directions
	Туре	Grams per active	Per 10I water or as	
		ingredient	indicated	
1 st generation				
Coumatetrayl*	BB	0.375g/kg	-	
	CB	7.5 g/kg	Undiluted	Dust entrance of burrow and along runways
Diphacinone	RB	0.05 g/kg	-	
Warfarin/sulphquinoxaline*	BB	0.25/-g/kg	-	
Second generation				
Brodifacoum*	BB	0.05g/kg	-	
Bromadiolone*	DP	1.5g/kg	-	Apply to mouse and rat runs & harbourages
	RB	0.05g/kg	_	
Difenacoum*	BB	0.1g/kg	-	
Flocoumafen*	BB	0.05g/kg	_	

BB=Bait block- special forms of bait

CB=Bait concentrate - A solid or liquid intended for dilution before use as a bait

DP=dusting powder – A free flowing powder, suitable for dusting

RB=bait ready for use - A formulation designed to attract and be eaten by the target pest

Annexure 5: Contact details and useful sources of information

National Institute for Communicable Diseases (NICD) Special Bacterial Pathogens Reference Unit No 1 Modderfontein Road Sandringham, Johannesburg. Tel: + 27 011 555 0331/0306/0308 Fax: + 27 011 555 0447 / 386 6594

CDC website: www.cdc.gov/ncidod/dvbid/plague

World Health Organization: www.who.int

PROF GERHARD H VERDOORN Agrochemical-environmental consultant **Poison Working Group** P.O. Box 72334 Parkview 2122 nesher@tiscali.co.za NASHUA Helpline 082 446 8946 Ms Nicola van Zijl Poison Working Group Poison Working Group P.O. Box 72334 Parkview 2122 pwg@ewt.org.za 011 486 1102

Maps and photos can be ordered from: Chief Directorate: Surveys and mapping Private bag X10 Mowbray 7705 Or http://w3sli.xcape.gov.za

National Department of Health Tel (012) 312-0000 Directorate: Communicable Disease Control Private Bag X828, Pretoria 0001

CDC Coordinators

Department of Health Northern Cape Province Private Bag X5049 KIMBERLEY 8301 Tel: 053 830 0529/660 Fax: 053 830 0655

Mpumalanga Department of Health Private Bag X11285 NELSPRUIT 1200 Tel: 013 766 3411 Fax: 013-766 3473

Limpopo Department of Health Private Bag X9302 POLOKWANE 0700 Tel: 015-293 6059 Fax: 015-293 6200

North West Department of Health Cnr Victoria & Carrington Streets Commissioner Building MAFIKENG Tel: 018 397 2663 Fax: 086 690 2835

Eastern Cape Department of Health Private Bag X0038 BISHO 5605 Tel: 040 609 3409 Fax: 040 609 3784 Gauteng Department of Health Private Bag X085 MARSHALLTOWN 2107 Tel: 011-355 3867 Fax: 011-355 3551

Kwa-Zulu Natal Department of Health Private Bag X9051 PIETERMARITZBURG 3200 Tel: 033 395 2051 Fax: 033 342 5830

Free State Department of Health P.O. Box 227 BLOEMFONTEIN 9300 Tel: 051 408 1734 Fax: 051 408 1074

Western Cape Department of Health P.O. Box 2060 CAPE TOWN 8000 Tel: 021 483 5707/3737 Fax: 021-483 2682

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