TB Strain Typing Cluster Investigation Handbook for Health Protection Units

2nd Edition, September 2011

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Document Control

Only approved numbered versions of the document should be referenced. All versions to date are described below.

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Table of Contents

1.0 Introduction 7

1.1 Purpose of the handbook 7
1.2 Background 7

2.0 Definitions 9

2.1 Clustered cases 9
2.2 Epidemiological cluster 9
2.3 Strain-type cluster 9
2.4 Epidemiologically confirmed strain-typing cluster 10
2.5 Epidemiological links 10

3.0 Cluster investigation processes and thresholds for action 11

3.1 Mechanism for reporting strain typing results and identifying clusters for investigation 11
3.2 Preliminary Strain Type Cluster Review (PSCR) 11
3.3 Thresholds for full cluster investigation 12
3.4 Conducting a full cluster investigation 13
Fig.1 Flow chart for cluster investigation 16
3.5 Possible outcomes following a cluster investigation 18
3.6 Expanding clusters 19

4.0 Recording cluster investigation activities and reporting the outcomes 20

4.1 Location of records 20
4.2 Recording cluster investigations on HPZone 20
4.3 Recording a cluster investigation on IRIS 26
4.4 Reporting the outcomes of cluster investigations 27

5.0 Roles, responsibilities and standards for strain typing service and response 28

6.0 Appendices 31

Appendix 1: Examples of Strain typing monthly cluster reports 33
Appendix 2: Cluster investigation Questionnaire 35
Appendix 3: Examples of useful cluster investigation tools 39
Appendix 4: Cluster Reporting Form 41
Appendix 5: Glossary and abbreviations 43
Appendix 6: Bibliography 45
Appendix 7: Key Contacts 47
Appendix 8: Feedback / comment form 49

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1.0 Introduction

1.1 Purpose of the handbook

- This handbook provides guidance and support to HPUs for the investigation of TB strain typing clusters identified through the new national TB strain typing programme.
- It has been produced primarily as guidance for HPA staff.
- It includes agreed standards and criteria for the investigation of TB strain type clusters by Health Protection Services in the HPA including guidance on the recording of the processes and outcomes of such investigations for purposes of evaluation.
- It is not intended to provide instruction on all aspects of the application of TB strain typing but as a public health tool. References to appropriate sources of detailed information on the wider applications of TB strain typing are included in the bibliography of the handbook.
- As the national TB strain typing programme evolves and our expertise increases, thresholds for cluster investigation may change to reflect improved understanding of the application of this tool in the UK. Therefore, this handbook is primarily guidance for good practice but will remain an evolving document that will be modified over time to reflect current knowledge.

The online version of this handbook, available from HPAnet, will be the most up to date version. Caution should be exercised when referring to paper copies.

1.2 Background

1.2.1 The role of strain typing in TB prevention and control

TB strain typing results, when combined with epidemiological data, help to identify TB patients who may be involved in the same chain of recent TB transmission and assist in the initiation of timely and appropriate control measures following cluster and outbreak investigations. TB strain typing also helps to distinguish TB patients whose disease is a result of reactivation of an infection acquired in the past and cases of re-infection with a new TB strain.

The introduction of universal TB strain typing i.e. submitting one isolate from every culture-positive patient with TB for strain typing will provide the best understanding of the epidemiology of TB transmission and help to uncover unexpected outbreaks, clusters, and false positives. It will also allow HPA, for the first time, to monitor our progress towards eliminating TB transmission by monitoring the changes in the percentage of strain type clustered cases.

1.2.2 The main objectives of strain typing:

- To identify epidemiological links between TB patients to detect and control outbreaks early and rapidly.
- To identify erroneous TB diagnoses based on false-positive cultures and thus avoid unnecessary investigation and treatment.
- To distinguish exogenous re-infection from endogenous reactivation in patients with a past history of TB.
- To monitor effectiveness of TB control activities by using recent TB transmission rates as a surrogate measure.
- Additional benefits:

- Strain typing can also be a very useful tool to identify nosocomial transmission that cannot be identified by conventional methods, and to identify transmission that occurs between patients in different jurisdictions more readily.
- It can also be useful to show that TB cases occurring in the same time and place can have unrelated strain typing and not belong to the same chain of recent transmission, thus requiring no further action.
- It is a useful tool to distinguish the overall diverse *Mycobacterium tuberculosis* strain pattern and identify endemic strains circulating in a given population. It may support the identification of different genetic lineages and the study of their geographical distribution and pathophysiology, which has implications for the development of new tools for TB control.

2.0 Definitions

2.1 Clustered cases

Two or more persons with TB who are **linked in time** and share **possible** epidemiological links.

2.2 Epidemiological cluster

Two or more persons with TB linked in time and with **known or definite** epidemiological links.

2.3 Strain-type cluster

Two or more persons with TB caused by **indistinguishable 24 loci strains** occurring within **24 months (2 years).**
Epidemiological information (see section 3.2) is required to determine if a strain type cluster is a genuine cluster, requiring further public health action. A strain type cluster may be discarded as a cluster once initial assessment excludes epidemiological association.

For purposes of this handbook and this programme, a strain type cluster may contain cases with TB isolates with the following characteristics:

- all 24 loci of the MIRU VNTR profiles of the isolates are complete and identical, or
- some members of the cluster may have up to, but no more than, one (1) missing / unmapped locus, providing that the missing locus is the same for all incomplete isolates within the cluster.

Examples:

- Cluster E0011: 3 cases, all three case isolates fully mapped and identical. This is a strain-type cluster.
  Case 1: 642652632622313264323541
  Case 2: 642652632622313264323541
  Case 3: 642652632622313264323541

- Cluster B0012: 3 cases; one case isolate has one missing / unmapped loci. This is a strain-type cluster.
  Case 1: 642652632622313264323541
  Case 2: 642652632622313264323541
  Case 3: 6426526326223_3264323541

- Cluster E0013: 3 cases; two cases have isolates with one missing / unmapped loci. The missing / unmapped loci are the same for cases 2 and 3. This is a strain-type cluster
  Case 1: 642652632622313264323541
  Case 2: 6426526326223_3264323541
  Case 3: 6426526326223_3264323541

- Cluster C0014: 3 cases; two cases have isolates with one missing / unmapped loci. The missing / unmapped locus is NOT the same for cases 2 and 3. This is a **NOT** a strain-type cluster.
  Case 1: 642652632622313264323541
  Case 2: 6426526326223132643235_1
  Case 3: 64265263262231_264323541

- Cluster B0015: 3 cases; Case 3 has two (2) missing / unmapped loci. Case 3 is **NOT** part of this strain-type cluster.
  Case 1: 642652632622313264323541
  Case 2: 642652632622313264323541
  Case 3: 6426526326223132643 2_5_1

2.4 Epidemiologically confirmed strain-typing cluster

This is a cluster of two or more persons with TB caused by **indistinguishable 24 loci strains** occurring within **24 months (2 years) AND** with **known or definite** epidemiological links. These are true clusters requiring public health action.

2.5 Epidemiological links

Based on information collected from two or more TB patients during the initial interview, contact tracing or cluster investigations, epidemiological links between TB patients can be characterised into three broad categories: known or definite epidemiological links, possible epidemiological links and no epidemiological links.

2.5.1 Known or definite epidemiological links

TB patients have a known or definite epidemiologic link if either of the following conditions is met:

- One patient volunteered the name of the other as a contact while **potentially** infectious. This applies to pulmonary TB cases, irrespective of sputum smear status **OR**
- The patients were in the same setting at the same time when either of them could have been potentially infectious. This applies to pulmonary TB cases, irrespective of sputum smear status.

In larger clusters, if any of the above epidemiological links are identified **between all of the cases within the cluster,** the patients are said to have definite epidemiological links.

2.5.2 Possible epidemiological link

TB patients have possible epidemiological link, if within the previous 24 months any of the following conditions are met:

- Two patients spent time in the same setting around the same time, but the timing of when they were there or the timing of the infectious period was not definite enough to meet the criteria for a definite epidemiological link **OR**
- Two patients lived in the same setting around the same time **OR**
- Two patients worked in, or were at the same setting, around the same time and shared social or behavioural traits that increased the chances of transmission **OR**
- One patient volunteered the name of the other as a contact but both patients have non-pulmonary TB **OR**
- Two patients were in the same setting at the same time but both patients have non-pulmonary TB.

In larger clusters, if any of the above epidemiological links are identified **between some but not all of the cases within the cluster**, the patients are said to have possible epidemiological links. Please note that the above list is not exhaustive.

2.5.3 No identified epidemiological link

Two patients should be classified as having no identified epidemiological link if they do not meet the criteria in 2.5.1 or 2.5.2.

For the purposes of this handbook, the term 'cluster' will be subsequently used to refer to strain type clusters, unless otherwise stated.

3.0 Cluster investigation processes and thresholds for action

Investigation of cases belonging to a strain type cluster aims to uncover epidemiological links between members of that cluster through systematic review of patient records and, where indicated, re-interviewing the patients involved.
Identification of previously unknown epidemiological links between members of a strain type cluster may indicate the need for subsequent extended contact tracing and screening.

3.1 Mechanism for reporting strain typing results and identifying clusters for investigation

Strain typing results will be available within 21 days of species identification for 90% of isolates. The MIRU-VNTR profile will be uploaded from the reference laboratory into the Enhanced Tuberculosis Surveillance (ETS) database, where isolates will be matched to notified clinical cases.

At the time this version of the handbook is produced, the ETS strain typing module (STM) is currently under development and will provide a mechanism for automated identification and reporting of clusters. Monthly cluster reports will be generated by the mycobacterium reference laboratories for HPUs and Regions. National clusters will be generated at Health Protection Services Colindale. The STM will also act as a cluster management tool by allowing the collation of demographic and clinical information from ETS and extra information on the social characteristics of cases.

Prior to the activation of the STM, the TB cluster investigators will obtain the strain typing information from the mycobacterium reference laboratories and, after performing a Preliminary Strain Type Cluster Review (as described below in section 3.2), will notify the relevant HPU of any clusters identified along with recommendations for further action.

All clusters (2 cases or more), will require some degree of assessment and the outcome of that preliminary assessment will determine the threshold at which a full cluster investigation is commenced. This is called a **Preliminary Cluster Review.**

3.2 Preliminary strain type cluster review (PSCR)

When a cluster is first identified, a review of known information on the cases involved is used to determine if further investigation is required, or if the epidemiological link between cases in the cluster is already known and thus, that no further investigation is required. It is also used to identify characteristics that may indicate a need for earlier and more rapid investigation.

In most circumstances, this Preliminary Strain Type Cluster Review (PSCR) is undertaken by the HPS Cluster Investigators. The information required for a Preliminary Strain Type Cluster Review will usually be available from the standard ETS or London TB Register (LTBR) notification or from the routine records of the TB clinical team. If the information required for the Preliminary Strain Type Cluster Review is unavailable from ETS / LTBR, the cluster investigator will highlight this on the cluster review. In such circumstances, responsibility for PSCR lies with the relevant HPU.

The TB Cluster Investigators will provide the following information on all clusters identified:

- National and local cluster name[1]
- Details on each case in the cluster[2]: Name of case, date of birth, NHS number, ETS/LTBR number, first part of postcode, HPU of residence, demographic characteristics available from ETS/LTBR (age, gender, ethnicity, country of birth, year of entry to UK), clinical characteristics (site of disease, sputum smear status, onset of symptoms, antibiotic sensitivities), and laboratory information (sample date, originating laboratory and MIRU-VNTR profile).
- Recommended action based on assessment of existing information.

The Preliminary Strain Type Cluster Review will also attempt to identify the following factors, the presence of which indicates that further investigation should be **considered** at an earlier stage (where a cluster size is below the standard thresholds outlined in section 3.3):

- The cluster includes a child (under 16 years)
- The cluster includes a health care professional
- The cluster includes a drug-resistant strain
- The cluster includes a case with known HIV infection
- The cluster includes cases with the following characteristics indicating high risk of transmission:
  - Homelessness or residence in a hostel or similar temporary accommodation
  - Recent incarceration in a prison / offender institute
  - Previous TB treatment failure (where known/ information available)
  - Problem drug or alcohol use
  - History of severe mental health problems[3]

In the absence of these indicators, then the thresholds in section 3.3 should be applied in determining when to start a full cluster investigation. **However, if local knowledge indicates that this is appropriate, a local team has the discretion to begin a full cluster investigation at levels below these defined thresholds.**

Examples of monthly cluster reports currently produced by the TB cluster investigators are shown in appendix 1.

3.3 Thresholds for full cluster investigation

Thresholds for cluster investigation have been set at three levels:

- HPU threshold
- Regional threshold
- National threshold

3.3.1 HPU threshold for cluster investigation

This is the threshold for triggering an active cluster investigation where all the cases in the cluster reside within a single health protection unit.

> *5 or more persons within 24 months (2 years), of which 2 occurred in the last 6 months; with TB caused by indistinguishable strains (see section 2.3 for definition of 'indistinguishable' strain type cluster).*

[1] Cluster nomenclature: A national agreed nomenclature to be generated by the reference laboratories is under development.
[2] LTBR currently contains more risk factor details than ETS
[3] Mental health problems likely to interfere with ability to adhere to treatment or cooperate with contact tracing

If the Preliminary Strain Type Cluster Review reveals the presence of the high risk factors defined in section 3.2, consideration should be given to starting active cluster investigation for fewer cases.

3.3.2 Regional threshold for cluster investigation

This is the threshold for triggering an active cluster investigation where the cases in the cluster reside across more than one HPU within a single region.

> *10 or more persons within 24 months (2 years), of which 2 occurred in the last 6 months; with TB caused by indistinguishable strains (see section 2.3 for definition of 'indistinguishable' strain type cluster)* [4].

If the Preliminary Strain Type Cluster Review reveals the presence of the high risk factors defined in section 3.2, consideration should be given to starting active cluster investigation for fewer cases.

3.3.3 National threshold for cluster investigation

This is the threshold for triggering an active cluster investigation where the cases in the cluster reside across more than one region.

> *10 or more persons within 24 months (2 years), of which 2 occurred in the last 6 months; with TB caused by indistinguishable strains (see section 2.3 for definition of 'indistinguishable' cluster).*

If the Preliminary Strain Type Cluster Review reveals the presence of the high risk factors defined in section 3.2, consideration should be given to starting active cluster investigation for fewer cases.

3.3.4 Note

It is important to remind users of this handbook that the thresholds provided here are for guidance but DO NOT replace professional judgement. If the responsible professional has cause to believe that investigation is necessary at a lower threshold, or that cases with a different strain type, or no strain typing information should be included in the cluster, then they should do so and clearly document their reasons for the decision. As this will be a relatively new area of work for many, advice and support for such decisions should be sought from TB lead colleagues at regional and national level (see Appendix 7 for key contacts).

3.4 Conducting a full cluster investigation

3.4.1 Leadership of cluster investigations

Responsibility for leading the investigation of a cluster will vary depending on the size and spread of the cluster and local expertise. The following are recommendations. However, it is essential that the agreed leadership of a cluster investigation is made clear and appropriately recorded to ensure effective coordination of an investigation.

Cluster wholly within a single HPU: The investigation should be led by the HPU TB lead or an appropriately senior / experienced member of the HPU clinical team.

[4] Full investigation of regional clusters may commence at a threshold of between 5 and 10 if local circumstances indicate that this is appropriate e.g. – cases in geographically contiguous areas.

Cluster within a single region: There are a number of options under these circumstances:

- The unit TB lead of the HPU with the majority of the cases within the cluster at the start of the investigation,
- The Regional TB lead, or
- A Regional Epidemiologist

The lead will nominate an HPU that is part of the cluster to hold the HPZone record of the investigation.

National cluster (cluster spreading beyond a single region): There are a number of options under these circumstances, depending on the size and spread of the cluster:

- **Where cluster size is moderate (10 cases or less):** led by the regional TB lead and / or the regional epidemiologist from the region with the most cases within the cluster at the start of the investigation. Where there is no clear concentration of cases within a single region, the investigation will be led by HPS Colindale. The lead will nominate a HPU that is part of the cluster to hold the HPZone record of the investigation.
- **Where cluster is large (more than 10 cases):** Led by HPS Colindale. The lead will nominate a HPU that is part of the cluster to hold the HPZone record of the investigation.

3.4.2 Membership of Cluster Investigation Team

As with other incident management teams, membership of the cluster investigation team will vary depending on local circumstances and resources, the size and distribution of the cluster and the characteristics of the cluster. The membership listed below is a recommendation:

Core:	Additional:
• CCDC / HPN representatives for HPUs with cases in the cluster • Relevant NHS TB service(s) • Health Protection Services TB Cluster Investigators • HPU TB lead • NHS Microbiological Services	• HPA Regional Epidemiology Unit • HPA Regional TB lead • Relevant HPA Mycobacterium Reference Laboratory • HPS Colindale (essential for all national clusters)

3.4.3 Steps in conducting a full strain typing cluster investigation

The following steps are recommended for a full investigation of a cluster:

1. **Review recommendations from Preliminary Cluster Review**
   HPU reviews the recommendations of the Preliminary Strain Type Cluster Review and decides whether to launch a cluster investigation based on this, local knowledge and the thresholds (section 3.3).
2. **Gather additional information on cases in the cluster**
   HPU sends out cluster investigation questionnaire (Appendix 2) to NHS TB case managers / teams.
   NHS TB teams review patient records and complete and return the cluster investigation questionnaires.
3. **Determine if epidemiological links exist between any or all of the cluster members**
   HPU team reviews the cluster questionnaires to identify similarities in time, place, person, overlapping infectious periods, and to determine if epidemiological links exist between any or all of the cluster members.

If no epidemiological links are identified, take standard TB control measures and close the investigation.

If evidence of potential epidemiological links is identified, consider if there is the possibility of an on going risk of transmission and if so, begin an outbreak investigation and conduct expanded contact tracing and screening in line with existing guidelines and best practice.

At this stage any potentially linked cases with previously unidentified epidemiological links should be added to the cluster. Thus, cases with no strain typing information or where the strain type may have more than one missing loci may be added to the cluster if epidemiological links indicate that they may be part of the same chain of recent transmission.

Appendix 3 contains an example of a useful approach to collating information obtained from cluster investigations that may assist with determining the presence of epidemiological links.

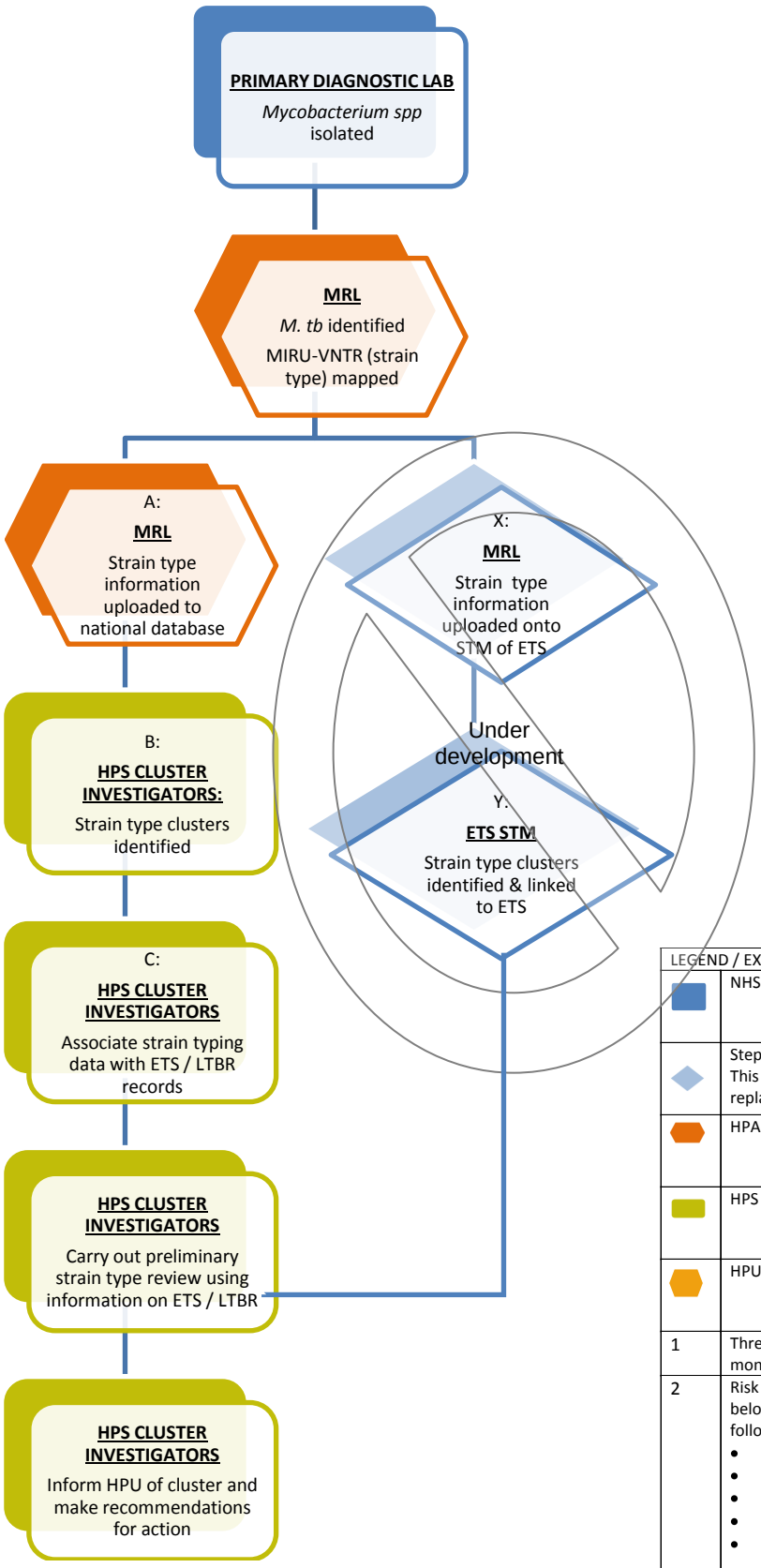
3.4.4 Expanded contact tracing (widening the search)

The aim of expanding contact tracing is to ensure that all contacts of an infectious TB patient are identified, evaluated and treated. The goals of standard contact tracing and expanded contact tracing are similar. Expanded contact tracing involves applying greater resources to identify and evaluate contacts since at this stage the possibility of recent transmission to contacts has been established from strain typing information.

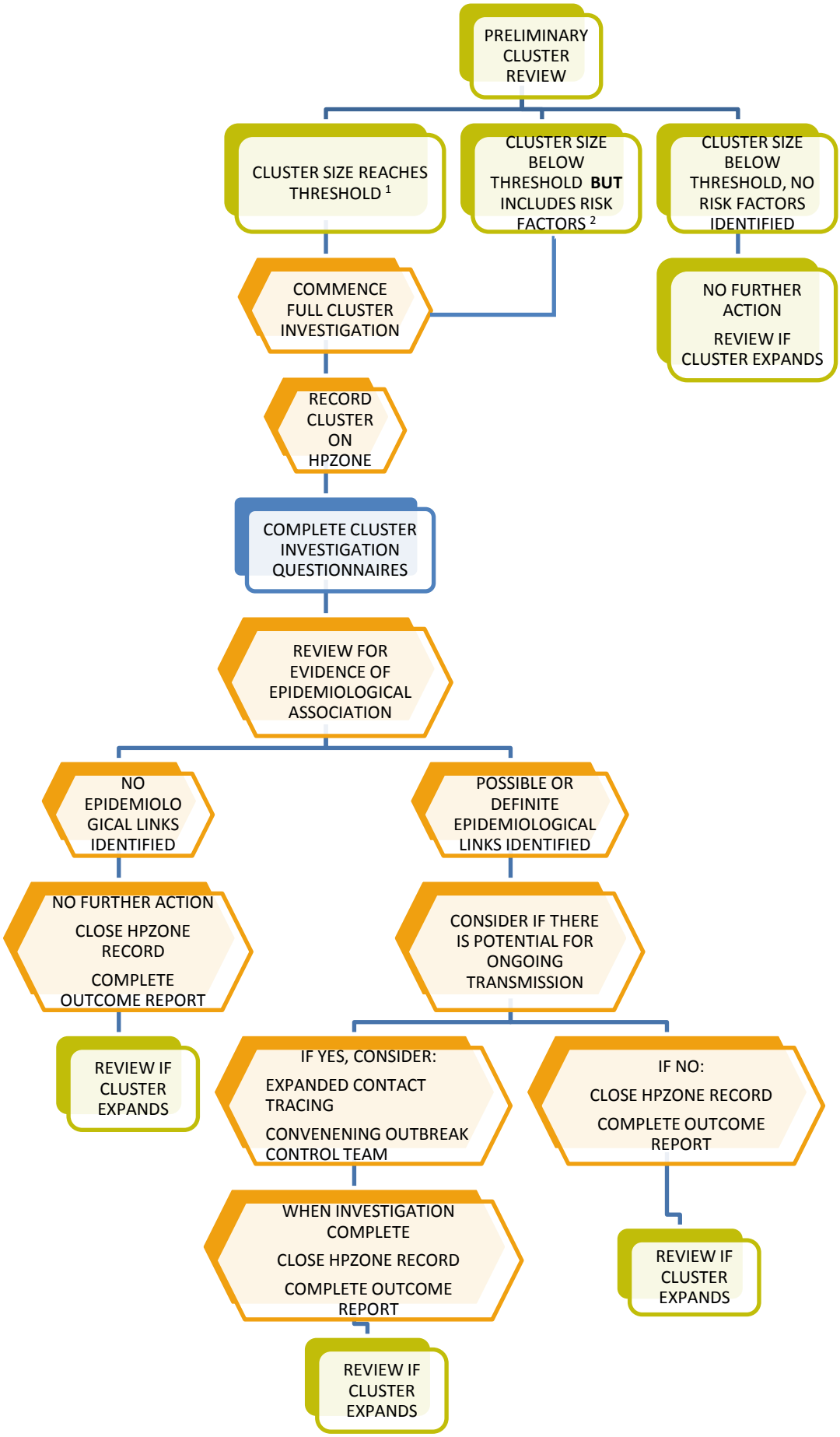
The first step in expanded contact tracing is to ensure completeness of the initial contact tracing of close contacts. Information on all contacts should be entered into HPZone (see section 4.2), or ETS contact tracing module (CTM) when available. For each contact, information on the key components of contact tracing should be collected: contact interview, symptom screening, tuberculin skin testing / interferon gamma release assay tests, evaluation of active TB for contacts with positive Tuberculin Skin Tests (TSTs), IGRAs or symptoms, and the treatment of LTBI.

Expanded contact tracing includes second and third tier contacts (using NICE / BTS ‘stone in the pond’ approach). This is not routinely done in the initial contact tracing and may extend into leisure and work place contacts. Similar information as above is collected for second and third tier contacts.

Figure 1: Flow chart for cluster investigation



LEGEND / EXPLANATORY NOTES	
	NHS Lab / NHS TB team
	Steps X & Y. This system is under development and will replace Steps A - C
	HPA Mycobacterium reference laboratories
	HPS Cluster investigators role
	HPU role
1	Threshold: ≥ 5 cases in 2 years + 2 in last 6 months)
2	Risk factors: The cluster includes cases who below to the following groups or have the following characteristics: • Child (under 16 years) • Health care professionals • The cluster includes a drug-resistant strain • Known HIV infection • Homelessness or residence in a hostel or similar temporary accommodation • Recent incarceration in a prison / offender institute • Known previous TB treatment failure • Problem drug or alcohol use • History of severe mental health problems


PRELIMINARY CLUSTER REVIEW
CLUSTER SIZE REACHES THRESHOLD [1]
CLUSTER SIZE BELOW THRESHOLD BUT INCLUDES RISK FACTORS [2]
CLUSTER SIZE BELOW THRESHOLD, NO RISK FACTORS IDENTIFIED
COMMENCE FULL CLUSTER INVESTIGATION
NO FURTHER ACTION
REVIEW IF CLUSTER EXPANDS
RECORD CLUSTER ON HPZONE
COMPLETE CLUSTER INVESTIGATION QUESTIONNAIRES
REVIEW FOR EVIDENCE OF EPIDEMIOLOGICAL ASSOCIATION
NO EPIDEMIOLOGICAL LINKS IDENTIFIED
POSSIBLE OR DEFINITE EPIDEMIOLOGICAL LINKS IDENTIFIED
NO FURTHER ACTION
CLOSE HPZONE RECORD
COMPLETE OUTCOME REPORT
CONSIDER IF THERE IS POTENTIAL FOR ONGOING TRANSMISSION
REVIEW IF CLUSTER EXPANDS
IF YES, CONSIDER:
EXPANDED CONTACT TRACING
CONVENENING OUTBREAK CONTROL TEAM
IF NO:
CLOSE HPZONE RECORD
COMPLETE OUTCOME REPORT
WHEN INVESTIGATION COMPLETE
CLOSE HPZONE RECORD
COMPLETE OUTCOME REPORT
REVIEW IF CLUSTER EXPANDS
REVIEW IF CLUSTER EXPANDS

3.5 Possible outcomes following a cluster investigation

A number of outcomes are possible following a full cluster investigation:

3.5.1 Epidemiological links are identified between ALL members of the cluster

If definite or possible epidemiological links (see definitions in section 2.5) are identified linking members of the cluster, this is good evidence that they are involved in the same chain of recent transmission.

The **next step** in these circumstances is to decide if expanded contact tracing or a full outbreak investigation is necessary to interrupt further transmission. This step should be considered if:

- the cluster is expanding, i.e. contains cases diagnosed within last 3 months
- the cluster includes high risk cases or vulnerable cases - homeless, drug resistant (especially MDR & XDR- TB) or immunocompromised.

3.5.2 No epidemiological links identified OR epidemiological links are identified between SOME members of the cluster

If a full cluster investigation fails to identify epidemiological links between cases in a cluster, or definite or possible epidemiological links are identified between some but not all members of the cluster, then it becomes less clear if all the cases are involved in the same chain of recent transmission. The possible explanations for such a situation include:

- Chance occurrence that members have the same strain.
- Imported cases where infection was acquired from the same region abroad but with no local epidemiological links.
- The transmission of common endemic strains of *M. tuberculosis* can occur in closed populations[5]. In such situations there may be indistinguishable strain typing isolates but with no evident epidemiological links.
- In rare circumstances, the culture may have been contaminated in the laboratory or there may have been other laboratory errors in reporting the isolates as indistinguishable (e.g., primary diagnostic laboratories may have sent the wrong specimen to the reference laboratories; mislabelling of the specimen in the primary or reference laboratories; reference laboratories may have performed the strain typing incorrectly or even mixed up the reports). Reference laboratories will have protocols for ruling out false positives before sending out strain typing reports.
- Investigators are not asking the right questions or the persons interviewed are unable or unwilling to give complete answers.
- An extensive outbreak of TB in the past could have led to a large number of people becoming infected with an indistinguishable strain of *M. tuberculosis* and several years later these people may reactivate their infection and develop active TB. Contact tracing may fail to establish an epidemiological link between patients if the actual links between these patients occurred several years in the past and are not recalled.

The next step is to decide if the cluster requires further investigation.
Further investigation should include a consideration of the following:

[5] A closed population is defined as a population that gains no new members and loses members only to death. A Dictionary of Epidemiology. 5th Edition. Editor Miquel Porta. Oxford University Press 2008

- A review of the strain typing information with the reference and NHS laboratories to exclude false clusters.
- A discussion with the reference laboratories to consider the possibility and potential benefit of further tests to extend the strain typing to include further loci.
- Extended contact tracing to identify potential shared contacts not already identified as linked to the cluster.

It may be appropriate to put further action on hold to see if further cases with the same strain type emerge which may bring an epidemiological association to light.

3.6 Expanding clusters

When a cluster begins to grow to include more TB patients with indistinguishable strain types, more information about epidemiological links may become available. The greater the number of leads an investigator has to follow-up, the greater the chance of identifying a shared link among patients in a cluster.

When a TB programme first initiates a strain typing service it is difficult to identify endemic strains until data from many patients are collected and analysed. Over time, it will become easier to identify *M. tuberculosis* strains that are commonly detected in an area but are rarely associated with a chain of recent transmission (endemic strains). This may then lead to a reduction in the number of cluster investigations where no epidemiological link is found.

4.0 Recording cluster investigation activities and reporting the outcomes

4.1 Location of records

The decisions and outcomes of cluster investigations should be recorded on HPZone by the team leading the cluster investigation.

Preliminary Cluster Reviews, where the decision is not to take any further action do not need to be recorded on HPZone. These will be recorded by the TB Cluster Investigators on a separately managed TB Cluster Investigators' database.

Where a Preliminary Strain Type Cluster Review indicates the need for further cluster investigation or where a cluster size reaches the threshold for cluster investigation, these MUST be recorded on HPZone as a **CLUSTER**.

- If all the cases in a cluster are within a single HPU, that HPU should record the cluster on their HPZone system.

- If cases within a cluster occur in more than a single HPU, then the HPS cluster investigators will recommend which HPU will hold the core HPZone record following discussions with the HPU TB leads. The HPZone record host could be either:
  - The HPU with the greatest number of cases
  - The HPU with the most recently identified case
  - The HPU in which the suspected source / exposure occurred (where known)

HPUs with cases forming part of a multi-HPU cluster should record the case related to the cluster as a **CASE** using the **'CONTEXT'** information on HPZone to link the **CASE** to the relevant **CLUSTER** record.

Detailed instructions for recording cluster investigations on HPZone are shown in section 4.2.

4.2 Recording cluster investigations on HPZone

In order to allow effective and full evaluation of the national universal TB strain typing service, it is essential that all cluster investigations are recorded systematically and consistently to allow extraction of information nationally.

HPZone is an integrated support tool designed to facilitate best practice for Health Protection professionals. It is used by Health Protection Units for managing cases of communicable disease

This section gives step by step instructions for recording TB strain typing cluster investigations on HPZone. Screen shots from a fictitious entry have been included for clarity. Key records are highlighted in red.

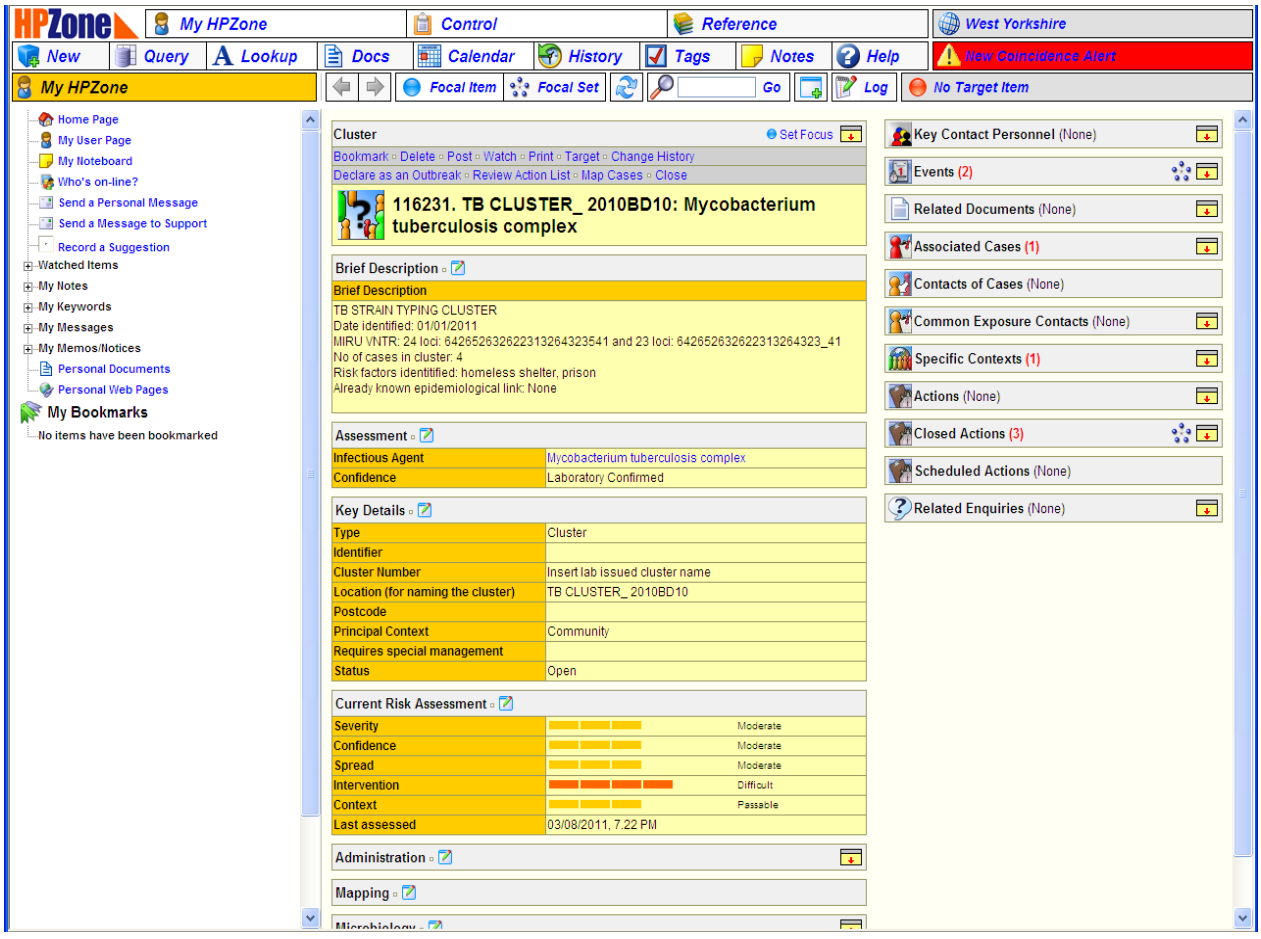
4.2.1 Creating an HPZone record: Start by creating a **NEW SITUATION** and selecting **CLUSTER**

HPZONE OPTIONS		ACTION / INFORMATION TO RECORD
BRIEF DESCRIPTION		**See screen shot 1** Record the following information: 1. Date cluster identified 2. MIRU VNTR profile of the isolates: If the cluster includes cases with a full 24 loci profile as well as cases with 23 loci, record both loci here. 3. Number of cases in the cluster at time of recording 4. Risk factors identified from preliminary review (if any) 5. Known epidemiological links between any cases in the cluster (if any) (As investigation progresses, you may add key new information to this BRIEF DESCRIPTION box by recording date of update and key finding (see screen shot 7).
ASSESSMENT	SCENARIO	Leave blank
	INFECTIOUS AGENT	Select 'Mycobacterium tuberculosis complex'
	CONFIDENCE	Select 'Laboratory confirmed'
KEY DETAILS	CLUSTER NUMBER	**Record the NAME OF THE SPECIFIC CLUSTER as issued by the reference laboratory or HPS cluster investigator**
	LOCATION	**See screen shot 1** **Record the NAME OF THE SPECIFIC CLUSTER as issued by the reference laboratory or HPS cluster investigator, prefixed with 'TB CLUSTER'** (This will determine the title of the HPZone record). It is good practice to include a geographical location such as 'London', 'West Midlands' 'South West Region', National' based on the agreement of the incident management team
	POSTCODE	Leave blank as cases are likely to have multiple postcodes. First part of the postcode may be recorded if all the same e.g. SE1
	PRINCIPLE CONTEXT	Select from drop down list based on information obtained from preliminary review or record 'unknown'. (At the beginning of an investigation, most clusters will be community based but as information becomes available, the context may be changed to a more specific location if appropriate)
	REQUIRES SPECIAL MANAGEMENT	Tick if an incident management / outbreak control team has been or will be convened.
AUTOMATICALLY GENERATED ACTION LIST		Manage the automatically generated action list as per the usual approach in your HPU
CURRENT RISK ASSESSMENT		Complete as normal
ADMINISTRATION	MANAGER	Record name of agreed investigation lead
	PCT	If all or majority of the cases are within one PCT select that PCT, otherwise leave blank.
MICROBIOLOGY	PHAGE TYPE / CODING	**See screen shot 2** **Record 24 LOCI MIRU VNTR here. If cluster includes cases with a missing loci, include this MIRU VNTR profile in BRIEF DESCRIPTION (see screen short 1)**

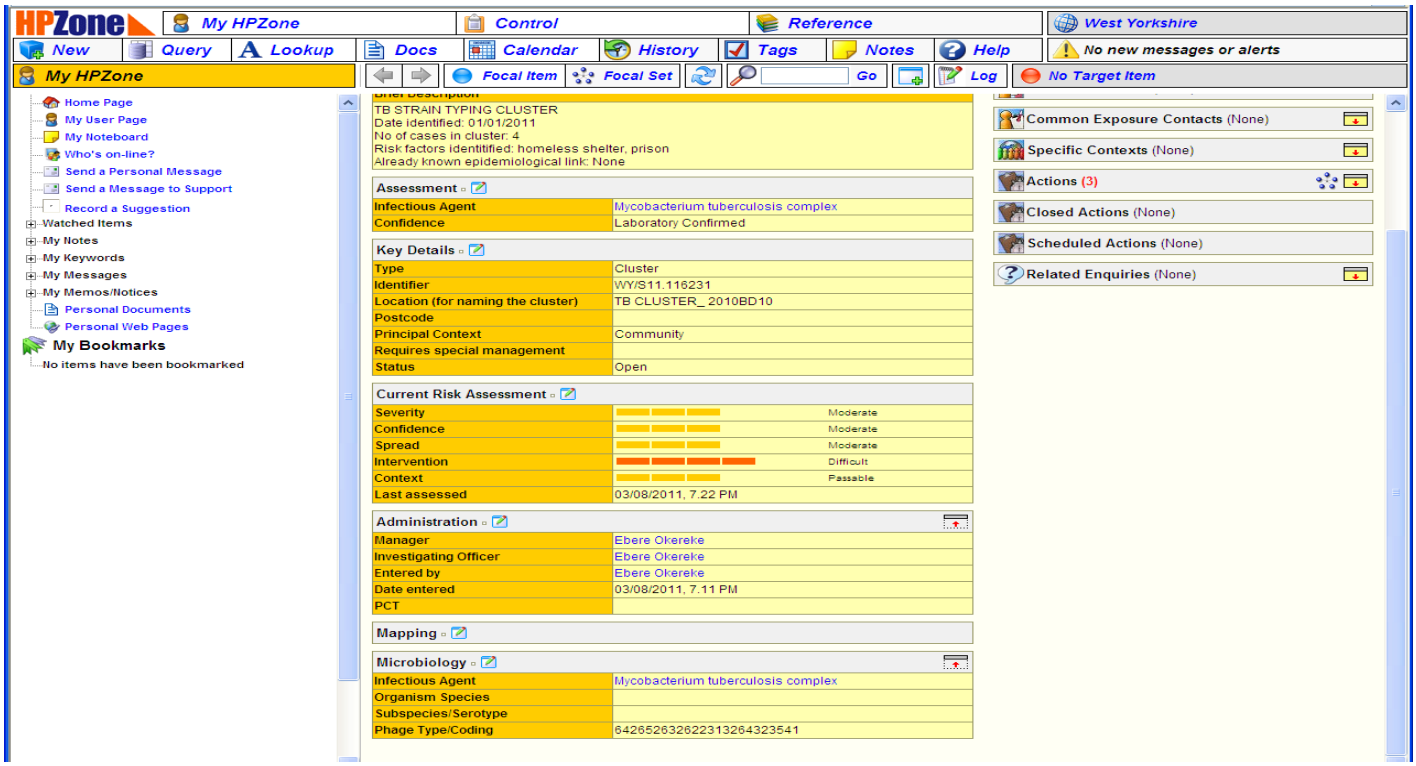
HPZONE OPTIONS	ACTION / INFORMATION TO RECORD
Specific context	**See screen shot 3 - 6** 1. Select **ADD A NEW CONTEXT** 2. Select **CONGREGATION** from the list of options. This will bring up a list of all relevant contexts nationally. 3. If your cluster is part of a cluster already being investigated elsewhere, the name will appear in the list of contacts and can be selected. **4. If your cluster has not yet been recorded on HPZone anywhere in the country, it will not appear in the list, you should then enter the FULL 24 LOCI MIRU-VNTR for the cluster in the search box. PRE-FIX THE 24 DIGITS WITH THE LETTERS 'VNTR' (SEE SCREEN SHOT 4).** **5. The next section (see screen shot 6) can be left blank and saved.** **This is an important step as it allows us to link all cases that form part of any cluster at HPU, regional and national level.**
ASSOCIATED CASE	Record all case details as usual. **Complete a cluster investigation form for each case (appendix 2).**
ASSOCIATED CONTACT	You **may wish** to enter the details of known close contacts of each TB case in the cluster here (optional)

HPZone screen shots

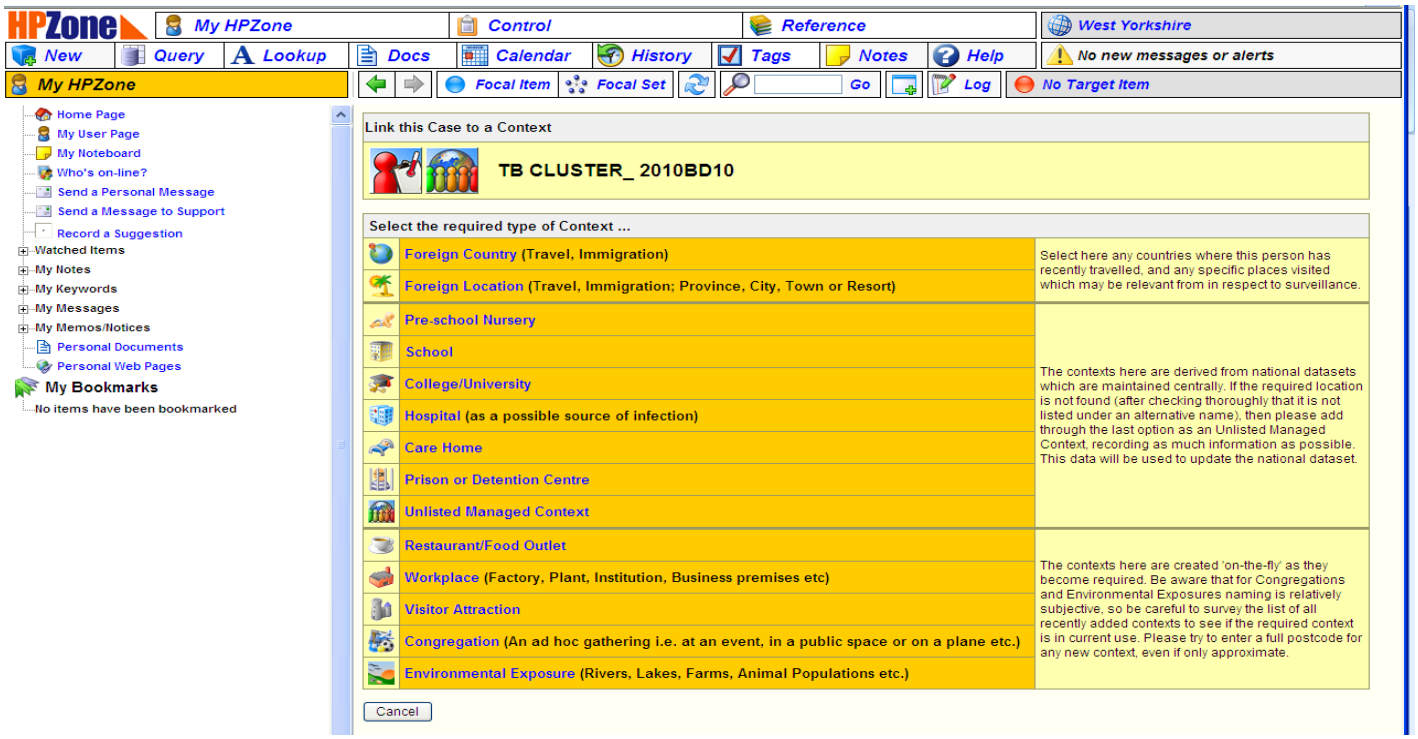
Screen shot 1



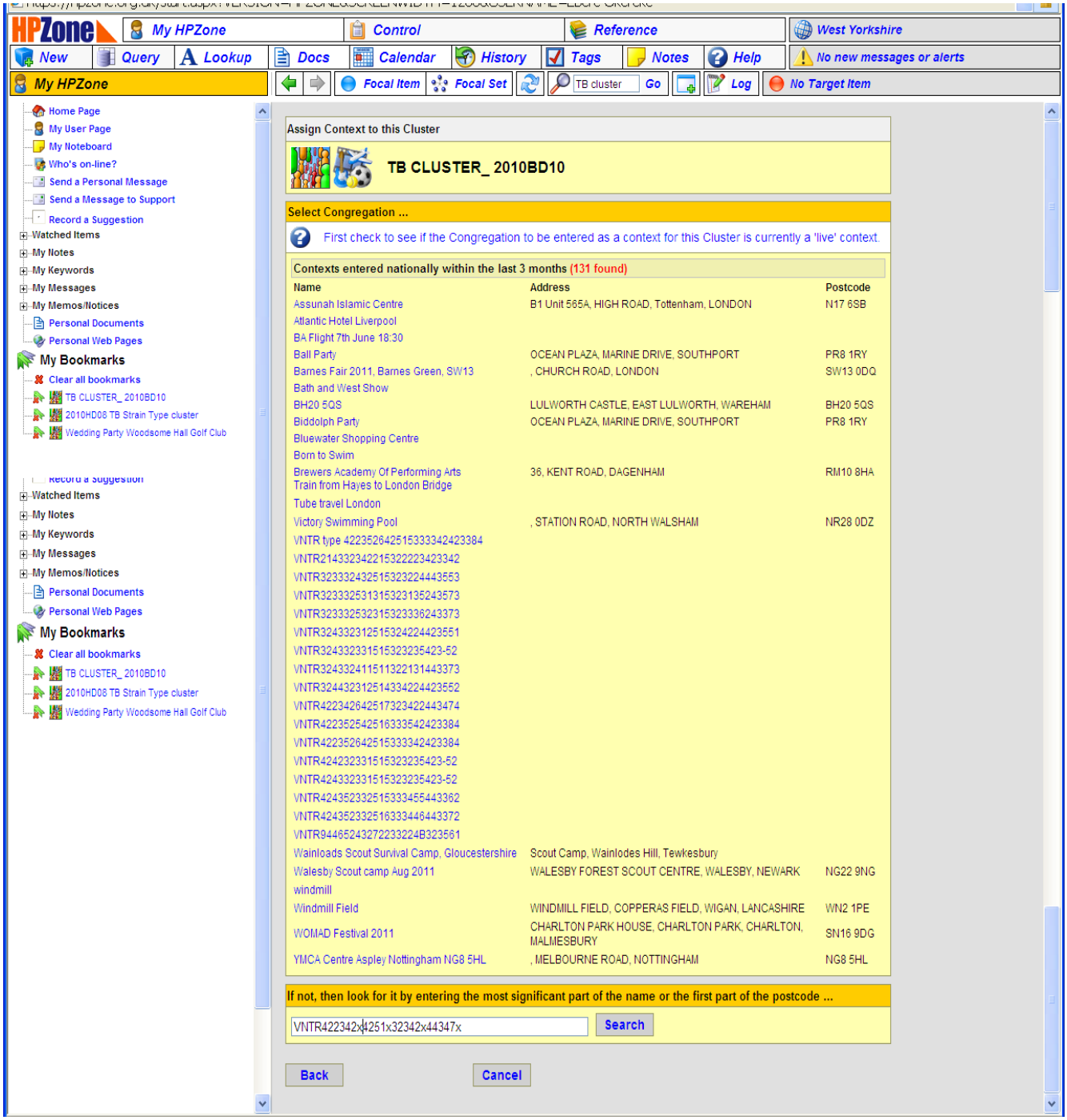
Screen shot 2



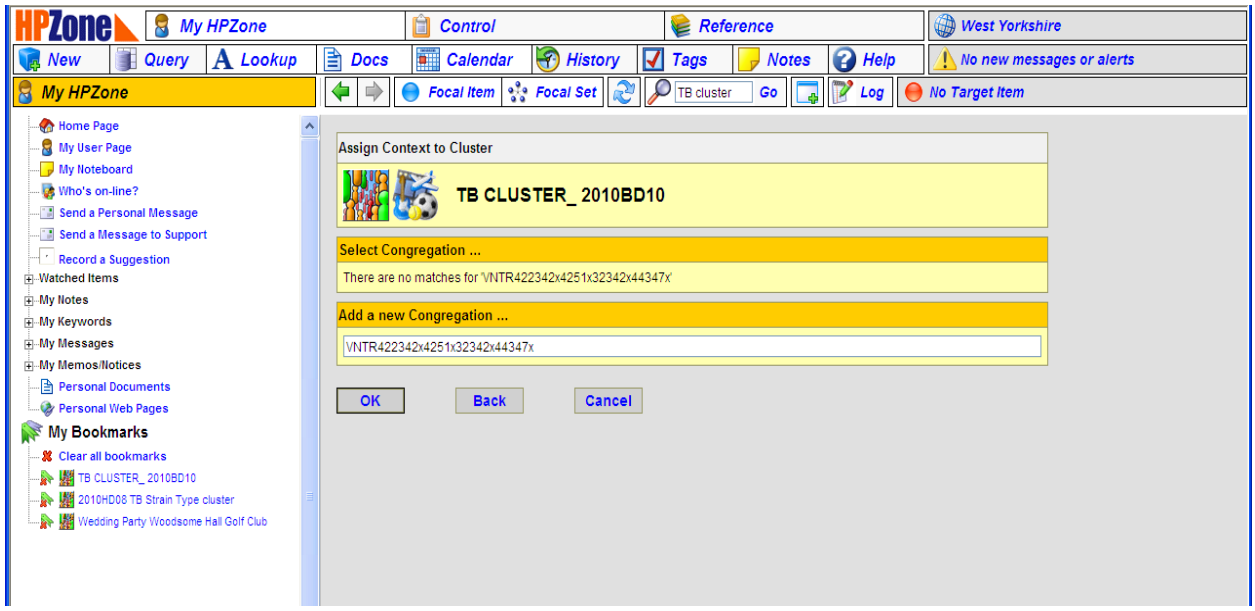
Screen shot 3



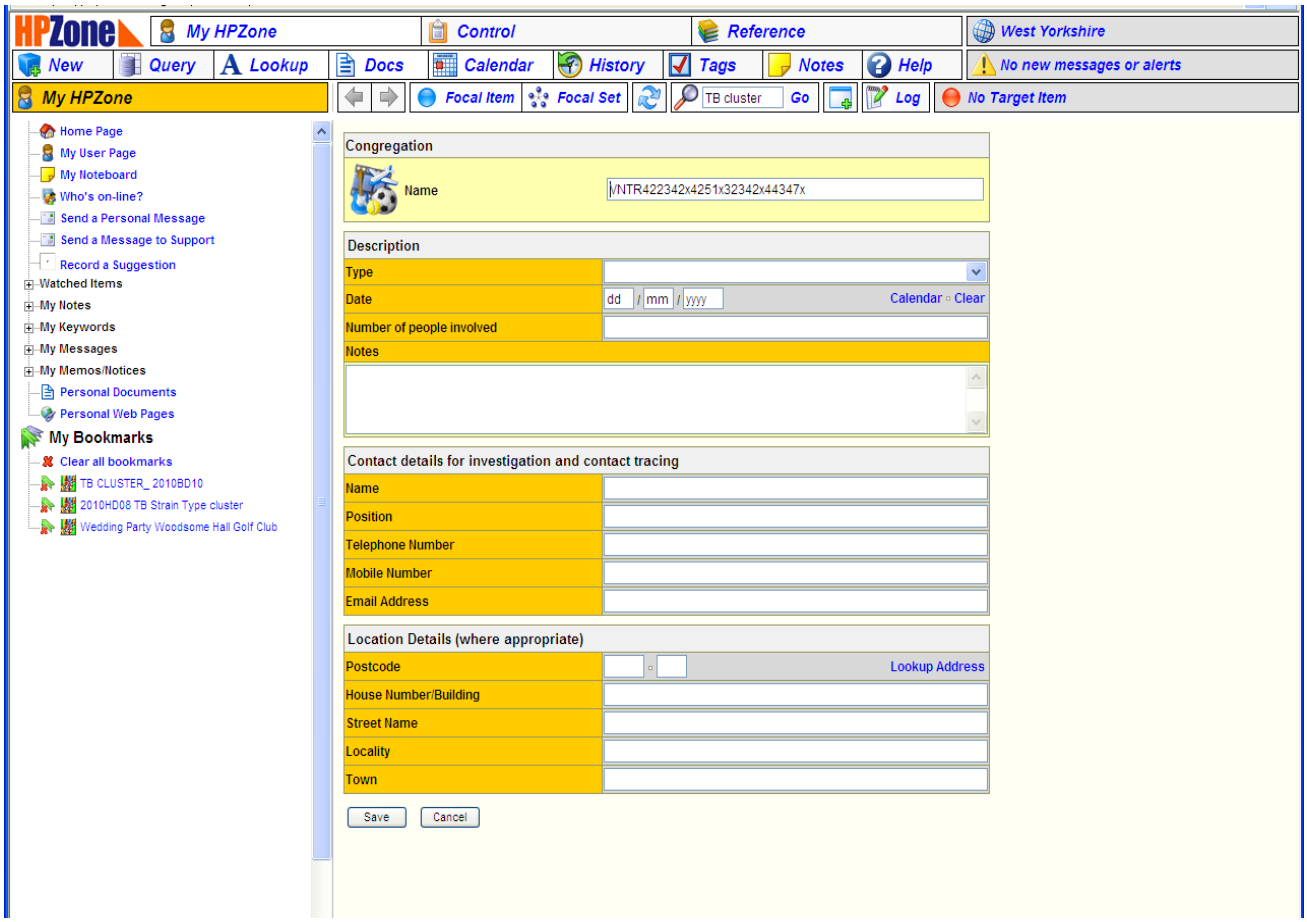
Screen shot 4



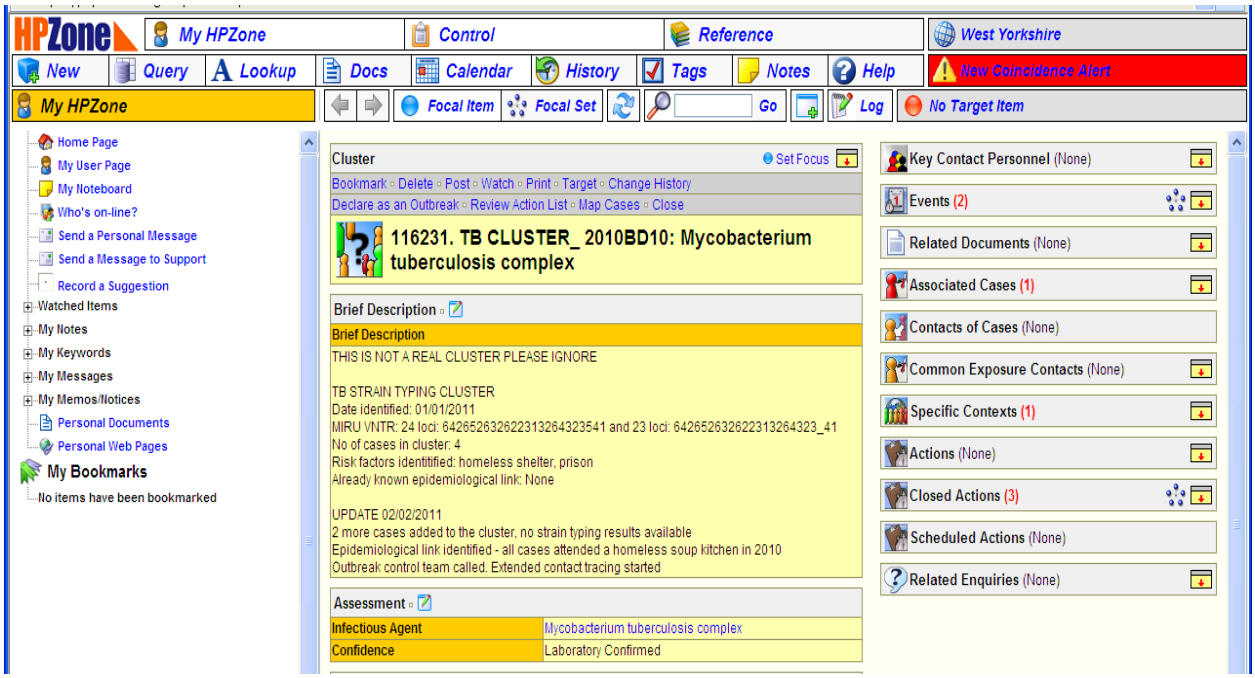
Screen shot 5



Screen shot 6



Screen shot 7



4.3 Recording a cluster investigation on IRIS

IRIS (Incident Reporting Information System) is the HPA's intranet-based centralised incident capture and information service. It aims to provide secure centralised incident alerting and information system to support the HPA Incident and Emergency Response activities and to provide readily accessible and timely information to Agency, Divisional, Regional and HPUs management levels about events/incidents affecting Agency resources. It is anticipated that IRIS will shortly be replaced by the HPZone dashboard, so this section will soon be redundant.

Consideration should be given to recording TB cluster investigations on IRIS if an incident management team has been convened.

Most TB strain type clusters will be IRIS level 1 incidents[6]. Occasionally, large or complex regional and national clusters may meet the criteria for IRIS level 2[6], but it is unlikely that a TB strain type cluster will be an IRIS level 3 incident, requiring central government involvement.

A decision to record a TB cluster investigation at IRIS level 2 or above should be discussed with the HPS TB cluster investigators and the regional TB lead.

[6] Health Protection Agency – Incident and Emergency Response Plan Version 8 20 October 2010, page 5 (HPAnet http://hpanet/webc/HPAnetFile/HPAnet_C/1287142611550)

4.4 Reporting the outcomes of cluster investigations

Health Protection Services will be holding national biannual Cluster Investigation Review Meetings to review the outcomes of TB cluster investigations. The purpose of these meetings will be to ensure that investigations are being conducted appropriately, to determine the workload implications of this new service and ensure that appropriate resources are available. A summary report from these meetings will be shared with HPUs via the HPS TB leads network and with the relevant NHS colleagues via the HPUs.

In addition, the HPA TB Programme Board has commissioned a full evaluation of the universal TB strain typing service, and this evaluation includes an assessment of the effectiveness of cluster investigations. Accurate information about the outcomes from cluster investigation is therefore essential for these purposes.

A TB strain typing cluster investigation outcome reporting form has been produced (appendix 4). It will be available on HPZone and it is envisaged that some of the fields will be automatically populated from information correctly recorded on HPZone. Until the automatic completion is operational, the outcome form should be manually completed and sent to the relevant TB Cluster Investigators and Regional TB Lead. A completed copy should also be uploaded to the HPZone cluster investigation record.

5.0 Roles, Responsibilities and Standards for Strain Typing Service and Response

Primary Diagnostic Laboratory

- If the local or primary microbiology laboratory does not provide microscopy and mycobacterium culture, the specimen should be referred to the Mycobacteria reference laboratory within one working day of receipt.
- The results of direct smear microscopy should be reported within one working day of receipt to the patient's clinician and the TB service.
- All samples for culture should be set up within one working day of receipt
- Culture, isolation and identification of 90% of all cases should be completed within 21 days of laboratory receiving the specimen.
- Culture that is positive for AFB should be sent to Reference Laboratories for strain identification within one working day of identification in the laboratory.
- Should work with the Mycobacteria Reference Laboratory to establish if any cross-contamination might have occurred.

Mycobacterium Reference Laboratories

- All new isolates of *M. tuberculosis* complex should be strain typed using MIRU-VNTR analysis.
- At least one initial isolate from all patients with culture confirmed result will have both susceptibility testing and molecular strain typing performed.
- At least 90% of all *M. tuberculosis* isolates should have 24 loci typing results available within 21 days of confirmation of identification.
- Report strain typing to primary laboratory within one working day of availability of typing result.
- Consider the possibility of cross contamination and false positive clustering and using agreed criteria rule that out as far as possible.
- Report strain typing results to HPU and NHS primary laboratory via agreed local mechanisms for onward dissemination to TB clinical teams.
- Strain typing data should be entered into the web-based National Strain Typing Database within one working day of results being available by the typing centre[7].
- Isolates found to have molecular profiles indistinguishable to previous isolates are grouped and highlighted to HPS TB cluster investigators.
- Reporting of results: a written and electronic report is provided to the requestors with the following information: The name of the originating laboratory; patient's name; patient's date of birth; referring laboratory reference number; provider laboratory number; date of isolate receipt by provider; molecular strain typing result which should have the complete 24 loci MIRU-VNTR profile.
- Participate in biannual cluster investigation review process.

[7] Exact mechanism to be determined

Health Protection Services Local Services (Health Protection Units and Regional Epidemiology Units)

- To identify a lead for investigating clusters within a HPU. The HPU and regional TB leads should work with the Regional Epidemiology Unit to identify leads for investigating regional and sub-regional clusters.
- To be responsible for collaborating with NHS and taking the lead in the investigation of potential local and regional clusters based on information provided by reference laboratories, working in collaboration with the NHS.
- Timely response to investigation of clusters.
- Record all cluster investigations on HPZone.
- Prepare summary reports of outcomes of cluster investigations and share with NHS and HPA through appropriate TB reports (e.g. annual or quarterly TB reports).
- Monitor and report on cluster expansion.

Health Protection Services Colindale TB Section

- National Cluster Investigator undertakes similar roles and responsibilities as described for the HPS TB Cluster Investigators but for national clusters.
- Responsible for undertaking monthly Preliminary Cluster Reviews of all national clusters reported from the reference laboratories.
- Lead the review and investigation of national clusters working with the HPS TB cluster investigators, regional TB leads and HPU TB leads.
- Record national clusters being investigated on cluster investigation database.
- Undertake epidemiological analysis of national cluster information.
- Undertake biannual reviews of national cluster investigations.

Health Protection Services TB Cluster Investigators

- Responsible for undertaking monthly Preliminary Cluster Reviews of all local and regional clusters reported from the reference laboratories and reporting these to the HPUs / regional TB leads.
- Using criteria defined in section 3.3 to make recommendations to HPUs for which clusters should be investigated.
- Provide support and advice to HPUs and regional TB leads where needed for any cluster investigations.
- Maintain regular liaison with HPUs and regional TB leads to ensure the timeliness of cluster investigations.
- Help to co-ordinate epidemiological investigation of clusters across more than one HPU.
- Record clusters being investigated on cluster investigation database.
- Undertake epidemiological analysis of cluster information.
- Report quarterly to HPA TB Strain Typing Board on activities and outcomes.
- Co-ordinate biannual reviews of cluster investigations with HPUs and produce reports for HPUs, the NHS, the HPS TB leads group, and the HPA Strain Typing Project Board.
- Produce annual report for stakeholders on HPS cluster investigations.
- Deliver training on cluster investigation process as required by HPUs and NHS.

NHS TB Services

- Responsible for collecting and reporting information to the HPA/HPU relating to individuals who are identified to them as being in clusters or outbreaks.
- Involved in local Outbreak Control Committees in the event that outbreaks are identified (as would be normal practice).

NHS Commissioners and Directors of Public Health

- Use the commissioning process to ensure that TB services support additional activity required to make strain typing effective.
- Receive and consider the recommendations in cluster investigation reports in service planning and development.
- Support and commit resources to cluster and outbreak investigations, as required.
- Respond to any recommendations jointly made, which may include need for new resources to augment TB control.
- The local Director of Public Health (DPH) is expected to be represented or made aware should an incident management team be convened to manage significant clusters or outbreaks (in line with usual local practice).

6.0 APPENDICES

Appendix 1: Sample strain typing cluster reports

Appendix 2: Cluster investigation questionnaire

Appendix 3: Example of cluster investigation tool

Appendix 4: Cluster investigation outcome reporting form

Appendix 5: Glossary, abbreviations and bibliography

Appendix 6: Bibliography

Appendix 7: Key contacts

Appendix 8: Feedback / comment form

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Appendix 1: Examples of Strain typing monthly cluster reports

1a: West Midlands Monthly cluster Report

Cluster No. EOO11		**Part of National Cluster - NO**			**VNTR24** 21433242261532143441528 2			
Notified	**Forename**	**Surname**	**Age**	**Postcode**	**ETS**	**HPU**	**Ethnicity**	**Preliminary Stain Type Review**
June 2011			22	B24		WME	Black Caribbean	Community care worker
May 2011			24	B38		WME	Black Caribbean	No risk factors identified on ETS
Recommendations		No further action required based on just 2 cases with no known risk factors						

Cluster No. C0012		**Part of National Cluster – NO**			**VNTR24** 32433251250132234244338 3			
Notified	**Forename**	**Surname**	**Age**	**Postcode**	**ETS**	**HPU**	**Ethnicity**	**Preliminary Stain Type Review**
Nov 2010			67	B26		WME	Indian	Previous pulmonary TB in 2007
Mar 2011			36	B11		WME	White	Drug & alcohol misuse
*June 2011			41	B20		WME	White	History of homelessness & alcohol misuse
Recommendations		Gather further information before considering moving to a full investigation						

Cluster No. D0013		**Part of National Cluster - YES**			**VNTR24** 22433233261532113251324 2			
Notified	**Forename**	**Surname**	**Age**	**Postcode**	**ETS**	**HPU**	**Ethnicity**	**Preliminary Stain Type Review**
*May 2011			43	WV14		WMW	Black African	Nurse, Pulmonary TB
Dec 2010			86	DY8		WME	White	Pulmonary TB, no known risk factors
Aug 2011			75	B11		WME	White	Hospital in-patient when notified
Recommendations		In-light of potential nosocomial transmission it may be worth reviewing the original contact tracing to complete the risk assessment locally – even though this is already being investigated nationally						

** Red indicates new isolates added to the cluster since the last monthly, i.e. an expanding cluster*
NB: Details shown are invented for demonstration purposes

1b: London HPU monthly report

Covering email
Dear HPU TB lead

Please find attached the Preliminary Strain Type Cluster Review for patients from xxx HPU in clusters that had either grown in size or are newly reported in xxx 2011. Those highlighted in red on the spreadsheet are newly reported in clusters this month.

RECOMMENDED HPU ACTIONS
Launch a cluster investigation for A0015 and review cluster E0160. Please see further details below and attached.

A0015
This is a local cluster of 5 patients which fulfils the threshold for investigation and therefore a cluster investigation should be launched. 3 patients have been reported in the last 6 months however no risk factor information has been recorded on LTBR for one of the patients

E0160
This is a local cluster of 2. One of the patients has a history of mental health problems and for the second patient this risk factor is recorded as unknown. Therefore I would recommend that this cluster was examined by yourselves in more detail to determine whether it warrants a cluster investigation.

Attached spreadsheet

NMRLclusterID	Cluster Level	Cluster size	Cluster investigator recommendations	DateReceived	Notification date	OnsetSymptoms	TreatmentOutcome	VNTR24	LTBR_No	Name	DOB	Age	Pulmonary	SputumPos
?B0033	National	3	No action-threshold not reached	26-Jul-11	05/08/2010	12/07/2010	Completed - Non-Pulmonary					46	Y	Yes
?B0033	National	3	No action-threshold not reached	26-Jul-11	08/04/2011	03/04/2011						31	Y	Awaiting
A0015	Local	5	Investigate - fulfills local threshold	07-Dec-10	19/08/2010	10/07/2010	Completed - Non-Pulmonary					51		Not done
A0015	Local	5	Investigate - fulfills local threshold	07-Dec-10	24/08/2010	01/06/2010	Completed - Pulmonary					23	Y	Yes
A0015	Local	5	Investigate - fulfills local threshold	18-Apr-11	01/03/2011							18	Y	Yes
A0015	Local	5	Investigate - fulfills local threshold	22-Jun-11	20/06/2011	01/04/2011						34	Y	Not done
A0015	Local	5	Investigate - fulfills local threshold	26-Jul-11	16/06/2011	20/04/2011						40		Not done
E0160	Local	2	?look into, new pt hist ment hlth probs?	17-May-11	18/04/2011	18/02/2011						24	Y	Yes
E0160	Local	2	?look into, new pt hist ment hlth probs?	26-Jul-11	01/06/2011	01/04/2011						21		Awaiting

Ethnicity	UKBorn	CountryOfBirth	YearOfEntry	PostCode	Occupation	PreviousDiagnosis	DST	DrugRes	Prison	Alcohol	Homeless	MentalHealth	Drug	CaseManager	Clinic
Black-African	N	Kenya	1996	IG5	Unemployed	N	SSSSS	N	N	N	N	Y	N		
Black-African	N	Kenya	2010	IG1	Student	N	SSSSS	N	N	N	N	N	N		
Bangladeshi	N	Bangladesh	2005	E1	Unknown	N	SSSSS	U	N	N	N	N	N		
	Y			IG5	Customer Service	N	SSSSS	N	N	N	N	N	N		
Bangladeshi				E1	Student	N	SSSSS	U							
Bangladeshi	N	Bangladesh		IG1	Unemployed	N	SRSSS	Y	N	Y	N	Y	N		
Bangladeshi	N	Bangladesh	1990	E1	Housewife	N	SSSSS	U	N	U	N	Y	N		
Black-Caribbean	Y	UK		E17	Unknown	U	SSSSS	U	N	N	N	U	U		
Black-Caribbean	N	Jamaica	2002	E5	Unemployed	N	SSSSS	N	N	U	N	Y	N		

NB: Details shown are invented for demonstration purposes

Appendix 2: Cluster investigation Questionnaire[8]

TB Cluster Investigation Questionnaire: Cluster No.

ETS No.		**Case's Initials**		**Hospital**	
No. in cluster		**Case's Dob**		**Treating Consultant**	
HPU		**Case's postcode**		**Site of Disease**	
Region		**Date notified**		**Onset / Rx Date**	

Dear colleague

The above patient is part of HPU cluster containing _ TB cases, some of whom are known to have one or more potential high risk factors (obtained from ETS). Other cases linked to this cluster are resident in ____ HPU / Region.

It would assist the investigation of this cluster if you could provide the following information and ask additional questions in relation to their place of work in the UK, and return the completed questionnaire to the HPU (see contact details below). We will analyse the questionnaires before sending you a summary report of the findings. Thank you very much for your co-operation[9].

Did patient regularly attend the following in the 2 year before diagnosis:	**Yes/ No/ Don't know**	**If yes, please provide name and address**	**If yes, please provide dates**	**Other comments**
Childcare/ Education (nursery, school, university, etc)	☐ Y ☐ N ☐ DK			
Work place (please provide address)	☐ Y ☐ N ☐ DK			
Place of worship (mosque, church etc.)	☐ Y ☐ N ☐ DK			

[8] *Available as a stand alone word document*

[9] The exact wording of this cover note will vary depending on the circumstances of the particular cluster under investigation.

Did patient regularly attend the following in the 2 year before diagnosis:	Yes/ No/ Don't know	If yes, please provide name and address	If yes, please provide dates	Other comments
Regular place of socialising – (Pub / clubs/ bar, gym/sports club, choir, dance class, language class etc.)	☐ Y ☐ N ☐ DK			
Prison (please provide dates if available)	☐ Y ☐ N ☐ DK			
Treatment /rehab centre for substance misuse	☐ Y ☐ N ☐ DK			
Treatment /rehab centre for alcohol misuse	☐ Y ☐ N ☐ DK			
Hostel/homeless shelter	☐ Y ☐ N ☐ DK			
Other places of interest (e.g. asylum seeker detention centre)	☐ Y ☐ N ☐ DK			

In the 2 year before diagnosis:	Yes/ No/ Don't know	Please provide details:	Other comments

Contact screening	Please provide details of any screening 'issues' identified	Other comments
No. of Household contacts identified		
No. of Other contacts identified		

Address in the previous 2 years			
Did they have previous history of exposure to TB (e.g. invited for screening as a contact)	☐ Y ☐ N ☐ DK		
Did they live or work overseas for more than 3 months?	☐ Y ☐ N ☐ DK		
Did they have visitors staying from overseas or elsewhere in the UK in previous 2 years?	☐ Y ☐ N ☐ DK	(If yes, please specify name of the countries and cities.)	
Did they regularly visit friends/family overseas or elsewhere in the UK?	☐ Y ☐ N ☐ DK	(If yes, please specify name of the cities.)	
Is/was the patient known by any other names or nicknames?	☐ Y ☐ N ☐ DK		

Please provide any additional details that you have identified that may aide this investigation

TB Cluster investigators:
Andy Burkitt, E: andy.burkitt@hpa.org.uk; T: 0844 2253550 F: 0191 2212584
Esther Hamblion E: esther.hamblion@hpa.org.uk; T: 020 7811 7228 F: 020 7811 7757
Laura Anderson: E: laura.anderson@hpa.org.uk; T: 020 8327 6165 F: 020 8327 6112

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Appendix 3: Examples of useful cluster investigation tools

Example 1:

(Author: Helen Bagnall, Epidemiological Scientist, West Midlands Regional Surveillance Unit)

ETS ID	Symptom Onset	Date Presented	Date of notification	Date Of Diagnosis	Start Of Treatment	Complete Course	Incomplete Reason	Death Date	End Of Treatment Date
000001*	14/10/2009		15/01/2010	14/01/2010	15/01/2010	Yes			15/07/2010
000003	01/12/2009	26/05/2010	04/06/2010	02/06/2010	04/06/2010	Yes			08/10/2010
000004	01/12/2009	14/09/2010	08/10/2010	29/09/2010	08/10/2010				
000005	31/05/2010	31/07/2010	11/08/2010	10/08/2010	11/08/2010		Patient died	17/10/2010	
000006	20/06/2010	27/07/2010	17/08/2010	10/08/2010	13/08/2010	Yes			18/02/2011
000002*	01/01/2011	14/04/2011	19/04/2011	14/04/2011	15/04/2011				

* Same person.

							2009			2010										2011					
No	ID	PCT	Sex	Age	Site	Smear	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	Epi links (D, P, N)	Comments / Additional information
1	000002*	PCT A	M	30	P	P																					
2	000003	PCT C	M	50	P	U																					
3	000004	PCT C	M	40	P	U																					
4	000005	PCT A	M	40	P	P																					
5	000006	PCT B	M	50	P	N																					

* also ETS ID 000001

Legend

- Infectious (date of onset - date start treatment)
- Infectious (start of treatment - two weeks after start of treatment)
- More than two weeks after start of treatment - date treatment completed
- More than two weeks after start of treatment - date of death
- ETS date of notification

Definitions

Please see ETS data dictionary for definitions.

Caveats

1. Data are based on ETS information *only*. Please note there may be other information available from other sources.
2. Dates are rounded to the nearest 1st / 15th of the month.
3. Dates, particularly dates of onset, may be estimates.

Key to fields

Site: P = pulmonary, N = non-pulmonary, PN = pulmonary & non-pulmonary, U = site not known.

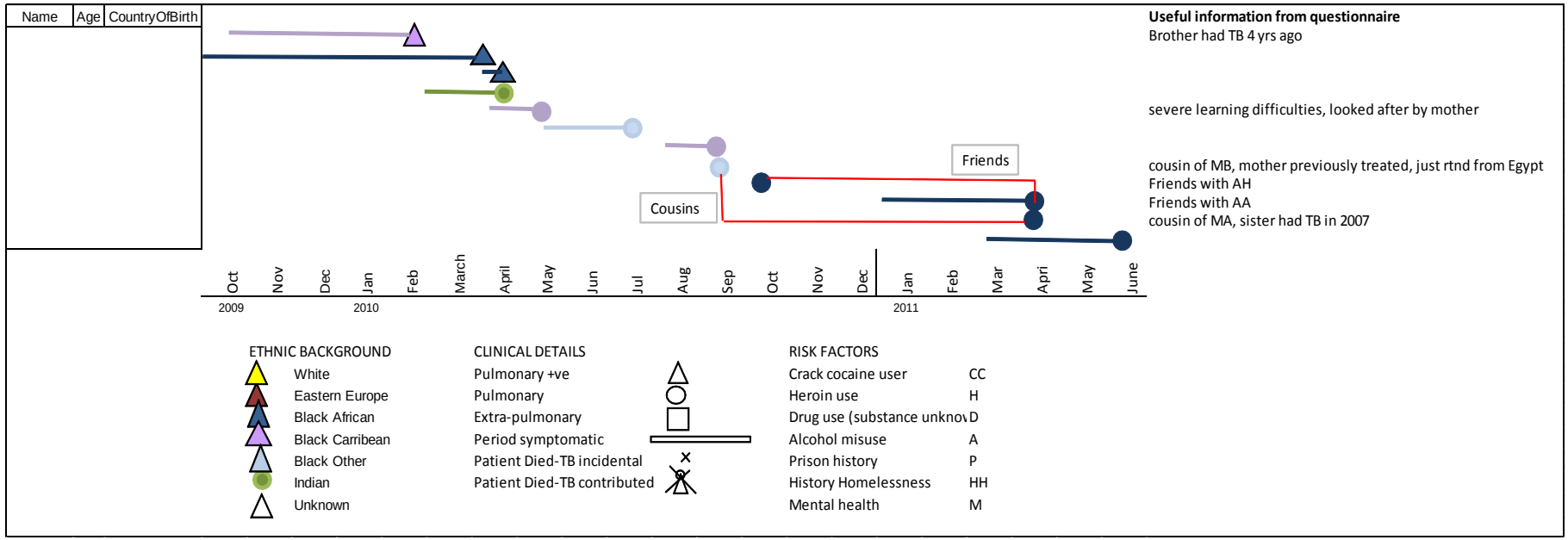
Smear: P = positive, N = negative, U = not known.

Epi links: Please provide any information on the epi links between cases e.g. definite, possible or none.

Comments: Please add any further relevant information.

Example 2:

Authors: Esther Hamblion / Sarah Anderson HPS London



Appendix 4: Cluster Reporting Form

TB STRAIN TYPING CLUSTER INVESTIGATION OUTCOME REPORTING FORM[10]

When complete, please:

1. Send copies to:
    a. HPS TB cluster investigator for your area (see end of this form for details)
    b. HPS TB Regional lead for your region
    c. HPS Regional Epidemiologists for your region
2. Upload a completed copy to the cluster record on HPZone

If you have any queries about completing this form, please contact your area TB cluster investigator

CLUSTER NAME / NUMBER		**HPZONE RECORD NUMBER**		**MIRU VNTR PROFILE**	
Name of reporter		**Email Address**			
Position		**Telephone**		**Fax**	
HPU		**Region**		**Date reported**	dd / mm / yyyy

Details of Lead Cluster investigator					
Name		**Email Address**		**Telephone**	
Position		**HPU**		**Region**	

CLUSTER DETAILS							
Type of cluster	☐	**HPU**	☐	**REGIONAL**	☐	**NATIONAL**	
Total number of cases in the cluster (include cases without matching strain type data where an epidemiological link identified)							
No of cases in the cluster with indistinguishable MIRU VNTR (24 loci or 23 loci, same missing locus)							
No of cases added to the cluster with unmatched loci (MIRU VNTR with more than 1 missing locus)							
No of HPUs with cases in this cluster							
List the HPUs involved and no of cases in each		**HPU**				**No of cases**	

Date investigation commenced	dd / mm / yyyy	
Reason for beginning investigation	☐	**HPU threshold reached**
	☐	**Regional threshold reached**
	☐	**National threshold reached**
	☐	**Below threshold, but Preliminary Strain Type Cluster Review identified risk factors**
	☐	**Other (Please explain):**

Please tick all actions taken in response to this cluster	☐	**Cluster Review meeting(s) / teleconference(s)**
	☐	**Incident Management meeting / Outbreak Control meeting**
	☐	**Additional strain typing information requested from reference laboratories**
	☐	**Extended contact tracing and screening of new contacts**
	☐	**Other (Please explain):**

[10] *Available as a stand alone word document*

Please summarise your findings from the cluster investigation. Please tick all options that apply and provide details			
☐	No epidemiological links found	Please comment:	
☐	Epidemiological links found but no additional public health action taken	Please comment:	
☐	New epidemiological links found.	Please describe:	
☐	Additional contacts identified and screened	If yes, how many: If additional contacts identified and screened: • How many new cases of active TB identified and treated? • How many new cases of latent TB infection identified? • How many new cases of latent TB infection given prophylaxis	
☐	Other	Please explain:	

Please indicate which factors you believe may have contributed to this cluster	
☐	Inadequate identification of and screening of contacts of early cases
☐	Delayed diagnosis of early cases
☐	Lack of cooperation from early cases
☐	Other. (Please explain):
☐	No factors identified

Final Public Health Outcome	
☐	Probable or definite chain of transmission identified and actions taken to interrupt further transmission
☐	No apparent chain of transmission identified, no further action deemed necessary
☐	Investigation inconclusive; to maintain a watching brief
☐	Other (Please explain):

Is a full incident report available?	☐ Yes	☐ No

General comments		
Was the strain typing information useful to you	☐ Yes	☐ No
The strain typing information disproved suspected links and provided reassurance	☐ Yes	☐ No
Any other comments:		

THANK YOU FOR COMPLETING THIS REPORT

TB Cluster investigators:
National clusters: Laura Anderson, HPS Colindale, laura.anderson@hpa.org.uk
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Rest of England: Andy Burkitt, HPS North East andy.burkitt@hpa.org.uk

Appendix 5: Glossary and abbreviations

Important definitions and abbreviations for understanding key terminologies for linking epidemiological data and strain typing results are defined below.

TERM / ACROMYN	DEFINITION
Cluster	A cluster in this handbook will refer to two or more *M. tuberculosis* isolates that share indistinguishable strain types.
Cluster investigation	An investigation to identify epidemiological links between TB patients whose isolates have indistinguishable strain types. A cluster investigation may consist of reviewing information from medical records and interviewing case managers. It can also involve interviewing TB patients.
Endemic strains	A strain of *M. tuberculosis* circulating in a relatively closed population for many years. Patients who are infected with endemic strains are often not involved in the same chain of recent transmission (i.e. within the previous 2 years) even though the strain type of the isolates from the patients are indistinguishable
Epidemiological cluster	Two or more persons with TB who share definite epidemiological links
Epidemiologically confirmed strain type cluster	Strain typing clusters that contain patients with known or definite epidemiological links.
ETS	Enhanced Tuberculosis Surveillance. ETS began in 1999 in England and Wales, and the following year in Northern Ireland, with the aim of providing detailed information on the epidemiology of TB.
HPZone	HPZone is an integrated support tool designed to facilitate best practice for Health Protection professionals. It is used by Health Protection Units for managing cases of communicable disease
Indistinguishable strain types	Two or more *M. tuberculosis* isolates that share the same strain type. Indistinguishable strain types may include missing data/loci
LTBR	London Tuberculosis Register is a web-based system surveillance and case management used in every tuberculosis clinic across London
IRIS	HPA Incident Reporting Information System
Loci / Locus	The specific location of a DNA sequence on the *M. tuberculosis* chromosome. Usually denoted by a number/letter for each VNTR
Matching strain types	Same as indistinguishable strain types, but fully identified, no missing data / loci
MIRU-VNTR	Myocobacterial Interspersed Repetitive Unit – Variable Number Tandem Repeats. MIRU is a PCR based strain typing assay. MIRU is a type of VNTR analysis.
MIRU-VNTR strain type	Finger printing designation that results from MIRU-VNTR analysis
Non-traditional setting	A setting where TB transmission took place that is not considered a traditional transmission setting, such as workplace or home. Non-traditional transmission settings identified during cluster investigation have included bars, social clubs, churches/ mosques/ temples.

TERM / ACROMYN	DEFINITION
PCR	Polymerase chain reaction is a method of amplifying small quantities of DNA up to amounts suitable for further analysis
Recent transmission	The transmission of TB that has occurred in the recent past, as opposed to reactivation of latent TB infection. Although the precise time period that distinguishes TB that resulted from 'recent' transmission and TB that resulted from reactivation of latent infection is not well defined; 'recent' transmission is often considered to be infection occurring within the preceding two years.
Re-infection vs. relapse	A case of relapsed TB represents a worsening of the disease after a period of improvement and is caused by the same strain of *M. tuberculosis* or endogenous infection. Re-infection is caused by a second infection with a strain that is different from the strain that caused the initial infection. Strain typing the initial and the subsequent *M. tuberculosis* isolate can distinguish these two possibilities.
RFLP	Restriction Fragment Length Polymorphism A strain typing technique based on measuring the number of length of the specific DNA fragments that are cut using specific restriction enzymes. The RFLP technique used to strain type *M. tuberculosis* is based on the IS6110 insertion sequence.
Standard TB control measures	Ensuring all TB cases complete treatment and all infected contacts are identified and treated appropriately.
Strain type cluster	A group of isolates that share the same strain typing pattern. The strain typing laboratories will report a PCR cluster designation for isolates with indistinguishable MIRU-VNTR patterns.
Traditional setting	Usual or suspected setting for TB transmission, such as home or workplace.
Universal strain typing	Policy of submitting one isolate from every culture-positive patient with TB for strain typing.
VNTR	see MIRU – VNTR

Appendix 6: Bibliography

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Appendix 7: Key Contacts

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[11] Samples from Gloucestershire and the South West may be processed by either Cardiff or London reference laboratories)

Appendix 8: Feedback / comment form

(Available as a stand alone word document)

TB Strain Typing Cluster Investigation Handbook for Health Protection Units 2nd Edition

Dear Colleague,

The national universal TB strain typing service has evolved in the year since its introduction, so the handbook has been modified to better suit the service.

We are therefore keen to capture the views of users on aspects of the handbook that may need review. We are therefore asking all users to use this form to provide feedback on the handbook, focusing on the general principles addressed in the handbook rather than specific local issues. This feedback will help us improve subsequent versions of the handbook and also identify aspects that may be addressed through specific training.

Please send the completed feedback form by email to tbsection@hpa.org.uk with the subject heading: TB Strain Typing Handbook Feedback.

Thank you

Name	
Email address	
Place or work	HPA / NHS
For HPA staff (Please tick appropriate option and provide details)	
☐	HPS: HPU, specify location
☐	HPS: Regional Epidemiology Unit, please specify location:
☐	HPS Colindale
☐	Microbiology services, please specify location:
For NHS staff, please indicate your workplace	
☐	Acute / Foundation Trust
☐	Community Trust / Social enterprise

Views about managing TB strain typing clusters:

1. Please rate your confidence about dealing with TB strain typing clusters from using the handbook and attending strain typing training (please circle one)				
Not at all confident 1	Moderately confident 2	Fairly confident 3	Mostly confident 4	Very confident 5

2. Please rate your confidence about knowing who you could contact to help you respond to strain typing clusters (please circle one)				
Not at all confident 1	Moderately confident 2	Fairly confident 3	Mostly confident 4	Very confident 5

3. How would you rate the overall quality of the handbook? (please circle one)				
Not at all confident 1	Moderately confident 2	Fairly confident 3	Mostly confident 4	Very confident 5

4. How would you rate the quality of specific aspects of the handbook? (Please tick one for each section)

Section	Poor	Fair	Satisfactory	Good	Excellent
1.0 Introduction					
2.0 Definitions					
3.0 Cluster Investigation Processes and Thresholds for action					
4.0 Recording cluster investigation activities and reporting the outcomes					
5.0 Roles, Responsibilities and Standards for Strain Typing Service and Response					
Appendix 1: Examples of Strain typing monthly cluster reports					
Appendix 2: Cluster investigation Questionnaire					
Appendix 3: Example of useful cluster investigation tool					
Appendix 4: Cluster Reporting Form					
Appendix 5: Glossary and abbreviations					
Appendix 6: Bibliography					
Appendix 7: Key Contacts					
Appendix 8: Feedback / comment form					

5. In what ways did the specific sections of the handbook not meet your expectations (please comment)

Section	Comment
1.0 Introduction	
2.0 Definitions	
3.0 Cluster Investigation Processes and Thresholds for action	
4.0 Recording cluster investigation activities and reporting the outcomes	
5.0 Roles, Responsibilities and Standards for Strain Typing Service and Response	
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Appendix 4: Cluster Reporting Form	
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Appendix 6: Bibliography	
Appendix 7: Key Contacts	
Appendix 8: Feedback / comment form	

6. How can we improve the handbook and what additional information do you think you require?

Section	Comment
1.0 Introduction	
2.0 Definitions	
3.0 Cluster Investigation Processes and Thresholds for action	
4.0 Recording cluster investigation activities and reporting the outcomes	
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Appendix 5: Glossary and abbreviations	
Appendix 6: Bibliography	
Appendix 7: Key Contacts	
Appendix 8: Feedback / comment form	

7. Further comments on any aspect of the handbook

Thank you for your comments; they will be considered and used to improve the next edition of the handbook.

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