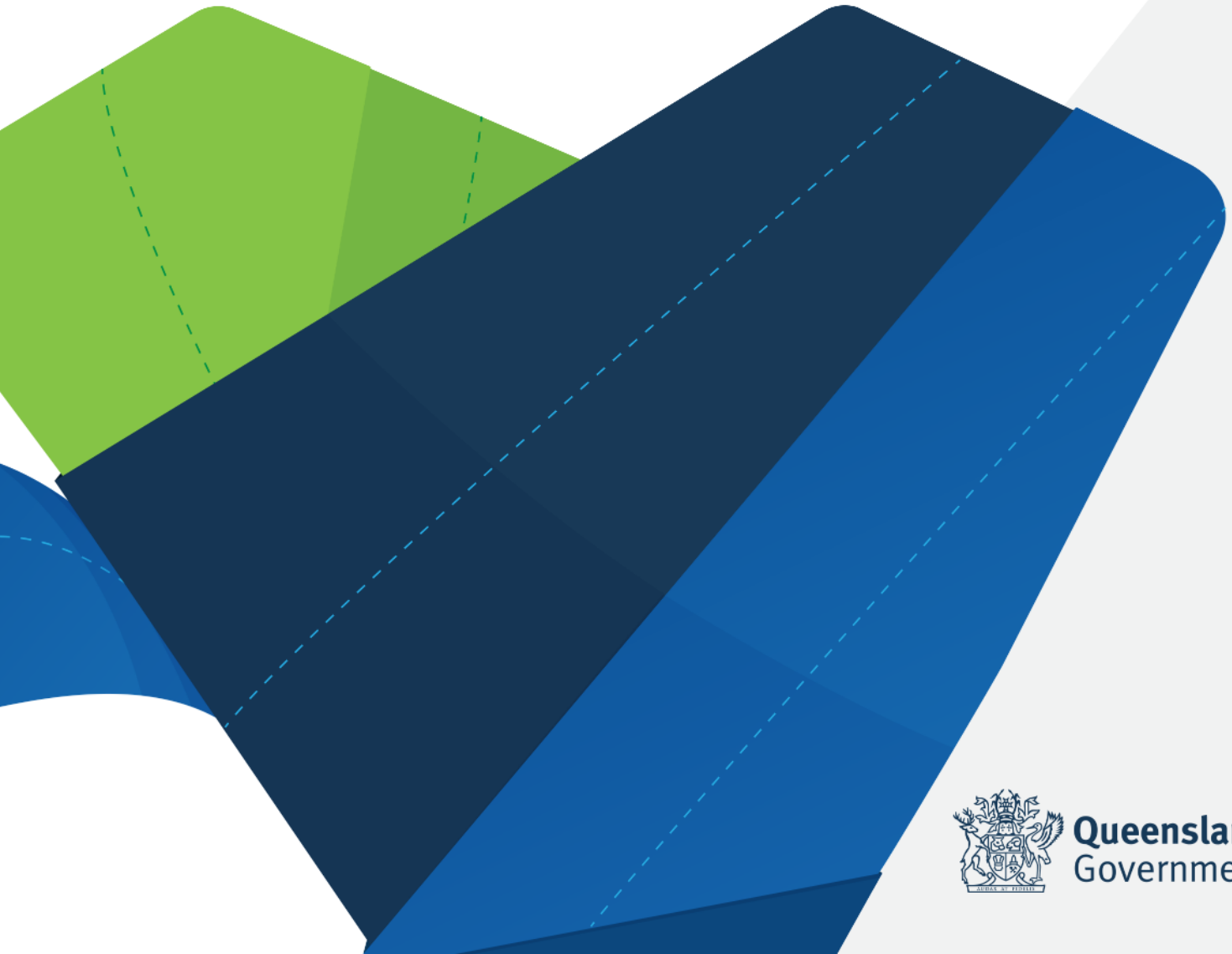
Queensland Health non-communicable disease cluster assessment guidelines 2019



Queensland Government

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About this report
The Queensland Health non-communicable disease cluster assessment guidelines describe the concepts and processes involved in the assessment of non-communicable disease clusters in Queensland. The guidelines are intended for use primarily by Queensland Health staff, although others may find it useful to know how Queensland Health responds to cluster concerns. For details of how to use the guidelines, please refer to the 'Users' guide' (page 5).

Version history
Original: 2009
Revision 1: 2012
Revision 2: 2018-19

Queensland Health non-communicable disease cluster assessment guidelines is available on the Queensland Health website: https://www.health.qld.gov.au/research-reports/population-health/cancer-clusters

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Table of Contents

Users guide

The **Queensland Health non-communicable disease cluster assessment guidelines** have been developed with the primary aim to assist Queensland Health staff to respond to and lead the assessment of suspected clusters of non-communicable disease such as cancer. Cancer is used as an example of non-communicable diseases throughout this guideline. Staff of other agencies involved in managing the assessment of clusters and communicating with the community may also find the guidelines useful. These guidelines are available publicly and are a resource to help the community understand the process of assessment and investigation.

The guidelines are divided into two parts.

Part 1 describes the step by step process of addressing the community concern regarding a suspected disease cluster. The process usually begins with an inquiry from a member of the public. Many concerns can be addressed in discussion with an experienced public health physician. In some instances, the enquiry progresses beyond the initial discussion to a type 1 or subsequent level of investigation, based on the degree of complexity of the issue. These guidelines describe the step by step process through the four types or levels of assessment, where type 4 is a research study. Table 1 (page 9) provides a convenient summary of what each type of investigation may entail. Management roles are described, epidemiological and environmental characteristics documented as are levels of approval and accountability. Part 1 includes a description of the cluster assessment register.

Part 2 describes in detail the role of Queensland Health and potentially other agencies in the assessment. It explains in greater detail the epidemiological and environmental processes, statistical analysis, communication strategy and media processes.

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1 The guidelines

1.1 Overview

Queensland Health (QH) takes community concerns about possible environmental causes of non-communicable disease seriously. Cluster inquiries are based on best-available evidence and are to be managed in a timely, empathetic and effective manner.

The *Queensland Health non-communicable disease cluster assessment guidelines* were originally developed in 2009 in a series of consultations involving QH staff and external experts in reference to the NHMRC Statement on Cancer Clusters[2] and international guidelines.[3-6] This 2019 edition has updated this guidance and simplified it where possible.

1.1.1 Purpose of the guidelines

Definitions
Cluster - The aggregation of cases in space and/or time, in amounts that are believed or perceived to be greater than would be expected by chance.[1]
Cluster assessment - Cluster assessment is a 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/s for the disease.

The purpose of these guidelines is to facilitate a systematic and multidisciplinary approach by QH officers in response to inquiries and concerns from the community and others about potential clusters of non-communicable disease.

The *Queensland Health non-communicable disease cluster assessment guidelines* have been developed for use specifically when QH is the lead agency in the assessment of potential non-communicable disease clusters. In addition, these guidelines should be used for all components of cluster assessments which QH undertakes or participates in. They do not apply to acute situations such as communicable disease outbreaks or bioterrorism events for which relevant guidelines should be followed. Section 1 of these guidelines describes the process for initial inquiry and cluster assessment of the four types. Supporting and more detailed information can be found in Section 2.

Components of cluster assessment described include:

- the role of QH in investigating and advising on reported clusters
- scope and processes of the different types of assessment
- roles and responsibilities of people and groups involved
- processes for recording, conducting, reporting and communicating an assessment
- evaluation and review of the assessment process.

Since the initial release of these guidelines in 2009, QH has developed a suite of resources for staff to effectively address public concerns about non-communicable disease clusters.

These are available on QH intranet: https://qheps.health.qld.gov.au/dcho/epidemiology/resources. QH also developed a suite of fact sheets describing common cancers and the cancer cluster assessment process for the public (https://www.health.qld.gov.au/research-reports/population-health/cancer-clusters).

1.1.2 Background to cluster assessments

Non-communicable disease cluster assessments often don't identify a common cause. Even when no cause is found, the investigation and explanation provided to the public can be reassuring and allay fears and anxieties. Investigations should consider the public's perception of risk and influence of the media, as maintaining trust and transparency with the community is important throughout the assessment.

Most reported non-communicable disease clusters have no identifiable cause and most do not require extensive evaluation. Experience in Queensland[7], other Australian jurisdictions, and internationally[8] suggests that 75–95% of reported suspected clusters can be completed quickly after initial contact. These guidelines aim to ensure potential clusters are not overlooked, and equally that resources are not allocated to unnecessary assessments, nor escalated unnecessarily.

In Queensland, reports of potential disease clusters can come from a range of sources but usually are from a concerned individual, health professional, political representative, workplace representative or government agency (e.g. education department). These usually concern a workplace, school or specific geographic area. Concerned communities will often assume an environmental hazard is responsible for an apparent cluster of disease when witnessed in a geographical area, time-period or particular group of people. Exposure to environmental toxins is generally quite unlikely in settings such as schools, suburban neighbourhoods or office buildings.

Cluster assessments, even with an excess case number, rarely result in important scientific findings of relationships between exposures and disease.[8, 9] There are well-known instances in which the cluster assessment of an unusual cancer has led to identification of a previously unrecognised human carcinogen.[2] These all involved clusters of a rare type of cancer in people with prolonged high-intensity exposure to an industrial/occupational or medical carcinogen,[9, 10] 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 or low incidence are observed.[11]

About 80% of non-communicable disease cluster reports have been related to cancer concerns. 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'.

1.1.3 Role of Queensland Health

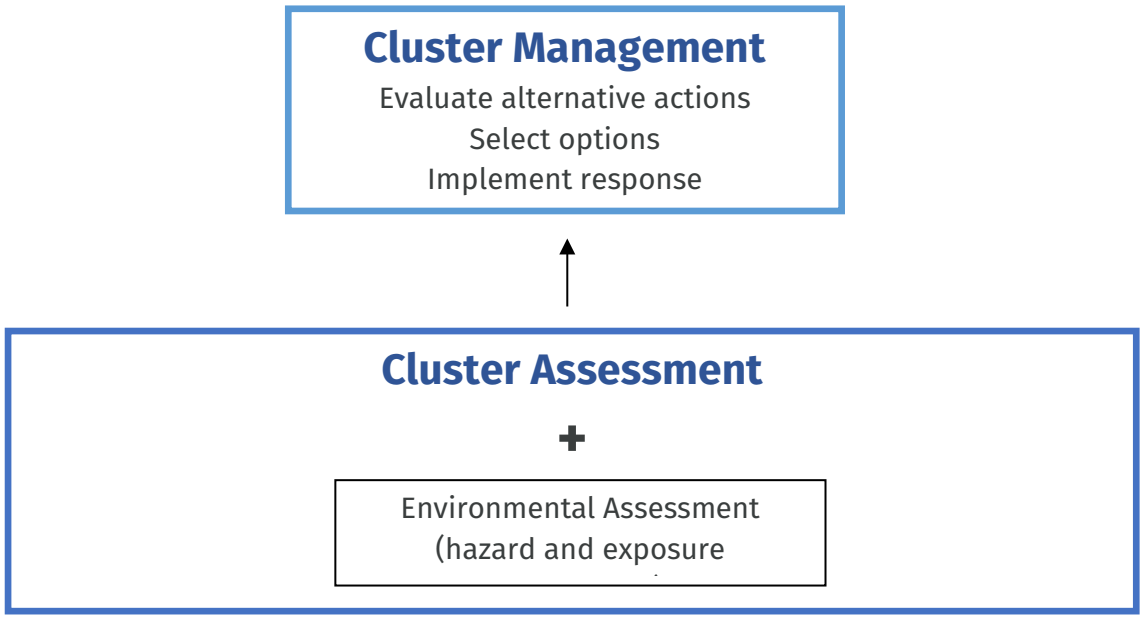
The role of QH during cluster assessment must be determined as soon as possible after the initial inquiry by an informant, before any other action is taken. QH may not be the cluster assessor, and it is important to determine what role it has (see Section 2.1).

When QH has a clear role, the cluster manager and the agency responsible for each component of assessment must be identified as a priority.

1.1.4 Cluster management

Before assessment begins, the cluster manager must be identified. 'Cluster management' is defined as the process of evaluating alternative actions, selecting options and implementing them in response to cluster assessment findings. The QH designated public health physician (PHP), delegate or chair of the cluster assessment team should liaise with the cluster manager as appropriate.

Figure 1: Overview of cluster management and cluster assessment



QH is cluster manager when QH facilities such as public hospitals are involved. Another example of a site-specific cluster manager would be the Queensland Department of Education for a cluster in a state school. Site-specific cluster managers usually have accountability arising from their ownership of an affected site. Some other aspects affecting determination of cluster manager include workplace health and safety liabilities (e.g. employers of the relevant workforce) or jurisdictional/legal responsibilities (e.g. local government of a town). In community-based clusters, the cluster manager will be determined through discussions between QH and key organisational stakeholders. Cluster management is further described in Section 2.2.

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 then investigate if there is a biologically plausible causal agent for the disease.

Assessment, including communication, of a non-communicable disease cluster is undertaken by a multidisciplinary team, including PHPs, epidemiologists, statisticians, environmental health officers (EHOs) and media and communications staff.

A cluster assessment is comprised of two essential components:

a. epidemiological assessment

b. hazard and exposure assessment (also called environmental assessment).

Initially an epidemiological assessment identifies 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. If a greater-than-expected number of cases is found, an environmental or hazard assessment determines if there is a biologically plausible causal agent for the disease.[12]

Both components are necessary to complete a cluster assessment. Lifestyle and genetic factors should also be taken into consideration because of their importance in disease causation. While these factors are of substantial importance, the primary data sources (e.g. Queensland Cancer Registry) for comparing observed and expected case numbers do not enable a quantitative appraisal of these factors. Assessment of such factors is feasible when addressing initial inquiries with the informant while conducting Type 1 or 2 cluster assessment. In Type 3 assessments, more detailed qualitative assessment of lifestyle and genetic factors may be required. Type 4 cluster assessments are research studies, usually involving a broad scope of data collection and assessment.

1.1.6 Communication

Communication is an integral part of all cluster assessments

Open and clear communication between the informant and the cluster manager and assessment teams is vital to ensure transparency, trust and two-way communication throughout the assessment. This is especially important in cluster assessments which may or have escalated. Communication of assessment process and findings is primarily the responsibility of the cluster manager, and may focus on affected individuals, concerned community and the media. This requires careful, sensitive consideration, and potentially QH media and communications staff and senior management input. Further information is described in Section 2.10.

Important points:

- Each of the four types is an assessment in its own right.
- Assessment typically begins with an initial inquiry from a concerned individual, usually relating to a school, workplace or neighbourhood.
- Based on initial contact and information provided by the informant, QH should determine if the reported concerns could potentially be a cluster.
- Open dialogue and transparency is key to interaction with informants.
- Investigations may require a mix of elements from the four assessment types, and analytic steps may occur concurrently or repeatedly.

- In unusual circumstances where significant exposure to a known hazardous agent is identified, a rapid transition from one type of cluster assessment (e.g. Type 1) to another (e.g. Type 3) may need to occur.
- The assessment process as presented in the guidelines is not necessarily a linear process in practical circumstances.

Based on QH's past experience and available evidence nationally[2] and internationally,[3-6, 8] most inquiries or concerns related to non-communicable disease clusters require only 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 required, and Type 4 research study assessments are very rarely undertaken.

1.1.7 Authority

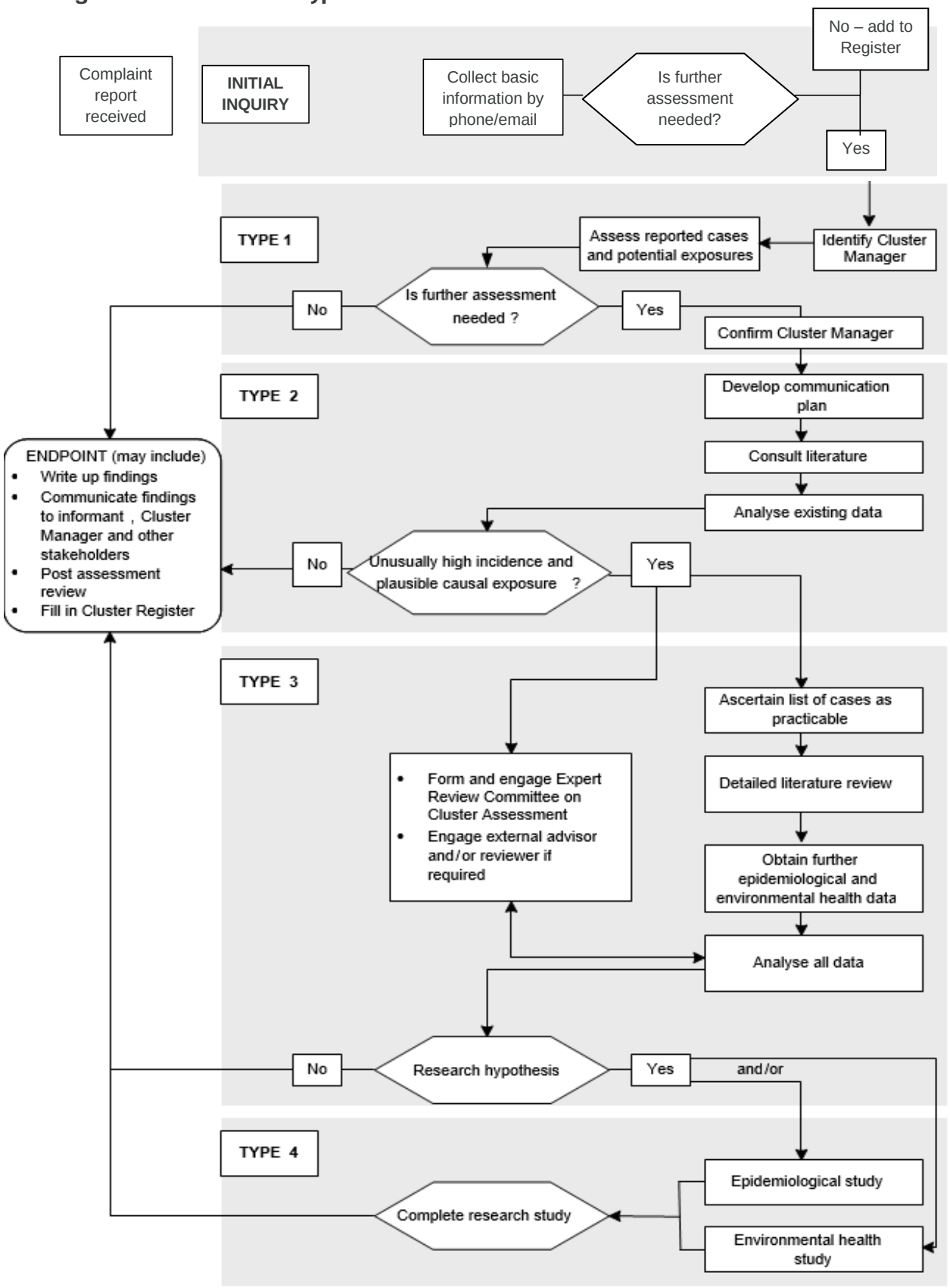
The authority to proceed and determine an appropriate type of assessment is made by the designated PHP and other QH appointed officers. Cluster assessment should follow best practice guidelines in planning, implementation and communication.

Table 1 - Features of each type of cluster assessment

	Initial inquiry	Type 1 cluster assessment: Inquiry response	Type 2 cluster assessment: Data assessment	Type 3 cluster assessment: Analytical assessment	Type 4 cluster assessment: Research study
Purpose	To assess whether the concern reported by the informant requires further assessment	To assess whether the cases reported by the informant could potentially be a cluster	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	To quantify the excess of disease and undertake a detailed exposure assessment of biologically plausible causal agents	To investigate biologically plausible hypotheses generated by the Type 3 assessment
Decision-maker	Public Health Physician	Public Health Physician	Type 2 cluster assessment team (+/- Expert Advisory Committee to be formed)	Type 3 cluster assessment team with advice from Expert Advisory Committee on Cluster Assessment (to be formed)	Large and specialised team (commonly outsourced)
Research question definition, data collection and analysis	n/a	Use informant data on cases and exposures May include use of standard literature and texts and/or use of additional existing data – Queensland Cancer Registry (routine inpatient data is rarely justified)	Use existing data Consult literature Validate cases Ascertain complete list of cases Quantify study population Determine expected case numbers from reference population Conduct environmental appraisal of setting +/- sampling	New data collected and analysed – epidemiological and/or environmental	New data collected and analysed – epidemiological, environmental and/or experimental

	Initial inquiry	Type 1 cluster assessment: Inquiry response	Type 2 cluster assessment: Data assessment	Type 3 cluster assessment: Analytical assessment	Type 4 cluster assessment: Research study
Cluster Assessment Team	n/a	**Assessment** Public health physician +- Senior local officer/s of: • Epidemiology and/or • Environmental health and/or • Media and communications +/- Other experts	**Assessment** Public health physician +- Senior local officer/s of: • Epidemiology and/or • Environmental health and/or • Media and communications +/- Representatives of other stakeholder groups +/- Other experts	**Assessment** Public health physician +- Senior local officer/s of: • Epidemiology and/or • Environmental health and/or • Media and communications +/- Representatives of other stakeholder groups +/- Senior statistical officer/s of Queensland Cancer Control Analysis Team (QCCAT) and/or Queensland Health Statistical Services Branch (SSB) +/- Other experts	As required
Indicative level of time	<6 hours	0.5–20-person days	10–50-person days	50–300-person days	>300-person days Very high human resource
Likely duration	Less than a week	Less than a week	Weeks–months	Months–year	Months–year

Figure 2: Overview of the types of cluster assessment*



*assessment process may not always follow a linear process and transition between Types may vary with situational circumstances

1.1.8 General assessment approach

A step-by-step approach that follows principles of good epidemiological and environmental health research is required.[5] The extent and nature of these steps will depend on the type of cluster assessment, and may not occur in the exact order below. A summary of the general steps taken in cluster assessment is described, noting that some of these steps would be unnecessary for Type 1 and 2 assessments.

Initial contact: Establish that a concern exists. Understand the social, economic and political context of the reported cluster.

Identify Cluster Assessor and Cluster Manager: The cluster assessment team and cluster manager will depend on the location and nature of the reported cluster.

Establish a case definition: Develop an appropriate case definition and adequately ascertain cases.

Epidemiological assessment: Identify the study population i.e. the denominator. Determine the expected number of cases. Understand the biology of the disease (e.g. cellular basis, casual factors, latency, development and progression) and how the disease has been diagnosed. Look for patterns, relationships and trends.

Environmental assessment: Collect data on all relevant environmental exposures and specify the potentially exposed population. Specify the biologically plausible causative agent. Quantify the period and the dose (intensity) of exposure. Characterise the epidemiological factors in relation to the event and undertake an exposure assessment of the relevant population.

Synthesize hypothesis: Formulate the hypothesis consistent with epidemiological and exposure data. Test the hypothesis.

Communication: Report findings, obtain peer review and communicate results—reports of similar assessments should be sought. Communication with affected communities/workplaces should occur through-out assessment to maintain relationships and trust.

1.1.9 Common challenges

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 assessment
- incorporating disease latency periods
- 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
- communicating with key stakeholders
- ensuring a clear and shared understanding between QH and other key stakeholders.

1.1.10 Government and cost

QH utilises established reporting and advisory pathways to undertake cluster assessment. Section 2.3.4 details the parameters under which external advisors and reviewers are engaged.

An indication of time required for each type of cluster assessment is provided in Table 1. Predicting time required and financial costs for cluster assessment is difficult, and the final amount is the cumulative cost incurred for **each type** of assessment undertaken. This 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 cost US$12 million.[13] It is often difficult to predict the time and financial costs required for a cluster assessment, and the final cost is the cumulative incurred for each type of assessment undertaken.

1.1.11 Terminology

Key terms such as 'cluster', 'risk', 'hazard' and 'latency' are defined in the Glossary (Section 2.11). Consistent with national and international documents, cluster is defined 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'. Importantly, the identification of a cluster using this definition does not imply there is a definite causal agent. It does however indicate the need to assess whether the cluster is related to factors other than chance.[2] This added layer of assessment uses environmental health, toxicological and risk assessment expertise.

1.1.12 Review

It is recommended that both the guidelines and cluster assessment resources be reviewed periodically as needs arise.

1.2 Initial inquiry

Most cluster inquiries or concerns are resolved in the first phone call.

Responding to an initial inquiry usually takes less than half a day.

For most suspected clusters of cancer and other non-communicable diseases, no plausible explanation is found. Regardless of the outcome of assessment, it is important that the informant's concerns are addressed at the initial phone call. The effectiveness of the initial discussion will have a significant impact on whether further assessment and reassurance is sought and, if so, the nature, duration and scale of further assessment.

Initial inquiries about a suspected cluster may come from a concerned individual or group, health professional, political representative, or 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. If after the initial inquiry the PHP makes the decision not to progress the assessment, basic information should be recorded on the Cluster Assessment Register (see Section 1.7).

A suite of resources, including an initial informant data sheet, exist on the QH intranet website to assist with non-communicable disease cluster assessment. Given the complexity of assessing and responding to a potential disease cluster, it is crucial that the initial inquiry is addressed prudently. The following guidance may be helpful:

- **Initial response**: Advise front office staff to collect contact details of the informant for a return call. Allow time to prepare for a detailed discussion with the informant.
- **Preparation**: Prepare with sufficient information to answer likely questions from the informant. QH's online 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 QH staff should attempt to make initial contact an empathetic conversation with information provided (e.g. fact sheets) to assist the informant with their concerns.
- **Respond promptly**: Generally, the inquiry should be satisfactorily addressed in the first conversation. In the few instances which warrant progression to further assessment, ensure the informant's concerns are addressed quickly, by phone or in person.
- **Implicate prudently**: The informant should be given sufficient information to help understand and appreciate that cluster assessment is complex and often there are no simple answers to completely satisfy everyone.

1.3 Type 1 cluster assessment – Inquiry response

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

Determination of the concerns of the individual or group is a priority of cluster management and should be clarified before any assessment commences.

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

	Type 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 is rarely justified
Cluster assessment team	• Public health physician +- Senior officers of: – Epidemiology and/or – Environmental health and/or – Media and communications +/- Other experts Cluster management • +/- Cluster manager
Indicative level of time	0.5–20-person days
Likely duration	Day–months

1.3.1 Initiating a Type 1 cluster assessment – briefing

If a cluster inquiry

- involves a Queensland Government facility the Executive Director, Health Protection (ED-HP), should be notified as soon as possible. The ED-HP will notify the Chief Health Officer (CHO) or Director-General, as appropriate.
- is likely to attract substantial public concern or media interest, the ED-HP should be notified in writing and the degree of concern/interest may need assessment.
- involves a Queensland Government facility and/or is likely to attract significant public concern or media attention, the relevant HHS Chief Executive should also be notified.

QH media and communications may also be informed, if the situation requires it.

1.3.2 Conducting a Type 1 cluster assessment

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

Type 1 cluster assessment requires expert judgement of the reported situation by the PHP. The PHP may seek expertise of epidemiology, environmental health, and media and communications across the QH state-wide operations.

The PHP will identify the cluster manager and provide them with these guidelines.

The principal data source for Type 1 assessment of cases and exposures is from the informant. A Type 1 assessment does not involve detailed examination of the literature, and collection of new data beyond that provided by the informant is rarely justified. The initial information collected from the informant as well as the standard literature search is expected to help answer questions such as:

- Who is the cluster manager?
- Who are the stakeholders?
- How many diagnoses of the same cancer or illness types are there?
- Who is included in the study population?
- Are the number of reported cases appearing to be more than would be expected for the study population?
- Are there any particular exposures that the informant is concerned about?
- Is there unusual or high exposure/s to a biologically plausible causal agent apparent for the disease in question?

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.

Type 1 cluster assessments generally will not require quantitative epidemiological assessment to determine if there is a potential excess number of cases given the size and demographics of the population. Expected case numbers can be drawn from expert knowledge or published literature including QH's Chief Health Officers report[14] or Queensland Cancer Registry documents. Observed case numbers are based upon information provided by the informant.

In a Type 1 assessment, exact rates of the relevant disease within the study population are not usually calculated. Similarly, quantitative comparison of observed and expected rates is rarely required. 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.

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.

Next, the PHP will consider any known or suggested biologically plausible causative agents, whether they exist in the alleged cluster community, and whether there is evidence of association with this type of cancer. The informant's perception of possible exposures associated with the disease should be sought. Environmental aspects including nearby industrial activities and workplace occupational activities should be detailed.

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

1.3.3 Decision points for the Type 1 assessment

The authority and decision to finalise a Type 1 cluster assessment is made by the PHP or delegate (Table 2). If multiple PHU regions are involved, the PHP may consult other PHPs, epidemiologists and environmental health professionals, to reach a decision.

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

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: Decision marker: PHP or delegate

Criteria to finalise Type 1 cluster assessment	Criteria to undertake a Type 2 cluster assessment
• no apparent excess number of cases given the demographic profile of the population • small numbers of a common disease for the study population • range of different diseases reported • insufficient exposure to a biologically plausible causal agent to account for the number of cases of the disease reported • inadequate latency period based on available evidence	• apparently higher than expected number of cases given the demographic profile of the population • unusual types of disease • plausible exposure to a plausible causal agent for the reported disease • adequate latency for the reported disease • identification of multiple cases of a rare disease, or a common one in an unusual age group • significant community concern or public interest

1.3.4 Finalisation of a Type 1 cluster assessment

Communication is the key aspect of cluster assessment and cluster management in addressing community concerns

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

1. Communication

Following the decision to finalise the assessment, a response outlining the decision and rationale should be provided to the informant, cluster manager and other key stakeholders. This can be by telephone, followed by written report if necessary. The response should be clearly articulated, empathetic, and based upon communication strategies as described in Section 2.10. The response could include information about the alleged cluster, and general information on disease clusters including fact sheets and preventive health messages.

2. Documentation

Documentation (e.g. file note) and/or written report should outline details of:

- the initial inquiry or concern
- the data considered in the cluster assessment including epidemiological, environmental or toxicological aspects
- any broader public concern or potential for high-level public concern
- communication with the informant

The documentation and/or written report, if prepared are a sufficient record for Type 1 cluster assessment.

3. Briefing

If the cluster inquiry is likely to attract substantial public concern, the ED-HP should be notified initially and at finalisation of the assessment. If notified at commencement, the HHS Chief Executive and QH media and communications should be informed of finalisation. Briefing to the ED-HP should include the response to the informant and other key stakeholders, and the written report if prepared.

4. Cluster assessment register

The PHP should ensure details of the assessment including a record of decisions and actions are entered into the cluster assessment register (see Section 1.7) held by Preventive Health Branch Epidemiology, Queensland Health.

1.4 Type 2 cluster assessment: data assessment

A Type 2 cluster assessment is initiated based on the 'Criteria to undertake a Type 2 assessment' in Table 2. It 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.

	Type 2: Data assessment
Purpose	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.
Decision marker	Type 2 cluster assessment team (+/- Expert Advisory Committee to be formed)
Research question definition, data collection and analysis	• 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 +/- sampling
Cluster assessment team	• Public health physician +- Senior officers of: – Epidemiology and/or – Environmental health and/or – Media and communications • +/-Representatives of other stakeholder groups • +/- Other experts • Cluster management – Cluster manager
Indicative level of time	10–50-person days
Likely duration	Weeks, months

1.4.1 Briefing and approval to initiate Type 2 cluster assessment

- If the focus of the inquiry involves a Queensland Government facility, the ED-HP should be notified as soon as possible. The ED-HP should notify the CHO or Director-General, as appropriate. 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-HP should be notified in writing and the degree of concern/interest may need assessment.
- QH media and communications should be informed if appropriate.
- When notifying the ED-HP, consider detailing:
  - rationale for proceeding to Type 2 assessment
  - why QH is involved
  - nature of QH's role, scope, duration and reporting processes
  - human and financial resource requirements, options for resource allocation including potential position backfill
  - potential opportunity costs.
- An Expert Advisory Committee on Cluster Assessment (EAC) may be formed and convened to provide advice regarding cluster assessment (see 1.5.5 and 2.6 for further information).

1.4.2 Role of Queensland Health

The role of QH as cluster assessor (epidemiological and/or environmental health assessor) must be determined before initiation of Type 2 cluster assessment. If QH is not cluster assessor for both components, then it is important to determine which agency is cluster assessor and if QH has a role.

1.4.3 The Type 2 cluster assessment team

The role of the Type 2 cluster assessment team (T2CAT) is defined in Table 3. Membership of the T2CAT should be confirmed before assessment begins and roles and responsibilities should be clarified at the outset. The T2CAT reports to the ED-HP.

The T2CAT may include the following:

- PHP
- Epidemiology staff, and

Senior officers of:

- Environmental health
- Media and communications
- Representatives of other stakeholder agencies, e.g. relevant local government agency, departments of environment employment and industrial relations
- Other experts.

The roles and responsibilities of the T2CAT are described below:

- The designated **PHP** is to chair and coordinate the T2CAT and ensure that resources to undertake the assessment are identified and managed. The role of chair can be delegated 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 the assessment
  - liaise with the affected community
  - undertake statistical analysis with advice and technical assistance as required
  - provide expert advice
- **Other department staff** are to provide further expert epidemiology, environmental health and toxicology advice if required.
- **Queensland Health media and communications staff** are to develop and implement the cluster-specific communication plan.

The T2CAT conducts the assessment with assistance from specialist teams including Queensland Cancer Control Analysis Team (QCCAT) and Queensland Health Statistical Services Branch (SSB) staff to provide advice regarding:

- epidemiological data analysis and statistical interpretation
- availability and limitations of relevant data (mortality, cancer registry, perinatal, and population data for the relevant denominators).

The T2CAT may also seek advice from the EAC.

1.4.4 Conducting the Type 2 cluster assessment

Type 2 cluster assessment conducted by the T2CAT should include (Table 3):

- a literature review of biology and risk factors for the disease, including latency and natural history, how these relate to reported period of exposure, and the period when the cases of disease were diagnosed
- a review of the study population epidemiology to ascertain if a statistical excess has occurred. Principles of epidemiological analysis are described in Section 2.8
- an environmental health assessment of agents and exposures to determine if there is a biologically plausible causal process (plausible agent and significant exposure) involved.

For this type of assessment appraisal of the setting is required. Environmental appraisal involves consideration of site history and a site inspection by experienced environmental health or occupational health professionals. Environmental sampling should only be conducted if there is clear and appropriate rationale, sampling plan, and resource allocation (Section 2.9).

Key documents to assist with the epidemiological, environmental health and toxicological evidence appraisal are listed in Section 2.9. These components are complementary and address the overall goals of the cluster assessment. Resources to assist with assessment are available on the QH intranet website (QHEPS).

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

Process	Analytic actions
• Confirm cluster manager and provide QH guidelines for cluster assessment. • Confirm epidemiological and environmental health cluster assessors. • Continuously review the endorsed plan for the cluster assessment, including roles, responsibilities (e.g. report writing), timelines, communication and resources required (human, time, funds). • Develop and implement a communication plan (Section 2.9). • Key stakeholders should be kept informed of progress at each step	• Develop a case definition describing disease/condition, geographical area, population group and time period. • Determine the research questions (Section 2.5). • Specify the study population • Scope and plan the assessment- includes case ascertainment (Section 2.4), study population determination methods, available sources of epidemiology, toxicology, environmental health and other scientific data • Assess epidemiology and environmental health using literature and existing data sources • Conduct environmental appraisal of setting to determine any links with biologically plausible causative agent • Interpret data and results and prepare scientific reports

1.4.5 Decision points for Type 2 cluster assessment

The decision to finalise the Type 2 cluster assessment or move onto a Type 3 cluster assessment is made by the T2CAT, based on expert multidisciplinary knowledge (Table 4) and the following considerations:

- 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?

Approval to undertake a Type 3 cluster assessment must be obtained from the ED-HP before proceeding. Such approval will be based on:

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

Table 4 – Decision making at conclusion of Type 2 assessment: Decision marker Type 2 cluster assessment team

Criteria to finalise the Type 2 cluster assessment	Criteria to undertake a Type 3 cluster assessment
• considering biological processes including latency periods, no excess of cases beyond what could be expected by chance alone for the study population • lack of sufficient exposure to a biologically plausible causal agent for the disease reported	• unusually high number of cases based on data from existing data sources • biologically plausible cause identified and sufficient exposure likely: Type 3 cluster assessment should not be undertaken if no likely sufficient exposure pathways or biologically plausible causal agents are identified • practicability of further assessment • new evidence about causation or methods of assessment become available.

1.4.6 Finalisation of the Type 2 cluster assessment

a. Governance to finalise the Type 2 cluster assessment

The decision to finalise the Type 2 cluster assessment is made by the T2CAT and approval should be obtained from the ED-HP.

b. The Type 2 cluster assessment report

A final report for the Type 2 cluster assessment will include:

- rationale for 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.
- an estimate of resources used (staff time and financial)

It may be necessary to undertake an internal review prior to release of the report. This review may be done by relevant QH staff not involved in the assessment. In addition, external review may be required, based on results of the assessment and social, economic and political implications and interests in the report. External review should be initially undertaken by the EAC (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 provided to the ED-HP prior to public release, who will also forward the report to the cluster manager and senior officers in QH.

c. Briefing to finalise the Type 2 cluster assessment

Following decision to finalise the assessment, depending on the situation, it may be appropriate to prepare a Briefing Note for information to the HHS Chief Executive, the Minister for Health, the Director-General, the CHO, and/or senior directors/managers of relevant public health units. This may include:

- 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.

d. Communication of the Type 2 cluster assessment report

- QH media and communications staff, will develop and implement the communication plan if required. This will include information which guides the release of the Type 2 cluster assessment findings to the affected and the wider communities (Section 2.10). Communication needs to be trustworthy and empathetic, in plain English, include a response about the specific alleged cluster, and general information on disease clusters.
- Summary findings of the assessment 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; and where appropriate also consider providing to:
    - relevant health workers in the affected area
    - representatives of other stakeholder agencies (for example local government, departments of environment, education, employment and industrial relations) in the affected area.

e. 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).

f. 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 in Table 4. Type 3 cluster assessment involves a multidisciplinary team using information from previous assessments as well as potentially 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 Type 3 cluster assessment are rarely satisfied, therefore this level of assessment is rarely undertaken.

	Type 3 – Analytical assessment
Purpose	To quantify the excess of disease and undertake a detailed exposure assessment of biologically plausible causal agents
Decision maker	Type 3 cluster assessment team with advice from the Expert Advisory Committee on Cluster Assessment
Research question definition, data collection and analysis	New data collected and analysed—epidemiological and/or environmental
Cluster Assessment Team	• Public Health Physician + Senior officers of: – Epidemiology and/or – Environmental health and/or – Media and communications • +/-Representatives of other stakeholder groups • +/- Senior statistical officer/s of Queensland Cancer Control Analysis (QCCAT) and/or Queensland Health Statistical Services Branch (SSB) • +/- Other experts • Cluster management – Cluster manager
Indicative level of time	50–300-person days
Likely duration	Months, year

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-HP should be notified as soon as possible 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-HP should be notified. The degree of public concern or media interest should be assessed.

- QH media and communications unit must be engaged.
- A detailed report must be provided to the ED-HP for approval prior to undertaking a Type 3 cluster assessment. The report will address:
  - QH's involvement
  - nature of QH's role, scope, duration, reporting processes, resources required and budget allocation
  - reasons for proceeding with assessment.

1.5.2 Role of Queensland Health

The role of QH as cluster assessor (epidemiological and/or environmental health assessor) must be determined at the initiation of assessment. If QH is not leading assessment then it is important to determine which agency is cluster assessor and the role of QH.

1.5.3 The Type 3 cluster assessment team

The principal role of the Type 3 cluster assessment team (T3CAT) is to manage and undertake the cluster assessment, as described in Table 5. Membership of the T3CAT must be confirmed before assessment begins and roles and responsibilities of the team and its members should be clarified. The T3CAT reports to the ED-HP.

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

- PHP
- Regional epidemiology staff

Senior officers including:

- Epidemiologists
- Environmental Health Officers
- Media and communications, Hospital and Health Service Communications
- Senior statistician, QCCAT and SSB representative
- Representatives of other agencies (such as local government, departments of education, environment, employment and industrial relations)
- Other experts.

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 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 SSB and/or QCCAT

  - liaise with appropriate experts for the toxicological and environmental health assessment
  - liaise with the community and media.
- **QH media and communications staff** are to develop and implement the communication plan.
- **Senior medical officer (Environmental Health)** to provide advice to the T3CAT regarding:
  - potential causative agents and toxicological properties
  - routes of potential exposure
  - potential biological monitoring requirements.
- **Preventive Health Branch epidemiology** 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 SSB** 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 (cancer in the Queensland Cancer Registry or 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 PHP and regional epidemiology staff. It may be necessary to recruit a senior project officer to assist the T3CAT.

1.5.4 Conducting the Type 3 cluster assessment

As described in Section 2.3, a Type 3 cluster assessment will include (as required by case definition and research questions):

- literature review of biology of the disease including latency and natural history, how these relate to the period of exposure, and the period when the cancers were diagnosed
- review of epidemiology to determine if a statistical excess has occurred (see Section 2.8)
- environmental health and toxicological assessment to build on data collected in the Type 2 cluster assessment and may include more detailed reviews of the literature concerning hazard assessment (see Section 2.9). Environmental sampling may be recommended, with testing by Queensland Health Forensic and Scientific Services potentially being most cost-effective. However, the need for credibility associated with independent testing should be considered.

Several key documents to assist with the epidemiological, environmental health and toxicological evidence appraisal are listed in Section 2.9. These components are complementary and address the overall goals of the cluster assessment.

Table 5 – The process and analytic actions of a Type 3 cluster assessment

Process	Analytic actions
• Confirm Cluster Manager, and provide these Guidelines • Confirm epidemiological and environmental health cluster assessors. • Develop a detailed plan including roles, responsibilities, timelines, communication and resources required (human, time, cost) before assessment proceeds • Provide detailed plan to ED-HP • ED-HP to ensure adequate staff and resources are available to undertake assessment • Assess community perceptions, concerns, reactions and needs • Develop and implement communication plan which guides communication with external stakeholders, including affected individuals as well as affected and wider communities, during the assessment (Section 2.10). • Liaise with the EAC • Conduct debriefing and evaluation of cluster assessment	• Review and adapt the case definition developed in the Type 2 cluster assessment. • Review and confirm research questions (Section 2.5). • Conduct a detailed literature review to assess natural history of the disease, toxicology of relevant agents and their environmental behaviour, and epidemiological plausibility of the association with an exposure • 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. – Review methods for case ascertainment (Section 2.4). – Specify the study population – Use exposure assessment (as described by the enHealth Environmental Health Risk Assessment Guidelines15) in the design of any environmental sampling (see Section 2.9). – 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 – In epidemiological and environmental assessments, consider potential cause and effect relationships (Section 2.7) and weight of evidence for matters such as carcinogenicity in choosing analytes. • Verify cases and study population • Collect, analyse and interpret data and results and prepare scientific reports

1.5.5 Expert advisory committee on cluster assessment

The EAR may be formed to provide advice on all Type 3 cluster assessments. Membership may include experts in related fields such as toxicology or occupational health and safety. The terms of reference for the EAC can be found in Section 2.6.

1.5.6 Engaging advisers for the T3CAT

External advisors may be engaged to provide specific specialist advice to the T3CAT and/or the EAC. This may be relevant to epidemiology, environmental health, toxicology, or communication issues. The rationale for seeking external advice and the nature of advice sought must be clearly documented.

1.5.7 External review

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 external reviewer is to:

- review methodologies used for epidemiology, environmental health and toxicology components
- review reporting of results
- provide informed and independent comment to media and/or 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-HP may appoint an external reviewer from another government agency, interstate health department, non-government organisation or an academic institution. If appointed, the external reviewer reports to the T3CAT.

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 EAC, with the decision endorsed by the ED-HP. Criteria to finalise or recommend areas of research are case specific (Table 6). The decision to undertake research 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 6 – Decision making at conclusion of Type 3 assessment. Decision maker: Type 3 cluster assessment team

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

Approval to undertake Type 4 cluster assessment must be obtained from the ED-HP before proceeding. Approval is based upon a proposal to undertake a Type 4 cluster assessment containing:

- rationale for recommendation, including overview of the research questions to be answered
- proposed role of QH
- QH resource requirements
- a work plan for the study outlining questions, scope and timelines.

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. Approval of this decision should be obtained from the ED-HP.

The Type 3 cluster assessment report

The final report should be prepared and endorsed by the T3CAT. The report should include:

- rationale for 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.
- an estimate of resources, detailing staff and time requirements and financial costs

If the T3CAT have not already done so, the ED-HP may seek review by the EAC including:

- internal review by relevant QH staff not involved in the assessment and/or
- review by an external reviewer.

The report must be endorsed by the ED-HP prior to public release, who will also forward the report to cluster assessor and cluster manager (if these positions are not undertaken by QH), the EAC, and to senior managers in QH.

Briefing to finalise the Type 3 cluster assessment

Following the decision to finalise the assessment, a Briefing Note for information to the Minister for Health, Director-General, CHO, ED-HP, Chief Executive of relevant HHSs and senior directors/managers of relevant regional public health units may be prepared providing:

- 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 to:

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

Communication of the Type 3 cluster assessment report

- QH media and communications branch staff, if involved, will develop and implement the communication plan. This will include information which guides the release of the Type 3 cluster assessment findings to the affected and the wider communities (Section 2.10). Communication needs to be trustworthy and empathetic, in plain English, include a response about the specific alleged cluster, and general information on disease clusters.
- 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; and where appropriate also consider providing to:
    - relevant health workers in the affected area
    - representatives of other stakeholder agencies (such as the local government, departments of education, environment, employment and industrial relations) 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 decision to finalise the assessment, additional communication tasks include:

- **Post assessment debrief**: It is recommended that within three months of assessment finalisation a formally convened debrief may be conducted. The purpose being to review and document the learning, identify key problems and issues, and possible future solutions.
- **Peer-review publication**: Consideration should be given to 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 should be reviewed three months after release of the final report. The review could 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 Manager, Preventive Health Branch Epidemiology recommending changes to these guidelines.

1.6 Type 4 cluster assessment – research study

	Type 4 – Research study
Purpose	To investigate biologically plausible hypotheses generated by the Type 3 assessment
Decision maker	Large and specialised team (commonly outsourced)
Data collection and analysis	New data collected—epidemiological, environmental and/or experimental
Cluster assessment team	As required
Resources	Very high human resource and cost
Likely duration	Months, years

The Type 4 cluster assessment is a discreetly planned and conducted research study and not a continuum of a Type 3 cluster assessment. This type of assessment is approved and undertaken based on the criteria in Table 6. The goal is to explore hypotheses that have arisen during Type 3 cluster assessment and were not addressed in past assessments. Rarely would this assessment contribute 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 including:

- definition of research questions and hypothesis to be tested
- appropriate study designs including 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, this might warrant further assessment 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 QH is responsible for undertaking the study, funding sources and processes for engaging partners and coordinating the study (including governance) must be determined. The study/steering committee should be established and could include senior QH professionals, members of the EAC, other academics or researchers from universities or research institutes. The roles and responsibilities of the committee and its members should 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 will include:

- Justifying the need for the study.
- Securing resources as the study will require a major commitment of resources.
- Seeking funding for financial, in-kind and technical contributions.
- Scoping and planning the assessment.
- Applying for ethics approval.
- Conducting the assessment.
- Finalising assessment.
- Reporting the outcomes of assessment.
- Developing communication plan when scoping the research study and being guided by any public comment.
- Keeping the ED-HP informed throughout the process, and ensuring report is reviewed before releasing.

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

As per Division 2 of the *Public Health Act 2005*,[16] the chief executive may establish and keep an environmental health register for environmental health events which have significant direct or indirect adverse effects on human health. This functions to monitor and analyse adverse effects occurring as a result of an event or exposure.

1.7 Cluster assessment register

A confidential Cluster Assessment Register commenced in 2004 to record summary details of cluster assessments undertaken by QH. The register contains personal data related to health status and therefore must remain confidential, however it does not contain names or addresses of cases.

The register includes information of all assessments including those that did not progress past the initial inquiry. It is the responsibility of assessment teams to ensure details are recorded at 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, involvement of committees, formation of assessment team, consultation with QH media and communications branch, 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 Access

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

- PHPs from the regional public health units
- Regional epidemiologists
- Senior epidemiology staff from the Preventative Health Branch.

1.7.3 Management of register

The register is managed by the Preventive Health Branch. To gain access to the register, please contact Preventive Health Branch Epidemiology at population_epidemiology@health.qld.gov.au

2 Supporting information

2.1 Role of Queensland Health in cluster assessment

For each type of cluster assessment, the role of QH must be determined as soon as possible, with cluster assessor and manager identified.

QH **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 QH expertise that is not available elsewhere.

QH **should not be** leading a cluster assessment when another party has clear responsibility for the cluster assessment, such as a workplace or other government department. QH can provide a supportive and advisory role to other agencies who may not be familiar with leading a cluster assessment.

For cluster assessments in a workplace, relevant departments including the Department of Employment will provide support on a case by case basis. This may involve literature searches of occupational and environmental studies, attending worksite meetings with QH to foster communication, advising on the scope of environmental monitoring and reviewing reports.

QH may provide advice on environmental testing but will not ordinarily undertake or fund such work, unless the cluster relates to a QH facility or requires specialist knowledge available in a QH department.

QH 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*.[16]

2.2 Cluster management

Cluster management is defined as the process of evaluating alternative actions, selecting options and implementing them in response to cluster assessment. The process incorporates information relating to environmental science, epidemiological, social, economic and political aspects. Cluster assessment informs the cluster management process by providing clear information (including uncertainties about the circumstances or concerns). As cluster assessment and management are interdependent, both processes should commence simultaneously.

Before assessment begins, the cluster manager should be identified, and governance provisions established. Cluster managers will usually have accountability arising from their responsibility with an affected site (e.g. education department for a state school, QH for a public hospital), workplace health and safety liabilities (e.g. employers of the relevant workforce) or jurisdictional or legal responsibilities (e.g. local government). For assessments

of community-based clusters, discussions between QH and key organisational stakeholders are required to determine the appointment of the most appropriate cluster manager.

In some situations, there may be multiple entities appointed as cluster manager, therefore the roles and responsibilities must be clearly defined. These may need to be reviewed and changed as the assessment progresses (e.g. when a causal agent and its source are identified).

Cluster assessment is one strategy available to cluster managers in addressing public concerns about potential environmental hazards. Other important strategies include:

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

In summary, cluster management involves:

- Establishing the governance and processes for cluster management, including accountability for management activities.
- Identifying the information needed for cluster assessment.
- Appraising results of cluster assessment.
- Defining available management options.
- Evaluating options according to the health, economic, social and political aspects.
- Deciding on appropriate action and overseeing implementation.
- Monitoring and evaluating effectiveness of actions taken.
- Implementing any changes to cluster management cycle.

2.3 Cluster assessment

2.3.1 Introduction

Cluster assessment is more than a statistical or environmental health exercise– it requires the integration of well-planned epidemiological, environmental health, toxicological and sociological assessment. This will include examination of specific or local circumstances as well as analysis of evidence drawn from literature. It 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, and seeking an explanation for their condition. Most reports of alleged non-communicable disease clusters are not true clusters, and therefore the emotional and communication components are very important. For the layperson, the ‘appearance’ of a cluster understandably leads to the assumption that there must be a common cause, but cluster assessments very rarely result in this finding. The most likely explanation is the chance distribution of biological events with complex multifactorial causation, operating differently in various individuals. Communication of such concepts to the community requires mature communication skills. It is important to recognise the social dimensions of

cluster reporting and maintain trust with the community, while not excessively depleting resources.

2.3.2 Issues identification

Before commencing an assessment consider:

- What is the concern?
- What is causing the concern?
- How was the concern initially identified?
- 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 (it 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 (output from assessment and timeframe required)?
- What are the project management aspects (objectives, nature of the risk assessment to be undertaken and timeframe)?

2.3.3 Cluster assessment principles

- **Protection of human health is the primary objective.**
- Cluster assessments should be undertaken with transparency and diligence.
- The processes are documented and communicated internally (within the cluster assessment team) and externally (to other relevant QH staff and stakeholders).
- Cluster assessments should be based on best available evidence, in accordance with current scientific knowledge, following best practice guidelines
- Good project management skills ensuring:
  - comprehensive planning and documentation
  - completion in a timely, transparent and scientifically rigorous manner
  - effective and efficient use of resources
  - effective application of skills and expertise of a range of relevant professions using a multidisciplinary approach (e.g. public health medicine, epidemiology, environmental health, toxicology and communications)
- The project identifies and addresses concerns and information needs of affected individuals, informant, communities and other key stakeholders by:
  - providing a systematic and well written ‘plain English’ documentation of the findings inclusive of file notes, letters and/or reports.

  - utilising good communication skills through mutual understanding and addressing any conflict between the public's expectation of cluster assessment and the science of carrying out such an analysis within existing limitations.[17]
- The project team identifies and acknowledges the uncertainties encountered and provides an uncertainty analysis about each aspect of the assessment to adequately inform the cluster manager.
- The aims, rationale and management of results need to be clearly documented for initial assessment, epidemiological or environmental components undertaken, or any escalation of assessment.
- Adequate identification and appraisal of relevant biological processes (e.g. latency period of carcinogens) and toxicological factors (e.g. potency of agents) and whether these are sufficient to account for the excess observed cases compared to the expected number.
- A cluster assessment rarely identifies a specific cause but should be undertaken to a level that reasonably excludes the presence of causal agents in sufficient concentration to account for a cluster.

Key questions

There are many key questions to ask during 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?
- Why have they informed us now?
- Is there a robust case definition that all reported cases been assessed against?
- 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, considering issues with disease classification, diagnostic tools and reporting processes?
- Is the disease rare?
- Does statistical evidence suggest the number of cases in the study population exceeds the number compared to a reference population?
- Do the disease types have any known cause?
- Does this known cause exist in these particular circumstances?
- Were all the people diagnosed with the disease exposed to the known cause?
- Was there an appropriate latency period?
- 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, 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?

2.3.4 Engaging advisors and reviewers

Advisor

Advisors may be engaged for specific cases to provide specific specialist advice to the cluster assessment team and/or the EAC, for example on epidemiology, environmental health, toxicology, occupational health or communication. Such specialist advice may be available in QH or externally. The rationale for seeking external advice and the nature of the advice sought should be clearly documented.

External review

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.

External reviewers should have a background and experience within population health, and expertise in cluster assessment. They require excellent communication skills, and credibility with the cluster assessors and stakeholders. An external reviewer will be appointed by the EAC and be external to QH. They may be from another government agency, an interstate health department, a non-government organisation or academia. Their purpose is to provide advice to the cluster assessment team.

2.4 Case ascertainment

Case ascertainment is a measure of the extent to which all cases meeting the case definition can be identified in a cluster assessment. Completeness depends on availability and quality of information and data sets, and resources required to investigate them. The goal of case ascertainment is to achieve the best practicable ascertainment based upon the available information at the time. A written record (e.g. 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. This involves investigating and accumulating information about suspected or actual cases of disease in

the population being assessed. Initially it may lead to accumulation of information on many individuals with multiple cancers, although some individuals will subsequently be excluded from further assessment based on the case definition.

For a Type 1 cluster assessment, potential case information will initially be gathered from the informant. It may also come from the cluster manager. For cluster assessments progressing beyond Type 1, more complex strategies will be used to ensure case ascertainment is as complete as practicable. Other sources of information include social networks, local knowledge and accessing data from the Queensland Cancer Registry. In many instances a potential case is identified by self-report. Due to the potential increased media interest of Type 2, 3 and 4 assessments, reporting of potential cases to the cluster manager is encouraged and can be facilitated through providing cluster manager contact details early on.

If additional cases are notified after completion of cluster assessment, a plan for appropriate action should be in place to manage these cases. Case ascertainment limitations should be described in the cluster assessment reporting.

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 should be developed for all other non-communicable cluster assessments. Establishing a case definition requires specialist knowledge and involves appraising potential cases and considering the natural history of the particular disease. It also includes the potential period of exposure (see Section 2.9). There is no set formula for the derivation of case definitions as they are affected by diverse factors such as geographical sites and diseases. A case definition could be: all reported incident cases of 'x' cancer among 'y' employed/residing/attending at 'z' workplace/area/school between YYYY and YYYY. For example, '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 similarity required between cases must be determined through consideration of alleged hazards, histopathology of disease, diagnostic criteria, availability and limitations of data sources. It is important to note that case ascertainment relates to individuals, not numbers of conditions. Multiple cancers may be reported for an individual however each of these cancers do not represent a unique case. Multiple primary cancers in an individual will usually relate to genetic predisposition or particular types of treatments. A small proportion of cancers are familial (<5%), involving a changed gene that is passed down through families, increasing individual risk of developing certain cancers. 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 in the development of their cancer are difficult to establish. Furthermore, having a risk factor/s, does not mean that a person will get the

disease. People develop cancer in the absence of known risk factors. It is particularly difficult to pinpoint the mix of causes of an individual cancer.

If there are a variety of different cancers reported in the community or workplace of concern, it is very unlikely that they share a common cause. For this reason, cluster assessment is undertaken when cases have disease of the same or similar histological type, rather than grouping multiple types of cancer. Inclusion of 'all cancers' in the case definition and assessment of all cancer rates is not advisable, except under 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 ordinarily excluded from cluster assessments[18] and in annual reporting of breast cancer by the Queensland Cancer Registry.[19] DCIS is usually asymptomatic and diagnosed through radiological screening programs and 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. An example would be in a workplace assessment, deciding if the study population is employees only, and excluding contractors and volunteers. Consideration should be given to whether the study population takes 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. 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 steps for appraising potential cases and finalising 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 be specific to the assessment (e.g. exclusion of contractors or staff with limited exposure to the putative hazard).
- All cases should be confirmed from a written record (e.g. Queensland Cancer Registry entry, pathology result), except under exceptional circumstances.
- Latency period (time from exposure to diagnosis of cancer) 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 (see Section 2.11). Latency period should be included in the case definition.

2.4.2 Confirmation of cases

With the approval of the Director-General of QH, data about relevant potential cases can be sought from the Queensland Cancer Registry. If information is required from primary health care records, written consent from the potential case is required to access data. Consent forms are included in resources for cluster assessment. 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 used to provide state and localised rates (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. If written consent has been given, the best practice case ascertainment is to access data from the doctor.
- Australian Cancer Registry data uses the address at the time of diagnosis. If a potential case moves address from the geographic area being assessed, this limitation needs to be noted and acknowledged.
- Queensland Cancer Registry data is most useful for clusters in a defined geographical area where rates can be checked for an entire statistical area. Importantly, misclassification of cases to an area may occur due to incorrect coding practices. This occurs when the assignment to the area is based upon postcode or suburb rather than geo-coding the place of residence. Assessing a cluster in a localised area must take into consideration whether misclassification bias has occurred in a geographic entity and whether a broader geographic area must be considered.
- While the Queensland Cancer Registry contains a variable field for occupational data, it is recognised as an incomplete field with inconsistent accuracy.

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 (e.g. leukaemia, lymphoma, brain cancers). If there is conflict between a pathology report and a Queensland Cancer Registry entry, the pathology report is more likely to be correct. Cancer registry data outside Queensland will not usually be accessed in a Type 2 cluster assessment but may need to be considered in a Type 3 assessment.

2.5 Research questions for Type 2 and Type 3 cluster assessments

For types 2, 3 and 4 cluster assessments, research questions should be defined at the planning phase. Examples of research questions 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?
- How do you define the time period of interest?
  - consider latency period
  - consider whether 'at risk' period should begin with the diagnosis date for the first case and end with the diagnosis date for the last case.
- Are there any exclusion and inclusion criteria in the case definition and are these also 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 other data sources (e.g. 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 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 considered?
- What is the expected number of cases in the reference population, and how is the reference population identified (e.g. Queenslanders of the same sex and same age groups)?
- What is the standardised incidence/mortality ratio (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 assessor deal with the emergence of new cases in the future? Will the O/E ratio be recalculated for each newly identified case?

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 hypothesis is 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 disease? Is anything unusual about the agent and/or level of exposure?
- How can latency periods be considered in assessing 'exposure'? Sensitivity analysis will be required to cover the range of values
- Are there relevant previously reported cluster assessments where environmental exposures were identified? Undertake literature review: grey literature and published
- Is environmental testing warranted? An appraisal of the relevant environment would be required to determine if there is a rationale and, if so, the analyses 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 state environmental protection agency, local government authority, private audits.
- Is environmental testing justified? If so, what is the nature and scope of the testing?
  - Is this considered sufficient to assess possible environmental aetiologies?
  - Were there resulting environmental findings of public health significance resulting from this testing?
  - Has expert advice been sought?

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 extra information derived in 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 case definition from Type 2 cluster assessment need refining based on improved information from case interviews, interviews with physicians, review of medical records?
- Are 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 disease-causing agent) already known to be present in the study population environment (e.g. proximity to an industrial source)?
- If so, has sufficient testing been done 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 (e.g. 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 (e.g. further environmental sampling, 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 (e.g. 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 (e.g. what standards will be used as reference; what experts can be consulted)?

3. 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 (e.g. case-control study, cohort study, create disease/exposure register).

2.6 Expert Advisory Committee terms of reference

Purpose

The Expert Advisory Committee on Cluster Assessment (EAC) provides authoritative counsel to QH regarding epidemiological and environmental health assessments of suspected non-communicable disease clusters, including review of assessment reports prepared by QH. It is formed usually in the case of a Type 2 or higher assessment, and is initiated by the Chair, who may be the ED-HP or PHP involved.

Governance

QH assesses suspected clusters of non-communicable disease according to the *Queensland Health Guidelines: Assessment of clusters of non-communicable disease 2019*. The EAC provides advisory services to cluster assessments in accordance with the guidelines.

Roles

- Provide QH with advice on appropriate methodology in relation to the epidemiological, environmental health and toxicological components of the assessment.
- Review all Type 2, Type 3 and, where relevant, Type 1 cluster assessment reports prepared by QH.
- Assist QH to build capacity in the assessment of non-communicable disease clusters.

Membership

The EAC is comprised of experts and senior officers within different fields relevant to the cluster assessment, and varies depending on the type of assessment and potential hazard being investigated.

Committee membership is likely to include the following expertise:

- epidemiological analysis and interpretation
- public health medicine
- toxicology
- environmental science
- statistical analysis
- other relevant agency experts (e.g. Cancer Council, National Research Centre for Environmental Toxicology or Department of Employment and Industrial Relations).

QH public health medicine, epidemiology and environmental health staff who are conducting the cluster assessments under discussion by the EAC may participate in committee meetings. External advisors may also be engaged by the EAC for advice on specific bodies of work.

Meetings are called by the Chair or delegate. Advice from the EAC may be sought by the Chair or any member of the committee out of session.

Secretariat

Secretariat for the EAC will be provided by the Epidemiology Unit, Preventive Health Branch. The Secretariat will coordinate meetings and minutes of meetings.

2.7 Causality

QH uses the principles developed by Bradford Hill (1965),[20] reviewed by Lucas and McMichael (2005)[21] and further adapted from NHMRC 2006[22] to assess causality (Table 7).

Table 7 – Principles of causality (Bradford Hill viewpoints as reviewed by Lucas and McMichael 2005[21] and adapted from NHMRC 2006[22])

Criteria	Principle
Strength of association	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.
Consistency	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.
Strength of study design	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.
Dose-response	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.
Temporality	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.

Criteria	Principle
Specificity	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 & McMichael 2005).[21] 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.
Biological plausibility	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.
Coherence	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 & McMichael 2005).[21]
Analogy	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.
Confounding	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.
Sensitivity analysis	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.[23] 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.

These principles consider epidemiological, exposure and toxicological evidence to assess whether particular agents have a causal relationship to a cluster. In considering epidemiological evidence generally, 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.[24, 25] Both viewpoints and reservations should be considered in a cluster assessment.

At a population level, causality can sometimes 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 *more likely than not caused* by the specified exposure.

2.8 Epidemiological assessment

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 QH and the EAC should consider the applicability of alternative theories and use of related statistical methods.

2.8.1 Principles

1. Cluster assessments 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 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 meaning 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.[26] Because of the difficultly 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.[26]
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 Type 3 cluster assessment than Type 2.
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.

2.8.2 Guidelines for statistical analyses

This section of the guidelines describes general statistical analysis procedures to follow in cluster assessments. Recognising that every cluster assessment is unique, QH 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 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**: 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.27 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.28 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.

   In 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.[29]
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.[29] Studies have shown that when the latency period is taken into account it generally shows that a cluster is more likely due to chance.[30] 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 2.11).
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 artefactually 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.[26]
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’.

2.9 Environmental assessments

2.9.1 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.
2. The purpose of environmental assessments is to identify a cause or to seek a plausible causal process (plausible agent plus sufficient exposure) for the cluster of a specific disease.
3. The overall process is:

- Identify the specific disease.
- Identify whether there are known causal agents for the disease.
- Identify the dose–response relationship for the agent (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 a biologically plausible 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 Contaminated Land Register or Environmental Management Register nor does it have a Site Management Plan, or
- from what is known about the history of the site and opportunities for exposure, it cannot be reasonably expected that an environmental agent will be identified to explain the number of people with the range of health effects reported
- the type of assessment undertaken is a Type 1 cluster assessment.

2.9.2 Resources

The key reference to be used for environmental assessments is enHealth (2012) Environmental Health Risk Assessment, Department of Health, Canberra.[15] 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 primarily be sought from Level 1 categorised documents. If information is not available in Level 1 categorised documents, then seek the information from Level 2, acknowledging 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

Level 1 documents	**a. NHMRC documents** Based around ambient air issues, 'Ambient Air Quality Standards Setting' (2006) provides extensive detail on appraising and integrating animal (toxicological) and human (epidemiological) data and assessing potential carcinogens (https://www.nhmrc.gov.au/guidelines-publications/eh40)
	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.[31] 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[15] provides a framework and extensive detail on health risk assessment.
	d. NICNAS (National Industrial Chemicals Notification and Assessment Scheme) evaluations
Level 2 documents	**a. Casarett and Doull's toxicology**[32] **b. 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

2.9.3 Data requirements

The following data requirements enable efficient and accurate appraisal of environmental information for the hazard and exposure 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, e.g. downstream/upstream, or towards/away from a source point
5. **Nature of the analyte**: may be important when the valency (e.g. chromium) or chemical form (e.g. 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**: e.g. 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.

2.9.4 Environmental assessment activities

Type 1 cluster assessment

Undertaken by a PHP, 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 latency (e.g. 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 (e.g. department of environment 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 2012).[15]
- Assess the validity, integrity and relevance of the above information.
- Appraise the exposures of the potentially affected population (see Chapter 8 of enHealth 2012 and Section 10.3.3).[15]
  - 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 findings from the Type 2 epidemiology assessment?
- Write a report for submission to the T2CAT, including an uncertainty assessment. The report should satisfy the relevant sections of Chapter 10 of enHealth (2012).[15]

Type 3 cluster assessment

Undertaken by an environmental health and environmental science expert. May require more detailed review of the literature (hazard identification and dose-response assessment).

- Review the activities conducted in the Type 2 cluster assessment.
- Determine whether environmental sampling is required. If sampling is indicated with reasons adequately documented, develop a sampling plan specifying agents of interest and detail why they are of interest (see section 8.7 and Chapter 10 of enHealth 2012).[15]
- 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 (2012).[15]

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?

2.10 Communication and engagement in cluster assessment

Disease clusters concern the public. By the time a person reports a suspected cluster it is likely they will have developed a significant degree of concern, and in some cases, a level of distress.

The public will expect 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 cluster assessment team will be hampered. Managing perceptions, information and relationships is key to achieving good outcomes, and can be achieved by making effective communication integral to cluster assessment. Evaluating community concerns, context and surrounding issues are cluster manager responsibilities (Figure 1 and Section 2.2). Information on communication issues should be provided by the cluster manager.

2.10.1 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.

2.10.2 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 and the community should be given the opportunity to express their views where it is reasonable and practicable.

QH media and communications 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. They will also report to the cluster manager if QH is the cluster manager.

If QH is not cluster manager, QH media and communications may offer specialist advice to the nominated cluster manager, if requested.

2.11 Glossary

Term	Definition
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.[33]
Association	A statistical dependence between two or more events, characteristics or other variables.[33]
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.[3]
Carcinogen	A cancer-causing substance or agent.3[4]
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.[33]
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.[33]
Case definition	A set of diagnostic criteria that must be fulfilled in order to identify a person as a case of a particular disease.[33] 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.[33]
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

Term	Definition
	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.[1] 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.[2] 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.[35]
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.[33]
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.[33]
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 walkthrough inspection by an experienced, expert environmental health

Term	Definition
	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.[33]
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.[33]
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

Term	Definition
	defined period. The denominator is the population at risk of experiencing the event during this period, sometimes expressed as person-time.[33]
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*.[33] 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.[36] '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.[29] 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 of several years between the first exposure to a known carcinogen and a diagnosis of cancer.[37] 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 (≈10µm in diameter) to produce a tumour with a diameter of 2mm. This tumour size of 2mm is approximately the lowest detectable level by mammogram.[29] The median time for the tumour to grow from

Term	Definition
	mammographically detectable size to clinically detectable size is estimated to be approximately 1.7 years.[38] 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

Term	Definition
	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.

2.12 Abbreviations

QH	Queensland Health
ED-HP	Executive Director, Health Protection (Queensland Health)
CHO	Chief Health Officer
PHP	Public Health Physician
EAC	Expert Advisory Committee on cluster assessment
QCCAT	Queensland Cancer Control Analysis Team
HHS	Hospital and Health Service (Queensland Health)
SSB	Statistical Services Branch (Queensland Health)
T2CAT	Type 2 Cluster Assessment Team
T3CAT	Type 3 Cluster Assessment Team

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