Queensland Health Guidelines

Assessment of clusters of non-communicable disease

2012
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The revised guidelines have been endorsed by the Queensland Health Expert Review Committee on Cluster Assessment.

The *‘Queensland Health Guidelines: Assessment of clusters of non-communicable disease 2012’* is available on the Queensland Health website:

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Preface

Each year Queensland Health responds to about 20 inquiries about suspected non-communicable disease clusters. The majority of these inquiries relate to cancer. This is understandable as cancer is a common disease. Most concerns relate specifically to breast cancer, which is the most commonly diagnosed cancer in women. Internationally and nationally it is found that nearly all cases, suspected clusters or groups of disease in one place are found to be a normal occurrence, with no identifiable environmental cause.

Queensland Health takes these inquiries and concerns seriously. The assessment of an apparent cluster of non-communicable disease, such as a cancer cluster or a cluster of birth defects, can be a complex and resource intensive task, and one that requires thorough planning and careful assessment.

Because of the number of cancer cluster inquiries, these guidelines emphasise cancer related aspects of cluster assessment. However the guidelines are equally applicable to all non-communicable disease clusters.

These guidelines are intended to assist Queensland Health to carry out appropriate and efficient cluster assessments, address public concerns and provide advice based upon the available evidence.

This revised version of the guidelines (2012 edition) details the initial inquiry response, as the majority of the cluster concerns are addressed at the initial stage, usually by phone, by experienced public health physicians. Beyond the initial inquiry response, four types of assessments are detailed, providing a systematic multidisciplinary approach to the assessment of disease clusters. In addition, references are given to standard cluster assessment tools and supporting information is provided to assist in cluster assessments. Once a type of assessment is completed, a decision must be made as to whether to undertake another type of assessment or finalise the inquiry with no further assessment. Criteria for each type of assessment are suggested to assist in this decision making process.

Addressing inquiries and concerns from the public is an important part of cluster assessment and management. The affected community may feel anxiety and distress with the knowledge of an apparent cluster of a non-communicable disease, especially if it may possibly be attributed to a preventable hazard. The guidelines include suggestions for communicating risk, managing risk perceptions and negative feelings associated with the inquiry, and strategies for meeting the information needs of the affected population, the public and the media.

The guidelines are available on the Queensland Health website at www.health.qld.gov.au

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February 2012
# TABLE OF CONTENTS

1 **The guidelines** .................................................................................................................. 5
   1.1 Overview .............................................................................................................................. 5
   1.2 Initial inquiry ........................................................................................................................ 14
   1.3 Type 1 cluster assessment: inquiry response ................................................................... 15
       1.3.1 Initiating a Type 1 cluster assessment — briefing ..................................................... 15
       1.3.2 Conducting the Type 1 cluster assessment ................................................................. 15
       1.3.3 Decision points for the Type 1 assessment ................................................................. 17
       1.3.4 Finalisation of a Type 1 cluster assessment ............................................................... 17
   1.4 Type 2 cluster assessment: data assessment ................................................................... 19
       1.4.1 Briefing and approval to initiate the Type 2 cluster assessment ............................ 19
       1.4.2 Role of Queensland Health ......................................................................................... 20
       1.4.3 The Type 2 cluster assessment team ......................................................................... 20
       1.4.4 Conducting the Type 2 cluster assessment ................................................................. 21
       1.4.5 Decision points for the Type 2 cluster assessment .................................................... 21
       1.4.6 Finalisation of the Type 2 cluster assessment ............................................................ 22
   1.5 Type 3 cluster assessment: analytical assessment ........................................................... 24
       1.5.1 Briefing and approval to initiate the Type 3 cluster assessment ............................ 24
       1.5.2 Role of Queensland Health ......................................................................................... 24
       1.5.3 The Type 3 cluster assessment team ......................................................................... 25
       1.5.4 Conducting the Type 3 cluster assessment ................................................................. 26
       1.5.5 Expert Review Committee on Cluster Assessment .................................................. 27
       1.5.6 Engaging advisers for the T3CAT ............................................................................ 28
       1.5.7 External reviewer ......................................................................................................... 28
       1.5.8 Decision points for the Type 3 cluster assessment .................................................... 28
       1.5.9 Finalisation of the Type 3 cluster assessment ............................................................ 29
   1.6 Type 4 cluster assessment: research study ...................................................................... 31
       1.6.1 Conducting the research study .................................................................................... 31
   1.7 Cluster Assessment Register .............................................................................................. 33
       1.7.1 Information recorded .................................................................................................... 33
       1.7.2 Annual reporting .......................................................................................................... 33
       1.7.3 Register location and format ....................................................................................... 33
       1.7.4 Access .......................................................................................................................... 33

2 **Supporting information** ..................................................................................................... 34
   2.1 Role of Queensland Health in cluster assessment ............................................................. 34
   2.2 Cluster management .......................................................................................................... 35
   2.3 Cluster assessment ............................................................................................................. 36
       2.3.1 Introduction .................................................................................................................... 36
       2.3.2 Issues identification ..................................................................................................... 36
       2.3.3 Cluster assessment principles ..................................................................................... 36
       2.3.4 Engaging external advisors and reviewers ................................................................. 38
   2.4 Case ascertainment ............................................................................................................. 39
   2.5 Research questions for Type 2 and Type 3 cluster assessments .................................... 42
   2.6 Causality ............................................................................................................................ 45
   2.7 Epidemiological assessment of cluster assessments ......................................................... 47
   2.8 Environmental assessments in cluster assessments ......................................................... 51
   2.9 The role of communication and engagement in a cluster assessment .......................... 55
   2.10 Glossary ........................................................................................................................... 56
   2.11 Abbreviations ................................................................................................................... 60
   2.12 References ........................................................................................................................ 61
1 The guidelines

1.1 Overview
Queensland Health takes community concerns about possible environmental causes of non-communicable disease seriously. The purpose of these guidelines is to facilitate a systematic and multidisciplinary approach by Queensland Health officers in response to inquiries and concerns from the community, health professionals and others about potential clusters of non-communicable disease. These guidelines outline the principles of non-communicable disease cluster assessment and a systematic approach to addressing public concerns of disease clustering, including the:

- role of Queensland Health in assessing a reported cluster and advising on its management
- scope and processes of the different types of assessment
- roles and responsibilities of people and groups in each type of assessment
- processes for recording, conducting, reporting and communicating an assessment
- evaluation and review of the assessment process.

The guidelines are in two parts:
- The guidelines
- Supporting information.

Since the release of these guidelines in 2009, Queensland Health has developed a suite of resources for staff to effectively address public concerns about non-communicable disease clusters. It also developed a number of fact sheets providing information for the public on common cancers and the cancer cluster assessment process. These resources are available on the Queensland Health intranet and internet websites.

1.1.1 Role of Queensland Health
The role of Queensland Health during any phase of the assessment must be determined as soon as possible after the initial inquiry or point of contact by an informant, and certainly before any other action is taken.

If Queensland Health is not the cluster assessor, it is important to determine if it has any role in the assessment. It may have a limited role determined by the scope, duration and/or reporting procedures.

For cluster assessments in which Queensland Health has a role, the cluster manager and the agency or agencies responsible for each component of the assessment must be identified as soon as possible. The role of Queensland Health is fully defined in Section 2.1.

1.1.2 Cluster management
Cluster assessment informs cluster management (Figure 1). All cluster inquiries and concerns must be managed in a timely, empathetic and effective manner, based upon best available evidence. ‘Cluster management’ is defined as the process of evaluating alternative actions, selecting options and implementing them in response to cluster assessments and related matters. It is led by the cluster manager.

Effective cluster management requires the implementation of multiple strategies in a timely manner. Cluster management incorporates scientific, technological, social, economic and political information (Figure 1). Guidelines for cluster management are beyond the scope of this document.

Cluster management is further described in Section 2.2. Before undertaking any cluster assessment, the cluster manager must be identified. The public health physician (PHP), delegate or chair of the cluster assessment team should liaise with the cluster manager as appropriate.
Queensland Health is rarely the cluster manager, except when Queensland Health facilities are involved (for example public hospitals). Another example of a site-specific cluster manager is designation of the Department of Education and Training (DET) as cluster manager for a cluster in a state school. These examples of site-specific cluster managers will usually have accountability arising from their ownership of an affected site. Some other aspects which may have a bearing on determining a cluster manager include workplace health and safety liabilities (for example, employers of the relevant workforce) or jurisdictional/legal responsibilities (for example, local government of a town). In community-based clusters, the cluster manager will be determined through discussions between Queensland Health and key organisational stakeholders.

Figure 1: Overview of cluster management and cluster assessment

Cluster Management

Cluster Assessment

Epidemiological Assessment + Hazard Assessment and exposure assessment

Assessment of community concerns, context and surrounding issues.

Note: Hazard assessment and exposure assessment are also referred to as environmental health assessment.

1.1.3 Scope of the guidelines
The Queensland Health Guidelines: Assessment of clusters of non-communicable disease 2012, have been developed for use by Queensland Health, specifically when the Division of the Chief Health Officer is the lead agency in the assessment of potential non-communicable disease clusters. In addition, these guidelines must be used for all components of cluster assessments which Queensland Health undertakes or participates in.

These guidelines do not apply to acute situations such as communicable disease outbreaks or bioterrorism events for which relevant guidelines should be followed.

1.1.4 Context for guideline development
Non-communicable disease cluster assessments very rarely identify a common cause and therefore very rarely identify ways of protecting or improving the public’s health. Cluster assessment is one strategy available to a cluster manager in addressing inquiries or public concerns about potential environmental hazards including carcinogens. Other important strategies include:

- education about the causes, frequency and patterns of disease in communities
- appraisal of the social, economic and political context of the affected community and ways of addressing these aspects
- risk communication to respond to the underlying perceptions of risk.

Most reported non-communicable disease clusters involve situations that are clearly not clusters and do not require extensive evaluation. Experience in Queensland\(^2\), other Australian states and territories, and internationally\(^3\) suggests that 75–95% of reports of clusters can be completed quickly after initial contact. These guidelines will assist staff by ensuring that a potential cluster is not overlooked, and equally that resources are not allocated to unnecessary assessments, nor are they escalated unnecessarily.

Queensland Health non-communicable disease cluster assessment guidelines 2012 6
The public image of non-communicable disease clusters is that any apparent clustering of cases in a geographical area, time period, and/or defined group of people raises the concern that a localised source of environmental hazard may be causing the problem. Public concern focuses primarily on toxic exposures, even when the suspected cluster involves a school, suburban neighbourhood or office building where the likelihood of such exposures would be no different from that in many other unaffected settings.

Cluster assessments, even when an excess number of cases are found, rarely result in important scientific findings of relationships between exposures and disease. In fact, it is claimed that the only useful cancer cluster assessments have been case series that were identified and reported by observant clinicians. There are well-known instances in which the assessment of a cluster of an unusual cancer has led to the identification of a previously unrecognised human carcinogen. These all involved clusters of a rare type of cancer in people with prolonged high-intensity exposure to an industrial/occupational or medical carcinogen, where the high exposure was identified at the time of first reporting the cluster or shortly afterwards. While assessment of single clusters is rarely fruitful, research on generalised clustering over large areas can provide information on what is ‘usual’ and generate hypotheses when areas of high and or low incidence are observed.

In Queensland, reports of potential disease clusters can come from a range of sources but usually are from a concerned individual or group, a health professional (such as a general practitioner or community health nurse), a political representative, a workplace representative or another government agency (for example, DET). These reports generally concern a workplace, school or a specific geographic area.

In recent years, about 80% of reports of non-communicable disease clusters have been related to cancer concerns. Reports of other non-communicable health events include birth defects, injury, suicide and respiratory conditions. Throughout this document the term ‘disease’ is used to cover the range of non-communicable diseases and conditions including the diverse group of diseases generally referred to as ‘cancer’.

In February 2012 the National Health and Medical Research Council (NHMRC) released a Statement on Cancer Clusters. The aim of the document was to provide the general public with information on concerns relating to the assessment and management of cancer clusters. This 2012 review of the Queensland Health Guidelines: Assessment of clusters of non-communicable disease 2009 was undertaken in consultation with Queensland Health staff and in reference to the NHMRC Statement on Cancer Clusters and international guidelines.

1.1.5 Cluster assessment
Cluster assessment is the scientific process to determine if there is an increased number of cases of a specific disease and to determine if there is a biologically plausible causal agent for the disease. That is, a cluster assessment seeks to identify if a greater-than-expected number of cases of the same or similar type of disease have occurred within a group of people in a geographic area over a specified period of time, together with a biologically plausible causal agent for the disease.

Assessment, including communication, of a non-communicable disease cluster is undertaken by a multidisciplinary team, which typically includes PHPs, epidemiologists, statisticians, environmental health officers and Integrated Communications Branch staff.

<table>
<thead>
<tr>
<th>Definitions</th>
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<tr>
<td><strong>Cluster</strong></td>
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<tr>
<td><strong>Cluster assessment</strong></td>
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These guidelines describe four types of cluster assessment (Sections 1.3, 1.4, 1.5 and 1.6). The decision to commence and also to finalise each type of assessment is based upon available evidence and is described in these sections.

A cluster assessment is comprised of two essential components:
   a) epidemiological assessment
   b) hazard and exposure assessment (also called environmental assessment).

Both components are necessary to complete a cluster assessment. Hazard assessment and exposure assessment usually focus on environmental factors as the inquiry or concern is usually an environmental agent in a neighbourhood, school or workplace causing the disease. In recognition of this, for the remainder of these guidelines this is termed ‘environmental health assessment’. However, as part of the broader process of cluster assessment, lifestyle and genetic factors should be taken into consideration because of their importance in disease causation. While these factors are of substantial importance, the primary data sources (for example, Queensland Cancer Registry) for comparing observed and expected case numbers do not enable a quantitative appraisal of these factors. It is acknowledged that, for practical reasons, no qualitative assessment of these factors is feasible when addressing an initial inquiry and only limited qualitative assessment is feasible in types 1 and 2 cluster assessment. In Type 3 assessments, more detailed qualitative assessment of lifestyle and genetic factors may be justifiable. Type 4 cluster assessments are research studies.

The principles of cluster assessment are further described in Section 2.3, case ascertainment (including case definition, inclusions and exclusions, and confirmation of cases) are described in Section 2.4, research questions in Section 2.5 and principles of causality in Section 2.6. Principles and guidelines of epidemiological assessments are described in Section 2.7. Section 2.8 details the principles and types of environmental assessment in cluster assessments, including data requirements for appraisal of environmental information. The role of communication is detailed in Section 2.9. A glossary provides the definitions for the terms used in this document (Section 2.10).

It is important to note that each of the four types of cluster assessment is an assessment in its own right. Assessment of all reported clusters generally begins with an initial inquiry from a concerned individual or group, a health professional, a political representative, a workplace representative or another government agency. During the initial phases of the assessment, key tasks for Queensland Health are to determine, based on the information provided by the informant, if the reported concerns about the disease could potentially be a cluster, and then respond appropriately to the queries and concerns of the inquirer through an open dialogue. Although the guidelines outline the components for each type of cluster assessment, occasionally it may be appropriate for some investigative elements placed in one specific cluster assessment type to occur in another cluster assessment type, or for some analytic steps to occur concurrently or be repeated as information needs evolve. Similarly, in unusual circumstances where it has been identified that there has been a significant exposure to a known hazardous agent, a rapid transition from one type of cluster assessment (for example, Type 1 inquiry response) to another type of cluster assessment (for example Type 3 analytical assessment) may need to occur. That is, the assessment process as presented in the guidelines is not necessarily a linear process in practical circumstances.

Based on Queensland Health’s past experience and available evidence nationally and internationally, most inquiries or concerns related to non-communicable disease clusters require only a brief appraisal by a PHP. In some cases, these initial inquiries or concerns may need a Type 1 assessment. Occasionally Type 2 data assessments are warranted. Type 3 analytical assessments are rarely justified, and Type 4 research study assessments are very rarely justified.
## Table 1: Features of each type of cluster assessment

<table>
<thead>
<tr>
<th></th>
<th><strong>TYPE 1 CLUSTER ASSESSMENT: INQUIRY RESPONSE</strong></th>
<th><strong>TYPE 2 CLUSTER ASSESSMENT: DATA ASSESSMENT</strong></th>
<th><strong>TYPE 3 CLUSTER ASSESSMENT: ANALYTICAL ASSESSMENT</strong></th>
<th><strong>TYPE 4 CLUSTER ASSESSMENT: RESEARCH STUDY</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purpose</strong></td>
<td>To assess whether the cases reported by the informant could potentially be a cluster</td>
<td>To assess, using existing data, whether there is an excess number of cases meeting the case definition and sufficient exposure to a biologically plausible causal agent for the type of disease reported</td>
<td>To quantify the excess of disease and undertake a detailed exposure assessment of biologically plausible causal agents</td>
<td>To investigate biologically plausible hypotheses generated by the Type 3 assessment</td>
</tr>
<tr>
<td><strong>Decision-maker</strong></td>
<td>Public health physician</td>
<td>Type 2 cluster assessment team</td>
<td>Type 3 cluster assessment team with advice from Expert Review Committee on Cluster Assessment</td>
<td>Large and specialised team</td>
</tr>
<tr>
<td><strong>Research question definition, data collection and analysis</strong></td>
<td>Use informant data on cases and exposures Use standard literature and texts Use additional existing data—Queensland Cancer Registry, routine inpatient data is rarely justified</td>
<td>Use existing data Consult literature Validate cases Ascertain complete list of cases Quantify study population Determine expected case numbers from reference population data Determine observed/expected ratio for study population Conduct environmental appraisal of setting</td>
<td>New data collected and analysed—epidemiological and/or environmental</td>
<td>New data collected and analysed—epidemiological, environmental and/or experimental</td>
</tr>
<tr>
<td><strong>Discipline/expertise required</strong></td>
<td>Assessment Public health physician +/- Director Epidemiology +/- Manager Environmental Health +/- Senior Medical Officer Environmental Health Branch +/- Integrated Communications Branch staff Cluster management Cluster manager</td>
<td>Assessment Public health physician Director Epidemiology (regional) Manager Environmental Health Integrated Communications Branch staff +/- Director Environmental Health +/- Senior Medical Officer Environmental Health Branch +/- Director Population Epidemiology Unit +/- Representatives of other stakeholder agencies or experts Cluster management Cluster manager</td>
<td>Assessment Public health physician Director Epidemiology (regional) Director and Manager Environmental Health Senior Medical Officer Environmental Health Branch Director Population Epidemiology Unit Integrated Communications Branch staff +/- Senior statistician, QCCAT and HSC +/- Representatives of other stakeholder agencies or experts Cluster management Cluster manager</td>
<td>As required</td>
</tr>
<tr>
<td><strong>Indicative level of resources</strong></td>
<td>0.5–20 person days $250–$10,000</td>
<td>10–50 person days $5000–$25,000</td>
<td>50–300 person days $25,000–$150,000</td>
<td>Very high human resource +$$$$</td>
</tr>
<tr>
<td><strong>Likely duration</strong></td>
<td>Day–months</td>
<td>Weeks–months</td>
<td>Months–year</td>
<td>Months–years</td>
</tr>
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</table>

* indicative resources excludes costs of environmental sampling and external review/advice
Figure 2: Overview of the types of cluster assessment

**TYPE 1**
- Complaint report received
- Collect basic information by phone and/or mail
  - Identify Cluster Manager
- Assess reported cases and potential exposures
  - Is further assessment needed?
    - No
    - Yes
      - Confirm Cluster Manager

**TYPE 2**
- Develop communication plan
- Consult literature
- Analyse existing data
  - Unusually high incidence and plausible causal exposure?
    - No
    - Yes
      - ENDPOINT
        - Write up findings
        - Communicate findings to informant, Cluster Manager and other stakeholders
        - Post assessment review
        - Fill in Cluster Register

**TYPE 3**
- Engage Expert Review Committee on Cluster Assessment
- Engage external advisor and/or reviewer if required
- Ascertained list of cases as practicable
- Detailed literature review
- Obtain further epidemiological and environmental health data
- Analyse all data
  - Research hypothesis
    - No
    - Yes
      - and/or

**TYPE 4**
- Complete research study
  - Epidemiological study
  - Environmental health study
1.1.6 Communication
Open communication between the informant of the suspected cluster and the teams for cluster management and cluster assessment is vital to the maintenance of transparent and trusting two-way communication throughout the assessment. A clear and consistent communication approach is required to effectively respond to the community concerns of clusters including those arising or escalating during the assessment. Communication of the cluster assessment and the findings is primarily the responsibility of the cluster manager, potentially to the affected individuals, concerned community and the media. This communication requires careful and sensitive consideration and may require input from Queensland Health Integrated Communications Branch staff and senior management. The role of communication and engagement in cluster assessment is described in Section 2.9.

1.1.7 Authority
The decision to undertake and the nature and type of assessment undertaken are decisions made by PHPs and other health practitioners. Cluster assessment should follow best practice guidelines in planning, implementation and communication.

1.1.8 Assessment approach
A step-by-step approach that follows principles of good epidemiological and environmental health research is required.12 Some key components of the assessment approach, bearing in mind that the nature and extent of these components depend on the type of cluster assessment, are:

- Establish that a concern exists.
- Understand the social, economic and political context of the reported cluster.
- Develop an appropriate case definition and adequately ascertain cases.
- Specify the potentially exposed population.
- Specify the biologically plausible causative agent.
- Quantify the period and the dose (intensity) of exposure.
- Understand the biology of the disease (that is, cellular basis, causal factors, latency, development and disease progression) and how the disease has been diagnosed.
- Collect data on all relevant environmental exposures.
- Characterise the epidemiological factors in relation to the event and undertake an exposure assessment of the relevant population.
- Look for patterns, relationships and trends.
- Formulate the hypothesis consistent with epidemiological and exposure data.
- Test the hypothesis.
- Report findings, obtain peer review and communicate results—reports of similar assessments should be sought.

There are a number of key questions to ask in a cluster assessment, acknowledging that some questions can only be answered through the detailed approach used in Type 2 or Type 3 cluster assessments:

- What are the concerns of the informant and other stakeholders? Have they been addressed?
- Given that cases have probably arisen over months or years, why have they informed us now?
- Is there a robust case definition and have all reported cases been assessed against the same definition?
- Have all cases been identified?
- Has the potentially exposed population been clearly defined?
- Are all disease cases of the same or similar type?
• Can the observed and expected number of cases in the study population be determined, taking into consideration issues relating to disease classification, diagnostic tools and reporting processes?
• Is the disease rare?
• Is there statistical evidence suggesting the number of cases in the study population exceeds the number compared to a reference population?
• Do the disease types have a known cause, whether occupational or non-occupational?
• Does this known cause exist in these particular circumstances?
• Were all the people diagnosed with the disease exposed to the known cause?
• Did the disease occur after the exposure and with an appropriate latency?
• Is the known exposure of sufficient magnitude for the disease to have occurred?
• After considering whether there are any other high or unusual common exposures, are there any other plausible occupational or non-occupational causes for the apparent cluster?
• On the weight of evidence and using sound chains of plausible reasoning, is it plausible that the group of cases occurred as a result of any of the identified exposures?
• How the nature and origins of the cluster are best explained?

Some common challenges of cluster assessment are:

• communicating effectively with the community that cluster assessment of relatively common cancers very rarely finds a biologically plausible cause
• providing key stakeholders with clear rationale and explanation for escalating or finalising the assessment
• incorporating latency periods, which may extend historically into the assessment process
• determining whether environmental testing is warranted and, if so, the nature and extent of such testing
• incorporating and explaining the role of uncertainty and chance in case development
• key stakeholder communication
• ensuring a clear and shared understanding between Queensland Health and other key stakeholders.

Reference documents for conducting environmental assessments are listed in Section 2.8. In addition, a number of supporting tools and resources developed for use by Queensland Health staff in undertaking an assessment are available on the Queensland Health intranet website. The website is updated from time to time and additional tools and resources are published as need arises.

1.1.9 Governance
Queensland Health assesses inquiries and concerns about potential clusters by using established reporting and advisory pathways (Figure 3). Section 2.3.4 details the parameters under which external advisors and reviewers are engaged.

1.1.10 Cost
Some indicative costs for each type of cluster assessment are provided in Table 1. The cost of environmental testing (if it is undertaken) and engaging external reviewers are not included in these indicative costs. It is often difficult to predict the period of time and financial costs for a cluster assessment, and the final cost is the cumulative cost incurred for each type of assessment undertaken. The financial and time costs can be considerable. For example, a 10-year study of brain cancer cases in almost 250,000 workers at Pratt & Whitney in Connecticut, USA between the years 1952 and 2001 has cost US$12 million.²²

1.1.11 Terminology
In general literature relating to clusters, there is some variation in the meanings for terms such as ‘cluster’, ‘risk’, ‘hazard’ and ‘latency’. Users of these guidelines are advised to consult the Glossary (Section 2.10) of this document for the definitions of key terms used in this document. To be
consistent with other national and international documents, cluster is defined in epidemiological terms as an ‘aggregation of cases in space and/or time, in amounts that are believed or perceived to be greater than would be expected by chance’. The identification of a cluster using this definition does not imply that there is a causal agent, because clusters of biological events do occur by chance. It does, however, indicate the need to assess whether the cluster can be related to factors other than chance. This added layer of assessment uses environmental health, toxicological and risk assessment expertise.

Figure 3: Reporting and advisory relationships of cluster assessment

1.1.12 Review
It is recommended that the Queensland Health Guidelines: Assessment of clusters of non-communicable disease 2012 is reviewed in 2014 or earlier if significant development in cluster assessment occurs. The cluster assessment resources will be reviewed periodically, consistent with evolving processes to undertake these assessments. The current version of the resources is available on the Queensland Health intranet (QHEPS) and internet websites.
1.2 Initial inquiry

In nearly all instances of suspected clusters of cancer and other non-communicable diseases, no plausible explanation is found. However, it is important that the informant’s concerns are addressed as adequately as possible at the initial phone call. The effectiveness of the initial phone interaction will have significant impact on whether further assessment and reassurance is sought and, if so, the nature, duration and scale of further assessment.

The initial inquiry about a suspected cluster may come from a concerned individual or group, a health professional (such as a general practitioner, community health nurse), a political representative, or a workplace representative. Other triggers may be a media inquiry or report. The inquiry should be directed to the PHP in the local public health unit. An initial inquiry response usually takes no more than half a day. If further assessment is required, the assessment escalates to a Type 1 assessment.

Queensland Health has developed a suite of resources to assist staff in non-communicable disease cluster assessment. They are available on the Queensland Health intranet website. The initial informant data collection form or similar, should be used to record information provided by the informant. Given the complexity of assessing and establishing a disease cluster and based on the rarity of the events, it is of utmost importance that the initial inquiry, most commonly by telephone, is addressed prudently. The following guidance may be helpful:

- **Response to phone call**: To allow time to prepare for the discussion with the informant, it is usually beneficial to advise administration or reception staff to collect contact details of the informant and a suitable time to call them back.
- **Preparation**: Prepare for the discussion with sufficient information to answer likely questions from the informant. Queensland Health’s suite of resources will be helpful in this regard.
- **Consider the context**: Is the informant a person with cancer, a close relative of a person with cancer, or a person concerned about cancer in their community? Does it involve a school, a workplace or a hospital? Have these issues been raised previously?
- **Explain**: The responding Queensland Health staff should attempt to make the initial contact an empathetic conversation with sufficient information provided to assist the informant with their inquiries and concerns. The informant may be referred to the relevant fact sheets for additional information.
- **Respond promptly**: In nearly all instances, the inquiry should be able to be satisfactorily addressed in the first conversation. In the few instances where there needs to be a progression to further assessment, attend to the informant’s concerns quickly, by phone or in person.
- **Implicate prudently**: The informant should be given sufficient information to help understand and appreciate the fact that cluster assessment is complex and often there are no simple answers that would completely satisfy everyone.
1.3 Type 1 cluster assessment: inquiry response

Type 1 cluster assessment initiates a local response when an alleged cluster is initially reported to Queensland Health.

A Type 1 cluster assessment is defined as the response to an inquiry for an alleged cluster, where the assessment undertaken by Queensland Health takes more than half a day.

 Determination of the concerns of the individual or group is a key component of cluster management. These concerns should first be clarified as described in Section 1.1 (Assessment approach), before any assessment commences.

The features of a Type 1 assessment are summarised in Table 1.

### Table 1: inquiry response

| Purpose | To assess whether the cases reported by an informant could potentially be a cluster |
| Decision maker | Public health physician |
| Research question definition, data collection and analysis | • Use informant data on cases and exposures • Use standard literature and texts • Using additional existing data, e.g. cancer registry, routine inpatient data which are rarely justified |
| Discipline/ expertise required | Cluster assessment • Public health physician • +/- Director Epidemiology • +/- Manager Environmental Health • +/- Senior medical officer Environmental Health Branch • +/- Integrated Communications Branch staff Cluster management • +/- Cluster manager |
| Indicative level of resources | 0.5–20 person days $250–$10,000 |
| Likely duration | Day–months |

#### 1.3.1 Initiating a Type 1 cluster assessment — briefing

- If the focus of the cluster inquiry involves a Queensland Government facility the Queensland Health Executive Director, Health Protection Directorate (ED HPD) should be notified in writing as soon as possible after the assessment is initiated. The ED HPD should notify the Chief Health Officer or Director-General, as appropriate, of the cluster inquiry.
- If the cluster inquiry is likely to attract substantial public concern or media interest, the ED HPD should be notified in writing. The degree of public concern or media interest may need to be assessed.
- Inform Queensland Health Integrated Communications Branch in both situations.

#### 1.3.2 Conducting the Type 1 cluster assessment

Type 1 cluster assessment requires expert judgement of the reported situation by the PHP. The PHP may seek the expertise of the regional Director Epidemiology and Manager Environmental Health, and the Senior Medical Officer Environmental Health Branch, and/or Integrated Communications Branch staff.

An assessment is Type 1 if it involves at least a half a day’s work by Queensland Health staff

The PHP will identify the cluster manager and determine whether to engage the cluster manager. If the cluster manager is engaged, they will be provided with these guidelines.
The principal data source for a Type 1 assessment is the informant data on cases and exposures. A Type 1 assessment does not involve detailed examination of the literature, and data collected beyond that provided by the initial informant is rarely justified. Using the 'Initial informant data collection form’ or similar for a Type 1 assessment, collect sufficient information from the informant and standard literature and texts to decide:

- How many diagnoses of the same type are there?
- Who are the people in the study population?
- Does the number of reported cases appear to be more than would be expected for the study population?
- Do there appear to be any unusual or high exposures to a biologically plausible causal agent for the diseases?
- Who is the cluster manager?
- Who are the stakeholders?

A Type 1 cluster assessment generally will not require any quantitative epidemiological assessment to determine if there is or is not a potential excess number of cases given the size and demographic profile of the population. Expected case numbers can be drawn from expert knowledge or from published literature including Queensland Health’s report of the Chief Health Officer19 or Queensland Cancer Registry documents. Observed case numbers are based upon information provided by the informant.

Many Type 1 cluster assessments require only a brief appraisal by an experienced PHP, which may include consultation with epidemiology and/or environmental health colleagues.

In a Type 1 assessment, exact rates of the disease in question within the study population are not calculated. Similarly, quantitative comparison of observed and expected rates is rarely justifiable. If on a rare occasion a comparison of rates is justified, determining person-years of exposure will be beyond scope. In order to determine the denominator for the observed rate, a broader population (such as geographic area or large age group) rather than that identified by the informant (such as a specific workforce population) should be used. For example, if there is concern about elevated cases of brain cancer in staff at a school, the approach may be to select a geographic area around the school and using the most recent available data from the Queensland Cancer Registry for that area, estimate the expected number of cases in a group of people aged, for example, 50 years and older, and then followed up for 10 years.

Type 1 cluster assessment does not require medical confirmation of the disease being assessed, nor verification with the Queensland Cancer Registry if the assessment relates to cancer.

At this stage, the PHP will consider any known or suggested biologically plausible causative agents, whether they exist in the community of the alleged cluster, and whether there have been reports of association with this type of cancer. During the assessment, the informant’s perception of possible exposure linked to the disease should be sought. Descriptions of the environment of the affected population including nearby industrial activities and workplace occupational activities should be detailed, taking into account the type of the disease.

Type 1 cluster assessment requires a brief environmental appraisal, which takes into consideration the site history and, if necessary, a physical inspection conducted by an environmental health or occupational health professional.

Communication is an integral part of cluster assessment and management. The role of communication and engagement in a cluster assessment is described in Section 2.9.
1.3.3 Decision points for the Type 1 assessment

The decision to finalise a Type 1 cluster assessment is made by the PHP or delegate (Table 2). Approval from a higher officeholder is not required. If the inquiry or concern relates to cases or exposures spread across PHU boundaries, then the PHP may consult with others to reach a decision. The consultation may include other PHPs as well as epidemiology and environmental health professionals.

The decision to finalise a Type 1 cluster assessment or, alternatively, seek to undertake a Type 2 cluster assessment, is made by the PHP, based on expert multidisciplinary knowledge and taking into account both epidemiological and environmental aspects. Criteria to either finalise or undertake a Type 2 cluster assessment are case-specific, and should be based upon consideration of all the criteria in Table 2. It is noted that a Type 2 cluster assessment may be undertaken to address community concerns rather than solely on the basis of evidence of a potential cluster.

The decision to undertake further assessment must also consider these questions:

- Have the concerns of the informant been addressed?
- Have necessary public health actions been taken?
- Is further assessment feasible and likely to answer any remaining questions?
- If further assessment is not warranted or feasible, what other actions could be undertaken to address community concerns?

Table 2: Decision making at conclusion of Type 1 assessment

<table>
<thead>
<tr>
<th>Criteria to finalise Type 1 cluster assessment:</th>
<th>Criteria to undertake a Type 2 cluster assessment:</th>
</tr>
</thead>
<tbody>
<tr>
<td>no apparent excess number of cases given the demographic profile of the population</td>
<td>apparently higher than expected number of cases given the demographic profile of the population</td>
</tr>
<tr>
<td>small numbers of a common disease for the study population</td>
<td>unusual types of disease</td>
</tr>
<tr>
<td>different diseases</td>
<td>plausible exposures to a plausible causal agent for the reported disease likely to be present</td>
</tr>
<tr>
<td>clearly unlikely to be sufficient exposure to a biologically plausible causal agent to account for the number of cases of the disease reported</td>
<td>adequate latency for the reported disease</td>
</tr>
<tr>
<td>clearly inadequate latency period based on available evidence</td>
<td>identification of multiple cases of a rare disease, or a common one in an unusual age group</td>
</tr>
</tbody>
</table>

1.3.4 Finalisation of a Type 1 cluster assessment

Four key steps are required for the finalisation of a Type 1 cluster assessment:

**Communication**

Following the decision to finalise a Type 1 cluster assessment, a response outlining the decision and rationale should be provided by the PHP to the original informant, cluster manager and other key stakeholders, as required. The response can be provided by telephone, followed by a written report, if it is considered necessary. If a written report is prepared, it should be provided to the informant and other key stakeholders, if appropriate. The response needs to be clearly articulated, empathetic, and based upon communication and engagement strategies as described in Section 2.9. The response could include information about the alleged cluster, general information on disease clusters including fact sheets and preventive health messages, if deemed appropriate.
Documentation
A file note should be prepared that outlines details of:
- the initial inquiry or concern
- the data considered in the cluster assessment including any epidemiological, environmental or toxicological aspects
- any broader public concern or potential for high-level public concern
- communication with the informant (refer to Communication section above).

The file note and written report, if prepared, are usually sufficient documentation for a Type 1 cluster assessment. Other formal documentation is generally not required for a Type 1 cluster assessment. Reports from previous Type 1 cluster assessments can be used as a guide for the preparation of assessment documentation.

Briefing
If the cluster inquiry is likely to attract substantial public concern, the ED HPD should be notified in writing at the finalisation of the assessment. Queensland Health Integrated Communications Branch must be informed of the finalisation of the assessment. The briefing to the ED HPD should include the written response to the informant and other key stakeholders and the assessment report, if prepared.

Cluster assessment register
The PHP will ensure the details of the assessment including a record of decisions and actions are entered into the cluster assessment register (see Section 1.7) held by Population Epidemiology Unit, Division of the Chief Health Officer, Queensland Health.
1.4 Type 2 cluster assessment: data assessment

A Type 2 cluster assessment is approved and initiated based on the ‘Criteria to undertake a Type 2 assessment’ in Table 2. A Type 2 cluster assessment involves a multidisciplinary team and uses existing epidemiological and environmental health data sources to assess whether:
- there is an excess of cases meeting the case definition
- there has been sufficient exposure to a biologically plausible causal agent for the type of disease reported.

1.4.1 Briefing and approval to initiate the Type 2 cluster assessment

- If the focus of the cluster inquiry involves a Queensland Government facility, the ED HPD should be notified in writing as soon as possible after the assessment is initiated. The ED HPD should notify the Chief Health Officer or Director-General, as appropriate, of the cluster inquiry. If a Type 1 assessment has already been conducted, further notification may not be necessary.
- If there is likely to be substantial public concern or media interest the ED HPD should similarly be notified in writing. The degree of public concern or media interest may need to be assessed.
- Queensland Health Integrated Communications Branch must be informed.
- The ED HPD must provide written approval prior to undertaking a Type 2 cluster assessment. The request for approval should include the following:
  - rationale for proceeding to a Type 2 assessment
  - why Queensland Health should be involved
  - nature of Queensland Health's role, scope, duration and reporting processes
  - human and financial resource requirements and options for adequate resource allocation including potential position backfill
  - potential opportunity costs.
- The Expert Review Committee on Cluster Assessment should be notified of the initiation of the Type 2 cluster assessment by the Director Population Epidemiology Unit.

<table>
<thead>
<tr>
<th><strong>Type 2: data assessment</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purpose</strong></td>
</tr>
<tr>
<td><strong>Decision maker</strong></td>
</tr>
</tbody>
</table>
| **Research question definition, data collection and analysis** | - Use existing data  
- Consult literature  
- Validate cases  
- Ascertained complete list of cases  
- Quantify study population  
- Determine expected case numbers from reference population data  
- Determine observed/expected ratio for study population  
- Conduct environmental appraisal of setting |
| **Discipline/expertise required** | Cluster Assessment  
- PHP  
- Director Epidemiology (regional)  
- Manager Environmental Health  
- Integrated Communications Branch  
- +/- Director Environmental Health Branch  
- +/- Senior Medical Officer Environmental Health Branch  
- +/- Director Population Epidemiology Unit  
- +/- Representatives of other stakeholder agencies or experts  
Cluster Management  
- Cluster Manager |
| **Indicative level of resources** | 10–50 person days  
($5000–$25,000) |
| **Likely duration** | Weeks, months |
1.4.2 Role of Queensland Health
The role of Queensland Health as cluster assessor (epidemiological and/or environmental health assessor) must be determined before initiation of the Type 2 cluster assessment. If Queensland Health is not the cluster assessor for both the epidemiological and environmental health components, then it is important to determine which agency is the cluster assessor and if Queensland Health has any role in the assessment. If it does have a role, the scope, duration and reporting procedures associated with that role should be determined.

As stated in the Overview, these guidelines apply to situations where Queensland Health is the lead agency in the cluster assessment of non-communicable disease. In addition, Queensland Health requires the use of these guidelines for all components of cluster assessments which it undertakes or participates in.

1.4.3 The Type 2 cluster assessment team
The principal role of the Type 2 cluster assessment team (T2CAT) is to manage and undertake the process and the science of the assessment, as defined in Table 3. The membership of the T2CAT must be confirmed before the assessment begins. Initially the T2CAT should discuss and clarify the roles and responsibilities of the team and of individual team members. The T2CAT reports to the ED HPD (Figure 3).

The T2CAT should comprise the following Queensland Health officers (or delegates):
- PHP
- Director Epidemiology (regional)
- Manager Environmental Health and Director Environmental Health Branch if appropriate
- Integrated Communications Branch staff
- Senior Medical Officer Environmental Health Branch, if appropriate
- Director Population Epidemiology Unit, if appropriate
- Representatives of other stakeholder agencies, for example, relevant local government agency (LGA), Department of Environment and Resource Management (DERM), Department of Employment and Industrial Relations (DEIR), if appropriate
- Additional experts, as required.

The roles and responsibilities of the T2CAT are described below:
- **PHP** is to chair and coordinate the T2CAT and ensure that resources to undertake the assessment are identified and managed. The role of the chair can be delegated by the PHP to another team member. The chair can also delegate specific tasks to T2CAT members or other experts as required.
- **Public Health Unit staff** are to:
  - coordinate and undertake designated components of the assessment
  - liaise with the community
  - undertake statistical analysis for the assessment with Health Statistics Centre (HSC) advice and assistance as required.
- **Other Division of the Chief Health Officer staff** are to provide expert epidemiology, environmental health and toxicology advice.
- **Integrated Communications Branch staff** are to develop and implement the cluster-specific communication plan.

A Type 2 cluster assessment is conducted by the T2CAT with the assistance of the Queensland Cancer Control Analysis Team (QCCAT) and HSC. QCCAT is to provide advice to the T2CAT regarding:
- epidemiological data analysis and statistical interpretation
- availability and limitations of relevant data (mortality, cancer registry, perinatal, and population data for the relevant denominators).

Where necessary, the T2CAT may seek advice from the Expert Review Committee on Cluster Assessment.
1.4.4 Conducting the Type 2 cluster assessment

Management and implementation of the process and the science of the assessment is undertaken by the T2CAT. The process and the science of the assessment are defined in Table 3. In line with the principles for cluster assessment (Section 2.3), a Type 2 cluster assessment should include (as required by the case definition and research questions):

- a literature review of the biology of, and risk factors for, the disease including the latency and natural history of the primary disease considered, how these relate to the reported period of exposure and the period when the cases of disease were diagnosed
- a review of the epidemiological information of the study population to ascertain if a statistical excess has occurred. Principles of epidemiological analysis for this type of cluster assessments are described in Section 2.7
- an environmental health assessment of agents and exposures to determine if there is a biologically plausible causal process (that is, plausible agent and significant exposure) for the cluster of a specific disease. For this type of assessment an appraisal of the setting is required and limited environmental sampling may be justified. This environmental appraisal involves consideration of the site history and a site inspection by an experienced, expert environmental health or occupational health professional. If these provide evidence of potential problems, environmental sampling may be warranted. Environmental and/or other scientific sampling should only be conducted by Queensland Health if there is a clear and defined rationale and sampling plan, with appropriate resource allocation (Section 2.8).

There are numerous documents which can assist the appraisal of epidemiological, environmental health and toxicological evidence in a cluster assessment. Several key documents are listed in Section 2.8. These components should be considered to be complementary in a cluster assessment. They must address the overall goals of a cluster assessment, be well-integrated and conducted according to the type of assessment. Use the ‘S009A – Secondary data collection form for suspected cancer cases (Type 1)’ or ‘S009b – Enhanced data collection on potential cases (Type 2 and 3)’, as appropriate. These forms are available on QHEPS.

**Table 3: The process and analytic actions of a Type 2 cluster assessment**

<table>
<thead>
<tr>
<th>Process</th>
<th>Analytic actions.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Confirm the person in the role of cluster manager, and provide them with the Queensland Health guidelines for cluster.</td>
<td>• Develop a case definition describing the disease/condition, geographical area, population group and time period.</td>
</tr>
<tr>
<td>• Confirm the epidemiological and environmental health cluster assessors.</td>
<td>• Determine the research questions (Section 2.5).</td>
</tr>
<tr>
<td>• Continuously review the endorsed plan for the cluster assessment, including roles, responsibilities (including report writing), timelines, communication and resources required (human, time, funds), and seek approval from the ED HPD for any significant modifications to the original plan.</td>
<td>• Specify the study population.</td>
</tr>
<tr>
<td>• ED HPD to ensure adequate staff and resources are available to undertake assessment. An assessment may require a dedicated project officer.</td>
<td>• Scope and plan the assessment including case ascertainment (Section 2.4) and study population determination methods and available sources of epidemiology, toxicology, environmental health and other scientific data.</td>
</tr>
<tr>
<td>• Develop and implement a communication plan (Section 2.9).</td>
<td>• Assess epidemiology and environmental health using literature and existing data sources.</td>
</tr>
<tr>
<td>• Senior officers (ED HPD, Director Environmental Health Branch, senior director of relevant Regional Health Service) should be kept informed of progress at each step in this assessment.</td>
<td>• Conduct environmental appraisal of setting to determine any links with biologically plausible causative agent.</td>
</tr>
<tr>
<td></td>
<td>• Interpret data and results and prepare scientific reports.</td>
</tr>
</tbody>
</table>

1.4.5 Decision points for the Type 2 cluster assessment

The criteria for a decision to either finalise the Type 2 cluster assessment or undertake a Type 3 cluster assessment should be based on expert multidisciplinary knowledge and must take both epidemiology and environmental aspects into account (Table 4). The decision should consider all
the criteria in Table 4 and should be decided by the T2CAT. The decision to undertake further assessment must also consider:

- Have the concerns of the informant been addressed?
- Have necessary public health actions been taken?
- Is further assessment feasible and likely to answer any remaining questions?
- If further assessment is not warranted or feasible, what other actions could be undertaken to address community concerns?

<table>
<thead>
<tr>
<th>Criteria to finalise the Type 2 cluster assessment:</th>
<th>Criteria to undertake a Type 3 cluster assessment:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- taking into account biological processes including latency periods, no excess number of cases beyond what would be expected by chance alone for the study population</td>
<td>- an unusually high incidence of cases based on data from existing data sources</td>
</tr>
<tr>
<td>- lack of sufficient exposure to a biologically plausible causal agent for the disease reported.</td>
<td>- a biologically plausible cause identified and sufficient exposure appears likely: a Type 3 cluster assessment should not be undertaken if no likely sufficient exposure pathways or biologically plausible causal agents identified</td>
</tr>
<tr>
<td></td>
<td>- practicability of further assessment</td>
</tr>
<tr>
<td></td>
<td>- new evidence about causation or methods of assessment become available.</td>
</tr>
</tbody>
</table>

Table 4: Decision making at conclusion of Type 2 assessment

Approval to undertake a Type 3 cluster assessment must be obtained from the ED HPD before proceeding. The proposal requesting approval to undertake a Type 3 cluster assessment must contain the following:

- rationale for escalation
- work plan for the Type 3 cluster assessment outlining questions, scope and timelines and resource requirements.

1.4.6 Finalisation of the Type 2 cluster assessment

Governance to finalise the Type 2 cluster assessment
The decision to finalise the Type 2 cluster assessment is made by the T2CAT which is chaired by the PHP. Approval for this decision should be obtained from the ED HPD.

The Type 2 cluster assessment report
A final report for the Type 2 cluster assessment should include the following:

- rationale for the epidemiological and environmental assessments undertaken and for any external advice sought
- an uncertainty analysis including assessment of potency of the agent, exposure, latency of agent, case ascertainment and population at risk
- on the weight of evidence, findings from the assessment
- statement of impact if further cases are reported after finalisation of the assessment.

It may be necessary to undertake an internal review prior to release of the report. This review may be done by relevant Queensland Health staff not involved in the assessment. In addition, external review may be required, based on the results of the assessment and the social, economic and political implications and interests in the report. External review should be initially undertaken by the Expert Review Committee on Cluster Assessment (Section 1.5.5). Should further external expert review be required, the process outlined in Section 2.3.4 for the engagement of an external reviewer should be undertaken.

The report must be approved by ED HPD prior to public release. The ED HPD will forward the report to the cluster manager. In addition, an estimate of resources used in the Type 2 cluster assessment (staff time and financial) should be articulated.

Previous reports of Type 2 cluster assessments can be consulted when preparing the report.

Briefing to finalise the Type 2 cluster assessment

Queensland Health non-communicable disease cluster assessment guidelines 2012 22
Following the decision to finalise the assessment, a Briefing Note for information to the Minister for Health, the Director-General, the Chief Health Officer, ED HPD, Senior Director Environmental Health Branch, senior directors of relevant Public Health Units should be prepared providing information on:

- the scope, processes and findings of the assessment, including provision of the Type 2 cluster assessment report
- reasons for finalisation
- implementation of the communication plan.

Also consider briefing and providing reports for information to:

- political representatives for the affected area
- local government libraries.

**Communication of the Type 2 cluster assessment report**

- Integrated Communications Branch staff, as members of the T2CAT, will develop and implement the communication plan. This will be developed at the beginning of the Type 2 cluster assessment and include information which should guide the release of the Type 2 cluster assessment findings to the affected and the wider communities (Section 2.9). The communication needs to be trustworthy and empathetic, and include a response about the specific alleged cluster as well as general information on disease clusters. The explanation of the assessment should be written in plain English.
- The findings of the report should be provided prior to public release to key external stakeholders identified in the communication plan, including:
  - affected individuals, groups and communities, as well as the original informant and possibly the wider community
  - relevant health workers in the affected area
  - representatives of other stakeholder agencies (for example LGA, DERM, DET, DEIR) in the affected area.

**Assessment Register**

The T2CAT should ensure the details of decisions, actions and any scientific reports are recorded in the cluster assessment register (Section 1.7).

**Other communication to finalise the Type 2 cluster assessment**

A team meeting should be held with the T2CAT to ensure that learning from the process are discussed and captured through the other communication and briefing activities.
1.5 Type 3 cluster assessment: analytical assessment

A Type 3 cluster assessment is approved and undertaken based on the criteria to undertake a Type 3 assessment in Table 4. A Type 3 cluster assessment involves a multidisciplinary team using information and reviews from previous assessments as well as collecting and analysing new data. The purpose of a Type 3 cluster assessment is to quantify the excess of disease and undertake a detailed exposure assessment of biologically plausible causal agents.

The criteria required to undertake a Type 3 cluster assessment are rarely satisfied, and therefore this level of assessment is rarely undertaken.

1.5.1 Briefing and approval to initiate the Type 3 cluster assessment

- If a Queensland Government facility is the focus of the cluster inquiry, the ED HPD should be notified in writing as soon as possible after the assessment is initiated to ensure the Minister for Health is also notified. If a Type 1 or Type 2 assessment has already been conducted, further notification may not be necessary.
- If there is likely to be substantial public concern or media interest the ED HPD should similarly be notified in writing. The degree of public concern or media interest should be assessed.
- Queensland Health Integrated Communications Branch must be informed.
- A detailed report must be submitted to the ED HPD for approval prior to undertaking a Type 3 cluster assessment. The report must address the following issues:
  - Queensland Health’s involvement
  - nature of Queensland Health’s role, scope, duration, reporting processes, resources required and budget allocation
  - reasons for proceeding with assessment.
- The Expert Review Committee on Cluster Assessment should be notified by the Director Population Epidemiology Unit of the initiation of the Type 3 cluster assessment.

<table>
<thead>
<tr>
<th>Discipline/ expertise required</th>
<th>Cluster Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Public Health Physician</td>
<td></td>
</tr>
<tr>
<td>- Director Epidemiology</td>
<td></td>
</tr>
<tr>
<td>- Director and Manager Environmental Health</td>
<td></td>
</tr>
<tr>
<td>- Senior Medical Officer Environmental Health Branch</td>
<td></td>
</tr>
<tr>
<td>- Director Population Epidemiology Unit</td>
<td></td>
</tr>
<tr>
<td>- Integrated Communications Branch staff</td>
<td></td>
</tr>
<tr>
<td>- +/- Senior statistician, QCCAT and HSC</td>
<td></td>
</tr>
<tr>
<td>- +/- Representatives of other stakeholder agencies or experts</td>
<td></td>
</tr>
<tr>
<td>- Cluster Management</td>
<td></td>
</tr>
<tr>
<td>- Cluster manager</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type: analytical assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purpose</td>
</tr>
<tr>
<td>Decision maker</td>
</tr>
<tr>
<td>Research question definition, data collection and analysis</td>
</tr>
<tr>
<td>Indicative level of resources</td>
</tr>
<tr>
<td>Likely duration</td>
</tr>
</tbody>
</table>

1.5.2 Role of Queensland Health

The role of Queensland Health as cluster assessor (that is, as epidemiological and/or environmental health assessor) must be determined at the initiation of the assessment. If Queensland Health is not leading the assessment then it is important to determine if it has a role in the assessment and, if so, the scope, duration and reporting procedures for that role.

As stated in the Overview, these guidelines apply to situations where Queensland Health is the lead agency in the cluster assessment of non-communicable disease. In addition, Queensland
Health requires the use of these guidelines for all components of cluster assessments which it undertakes or participates in.

### 1.5.3 The Type 3 cluster assessment team

The principal role of the Type 3 cluster assessment team (T3CAT) is to manage the process and the science of the assessment as described in Table 5. The membership of the T3CAT must be confirmed before the assessment begins. Initially the T3CAT should discuss and clarify roles and responsibilities of the team and of individual team members. The T3CAT reports to the ED HPD Cost

Some indicative costs for each type of cluster assessment are provided in Table 1. The cost of environmental testing (if it is undertaken) and engaging external reviewers are not included in these indicative costs. It is often difficult to predict the period of time and financial costs for a cluster assessment, and the final cost is the cumulative cost incurred for each type of assessment undertaken. The financial and time costs can be considerable. For example, a 10-year study of brain cancer cases in almost 250,000 workers at Pratt & Whitney in Connecticut, USA between the years 1952 and 2001 has cost US$12 million.\(^\text{16}\)

**Terminology**

In general literature relating to clusters, there is some variation in the meanings for terms such as ‘cluster’, ‘risk’, ‘hazard’ and ‘latency’. Users of these guidelines are advised to consult the Glossary (Section 2.10) of this document for the definitions of key terms used in this document. To be consistent with other national and international documents, cluster is defined in epidemiological terms as an ‘aggregation of cases in space and/or time, in amounts that are believed or perceived to be greater than would be expected by chance’.\(^\text{17}\) The identification of a cluster using this definition does not imply that there is a causal agent, because clusters of biological events do occur by chance. It does, however, indicate the need to assess whether the cluster can be related to factors other than chance.\(^\text{17}\) This added layer of assessment uses environmental health, toxicological and risk assessment expertise. Initially, the T3CAT should discuss, clarify and confirm membership of the team, as well as the roles and responsibilities of individual team members.

The T3CAT should comprise the following Queensland Health officers (or delegates):

- PHP
- Director Epidemiology (regional)
- Director and Manager Environmental Health Branch
- Senior Medical Officer Environmental Health Branch
- Director Population Epidemiology Unit
- Integrated Communications Branch staff
- Senior statistician, QCCAT and HSC representative, as required
- Representatives of other agencies (such as LGA, DERM, DET, DEIR), as required
- Additional experts, as required.

The roles and responsibilities of T3CAT are described below:

- **PHP** is to chair and coordinate the T3CAT and ensure that resources to undertake the assessment are identified and managed. The role of the chair can be delegated by the PHP to another team member. The chair can also delegate specific tasks to T3CAT members or other experts as required.

- **Public Health Unit members** are to:
  - coordinate and undertake designated components of the assessment
  - liaise with the responsible physician/s if case verification is required
  - identify required epidemiological analysis, obtain data required for such analysis and liaise with HSC
  - liaise as required with appropriate experts for the toxicological and other aspects of the environmental health assessment
  - liaise with the community and media.
• **Integrated Communications Branch staff** are to develop and implement the communication plan.

• **Senior Medical Officer Environmental Health Branch** is to provide advice to the T3CAT regarding:
  - potential causative agents and toxicological properties
  - routes of potential exposure
  - potential biological monitoring requirements.

• **Director Population Epidemiology Unit** is to provide advice to the T3CAT regarding epidemiological data analysis and interpretation from a public health perspective, and cluster assessment reporting.

• **Senior statisticians, QCCAT and HSC** are to provide or facilitate T3CAT provision of:
  - expert advice on data analysis and statistical interpretation
  - advice on availability and limitations of relevant data (mortality, cancer registry, perinatal, and population data for denominators)
  - coordination of the detailed descriptive analysis and verification of cases in the relevant data collection (that is for cancer in the Queensland Cancer Registry or for birth defects in the Perinatal Data Collection)
  - statistical analysis.

Before committing to undertake a Type 3 cluster assessment, consideration must be given to backfilling of key positions such as the PHP and Director Epidemiology (regional). Furthermore, it may be necessary to recruit a suitably qualified senior project officer to assist the T3CAT.

### 1.5.4 Conducting the Type 3 cluster assessment

Management and implementation of the process and the science of the assessment is undertaken by the T3CAT. The process and the science of the assessment are defined in Table 5. In line with the principles for cluster assessment (Section 2.3), a Type 3 cluster assessment should include (as required by the case definition and research questions):

- a literature review of the biology of the disease to include the latency and natural history of the cancer, and how these relate to the period of exposure and the period when the cancers were diagnosed
- a review of the epidemiology to determine if a statistical excess has occurred (principles of epidemiological analysis of cluster assessments are described in Section 2.7)
- an environmental health and toxicological assessment to build on the data collected in the Type 2 cluster assessment and may include more detailed reviews of the literature concerning hazard assessment (Section 2.8 hazard identification and dose–response assessment). If required, environmental sampling will be recommended. Environmental testing by Queensland Health Forensic and Scientific Services may be most cost effective. However judgement should be made based on the need for credibility associated with independent testing. Limited environmental sampling using external consultants will cost at least $5,000–$30,000. Extensive sampling will cost considerably more.

There are numerous documents which support the appraisal of epidemiological, environmental health and toxicological evidence in a cluster assessment with several key documents listed in Section 2.8. These epidemiological and environmental health assessments must be complementary in a cluster assessment. They must address the overall goals of a cluster assessment, be well-integrated and conducted according to the type of the assessment.
Table 5: The process and analytic actions of a Type 3 cluster assessment

<table>
<thead>
<tr>
<th>Process</th>
<th>Analytic actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Confirm the Cluster Manager, and provide these Guidelines if they have not already been provided.</td>
<td>• Review and adapt, as appropriate, the case definition developed in the Type 2 cluster assessment.</td>
</tr>
<tr>
<td>• Confirm the epidemiological and environmental health cluster assessors.</td>
<td>• Determine the research questions (Section 2.5).</td>
</tr>
<tr>
<td>• Develop a detailed plan that includes roles, responsibilities(including report writing), timelines, communication and resources required (human, time, cost) before Type 3 cluster assessment proceeds</td>
<td>• Conduct a detailed literature review to assess the natural history of the disease, the toxicology of relevant agents and their environmental behaviour, and the epidemiological plausibility of the association with an exposure</td>
</tr>
<tr>
<td>• Provide detailed plan to ED HPD</td>
<td>• Scope and plan the assessment including possible sources of epidemiology, toxicology, environmental health and other scientific and data gathering processes to answer the research questions.</td>
</tr>
<tr>
<td>• ED HPD to ensure adequate staff and resources are available to undertake assessment</td>
<td>- Review methods for case ascertainment (Section 2.4).</td>
</tr>
<tr>
<td>• Assess community perceptions, concerns, reactions and needs</td>
<td>- Specify the study population</td>
</tr>
<tr>
<td>• Develop and implement a communication plan at the commencement of the Type 3 cluster assessment which guides communication with external stakeholders, including the affected individuals as well as the affected and wider communities, during the assessment (Section 2.9).</td>
<td>- Use exposure assessment (as described by the enHealth Environmental Health Risk Assessment Guidelines20) in the design of any environmental sampling (for further information see Section 2.8).</td>
</tr>
<tr>
<td>• Liaise with the Expert Review Committee on Cluster Assessment</td>
<td>- Use environmental sampling regimes that outline the rationale for chosen analytes, how the quality of the data will be ensured and processes for interpreting and managing results</td>
</tr>
<tr>
<td>• Conduct debriefing and evaluation of cluster assessment</td>
<td>- In epidemiological and environmental assessments, consider potential cause and effect relationships (Section 2.6) and weight of evidence for matters such as carcinogenicity in choosing analytes.</td>
</tr>
<tr>
<td></td>
<td>• Verify cases and study population</td>
</tr>
<tr>
<td></td>
<td>• Collect, analyse and interpret data and results and prepare scientific reports</td>
</tr>
</tbody>
</table>

1.5.5 Expert Review Committee on Cluster Assessment

The Expert Review Committee on Cluster Assessment provides advice on all Type 3 cluster assessments regarding:

- the methodology for epidemiology, environmental health, toxicology
- interpretation and reporting of results.

The Expert Review Committee on Cluster Assessment provides advice to the ED HPD and the T3CAT (Figure 3). The committee is comprised of Queensland Health and external agency members who have expert knowledge in assessing cancer and other non-communicable disease clusters. The committee is chaired by the ED HPD. Committee meetings should be attended by the chair, the T3CAT, as well as other relevant Queensland Health staff members such as Integrated Communications Branch staff and Population Epidemiology Unit staff to discuss related specific assessments. In addition, Queensland Health staff who are not members of the committee may attend as observers and provide information to the committee, as required.

Committee membership includes the following expertise:

- epidemiological analysis and interpretation
- public health medicine
- toxicology
- environmental science
- statistical analysis.
1.5.6 Engaging advisers for the T3CAT
External advisors may be engaged to provide specialist advice to the T3CAT and/or the Expert Review Committee on Cluster Assessment (Figure 3). The external advisors will provide specific specialist advice, for example, on epidemiology, environmental health, toxicology, or communication issues. The rationale for seeking external advice and the nature of the advice sought must be clearly documented.

1.5.7 External reviewer
External reviewers are not used routinely but may need to be engaged where:
- there is heightened or intense community concern, anxiety or distress
- the assessment is particularly complex
- cluster management processes are likely to be controversial.

Depending on the nature and complexity of the assessment, and the breadth of skills of the external reviewer, more than one reviewer may be required. The role of the external reviewer is to:
- review the methodologies used for the epidemiology, environmental health and toxicology components
- review the reporting of results
- provide informed and independent comment to media and/or the general and wider communities, if required.

An external reviewer will be expected to have experience and expertise in cluster assessment and in fields relevant to the cluster assessment. It is also expected they have excellent communication skills. With the advice of the T3CAT, the ED HPD may appoint an external reviewer who may be from another government agency, interstate health department, non-government organisation or an academic institution. If appointed, the external reviewer shall report to the T3CAT (Figure 3).

1.5.8 Decision points for the Type 3 cluster assessment
The decision to finalise the Type 3 cluster assessment or recommend areas of research under the Type 4 cluster assessment (research study) is made by the T3CAT. The T3CAT should seek advice from the Expert Review Committee on Cluster Assessment, with the decision endorsed by the ED HPD. Criteria to either finalise or recommend areas of research are case specific (Table 6).

The decision to undertake research must also consider the following elements:
- Have the concerns of the informant been addressed?
- Have necessary public health actions been taken?
- Is further assessment feasible and likely to answer any remaining questions?
- If further assessment is not warranted or feasible, what other actions could be undertaken to address community concerns?

Table 6: Decision-making at conclusion of Type 3 assessment

<table>
<thead>
<tr>
<th>Criteria to finalise the Type 3 cluster assessment include:</th>
<th>Criteria to undertake a Type 4 cluster assessment (research study) include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>taking into account the natural history of the disease including latency periods, no excess number of cases beyond what would be expected by chance alone for the study population</td>
<td>new data on the causes of the relevant disease becomes available</td>
</tr>
<tr>
<td>lack of sufficient exposure to a biologically plausible causal agent for the type of disease reported.</td>
<td>Type 3 cluster assessment indicates a reasonable likelihood of biologically plausible and sufficient causal exposure for which clarification is required and practicable</td>
</tr>
<tr>
<td></td>
<td>research hypotheses can be generated which are answerable by epidemiological and/or environmental health studies</td>
</tr>
</tbody>
</table>

Approval to undertake a Type 4 cluster assessment must be obtained from the ED HPD before proceeding. Approval is based upon a proposal to undertake a Type 4 cluster assessment containing the following:
• rationale for recommendation, including overview of the research questions to be answered
• proposed role of Queensland Health
• Queensland Health resource requirements, if applicable
• a work plan for the study which outlines the questions, scope and timelines, if applicable.

Approval recommending areas of research must be granted from the ED HPD before proceeding to a Type 4 cluster assessment.

1.5.9 Finalisation of the Type 3 cluster assessment

Governance to finalise the Type 3 cluster assessment
The decision to finalise the Type 3 cluster assessment is made by the T3CAT which is chaired by the PHP. Approval of this decision should be obtained from the ED HPD.

The Type 3 cluster assessment report
The final report should be prepared and endorsed by the T3CAT. It should withstand assessment according to the relevant sections of Chapter 10 ‘Appraisal of assessment’ of the Environmental health risk assessment guidelines. The report should include the following:
• rationale for the epidemiological and environmental assessments undertaken and any external advice sought
• uncertainty analysis including assessment of potency of the agent, exposure, latency of agent, case ascertainment and population at risk, and which may include sensitivity analysis on the weight of evidence and findings from the assessment
• statement of possibilities if further cases are reported after the period of assessment.

If the T3CAT have not already done so, the ED HPD may seek review by the Expert Review Committee on Cluster Assessment including an:
• internal review by relevant Queensland Health staff not involved in the assessment and/or
• review by an external reviewer.

The report must be endorsed by the ED HPD prior to public release. The ED HPD will forward the report to the cluster assessor and cluster manager (if these positions are not undertaken by Queensland Health) and the Expert Review Committee on Cluster Assessment.

In the report, an estimate of resources used to undertake the Type 3 cluster assessment, detailing staffing requirements, time requirements and financial costs should be articulated.

Previous Type 3 cluster assessment reports should be consulted.

Briefing to finalise the Type 3 cluster assessment
Following the decision to finalise the assessment, a Briefing Note for information to Minister for Health, Director-General, Chief Health Officer, ED HPD, Senior Director Environmental Health Branch, and senior directors of relevant regional health services should be prepared providing information:
• the scope, processes and findings of the assessment, including provision of the Type 3 cluster assessment report
• reasons for finalisation
• implementation of the communication plan.

Also, consider briefing and providing reports for information to:
• political representatives for the affected area
• local government libraries.

Communication of the Type 3 cluster assessment report
• Integrated Communications Branch staff, as members of the T3CAT, will develop and implement the communication plan. This will be developed at the beginning of the Type 3 cluster assessment and include information to guide the release of the Type 3 cluster assessment findings to the affected and the wider communities (Section 2.9). The communication needs to be trustworthy and considerate, and include a response about the
specific alleged cluster, as well as general information on disease clusters. The explanation
of the assessment should be written in plain English.

- The findings of the report should be provided, prior to public release, to key external
  stakeholders identified in the communication plan, including:
    - affected individuals, groups and communities, as well as the original informant and
      possibly the wider community
    - relevant health workers in the affected area
    - representatives of other stakeholder agencies (such as the LGA, DERM, DET,
      DEIR) in the affected area.

Assessment Register
The T3CAT should ensure the record of decisions, actions and any scientific reports are recorded
in the Cluster Assessment Register (Section 1.7).

Other communication to finalise the Type 3 cluster assessment
Following the decision to finalise the assessment, a number of additional communication tasks
need to be undertaken.

- **Post assessment debrief**: Within three months of finalising the assessment, a formally
  convened debrief will be conducted. The purpose of the debrief is to review and document
  the learning, identify key problems and issues encountered, and identify possible future
  solutions.

- **Peer-review publication**: Consideration should be given to the potential for the cluster
  assessment to be added to the literature in this field. The addition to the evidence base
  may relate to one or more of the following issues:
    - methodology of epidemiological and/or environmental health assessment
    - findings of the cluster assessment
    - methodology of cluster management
    - assessment and management of community concerns
    - cluster assessment communication.

- **Post assessment reviews**: The assessment will be reviewed three months after release of
  the final report. The review should cover:
    - an evaluation of the assessment response
    - whether the cluster assessment findings need to be reviewed if further cases have
      been reported
    - evaluation of the assessment process and capacity of this protocol to meet the
      requirements of the assessment
    - advice to the Director Population Epidemiology Unit recommending changes to
      these guidelines.
1.6 Type 4 cluster assessment: research study

The Type 4 cluster assessment should be regarded as an offshoot of the Type 3 cluster assessment. This type of assessment is approved and undertaken based on the ‘Criteria to undertake a Type 4 cluster assessment’ in Table 6. The goal is to explore hypotheses that have arisen during the Type 3 cluster assessment, and were not addressed in past assessments. Rarely would this assessment contribute to adding to the explanation of the cause of a cluster. A Type 4 cluster assessment explores a narrow, well defined research hypothesis and will not have the breadth of a Type 3 cluster assessment.

The decision to initiate a research study should be based on the hypothesis that important, biologically plausible risk factors are present and operating, as identified from the Type 3 cluster assessment. The feasibility of conducting a scientifically valid and socially useful study should have a sound basis.

The research study must be preceded by a detailed feasibility study covering:

- definition of the research questions and hypothesis to be tested
- appropriate study designs and the level of evidence which the study design will provide
- resource requirements
- timelines.

The research study should be undertaken according to standard fiscal accountability and research processes. A significant component of any research study needs trustworthy, considerate, comprehensive and effective public communication and briefing.

There are generally two types of major research studies: epidemiological studies and environmental health studies.

- **Epidemiological study**: If there is an excess of cases in the cluster and there is a biologically plausible connection between the cases and some environmental exposures, then this might warrant further assessment of the cases and their environment such as a nested case-control study or a genetic study.
- **Environmental health studies**: This may involve more detailed environmental sampling, biological monitoring, toxicological studies or genetic analysis.

1.6.1 Conducting the research study

As many clusters relate to workplaces, the responsibility for the study will be with the employer. If Queensland Health is responsible for undertaking the study, funding sources and processes for engaging partners and coordinating the study (including governance) must be determined by Queensland Health. The study/steering committee should be established and could include senior Queensland Health professionals, members of the Expert Review Committee on Cluster Assessment, and other academics or researchers from universities or research institutes. The roles and responsibilities of the committee and its members would need to be established through a Terms of Reference. An issues management plan should be developed using the communication plan developed in other cluster assessment types.

Steps for conducting a research study may include:

<table>
<thead>
<tr>
<th>Type 4: research study</th>
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<tbody>
<tr>
<td><strong>Purpose</strong></td>
</tr>
<tr>
<td><strong>Decision maker</strong></td>
</tr>
<tr>
<td><strong>Data collection and analysis</strong></td>
</tr>
<tr>
<td><strong>Expertise required</strong></td>
</tr>
<tr>
<td><strong>Resources</strong></td>
</tr>
<tr>
<td><strong>Likely duration</strong></td>
</tr>
</tbody>
</table>
• Justify the need for the study.
• Secure resources as the study will require a major commitment of resources.
• Seek funding for financial, in-kind and technical contributions.
• Scope and plan the assessment.
• Conduct the assessment.
• Finalise assessment.
• Report the outcomes of the assessment.
• Develop communication plan when scoping the research study and be guided by any public comment.
• Keep the ED HPD informed throughout the process, and have the report reviewed before releasing it.

Efforts should be made to publish the methodology and findings in a recognised peer-reviewed medical, environmental health or epidemiology journal. The initial planning of the publication should be made at the commencement of this assessment type, including agreement on issues such as audience, scope and authorship; and public communication and briefing.
1.7 Cluster Assessment Register

A confidential Cluster Assessment Register commenced in 2004 to record summary details of all cluster assessments undertaken by Queensland Health. The register contains personal data related to health status and therefore must remain confidential.

The register includes information of all assessments; from Type 1 to Type 4. The register does not include an assessment that involves less than four hours of work of Queensland Health staff. It is the responsibility of all assessment teams to ensure details are recorded at the commencement and upon finalisation of each assessment.

1.7.1 Information recorded

The following information is recorded in the register:

- **Data entry information**: cluster ID, name of person entering data into register
- **Details of initial contact**: region, public health unit, date notified, name of person receiving notification
- **Details of informant**: name, position, agency, phone and/or email address
- **Details of suspected cluster**: identifiable location, setting, whether or not children involved, disease/condition, sub-types, number of cases, sex, age, suspected hazard, population at risk
- **Action taken**: communication strategies applied, involvement of committees, formation of assessment team, consultation with Queensland Health Integrated Communications Branch, and briefing the Minister for Health
- **Assessment summary**: verification of details against Queensland Cancer Registry, study period or years of data considered, assessment status, and if the status of an assessment is inactive (that is, when an assessment has not progressed due to lack of sufficient information) the date that the assessment became inactive
- **Concluding remarks**: date of completion of assessment, approximate hours worked, highest level of assessment type, final comments.

1.7.2 Annual reporting

An annual report of activity is presented at the Health Surveillance/Epidemiology meeting each year around May–June. This report is prepared by the Population Epidemiology Unit of the Division of the Chief Health Officer.

1.7.3 Register location and format

The register is managed by the Population Epidemiology Unit to ensure staff access is updated and a confidential master register is maintained. The register is reviewed biennially in line with the review of the guidelines.

1.7.4 Access

The following positions have access to the register to enable regular updating:

- PHPs from the regional health services
- Director Epidemiology (regional)
- Director, and Advanced Epidemiologist, Population Epidemiology Unit, Preventative Health Directorate, Division of the Chief Health Officer.
2 Supporting information

2.1 Role of Queensland Health in cluster assessment

For each type of cluster assessment the role of Queensland Health in any component of cluster assessment must be determined as soon as possible after contact by an informant and before other actions are taken. If Queensland Health is not the cluster assessor then it is important to determine if it has any role in the assessment and, if so, its scope, duration and reporting procedures. For cluster assessments for which Queensland Health has a role, the agency for responsibility for all components of the cluster assessment and the cluster manager must also be identified as soon as possible.

Below is a checklist for evaluating whether Queensland Health should or should not be involved in a cluster assessment and, if so, what that role should involve.

Queensland Health should be involved in a cluster assessment when:

- the alleged cluster occurs in a community setting, such as a street, suburb or town
- the alleged cluster relates to a Queensland Government workplace
- there is a specific need for Queensland Health expertise that is not available elsewhere.

Queensland Health should not be involved in a cluster assessment when another party has clear responsibility for the cluster assessment, such as a workplace or other government department

In 2011, Queensland Health and DET co-signed the ‘Working Agreement for the Assessment of Clusters of Non-communicable Disease’. For cluster assessments in a workplace other than a Queensland Government facility, consultants should be engaged by the cluster manager to assess the cluster. Consultants should be experienced in cluster assessments and be able to couple the epidemiological and hazard assessment components of the cluster assessment. The consultant may need to engage a multidisciplinary team to assess the cluster. Potential consultants are listed on the websites of the Australasian Faculties of Occupational and Environmental Medicine (http://afoem.racp.edu.au/) and the Australasian Faculty of Public Health Medicine (http://afphm.racp.edu.au/).

For cluster assessments in a workplace, DEIR will provide support as required, on a case by case basis. Such support may involve preliminary literature searches of relevant occupational and environmental studies, attending worksite meetings with Queensland Health to foster communication, advising on the scope of any environmental monitoring and reviewing reports.

Queensland Health may provide advice on environmental testing but will not undertake or fund such work, unless the cluster relates to a Queensland Health facility.

Queensland Health also plays a role in the release of information for an alleged cluster assessment as outlined in Section 281 of the Public Health Act 2005.
2.2 Cluster management

As outlined in Section 1.1, cluster management is distinct from cluster assessment. Cluster management is defined as the process of evaluating alternative actions, selection options and implementing them in response to cluster assessment. The process incorporates information relating to environmental science, epidemiological, social, economic and political aspects. Cluster management must be conducted in a timely manner. The key role of a cluster assessment is to adequately inform the cluster management process by providing clear and objective information (including uncertainties) relating to the assessment.

As cluster assessment and cluster management are interdependent, both processes should commence simultaneously. Guidelines for cluster management are beyond the scope of this document. However, in summary, cluster management includes the following:

- Establish the governance and processes for cluster management, including identification of a cluster manager who will be accountable for cluster management activities.
- Identify the information needed for the cluster assessment.
- Appraise the results of the cluster assessment (including an assessment of the nature and magnitude of uncertainty).
- Define available management options.
- Evaluate the options according to the health, economic, social and political aspects.
- Decide on appropriate action and oversee implementation.
- Monitor and evaluate the effectiveness of the actions taken.
- Implement any changes to the cluster management cycle.

It is very rare to identify a common cause in non-communicable disease cluster assessments. Therefore, very rarely are ways identified to protect or improve the public’s health. Cluster assessment is one strategy available to cluster managers in addressing public concerns about potential environmental hazards including carcinogens. Other important strategies include:

- education about the causes, frequency and patterns of disease in communities
- appraisal of the social, economic and political context of the affected community and ways of addressing these aspects
- risk communication to respond to the underlying perceptions of risk.

Before undertaking any cluster assessment type, the cluster manager must be identified and governance provisions established. The identification of the cluster manager is determined by the circumstances. The cluster manager will usually have accountability arising from their responsibility with an affected site (for example, DET for a state school, Queensland Health for a public hospital), workplace health and safety liabilities (such as, employers of the relevant workforce) or jurisdictional or legal responsibilities (for example, LGA of a town). For assessments of community-based clusters, discussions between Queensland Health and key organisational stakeholders are required to determine the appointment of the cluster manager.

In some situations there may not be a single entity identified to act as cluster manager and several entities may be appointed. In these situations, the roles and responsibilities of each entity must be clearly defined. Such roles and responsibilities may need to be reviewed and changed as an assessment progresses (e.g. when a causal agent and its source are identified).

Recognising that cluster managers and cluster assessors may come from different stakeholder agencies, it is important that cluster managers note the following points:

- The Queensland Health guidelines: Assessment of clusters of non-communicable disease 2012 are for the assessment of potential non-communicable disease clusters and apply where Queensland Health is the lead agency. In addition, Queensland Health requires the use of these guidelines for all components of cluster assessments which it undertakes or participates in.
- The requirement to undertake, the nature and type of assessment undertaken are healthcare decisions made by PHPs and other health practitioners.
2.3 Cluster assessment

2.3.1 Introduction
Cluster assessments are more than a statistical or environmental health exercise. Instead they require high quality integration of well-planned and complementary epidemiological, environmental health, toxicological and sociological assessments. They require examination of individual circumstances as well as analysis of evidence drawn from literature. This exercise requires a diverse team comprising a broad range of disciplines.

Cluster assessments are challenging and resource intensive for a range of reasons. Investigators are usually dealing with people distressed by their disease, or that of a family member or friend, who are seeking a clear explanation for their condition. Most reports of alleged non-communicable disease clusters involve situations that are clearly not clusters, and rarely do assessments yield scientific finding of relationships between exposure and disease. The challenges relate to the complexities of the epidemiological and environmental health assessments and the emotional and communication components. For the layperson, the ‘appearance’ of a cluster understandably leads to a spontaneous observation that there must be a common cause. However, cluster assessments very rarely result in finding a clear, common cause. The most likely explanation is the chance distribution of biological events with complex multifactorial causation, where the multifactorial mix operates differently in different individuals. It takes a highly skilled communicator to empathetically and convincingly communicate concepts of such chance to the community. It is important to recognise the social dimensions of cluster reporting and develop a process that maintains trust with the community and which does not excessively deplete resources.

2.3.2 Issues identification
Issues should be identified that are amenable to cluster assessment. Issue identification assists in establishing a context for the cluster assessment. Before commencing a cluster assessment consider the following questions:

• What is the concern?
• What is causing the identified concern?
• How was the concern identified initially?
• How was the concern raised?
• Why is the concern an issue?
• How urgently does the issue need to be addressed?
• Is the issue amenable to cluster assessment?
• Is a cluster assessment appropriate (cluster assessment may not be appropriate if the result is obvious; will not assist policy making, risk management or the transparency or defensibility of the risk management process; or the opportunity costs of risk assessment will detract significantly from the scale and timing of the implementation of cluster management options)?
• Who is the cluster manager and what do they want (nature of the output from cluster assessment and timeframe)?
• What are the project management aspects of the cluster assessment (objectives, nature of the risk assessment to be undertaken and timeframe)?

2.3.3 Cluster assessment principles
• The protection of human health is the primary objective.
• Cluster assessments need to be done with transparency and diligence, using high level scientific skills.
• The processes are effectively documented and communicated both internally (within the cluster assessment team) and externally (to other relevant Queensland Health staff and stakeholders including affected individuals, groups, and communities appropriate to the type of assessment).
• Cluster assessments should be soundly based on the best available evidence, in accordance with current scientific knowledge and follow best practice guidelines (including the use of these guidelines) in planning and conducting cluster assessments.

• If a Type 2 or Type 3 cluster assessment is undertaken, a step-by-step approach is used following the principles of good epidemiological and environmental health research. Note: most of these steps are unnecessary for a Type 1 cluster assessment and some will be unnecessary for a Type 2 cluster assessment. The steps are:
  - establish that a problem exists
  - adequately ascertain cases
  - identify the study population i.e. the denominator
  - collect data on all relevant environmental exposures
  - characterise the events in terms of epidemiological factors and exposure assessment of the relevant population
  - look for patterns and trends
  - formulate and test hypothesis
  - write report
  - obtain peer review
  - finalise report and communicate results.

• Apply good project management skills ensuring the assessment:
  - is comprehensively planned and documented
  - is completed in a timely, transparent and scientifically rigorous manner
  - effectively and efficiently uses resources (noting the level of resources can be substantial for a Type 3 or Type 4 cluster assessment)
  - effectively applies the skills and core disciplines of a range of relevant professions using a complementary and multidisciplinary approach involving public health medicine, epidemiology, environmental health, toxicology and communication officers.

• The project identifies and addresses the concerns and information needs of the affected individuals, informant, general and wider communities and other key stakeholders (such as the local community, people tasked with cluster management) by:
  - providing a systematic and well written 'plain English' documentation of the findings inclusive of file notes, letters and/or reports, and information which demonstrates good records management systems
  - utilising good communication skills through mutual understanding and addressing any conflict between the public’s expectation of a cluster assessment and the science of carrying out such an analysis within the limits of available knowledge and resources.

• The project team identifies and acknowledges the uncertainties that arise from the assessment process and provides an uncertainty analysis about each aspect of the assessment as well as other information to adequately inform the cluster manager to enable informed decision-making.

• The aims, rationale and management of results need to be clearly established and documented for:
  - the cluster assessment
  - escalating the assessment to higher levels
  - any particular epidemiological or environmental assessments undertaken as part of the cluster assessment.

• Adequate identification and appraisal is required of the relevant biological processes (for example, latency period of carcinogens) and toxicological factors (such as the potency of agents) and whether there are sufficient of these to account for the excess observed cases compared to the expected number. The assessment should contain a detailed description of uncertainty, where the uncertainty arose during the assessment and the effect it has on the final conclusions.

• A cluster assessment rarely identifies a specific cause but should be undertaken to a level that, in the opinion of the cluster assessor, reasonably excludes the presence of causal agents in sufficient concentration to account for a cluster.
2.3.4 Engaging external advisors and reviewers

**External advisor**
External advisors may be engaged for specific cases to provide specialist advice to the cluster assessment team and/or the Expert Review Committee on Cluster Assessment. They will be engaged to provide specific specialist advice, for example, on epidemiology, environmental health, toxicology, or communication issues. The rationale for seeking external advice and the nature of the advice sought must be clearly documented.

**External reviewer**
External reviewers are not routinely used but may need to be engaged where:
- there is strong community concern and doubt
- the assessment is particularly complex
- cluster management processes are likely to be very controversial.

Depending on the nature and complexity of the assessment, and the breadth of skills of the external reviewer, more than one reviewer may be required. The role of the external reviewer is to:
- review the methodologies for epidemiology, environmental health and toxicology
- review the reporting of results
- provide informed and independent media comment and/or information to the community, if required.

An external reviewer will have a background and experience in population health, and have experience and expertise in cluster assessment. They will possess excellent communication skills, and have credibility with the cluster assessors and stakeholders. An external reviewer will be appointed by the Expert Review Committee on Cluster Assessment, and be external to Queensland Health. They may be from another government agency, an interstate health department, a non-government organisation or academia. The external reviewer is appointed to provide advice to the cluster assessment team. A list of potential external advisors and reviewers can be obtained from the Director Population Epidemiology Unit. This list will include external reviewers who have previously provided this service to Queensland Health. The cost of review or advice will depend upon the complexity and nature of the assessment, communication and reporting requirements with an approximate fee between $1,000 and $4,000.
2.4 Case ascertainment

Case ascertainment is a measure of the extent to which all actual cases meeting the case definition can be identified in a cluster assessment. Completeness depends on the availability and quality of information and data sets, and the resources required to investigate those data sets. The goal of case ascertainment is to achieve the best practicable ascertainment based upon the available information at the time and the purpose and scope of the assessment. A written record (for example, Queensland Cancer Registry entry, pathology result) is generally required for inclusion as a case in an epidemiological assessment.

Case ascertainment begins with determining the number of potential cases. Ascertaining potential cases is the broad process of investigating and accumulating information about suspected or actual cases of disease in the population being assessed. Ascertaining potential cases is not selective (for example, information on all types of cancer may be collected, not just one specific cancer) and will generally accumulate information on many individuals initially. Some of those individuals will, at a later stage, be excluded from further assessment, generally based on the case definition.

For a Type 1 cluster assessment, potential cases will initially be ascertained from information supplied by the informant at initial contact. It may also come from the cluster manager, and on this basis it would satisfy the case ascertainment requirements (see Table 1).

For cases more difficult than Type 1 cluster assessments, more complex strategies will be used to ensure ascertainment of potential cases is as complete as practicable. For types 2, 3 and 4 cluster assessments, the most useful initial sources of information about potential cases are obtained through social networks and local knowledge. In many instances a potential case is identified by self report. Concurrently for types 2, 3 and 4 cluster assessments, the cluster manager will be responsible for formal and informal communication with key stakeholders. Due to the increased media interest of types 2, 3 and 4 cluster assessments, reporting of potential cases to the cluster manager is encouraged. During the early phase of case ascertainment consideration should be given to announcing contact numbers and details of the cluster manager to enable reporting of potential cases.

For types 2, 3 and 4 cluster assessments further ascertainment of potential cases not identified by the above means may be justifiable. This may involve investigation of Queensland Cancer Registry data or other official records. This process depends on both the availability of data sets and the resources to investigate those data sets, as well as the appropriate authority to access confidential data. Social networks, including local knowledge, media coverage, and checking diagnosis of identified cases through data sources such as the Queensland Cancer Registry, are considered to provide a satisfactory level of case ascertainment for types 2 and 3 cluster assessments. Case ascertainment limitations should be described in the cluster assessment reporting.

Best practice case ascertainment is undertaking the cluster assessment using the available information at that point in time. If additional cases are notified, consideration should be given to the potential impact the additional cases have on cluster assessment (epidemiological and environmental health components) as well as to the cluster management. In reports of types 2, 3 and 4 cluster assessments, recommendation for appropriate actions following notification of additional cases after completion of assessments should be provided to the cluster manager.

2.4.1 Case definition, case inclusions and exclusions

While a ‘working’ case definition is used for a Type 1 assessment, a formal case definition must be developed for all other non-communicable cluster assessments. The case definition is a deductive process of appraising potential cases and takes into account the natural history of the particular disease. The case definition also includes the potential period of exposure, which is further discussed in Section 2.10. However, it must be emphasised there is no set formula for the derivation of case definitions as they are affected by highly diverse particulars such as
geographical sites and diseases. Establishing a case definition requires professional judgment and specialist knowledge. The case definition follows the form: all reported incident cases of ‘x’ cancer among ‘y’ employed/residing/attending at ‘z’ workplace/area/school between YYYYY and YYYYY. For example, an example may be ‘all reported incident cases of brain cancer among female staff members employed at workplace The Office between 1990 and 2005’. Once defined, the case definition will focus on the epidemiological component of the assessment.

Before case ascertainment can be finalised, decisions regarding which conditions to include and exclude in the case definition are required. The degree of required similarity of cases must be determined through consideration of alleged hazards, histopathology of disease, diagnostic criteria, availability of data sources to ascertain expected case numbers and limitations of available data. Specialist advice may be required and should be sought early in the cluster assessment. It is important to note that case ascertainment relates to individuals, not numbers of conditions. For example, multiple cancers may be reported for an individual, whether or not these are reported as primary or secondary cancers. Each of these cancers is not a unique case. Multiple primary cancers in an individual will usually relate to genetic predisposition and particular types of treatments. Specialist advice should be obtained to ensure that such conditions and cases are appropriately included in the cluster assessment.

Ascertainment of cancer is given as an example because non-communicable disease cluster assessments mostly relate to cancer. Cancer is a general term representing many diseases with a wide variety of causes. Overall, about one-third of all cancer cases and deaths are considered to be due to known behavioural risk factors. Exact causes for individuals and the contributions of known risk factors are very difficult to establish. Furthermore, having a risk factor, or even several, does not mean that a person will get the disease. Many people get cancer without having any known risk factors. It is particularly difficult to pinpoint the mix of causes of an individual cancer.

Exactly when a cancer becomes clinically evident and who it affects is largely determined by random factors. If there are a number of different types of cancer in a community or workplace then it is very unlikely that they share a common cause. For this reason, cluster assessment is undertaken of cases of disease that are of the same or similar histological type, rather than grouping multiple types of cancer. Inclusion of ‘all cancers’ in the case definition, that is the aggregate of all cancer types, and assessment of the rate of all cancer is not advisable except under extreme circumstances where a clearly identified hazard has been reported, for example exposure to large doses of radiation.

Cancer classification is important in case ascertainment. For example, ductal carcinoma in situ (DCIS) of the breast, which is a lesion whose cells have features of cancer cells, is a non-invasive condition that may or may not progress to invasive cancer. It is excluded from cluster assessments and in annual reporting of breast cancer by the Queensland Cancer Registry. DCIS is usually asymptomatic and is usually diagnosed through radiological screening programs and subsequent pathology testing of biopsy specimens. Due to these difficulties in ascertaining expected rates, DCIS should be excluded when determining expected rates in breast cancer cluster assessments.

Inclusion and exclusion criteria relate to the study population. For example, in a workplace assessment, is the study population the employees only, with exclusion of contractors and volunteers? Additionally, does the study population take into account migration in and out of the population at risk? It is important to ensure that the cases are part of the study population. As an example, volunteers can only be counted as cases if they are also included in the study population.

For types 2, 3 and 4 cluster assessments, the pre-defined steps for appraising potential cases and finalising the case definition are:

- The disease assessed must occur in more than one individual case and must have the same or similar histological type.
- Exclusion criteria must be considered and must be specific to the assessment, for example, exclusion of contractors or staff with limited exposure to the putative hazard.

Queensland Health non-communicable disease cluster assessment guidelines 2012 40
• All cases should be confirmed from a written record (such as Queensland Cancer Registry entry, pathology result), except under exceptional circumstances.
• Latency period (time from exposure to diagnosis of cancer) is a critical scientific factor for assessment. Latency period should be included in sensitivity analysis for all assessments, acknowledging there may be limited data available in the literature for guidance on accurately defining the expected time period. However, it is recommended five years is the minimum latency period used in assessment of solid tumours. Latency periods of 5, 10 and 20 years should be included in cluster assessments of cancers in order to assess the sensitivity of the calculations to varying latency periods. Slightly shorter latency periods may be the criteria for cancers such as leukaemia or longer latency periods for mesothelioma (Section 2.10). Latency period should be included in the case definition.

2.4.2 Confirmation of cases
With the approval of the Director-General of Queensland Health, data about relevant potential cases can be sought from the Queensland Cancer Registry. In some situations the PHP may require access to hospital and healthcare records. Written consent from the potential case is required to access data from patients’ doctors. Consent forms are included in resources for cluster assessment, as a template for a brief to the Director-General to access the Queensland Cancer Registry. The written consent of cases is needed for release of identifiable data to the informant, and it is the responsibility of the informant to seek such consent. If a report is to be made public and cases are identifiable, written consent from the cases is required. It is the responsibility of the cluster manager to seek such consent.

Queensland Cancer Registry data is useful for providing state-based rates where the Queensland population is the reference population. It should be noted Queensland Cancer Registry data has certain limitations for use in cancer cluster assessments:

• While Australian registers are close to complete, experience from the United States of America would suggest there is approximately a 2% undercount compared to hospital records. As the Queensland Cancer Registry is nearing completion of the collection and quality assurance processes for each year, in the situation where a suspected case is not listed on the registry, it may be the registry is incorrect. Therefore, if written consent has been given, the best practice case ascertainment is to access data from patients’ doctors.
• Australian Cancer Registry data uses the address at the time of diagnosis. Therefore if a potential case moves address from the geographic area being assessed, this limitation needs to be noted and acknowledged in the final report.
• Queensland Cancer Registry data is most useful for clusters in a defined geographical area and where rates can be checked for an entire Statistical Local Area (SLA). It is important to note that classification of cases to an SLA is prone to misclassification due to incorrect coding practices. Misclassification due to coding occurs when the assignment to the SLA is based upon postcode or suburb name rather than full address details. Data that has been assigned to an SLA based upon geo-coding of the place of residence can more accurately allocate the case to the SLA. Assessing a cluster in an SLA must take into consideration whether misclassification bias has occurred in a geographic entity and whether a broader geographic area must be considered, for example, the SLA and surrounding SLAs. Alternatively, reallocating the value of individual cases to correct residential SLA can be appraised.
• While the Queensland Cancer Registry contains a variable field for occupational data, it is recognised as an incomplete field with inconsistent accuracy. The occupational cluster data should not be relied upon for case ascertainment unless a comprehensive list of occupational names can be provided.

The Queensland Cancer Registry is an important information source for many cancers, but not all cancers. For some cancers, pathology reports are needed to precisely describe the disease, such as leukaemia, lymphoma and brain cancers. If there is conflict between a pathology report and a Queensland Cancer Registry entry, then the pathology report will be deemed to be correct. Cancer registry data outside Queensland will not be accessed in a Type 2 cluster assessment but may need to be considered in a Type 3 cluster assessment.
2.5 Research questions for Type 2 and Type 3 cluster assessments

During types 2, 3 and 4 cluster assessments, research questions should be scoped and defined at the planning phase. Examples of research questions to be used as a guide are listed below.

2.5.1 Research questions for Type 2 cluster assessment

There are two broad questions for this type of assessment:

- **Is there an excess number of cases above that expected in the study population?**
- **Is there a plausible environmental exposure that requires further assessment?**

1. **Is there an excess number of cases above that expected in the study population?**

   - What is the case definition? For example, ‘self reported incident brain cancer cases diagnosed after XX in women (aged YY–YY years) who were employed at workplace AAAA between YYYY and YYYY’
   - How do you define the time period of interest?
     - make allowance for a latency period
     - consider whether the ‘at risk’ period should begin with the date of diagnosis for the first case and end with the date of diagnosis for the last case.
   - Are there any exclusion criteria for contractors and volunteers and inclusion criteria for employees only in the case definition? The same exclusion and inclusion criteria should be applied in determining case numbers and the study population.
   - What is the current number of confirmed cases? Are all cases of same (or similar) type? Have the cases been confirmed through cross-checking with other data sources, such as the Queensland Cancer Registry, histopathology, physician?
   - How are person-years of exposure defined? Is it restricted to the years exposed? How is ‘part time’ exposure considered? Does it take into account the increased incidence of disease with ageing?
   - How is the study population defined? Who is considered at risk? How are the boundaries drawn around the at risk population justified?
   - What is the total number of people in the study population? Are the latency period and migration in/out of population taken into account?
   - What is the expected number of cases in the reference population, and how is the reference population identified, for example Queenslanders of the same sex and same age groups?
   - What is the standardised incidence/mortality ratio, that is, the ratio of observed/expected cases (O/E)?
   - What measures of statistical significance will be used? What cut-off for this ratio (O/E) has been pre-determined to be statistically significant?
   - How will the cluster manager and cluster assessor deal with the emergence of new cases in the future? Will the O/E ratio be recalculated for each newly identified case? Actions should be itemised in the report.

2. **Is there possible exposure to a biologically plausible causal agent for the type of disease reported?**

   - What known environmental causes for this kind of cancer/disease are reported in international literature? Has a review of databases such as International Agency for Research on Cancer (IARC), Agency for Toxic Substances and Disease Registry (ATSDR) and National Industrial Chemicals Notification and Assessment Scheme (NICNAS) been undertaken? It should be noted that most databases are designed according to substance or situation (such as occupational exposure) rather than outcome.
   - What is the hypothesis held by investigators about an environmental exposure? Do the cases have a common occupational or non-occupational exposure? Is there a hypothesis held by the affected population about an environmental exposure? Has the study population identified an exposure of interest?
• Are there any unusual exposures present which could potentially be (unrecognised) agents for this kind of disease? Is there anything unusual about the agent and/or the level of exposure?
• How can latency periods be taken into account in assessing ‘exposure’? Sensitivity analysis will be required to cover the range of values
• Are there any relevant previously reported cluster assessments where environmental exposures were identified? Undertake literature review: grey literature and published
• Is environmental testing warranted? For environmental health purposes, an appraisal of the relevant environment, such as the workplace, would be required to determine whether there is a rationale and, if so, the analytes and sampling plan.
• What is known about the history of the site? Has any environmental testing been done at the affected site either in the past or as part of the current assessment? Collect reports from sources such as the Environmental Protection Agency, LGA, private audits.
• Is environmental testing justified? If so, what is the nature, scope and quality of the testing?
  - Is this considered sufficient to assess possible environmental aetiologies?
  - What are the environmental findings of public health significance that resulted from this testing?
  - Has expert advice been sought from, for example, a toxicologist, Workplace Health and Safety?

2.5.2 Research questions for Type 3 cluster assessment
The overarching purpose is to quantify the excess of disease and undertake a detailed exposure assessment of biologically plausible causal agents. Questions for this type of cluster assessment are:
• What is the excess of cases following analysis of the extra information derived in the Type 3 cluster assessment?
• What is the hypothesis regarding a plausible environmental aetiology?
• Is it feasible to determine whether a causal relationship exists? What is the best way to determine whether a causal relationship exists?

1. What is the excess of cases?
• Does the initial case definition used in the Type 2 cluster assessment need to be further refined on the basis of improved information such as that gained through case interviews, interviews with physicians, review of medical records.?
• Are any additional exclusion/inclusion criteria needed?
• Is case ascertainment adequate? How and to what extent should active case-finding be undertaken?
• Can the denominator population be more accurately defined?

2. What is the hypothesis regarding a plausible environmental cause?
• Is a recognised potential carcinogen (or other disease-causing agent) already known to be present in the environment of the study population, for example, is there proximity to a significant industrial source?
• If so, has sufficient testing been done already to assess the level of exposure in the population?
• Is there any evidence that exposure may be occurring at unsafe levels?
• What variations in exposure might exist, for example, is there a highly exposed or sensitive subpopulation?
• What is the strength of evidence in the literature for a causal relationship between this exposure and the suspected cancer/disease?
• What is the weight of evidence for a proposed causal agent to be a carcinogen?
• What is already known about the dose–response relationship for this carcinogen?
• Would the dose experienced by the relevant population be likely to account for the population attributable risk?
• What is the nature and scope of testing that needs to occur to further assess exposure in the population (for example, further environmental sampling, and biological monitoring)?
• If no potential carcinogen is identified as being present in the environment during Type 2 cluster assessment, is testing required to exclude the presence of such?
• What testing should be carried out for potential carcinogens?
• What is the nature and scope of testing needed (for example, over what time period, what kind of testing, what medium, how many samples, how many sites, what level of detection will be used, who should do the testing)?
• How will the meaning of test results be assessed (for example, what standards will be used as reference, what experts can be consulted)?

1. **Assuming there is a hypothesis and it is feasible to investigate this causal relationship, what is the best way to ascertain causality?**

How would one design and scope further epidemiological and/or environmental health studies (for example, case-control study, cohort study, create disease/exposure register).
2.6 Causality

Queensland Health uses the principles developed by Bradford Hill (1965), reviewed by Lucas and McMichael (2005) and further adapted from NHMRC 2006 to assess causality (Table 7).

Table 7: Principles of causality (Bradford Hill viewpoints as reviewed by Lucas and McMichael 2005 and adapted from NHMRC 2006)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Principle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strength of association</td>
<td>Strong associations are more likely to represent a causal relationship than weak associations. In epidemiological studies, particularly those undertaken in advanced industrialised nations where exposures are unlikely to be extreme; it is relatively unusual to identify very strong associations. In the case of weak associations, the difficulty of separating a true causal effect from the ‘statistical noise’ induced by imprecise information, uncontrolled biases and various forms of confounding often proves an insurmountable problem.</td>
</tr>
<tr>
<td>Consistency</td>
<td>Causality is more likely if an observation has been made repeatedly in different settings, using perhaps different populations and study designs. The factors that may confound a relationship, however, may be the same in all observational studies.</td>
</tr>
<tr>
<td>Strength of study design</td>
<td>Evidence from ‘true experiments’ is most compelling. For example, randomised controlled trials of exposure to gaseous pollutants have been performed with human volunteers. Often, however, such experiments are not feasible or ethical. It is then necessary to rely on weaker observational designs including (in descending order of preference): cohort studies, case-control studies, cross-sectional studies (surveys) and ecological studies.</td>
</tr>
<tr>
<td>Dose-response</td>
<td>The data from observational studies can often be stratified according to the level of exposure. When the health effect appears greater amongst those with the higher levels of exposure (i.e. there is an apparent dose–response gradient), this may be a pointer to causality. In some settings, however, the higher the exposure, the higher are the levels of other confounders. For example, in early studies of the health effects of air pollution, it was noted that sulphur dioxide levels typically varied in accordance with particle levels, since both were partly derived from burning coal.</td>
</tr>
<tr>
<td>Temporality</td>
<td>Exposure to the environmental agent must precede the development of disease. The temporal sequence can only be reliably established by cohort studies and randomised controlled trials.</td>
</tr>
<tr>
<td>Specificity</td>
<td>One exposure should give rise to only one outcome. Whilst this requirement is satisfied for many infectious agents, it rarely applies to other environmental exposures (Lucas &amp; McMichael 2005). This suggests that a specific exposure, a specific outcome, or an outcome that only occurs under environmental conditions where genetic susceptibility is important, would be sufficient for the relationship to be considered causal.</td>
</tr>
<tr>
<td>Biological plausibility</td>
<td>Arguably this is the most important consideration in assessing causation. When an observational study provides information that is in keeping with expectations from animal or in vitro research, the acceptability of claims of a causal association are considerably greater. Such research may cover a broad range, including animal toxicology and human volunteer studies.</td>
</tr>
<tr>
<td>Coherence</td>
<td>Temporal patterns of exposure must fit with the observed pattern of disease. The hypothesis that fewer childhood infections are causing the rising prevalence of asthma (the popular 'hygiene hypothesis') is an example of such an association (Lucas &amp; McMichael 2005).</td>
</tr>
<tr>
<td>Analogy</td>
<td>While this is probably the least important consideration, the case for causation is strengthened if there is similarity to a previously established relationship. For example, it is plausible that diesel particle pollution could cause lung cancer because it contains many of the same polycyclic aromatic hydrocarbons as cigarette smoke.</td>
</tr>
<tr>
<td>Confounding</td>
<td>While not generally regarded as one of the classical Bradford Hill viewpoints, the issue of confounding is integral to assessing causation. A confounder is any factor associated with the exposure of interest (e.g. air pollution) that is itself a determinant of the outcome of interest (for example, COPD). A good example of a confounder would be cigarette smoking. In many study designs, unless reliable and valid smoking data are collected and allowed for in an analysis, it is not possible to disentangle the effects of air pollution on COPD. The method employed in time series studies avoids having to control for confounders that do not vary over time.</td>
</tr>
<tr>
<td>Sensitivity analysis</td>
<td>This is not one of the classical Bradford Hill principles, however the assessment of cause and effect relationships will be strengthened by the application of sensitivity analysis. If the introduction, deletion or adjustment of key variables in the dataset, or the introduction of other plausible explanatory factors, results in the significant change in the outcome of the analysis, there may be grounds for reassessing the validity of the proposed model.</td>
</tr>
</tbody>
</table>
These principles consider the epidemiological, exposure and toxicological evidence to assess whether particular agents have a causal relationship to a cluster. In considering epidemiological evidence generally, rather than in the context of cluster assessments specifically, Bradford Hill asked ‘in what circumstances can we pass from this observed association to a verdict of causation?’ Bradford Hill’s critics have reservations about causal viewpoints.\textsuperscript{26,27} Both viewpoints and reservations should be considered in a cluster assessment.

At a population level, causality can be conclusively established between a particular exposure and a particular disease. In contrast, it is not possible to establish such a link conclusively between an exposure and a particular disease in a given individual—for example, smoking in a person with lung cancer. It is possible, however, to infer deductively that a specific individual’s illness was \textit{more likely than not} caused by the specified exposure.
2.7 Epidemiological assessment of cluster assessments

The principles and guidelines for epidemiological assessment of clusters are described below. While the overall approach described in this document is based on frequentist statistical theory, alternative methods such as Bayesian theory may be more applicable in cluster assessment. When providing advice, specialist biostatisticians from within Queensland Health and the Expert Review Committee on Cluster Assessment should consider the applicability of alternative theories, and use of related statistical methods.

2.7.1 Principles

1. Cluster assessments are more than an epidemiological exercise or unidisciplinary process. They require high quality integration of well-planned and complementary epidemiological and environmental health assessments.

2. Epidemiological assessment within a cluster assessment seeks to determine whether there is an association between a putative exposure and disease, through to assessing whether an excess number of cases above that expected has occurred in the exposed population. This assessment addresses the question of statistical significance, and is a component of the assessment to address both the public health importance of a putative exposure and the community concerns.

3. It is necessary to set the parameters so that the epidemiological assessment has the potential to capture the suspected cluster without dilution of the possible observed health effects. For example, it may be necessary to select a geographic area or workforce component large enough to capture all potential cases but small enough to be able to detect any localised difference in outcome.

4. Most cluster assessments are post hoc assessments, that is, they relate to situations in which an observed excess is reported but no local environmental factor is suspected a priori. Statistical testing is not possible a posteriori. Because of the difficulty of determining the place and time to which cases were related and the great influence of the study population characteristics, no reliable information on the reality of an observed excess could be provided by any statistical tests. However, the public often seek a statistical assessment of an observed excess, and some statistical analysis may be required to at least partially meet the needs of the informant.

5. Case-control studies mainly carried out to ascertain and explain a perceived excess of cases are subject to several limitations: the role played by random fluctuations in the occurrence of a cluster; the ability to identify a potential risk factor, and the ability to evidence a real link between the environment and the disease.

6. All statistical analysis that is undertaken should be:
   a) simple
   b) robust
   c) subject to appropriate sensitivity analysis of both the numerator and denominator.

7. Analysis needs to be undertaken on the data available, documenting the data limitations. The quality of the data will vary between the types of assessment, with better quality and more complete data used in a Type 3 cluster assessment than a Type 2 cluster assessment.

8. The epidemiology research question should be defined and analysis undertaken to answer within the available data, consistent with the type of the cluster assessment. Research questions for types 2 and 3 cluster assessments are detailed in Section 2.5.

9. The data used to derive the expected and observed cases should be developed using comparable definitions and assumptions.
2.7.2 Guidelines for statistical analyses
This section of the guidelines describes the general statistical analysis procedures to follow in cluster assessments. Recognising that every instance of cluster assessment is unique, Queensland Health staff should seek expert statistical advice when conducting detailed assessment (Type 1 and above).

1. SIR/SMR: The standardised incidence or mortality ratio is the usual epidemiological analysis. The SIR is the ratio of the observed number of cases (meeting the case definition) to the expected number of cases. Steps include:
   - Calculate the age-specific rate in reference population (A).
   - Calculate the age-specific population at risk (B).
   - Multiply A * B to get the age-specific expected number of cases.
   - Add across the age groups to get the total number of expected cases (E).
   - Obtain the number of observed cases (O).
   - Calculate O/E, that is SIR or SMR = O/E.

2. Confidence intervals: Confidence interval of the SIR or SMR is a measure of the statistical uncertainty about the estimate (the narrower the interval, the more confident we are about the estimate). The conventional (although somewhat arbitrary) cut-off point for assessing statistical significance of 95% confidence interval should be used. The use of a two sided confidence interval allows for the possibility that the risk of disease in the study population may be lower or higher than in the reference population. While it is unlikely that the risk in the study population is lower, it cannot be discounted. Therefore, it is recommended that two sided confidence intervals are included.

   Use an exact confidence interval based on the Poisson distribution, as calculated by the statistical package STATA and based on an exact relationship between the Poisson distribution and the chi-square distribution. The width of the confidence interval is directly a function of the number of cases. Values of SIR greater than 1.0 indicate an increased risk compared to the reference population. If the lower bound of the confidence interval is also above 1.0, then we say the increased risk is statistically significant.

3. p values: Use of p values is not appropriate as a probability measure in epidemiological assessment of cancer clusters, as cluster assessment is a post hoc analysis. The p value can be used as a measure of the strength of the evidence, not as a probability of such an event occurring.

4. Statistical significance: In epidemiological assessment of clusters we have no control over the size of the population under assessment and the indicators of statistical significance are based on arbitrary cut-off points (95% confidence interval, p<0.05). Therefore, the emphasis in reporting should be on how important is the direction of the SIR, that is, the order of magnitude, not statistical significance.

5. Multiple comparisons: In essence, the p value is interpretable when only one comparison or one test is performed. Therefore, if a p value is reported, many statisticians adjust p values from a cluster assessment for implied multiple comparisons. More specifically, when a cancer cluster is reported from one population it implies that comparisons have taken place in many similar populations which go unreported because no clusters were found. Further, there are many other types of cancer and other time periods, which imply more comparisons. The more comparisons that are made, the greater the probability of observing the cluster in question is due to chance. Adjustment for multiple comparisons is by the Bonferroni adjustment:

   \[ P_{adjusted} = 1 - (1 - P_{unadjusted})^n \]

   where n is the number of multiple comparisons.

   Selection of a value of n is subjective. For example, in an epidemiological assessment in a school population, is n the number of other schools in Brisbane, Queensland or Australia? Is it only state schools or does it include private schools, or both primary and high schools? Rather
than selecting a particular value for \( n \), the effect of several different values should be assessed as a sensitivity analysis.

By convention, statistical significance is at the 95% level, which means there is up to a one in twenty probability the result will be due to chance. If about 50 specific comparisons (cancer diagnosis and/or cause of deaths and/or populations) are made, by definition, apparently statistically significant associations could arise for 2–3 comparisons (cancer diagnosis and/or cause of deaths and/or populations) by chance alone.

Because of the subjective determination of the number of multiple comparisons, both confidence intervals and \( p \) values are hard to interpret for cluster assessments. Confidence intervals have a minor advantage as they focus attention on the point estimate of the SIR to a larger extent than \( p \) values.

6. **Confounding:** The major confounders of non-communicable disease are age and sex. These are routinely accounted for in the assessment of differences in the rates of observed and expected cases.

Additional potential confounders, such as lifestyle and genetic factors, are not taken into account in most cluster assessments. While this information can potentially be collected from the observed cases in the assessment, this information is not available on all Queensland cases and cannot be determined and used in the assessment of the expected number of cases. For example, the Queensland Cancer Registry does not list genetic or lifestyle factors for each incident cancer case.

However, the broader process of cluster assessment, lifestyle and genetic factors should be qualitatively considered because of their importance in disease causation. Only limited qualitative assessment is feasible in Type 1 and Type 2 cluster assessments. In a Type 3 cluster assessment a more detailed qualitative assessment of lifestyle and genetic factors may be possible.

Taking confounders other than age and sex into account generally moves the SIR closer to the null value and therefore increases the likelihood that the cluster is due to chance.

7. **Sensitivity analysis:** Sensitivity analysis should be conducted and reported as part of the assessment. Variables to be considered in the sensitivity analysis include, but are not limited to: multiple comparison, reference population, latency period, case ascertainment and exposed population ascertainment.\(^{31}\)

8. **Reference population:** The reference population for the calculation of expected cases needs to be documented, and is a larger, relevant population, such as the state population. Choice of reference or standard population is dependent on known epidemiology of the disease of interest and available information. The reference population is usually the Queensland population. Different reference populations may be used as part of the sensitivity analysis.

9. **Latency period:** Latency periods are the time from exposure to diagnosis of cancer. These periods are for a risk factor/disease pair and are an average which might not apply to an individual.\(^{31}\) Studies have shown that when the latency period is taken into account it generally shows that a cluster is more likely due to chance.\(^{32}\) To date, the latency period has usually not been accounted for in standard epidemiological analysis: most case definitions determine that the time of putative exposure must be before diagnosis of disease but do not take into account a latency period.

Latency should be included in sensitivity analysis for all assessments, acknowledging that there may be limited data available in the literature to accurately guide defining of periods. It is recommended that five years is the minimum latency period used in the assessment of solid tumours and latency periods of 5, 10 and 20 years should be included in cluster assessments.
of such cancers. Slightly shorter latency periods may be required for cancers such as leukaemia and longer periods for mesothelioma. Latency is further discussed in the Glossary (Section 2.10).

10. **Time period within case definition**: A number of factors must be considered in determining the time period in the case definition. Latency is a critical scientific factor. As a minimum five-year latency period is recommended, the case definition should reflect the latency period used in the analysis. If the limits of the time period in the case definition are the date of diagnosis for the first and last cases, the resultant SIR will be artfactually increased.

11. **Method of calculation for lifetime risk**: Take into account ages of cases and ageing over time to determine person-years of exposure, which acknowledges genetic and other background exposures apart from the putative presumed exposure.

12. **Maps and/or visual objects**: Through maps or similar visual techniques, communication of the variation in incidence rates between small geographic areas of Queensland may provide a useful tool for public communication to dispel the hypothesis that through chance alone incidence rates are homogenous across geographic or population groups.

13. **Report in full number**: In communication, use whole integers for reporting expected case count. For example, 'about 3 expected cases per 100,000 population' instead of '2.7 cases per 100,000 population'.
2.8 Environmental assessments in cluster assessments

2.8.1 Principles

1. Environmental and epidemiological assessments are complementary in a cluster assessment. They must address the overall goals of a cluster assessment, be well-integrated and conducted according to the type of assessment. Each should contribute to the ‘reality check’ of the other.

2. The purpose of environmental assessments is to identify a cause or to seek a plausible causal process (that is, plausible agent plus sufficient exposure) for the cluster of a specific disease.

3. The overall process of an environmental assessment is:
   - Identify the specific disease.
   - Identify whether there are known causal agents for the disease.
   - Identify the dose–response relationship for the agent (that is, the percentage of the population affected at particular levels of exposure and assessment of potency of the hazard/exposure).
   - Identify whether there are significant exposures of the affected population to the known causal agent that could account for the increased rates of disease, or if a known causal agent is not identified, whether there are any significant exposures to some other agent that could plausibly account for the increased rates of disease.

4. Most environmental assessments can be done as a ‘desktop’ exercise. Types 2 and 3 cluster assessments should include a site appraisal.

5. Environmental sampling should only be recommended by the cluster assessment team if:
   - it clearly addresses the goals of the cluster assessment
   - there is a known causal agent or there is a biologically plausible, but not proved, causal agent likely to be present in significant levels
   - the reasons for doing the environmental sampling and how the results will be interpreted and managed are clearly documented in advance
   - there is a clearly documented sampling plan and reporting process.

Environmental sampling is not necessary if:
   - the site does not appear on DERM’s Contaminated Land Register or Environmental Management Register nor does it have an DERM Site Management Plan, or
   - what is known about the history of the site and the opportunities for exposure, it cannot be reasonably expected that an environmental agent will be identified that could explain the number of people with the range of health effects reported, or
   - the type of assessment undertaken is a Type 1 cluster assessment.

2.8.2 Resources
The key reference to be used for environmental assessments is enHealth (2002) Environmental Health Risk Assessment, Department of Health and Ageing, Canberra. Additional causal, dose–response and guidance values information should be sought from the sources in Table 8. Documents are categorised based on the level of endorsement/participation by Australian authorities and the depth of evaluation involved in the development of them. Information should be sought from Level 1 categorised documents. If information is not available in Level 1 categorised documents, then seek the information from Level 2 categorised documents. However, be aware that they may not be endorsed. If information is not available in Level 2 categorised documents, then proceed to Level 3. All the documents, particularly those in Levels 2 and 3 require rigorous appraisal for relevance, validity and accuracy.
Table 8: Documents to be used to obtain causal, dose response and guidance values

<table>
<thead>
<tr>
<th>Level 1 documents</th>
<th>a. NHMRC documents</th>
</tr>
</thead>
</table>

| b. WHO documents | These include: International Programme on Chemical Safety Environmental Health Criteria monographs and Concise International Chemical Assessment documents (CICADs). For carcinogenicity assessments, International Agency for Research on Cancer (IARC) evaluations provide information about specific substances and situations. Users of the IARC document should be acquainted with the classification system which is available through the ‘Preamble’ link. The human data for the cancer evaluations is from historical, usually occupational, cohorts that may have experienced higher than current exposures. |

| c. enHealth/National Environmental Health Committee documents. | In particular Environmental Health Risk Assessment provides a framework and extensive detail on health risk assessment. |

| d. NICNAS (National Industrial Chemicals Notification and Assessment Scheme) evaluations | |

| Level 2 documents* | a. Casaret and Doull’s toxicology
d. US Agency for Toxic Substances and Disease Registry documents |

| Level 3 documents* | Peer-reviewed journals |

* These should only be used if information is not available in Level 1 categorised documents, and as applicable with a full appreciation of their limitations

2.8.3 Data requirements

The following data requirements are intended to enable efficient and accurate appraisal of environmental information for the hazard assessment and exposure assessment components of the cluster assessment.

1. **Rationale**: for the sampling program and selection of analytes including sampling objectives sampling processes and environmental factors relevant to the choice of analytes, inclusion of unusual analytes and exclusion of common analytes

2. **Mapping**: of testing sites for easy identification of sampling sites in relation to relevant environmental sources

3. **Cross-referencing**: of results to maps: including between different parts of a report

4. **Linear geographic sequence**: of results, for example, downstream/upstream, or towards/away from a source point

5. **Nature of the analyte**: may be important when the valency (for example, chromium) or chemical form (for example, organic arsenic versus inorganic arsenic in fish, haem iron versus non-haem iron in animal samples) might be relevant for health risk assessment

6. **Levels of reporting**: for each analyte for each batch of results

7. **Presentation of results**: in the units for which the standards are written, for example, using milligrams/m3 instead of nanograms/m3 when sampling ambient air

8. **Key technical information**: for example, scales, sampling volume rates, time location and duration of activities that may have influenced the results

9. **Laboratories involved**: including their quality assurance/quality control procedures

10. **Collation of results**: into a single table when there have been several sampling periods to enable efficient appraisal of results and ready detection of trends

11. **Absence of results**: whether due to an absence of testing or because results were non-detects

12. **Composite samples**: where these have been used, including an explanation of compositing techniques, likelihood of significant heterogeneity in individual components and n is the number of samples, and reasons why guideline values should not be divided by n in the assessment process to aid in identifying high concentrations in one
or two individual components of a composite (note that compositing is specified practice for some types of food sampling)

13. **Censored data:** where this has been used and an explanation of data censoring methods

14. **Word-processing:** should allow for track changes, comments, and cutting and pasting into a Word document—note that documents created in Adobe Portable Document Format (PDF) hinder rapid transcription and increase potential for transcription errors.

### 2.8.4 Environmental assessment activities

#### Type 1 cluster assessment

As this is likely to be undertaken by a PHP in response to an initial inquiry, the following processes should be used:

- Ask the informant what they think might account for the number of cases they are reporting.
- Ask the informant to describe the environment of the affected population taking into account the type of disease and the latency (for example, nearby industrial activities, workplace occupational activities).
- Ask if the affected population is currently experiencing or have experienced in the past any unusual or high exposures.

#### Type 2 cluster assessment

This will be undertaken by an officer skilled in environmental health and environmental science.

- Collect a history of the area or the workplace.
- Gather environmental information about the area or workplace (for example, DERM or Workplace Health and Safety data).
- Undertake a site appraisal for the potential of high or exotic exposures to possible causal agents (see Section 8.7 of enHealth 2002).³³
- Assess the validity, integrity and relevance of the above information.
- Appraise the exposures of the potentially affected population (see Chapter 8 of enHealth 2002 and Section 10.3.3)³³.
  - Appraise individuals who have been exposed (all or some of the populations, sensitive subpopulations)
  - What is the nature of the exposure (magnitude, duration, constant or variable)?
- Review the standard literature to develop an understanding of the dose–response relationship for the relevant agent.
- Is the nature and level of exposure likely to explain the findings of the Type 2 epidemiology assessment?
- Write a report for submission to the T3CAT, including an uncertainty assessment. The report should satisfy the relevant sections of Chapter 10 of enHealth (2002).³³

#### Type 3 cluster assessment

This will be undertaken by an environmental health and environmental science expert. More detailed reviews of the literature may be undertaken concerning hazard assessment (that is, hazard identification plus dose–response assessment).

- Review the activities conducted in the Type 2 cluster assessment.
- Determine whether environmental sampling is to be undertaken. If sampling is indicated and the reasons are adequately documented, develop a sampling plan specifying the agents of interest and detail why they are of interest (see Section 8.7 and Chapter 10 of enHealth 2002).³³
- Implement the sampling plan.
- Write a report and submit to the T3CAT including an uncertainty assessment. The report should satisfy the relevant sections of Chapter 10 of enHealth (2002).³³

#### Type 4 cluster assessment
This will be undertaken by a person with both environmental health and environmental science skills and will address particular questions using an appropriately designed research study.

- Review the activities done in the types 2 and 3 cluster assessments.
- Develop and implement an appropriate research plan.

**Issues to be resolved**

- What are the reporting arrangements for the Type 4 research study?
- What else needs to be included to reinforce the integration of the epidemiological assessment with the environmental assessment?
2.9 The role of communication and engagement in a cluster assessment

Disease clusters concern the public. By the time a person actually reports a suspected cluster they will have developed a significant degree of distress.

The public expects to be involved in the investigation through a transparent and accountable process. Without a clear and consistent communication approach, the work of the cluster manager and the cluster assessment team will be hampered. Managing perceptions, information and relationships is the key to achieving good outcome for all parties. This can be achieved by making effective communication integral to a cancer cluster assessment. Evaluating community concerns, context and surrounding issues are some of the responsibilities for the cluster manager (Figure 1 and Section 2.2). In the cluster assessment, information on communication issues should be provided by the cluster manager.

2.9.1 Incorporating a communication role as part of a cluster assessment

The Queensland Health community engagement manual (2010)36 provides broad advice on developing and implementing a strategic community engagement plan. The manual is useful for types 2, 3 and 4 cluster assessments irrespective of whether the cluster manager is a government agency or not. It is the recommended communication approach for Queensland Government agencies responding to clusters of non-communicable disease. The majority of assessments will be initial inquiries or Type 1 cluster assessments. These are generally resolved by a brief telephone call or other form of communication and will not require application of the community engagement manual.

2.9.2 Objectives of communication and engagement

- Demonstrate established processes for assessments of clusters of non-communicable disease.
- Recognise the skills and abilities of the cluster assessment team as being experts in the field.
- Undertake an engagement process that values two-way communication and good community relations.
- Address public concerns and instil public confidence in the actions of the cluster assessment team.
- Build shared understanding about cancer clusters, the investigation process and the personal and community impacts associated with the assessment process.
- Demonstrate an accountable and transparent process aligned with the Community engagement manual.

2.9.3 Communication processes

All communications related to cluster assessment should aim to address the expectations and needs of the impacted community and other stakeholders. Cluster managers must acknowledge the views and concerns of the community. The community should be given the opportunity to express their views with the cluster management process where it is reasonable and practicable.

Queensland Health Integrated Communications Branch will nominate and appoint a communication or engagement officer who has responsibility for developing and implementing the communication plan. The appointed officer will be responsible to the decision-maker identified in each specific cluster assessment. The appointed officer will also report to the cluster manager if Queensland Heath is the cluster manager.

If Queensland Health is not the cluster manager, Queensland Health Integrated Communications Branch may offer specialist advice to the nominated cluster manager, if requested.
2.10 Glossary

**Agent:** Any chemical, physical, biological or social substance or factor being assessed, such as a chemical substance or form of radiation, whose presence or absence (in the case of a deficiency disease) is essential for the occurrence of a disease.\(^{37}\)

**Association:** A statistical dependence between two or more events, characteristics or other variables.\(^{37}\)

**Biological plausibility:** The likelihood that a given factor can cause a biological effect within an individual that leads to disease. It is based on current knowledge of biological processes.\(^{10}\)

**Carcinogen:** A cancer-causing substance or agent.\(^{38}\)

**Cancer risk:** The potential for exposure to a contaminant to cause cancer in an individual or population is evaluated by estimating the probability of developing cancer over a lifetime. Cancer risk is the likelihood, or chance, of getting cancer. The term ‘excess risk’ is used because we all have a ‘background risk’ of about one in four chances for women and one in three for men of getting cancer in their lifetimes, and excess risk is risk greater than this background risk.\(^{37}\)

**Case:** A person in the population or study group identified as having the particular disease under investigation. A variety of criteria can be used to identify cases, as detailed in the case definition.\(^{37}\)

**Case definition:** A set of diagnostic criteria that must be fulfilled in order to identify a person as a case of a particular disease.\(^{37}\) See also Section 2.4.

**Causality:** The relating of causes to the effects they produce. It must be emphasised that epidemiological evidence by itself is insufficient to establish causality though it can provide powerful circumstantial evidence.\(^{37}\)

**Causal agent:** A physical, chemical or biological agent where there is sufficient evidence or weight of evidence to attribute causation of particular disease or biological effects if sufficient levels of exposure occur.

**Chance:** The term chance is used with a number of meanings in the community. In this document, we use ‘chance’ according to the following meaning. Chance is something that happens unpredictably without discernible human intention or discoverable cause. In the context of a slightly increased number of cancer cases in a particular setting, the increase due to chance relates to something that happens unpredictably (or haphazardly) in the community without any particular factor being the cause.

**Cluster:** An aggregation of cases in space and/or time, in amounts that are believed or perceived to be greater than would be expected by chance. The identification of a cluster using this definition does not imply that there is a causal agent, because clusters of biological events do occur by chance. It does, however, indicate the need to assess whether the cluster can be related to factors other than chance.\(^{17}\) In some circumstances, the proposed cluster is initially reported in relation to a geographic location such as a community or site without initially clearly defined risk from a hazardous agent. Determination of a cluster using statistical methods does not imply a cause for the reported excess number of cases. A significant association between disease and exposure may indicate that one causes the other. Alternatively it may mean that both are related to a third variable that influences both, or it may be a coincidence.\(^{39}\)
Cluster assessment: The scientific process to determine if there is an increased number of cases of a specific disease or condition and to determine if there is a biologically plausible causal agent for the disease.

Cluster management: Is the process of evaluating alternative actions, selecting options and implementing them in response to cluster assessments. The decision-making will incorporate scientific, technological, social, economic and political information. The process requires value judgements, for example, on the tolerability of risks and the reasonableness of costs.

Confidence interval: The interval with a given probability, e.g. 95%, that the true value of a variable is contained within the interval.37

Confounding: A situation in which a measure of the effect of an exposure on risk is distorted because of the association of exposure with other factors that influence the outcome under study.37

Dose-response assessment: Determination of the relationship between the magnitude of the dose or level of exposure of a population to an agent and the incidence of specified associated adverse effects.

Environmental appraisal: Environmental appraisal is the consideration of the site history and a walk through inspection by an experienced, expert environmental health or occupational health professional. If these provide evidence of potential problems, environmental sampling may be warranted.

Environmental health: Those aspects of human health determined by physical, chemical, biological and social factors in the environment. Environmental health practice covers the assessment, correction, control and prevention of environmental factors that can adversely affect health, as well as the enhancement of those aspects of the environment that can improve human health.

Epidemiology: The branch of medicine that deals with the study of the causes, distribution, and control of disease in human populations.37

Exposure assessment: The estimation (qualitative or quantitative) of the magnitude, frequency, duration, route and extent of exposure to a potentially hazardous agent for the general population, for different subgroups of the population, or for individuals.

Hazard: The capacity of an agent to produce a particular type of adverse health or environmental effect.

Hazard assessment: The identification, from animal and human studies, in vitro studies and structure–activity relationships, of adverse health effects associated with exposure to an agent. Hazard assessment comprises hazard identification and dose–response assessment. It essentially identifies whether potentially hazardous agents are present, what type of health effects can arise with sufficient exposures and the incidence of those health effects at various levels of exposure. Exposure assessment is closely related to hazard assessment and assesses whether people are exposed to hazardous agents and, if so, how they are exposed and the magnitude of the exposure. In a cluster assessment the combination of hazard assessment and exposure assessment is to determine whether there are sufficient exposures to a hazardous agent to account for the rate of a particular disease.

Hazard identification: The identification, from animal and human studies, in vitro studies and structure–activity relationships, of adverse health effects associated with exposure to an agent.

Incidence: The number of new cases of disease in a defined population over a specific time period.37
**Incidence rate:** The rate at which new events, such as brain cancer diagnosis, occur in a population. The numerator is the number of new events that occur in a defined period. The denominator is the population at risk of experiencing the event during this period, sometimes expressed as person-time.\(^{37}\)

**Latency:** Also known as ‘latency period’. The period of time between exposure to a disease-causing agent and the appearance or diagnosis of a cancer or non-infectious disease known or suspected to be associated with that agent. This definition is consistent with the definition used in *A dictionary of public health*.\(^{37}\) The year of first exposure and the pattern and magnitude of exposure need to be considered.

There are other definitions used in other references and readers should be aware of these differences when using other texts. For example, they may refer to the ‘onset of cancer’: the context usually implies that this is the time of clinical or symptomatic appearance or diagnosis of a cancer rather than the time when it occurs at a microscopic level.

Issues regarding latency are well summed up in a document by the Australasian Faculty of Occupational Medicine on Occupational Cancer.\(^{40}\) ‘Therefore, before attributing a cancer to a past exposure, an estimate should be made of the period between the exposure and cancer onset to ensure that at least the minimum latency period has elapsed. Most epidemiological studies tend to exclude cancers within 10 years of first exposure and, because of the number of steps in the transformation from a normal cell to malignancy, greater confidence can be placed in a causal association with longer periods following exposure. There is good evidence that the latency period for benzene and radiation-induced leukaemia may sometimes be less than 10 years. However, evidence is scant on the minimum latency periods for most cancers. Therefore in the absence of good data, latency periods of less than 10 years cannot be totally ruled out.

There is often limited information available about latency for specific cancers.\(^{31}\) The best information is where there has been a well-defined exposure to a known disease-causing agent such as radiotherapy and the subsequent development of leukaemia. The latency period for more aggressive cancers tends to be shorter than for less aggressive cancers. There is often a long period (10 to 30 years or more) between the first exposure to a known carcinogen and a diagnosis of cancer.\(^{41}\) Longer periods (for example, 30 years) have been proposed for conditions such as mesothelioma. The latency period between exposure and development of mesothelioma is long—estimated between 20 and 30 years and even up to 45 years.

For breast cancer, more than 18 years is required from the first tumour cell (=10\(\mu\)m in diameter) to produce a tumour with a diameter of 2\(\)mm. This tumour size of 2\(\)mm is approximately the lowest detectable level by mammogram.\(^{31}\) The median time for the tumour to grow from mammographically detectable size to clinically detectable size is estimated to be approximately 1.7 years.\(^{42}\)

For cancer cluster assessments, a latency of five years is used as the minimum period for assessments. A shorter period of time should be used only if there is good evidence for the particular type of cancer. Average latencies of 10–20 years are more easily justified. While there are likely to be variations of latencies for individual cases of the same cancer in any particular cluster assessment, the distribution of these individual latencies would be expected to follow a Poisson distribution and therefore would not be a number of unusually short latencies for these cases.

**Multiple comparisons:** Adjustment of the \(p\) values from a cluster investigation for implied comparisons with similar populations. One common way to adjust for multiple comparisons is by the Bonferroni adjustment. Selection of the number of multiple comparisons is subjective.

**Potency:** This is a measure of the incidence of effects (‘the response’) in a population for particular levels of exposure (‘the dose’). Agent ‘A’ is more potent than agent ‘B’ if it has a higher incidence of effects for similar exposures. It is useful to consider in cluster assessment to decide whether the
levels of exposure of the affected population to a known causal agent could account for the increased rates of disease observed.

**Reference population:** This will usually be the Queensland Estimated Resident Population for the years included in the case definition.

**Study population:** The population referred to in the case definition. The population considered to be potentially at risk for the identified agent.

**Surveillance:** Data collection to detect events or identify trends to initiate public health action.

**Type 1 cluster assessment:** Assessment of whether the cases reported by the informant could potentially be a cluster.

**Type 2 cluster assessment:** Assessment, using existing data, of whether there is an excess incidence of cases meeting the case definition and possible sufficient exposure to a biologically plausible causal agent for the type of disease reported. In comparison to Type 1 cluster assessment, Type 2 cluster assessment includes more detailed case ascertainment, an assessment of the presence of exposure to a biologically plausible causal agent and exposure assessment of the relevant population, using existing data sources.

**Type 3 cluster assessment:** Assessment, using newly collected and existing data, to quantify the excess of disease and undertake a detailed exposure assessment of biologically plausible causal agents. A very detailed case ascertainment is undertaken. Further data collections are likely to occur when undertaking the type of assessment.

**Type 4 cluster assessment:** A research study to investigate biologically plausible hypotheses generated by the Type 3 cluster assessment. It will further explore and define causal and non-causal links between the disease and exposure. It is conducted only in the very rare situations where a Type 3 cluster assessment provides outstanding questions which can be answered through a research study. While other assessment types are essentially retrospective in nature a Type 4 cluster assessment may incorporate prospective elements. The research study requires a range of expertise and may be collaboration between government and the resources available through academic institutions.
2.11 Abbreviations

DEIR    Department of Employment and Industrial Relations
DERM    Department of Environment and Resource Management
DET     Department of Education and Training
ED HPD  Executive Director, Health Protection Directorate
HSC     Health Statistics Centre
PHP     Public Health Physician
QCCAT   Queensland Cancer Control Analysis Team
SLA     Statistical Local Area (Australian Bureau of Statistics)
T2CAT   Type 2 Cluster Assessment Team
T3CAT   Type 3 Cluster Assessment Team
2.12 References


