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1.0 Introduction

1.1 Purpose of the handbook

This handbook provides guidance and support for the use of tuberculosis (TB) strain typing data for investigating TB clusters. It has been produced primarily as guidance for Public Health England staff following the evaluation of the first three years of the National Strain Typing Service and resulting recommendations (please see section 1.2.3 for details).

This handbook shares good practice and will remain an evolving document that will be modified over time to reflect current knowledge. It is not intended to provide instruction on all aspects of the application of TB strain typing, but only on strain typing as a public health tool.

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, can help to identify TB patients who may be involved in the same chain of recent TB transmission. They can also assist in the initiation of timely and appropriate control measures following cluster and outbreak investigations. In addition, TB strain typing results combined with epidemiological data provide an opportunity to better understand the epidemiology of TB in a given setting.

1.2.2 The main objectives of strain typing are:

- to provide access to typing results in response to local or national incidents of suspected transmission, enabling the prospective, proactive, locally-led application of strain typing for TB control and public health protection
- to understand the national and local epidemiology of TB, including the identification of risk groups for TB attributable to recent transmission
- to understand the molecular epidemiology of TB, including diversity of circulating strains, geographical distribution, lineages and virulence
- to monitor TB programmes by analysing the trends in estimates of recent transmission
- to meet international obligations for molecular surveillance, Europe-wide and globally
- to create a national repository of strain types

In addition, strain typing data can be used:

- 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
It can also be useful to identify if TB cases occurring in the same time and place have unrelated strain types, thus do not belong to the same chain of recent transmission and hence not requiring further public health investigation.

1.2.3 The TB Strain Typing Service in England and Wales

In January 2010 the then Health Protection Agency (HPA) National TB Strain Typing Service was established in response to Stopping Tuberculosis in England: An action plan from the Chief Medical Officer, 2004. Prospective universal strain typing was undertaken on TB isolates using 24 loci Mycobacterial Interspersed Repetitive Unit-Variable Number Tandem Repeats (MIRU-VNTR). Molecular clusters of patients with indistinguishable 24 loci MIRU-VNTR profiles were investigated prospectively to identify epidemiological links and transmission settings when certain criteria were met. These criteria were five cases, resident in a Health Protection Unit (HPU) footprint, or ten cases nationally, within 24 months with two in the previous six months. Clusters were investigated at an earlier stage if they contained cases with factors suggesting a higher risk of transmission eg having prison or drug history or MDR TB.

A 3 year evaluation of the Strain Typing Service was completed in March 2013, and its recommendations were endorsed by the PHE TB Delivery Board. The recommendations relevant to the use of strain typing data as a public health tool were as follows:

- the need to continue the universal typing of all culture-confirmed TB cases
- cluster investigations should be reconsidered, as there was no evidence that the routine investigation of all clusters that met a certain threshold was effective or cost-effective
- local cluster investigations should be initiated from the local level in response to local demand
- regional cluster investigations should be discontinued
- routine investigation of national clusters should be discontinued, and national cluster investigation should be limited to clusters that have been identified to be of public health importance

This handbook has been produced to support PHE staff in using TB strain typing results to inform public health action.

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2.0 Definitions

2.1 Epidemiological cluster

Two or more persons with TB with known epidemiological links. Strain typing information is required to provide additional evidence as to whether a transmission event has occurred. Cases found to have different strain types in an epidemiological cluster should not be considered as being in the same chain of transmission.

2.2 Strain type cluster

Two or more persons with TB caused by indistinguishable 24 loci strains. Epidemiological information (see section 3.2) is required to determine if a strain type cluster is a genuine cluster representing recent transmission.

For the purpose of this handbook and this programme, a strain type cluster is defined as a cluster which contains cases with TB isolates exhibiting the following characteristics:

Two or more cases with indistinguishable 24 loci strains, with at least one case with a complete 24 loci MIRU VNTR profile. Additional cases in the cluster may each have one missing locus (-).

Examples:
Cluster X1051: 2 cases, both case isolates fully mapped and identical. This is a strain-type cluster.
  Case 1: 614642432722324263313461
  Case 2: 614642432722324263313461

Cluster E1704: 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 strain-type cluster.
  Case 1: 32463223516222517423182
  Case 2: 3246322351622251742-182
  Case 3: 324632235162225174231-2

Cluster C1065: 3 cases; Case 3 has two (2) missing / unmapped loci. Case 3 is NOT part of this strain type cluster:
  Case 1: 422352642517333542423384
  Case 2: 422352642517333542423384
  Case 3: 2235264251733354-423384

Exceptions to the above; some clusters have one untypable locus (U) in all cases in the cluster, and despite repeated attempts to type the locus, the locus is untypable and all cases in the cluster have this untypable locus.

Cluster E1237: 4 cases, all cases have the same untypable locus. These cases all form a strain-type cluster:
  Case 1: 424332331515323236423U52
  Case 2: 424332331515323236423U52
  Case 3: 424332331515323236423U52
  Case 4: 424332331515323236423U52
2.3 Epidemiologically confirmed strain-type cluster

This is a cluster of two or more persons with TB caused by indistinguishable 24 loci strains with known epidemiological links between at least two members of the cluster.

2.4 Epidemiological links

Based on information collected from two or more TB patients who are linked in time and place during 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.

2.4.1 Known epidemiological link

TB patients have a known epidemiological link if either of the following conditions is met:

- one patient volunteered the name of the other as a contact while either was potentially infectious (ie had pulmonary TB, 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

2.4.2 Possible epidemiological link

TB patients have a possible epidemiological link, if 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 in the same setting, around the same time and shared social, occupational or behavioural characteristics 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.

2.4.3 No identified epidemiological link

Two patients should be classified as having no identified epidemiological link if they do not meet the criteria in 2.4.1 or 2.4.2.

For the purposes of this handbook, the term ‘cluster’ will be subsequently used to refer to strain type clusters, unless otherwise stated.
3.0 Use of TB strain typing results to inform public health action

Access to TB strain typing results, in combination with epidemiological data, can help determine whether recent transmission of TB has occurred, and so help direct additional control efforts.

3.1 Mechanism for reporting strain typing results

The MIRU-VNTR profile of each TB isolate, where available, will be uploaded from the TB reference laboratories into the Enhanced Tuberculosis Surveillance (ETS) database, where isolates can be matched to notified cases.

The ETS Strain Typing Module (STM) automatically identifies and reports clusters. Cluster reports will be generated by the TB Section at Centre for Infectious Disease Surveillance and Control (CIDSC). Reports will be generated according to HPA geographical footprints (until structural changes are made to ETS); i.e. for each pre-2013 HPU, each pre-2013 region and for the entire country. Reports will be regenerated weekly, and be available to view by users at the Health Protection Team (HPT), Field Epidemiology Services (FES) and national level.

STM Screen shot 1

The STM will also act as a cluster identification and management tool by allowing the collation of demographic and clinical information from ETS with additional information on the social characteristics of cases, collected through the cluster questionnaire.
Screen shot two shows an example cluster with a recent case in yellow (isolate with a specimen date in the last three months), and a summary of clinical, demographic and risk factor information for the cases in the cluster.

For full details of the features and technical guidance on the use of the strain typing module, please refer to the STM user manual (available for download in the ETS help tab).

3.2 How to use TB strain typing data to inform the need for cluster investigation

3.2.1 Local level

At a local level, individual Health Protection Teams (HPTs) should determine how they will use the reports of TB strain typing clusters provided in the STM to decide whether to investigate local TB clusters. This decision should be informed by their experiences of conducting cluster investigations in their local area in the first three years of the strain typing service, combined with knowledge of their local epidemiology, pre-existing communication channels with their local TB services, and their clinical judgement.

Possible approaches to using STM include a periodic review of clusters to identify features that may require further investigation, or the use of strain typing data to provide additional information about potential clusters identified through epidemiological links between cases.

If an HPT is actively reviewing clusters to identify those that may require investigation, it may be helpful to consider if cases in the cluster have any of the following factors that may indicate recent transmission:
• the cluster includes a child (under 16 years), especially if under five years old or a child born in the UK
• the cluster includes a case with known HIV infection
• the cluster includes cases with the following characteristics:
  o homelessness or residence in a hostel or similar temporary accommodation
  o recent incarceration in a prison / offender institute
  o previous TB treatment failure (where known/ information available
  o problem drug or alcohol use
  o history of severe mental health problems

In addition, the following factors may warrant further investigation:
• the cluster includes a health care professional
• the cluster includes a drug-resistant strain
• a cluster of *M. bovis* cases

### 3.2.2 Regional level

Following the evaluation of the Strain Typing service, routine investigation of regional clusters will no longer be conducted. However, Field Epidemiology Services (FES) will review cluster reports at former HPA regional level periodically, to enable prioritisation for example of serious, or large and rapidly growing clusters of public health concern that might otherwise not be recognised as such, in order to assist colleagues at HPT level within the region in their own reviews and investigations.

### 3.2.3 National level

At a national level, national clusters (clusters containing cases that cross pre-2013 HPA regional boundaries) will be reviewed periodically by the TB Surveillance Team at CIDSC, to identify whether there are any national clusters of public health concern which require further investigation.

### 3.2.4 Practical considerations

Clusters illustrated on the STM may not always show all TB cases that are potentially part of a cluster from a particular HPU area. On occasion it may be necessary for the HPT to manually add cases to particular clusters. Examples of this may include;

• a clinical diagnosis of TB where no sample was obtained for culture but epidemiological links are identified
• a historical but still relevant case that may have had no typing or incomplete typing
• epidemiologically linked cases where incomplete typing occurs

• a case that was incorrectly assigned to an HPU report due to the hospital laboratory where their specimen was submitted (cases are assigned to HPU reports based on where specimens are submitted as opposed to the case’s postcode of residence)

In addition, as only cases within a particular HPU are included in a HPU cluster report, any cases in a neighbouring HPU area will not be included. Caution should be exercised when adding cases to clusters with no complete strain typing result. Manually added cases should be reviewed regularly to ensure they should still be in the cluster.

Cases with one missing loci will be automatically added to a cluster by the STM (provided there is at least one case within the cluster with a complete 24 MIRU-VNTR). It should be noted that cases that have one or more missing loci from their 24 MIRU-VNTR profile could be part of more than one cluster, and if their strain typing were to be repeated and the missing loci filled, they may no longer be part of all clusters to which they were originally assigned. Updated 24 MIRU-VNTR profiles with additional loci typing information will be highlighted on the STM report and should be reviewed, and accepted where appropriate (see STM User Manual for more detail).

Some isolates that appear in the cluster report will not have ETS IDs associated with them; this could be for a number of reasons including that the case may not have been notified on ETS but has had a sample sent to the laboratory; others may have been notified but the case and laboratory isolate may not have been matched in the system.

It is also acknowledged that ETS data may not be complete e.g. risk factor information may not be present. Furthermore, certain ‘risk’ information is not captured in the ETS system such as HIV status and cognitive impairment.

Please note: If a case is added to a cluster their association with the cluster should be recorded in the epidemiological link section and the notes section on the STM. A case can only be added to a cluster if they have an ETS number. For further technical details please refer to the STM User Manual.

3.2.5 Cluster ‘status’ definitions

When a new cluster is shown on the STM, the status of the cluster automatically defaults to a setting titled ‘Awaiting Preliminary Review’. If the cluster is reviewed by an HPT this status should be updated.

A cluster may have one of the following statuses listed below:

Awaiting Preliminary Review
A status given to all clusters prior to an assessment on whether or not they are to become active.

No Action Required
This status can be given to clusters that do not require active investigation. Please note this can only be given to clusters that have never been active before.

Active Investigation
This is the status given to active clusters that are currently undergoing investigation. Please note clusters can only have this status if this is the first time they have been active.
**Watchful Waiting**
This may be given to clusters that have been previously active but that are not currently being actively investigated. This identifies those clusters that have recently been investigated but there is uncertainty about whether they should be formally “closed”. For example, this could include those clusters that may be expected to grow following the addition of any new patients that could change the investigation status.

**Re-opened for active investigation**
This may be given to clusters that have been either “Closed” or in “Watchful Waiting” in the past, but have now been re-opened for a specific reason, such as the addition of new cases to the cluster requiring active investigation, or if cases within the cluster have been subsequently found to have risk factors. This is important to distinguish from “Active Investigation”, as it will signal that those investigating will perhaps want to look back at historical records of epidemiological links found and seek out previous investigation information.

**Closed**
This may be given to clusters that have no further action remaining following an investigation; public health action has been carried out, and there is little likelihood of the cluster becoming active in the near future. Please note, this status is also subject to change, as new patients could still arise in these clusters and cause them to be “Re-opened”.

A chronological record of the previous cluster status(es) are stored on the STM.

### 3.3 Conducting a full cluster investigation

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.

Prior to the strain typing evaluation, clusters were investigated based on thresholds (number of cases in a cluster in a given time). Cluster thresholds were set at five or more persons within 24 months, of which two occurred in the last six months in a HPU area. The threshold was ten cases for regional and national clusters. Cluster investigations were often initiated before the threshold was reached if cases in the cluster had risk factors.

Following the evaluation, routine investigation of clusters that meet a certain threshold or fulfil certain criteria is no longer recommended. It is the responsibility of the HPT to use their local knowledge and professional judgement to determine whether a TB cluster requires investigation. If required, advice and support for such decisions could be sought from TB lead colleagues at PHEC, FES or national level (see Appendix 6 for key contacts).

### 3.3.1 Recommended steps in conducting a full strain typing cluster investigation

In the event that the local HPT consider that the situation or circumstances warrant a full investigation the following steps are recommended:

**Local clusters**

1. Gather additional information on cases in the cluster
The cluster investigation questionnaire should be used to gather additional information on cases in the cluster. The questionnaires on STM can be edited to add specific questions based on the local information gathered to date relevant to the cluster (Appendix 1). For cases where a questionnaire is required, the questionnaire can be submitted to the NHS TB case manager through the STM (although not for London cases). For questionnaires submitted through STM, NHS TB case managers will be alerted on ETS that they have a case which is part of a cluster that requires a questionnaire to be completed.

For cases that are children, the information about both the child and the parent should be collected in the questionnaire. This information will usually need to be requested from the NHS TB case manager who may need to review patient records or interview the patient directly. For all cases that have had a previous history of TB in the UK, the reference laboratory should be contacted to ask for the previous specimen to be typed if it has not previously been typed.

2. Determine if epidemiological links exist between any or all of the cluster members
Information gathered should be reviewed to identify similarities in time, place, person, overlapping infectious period(s), and to determine if any other epidemiological links exist between any or all of the cluster members. Epidemiological links, and other information gathered should be recorded in the STM.

Appendix 2 contains examples of a useful approach to collating information obtained from cluster investigations that may assist with determining the presence of epidemiological links.

Investigation could include consideration of the following:

- 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 or to conduct Whole Genome Sequencing (WGS)
- consider collating further information on a revised locally tailored questionnaire, specific to the cluster

3. Actions to take
If evidence of potential previously unrecognised epidemiological links are identified, consideration should be given to whether there is an on-going risk of transmission. If such a risk exists, the appropriate public health actions should be taken, such as expanded contact tracing and screening in line with existing guidelines and best practice, or TB awareness education.

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.

National clusters

In the event that CIDSC consider that the situation or circumstances warrant a full investigation of a national cluster, the following steps are recommended:

1. Gather additional information on cases in the cluster
When a national investigation is launched, HPTs with cases in the cluster under investigation will be informed by email that an investigation is being conducted.

Cases which require more information require a cluster questionnaire to be completed. National cluster investigators will edit questionnaires on STM and add specific questions based on
information gathered to date on the cluster. For cases where a questionnaire is required, the cluster investigator will submit the questionnaire through the STM, where possible, to the NHS TB case manager.

For cases that are children, the information about both the child and the parent should be collected in the questionnaire. For all cases that have had a previous history of TB in the UK, the reference laboratory should be contacted to ask for the previous specimen to be typed if it had not previously been typed.

2. NHS TB Case Managers alerted of questionnaires
NHS TB case managers will be alerted on ETS that they have a case which is part of a national cluster that requires a questionnaire to be completed. Users at a HPT level will also see the alerts for questionnaires for clinics within their area.

3. Determine if epidemiological links exist between any or all of the cluster members
The cluster investigator will review the cluster questionnaires to identify similarities in time, place, person, any overlapping infectious period(s), and to determine if any other epidemiological links exist between any or all of the cluster members. Epidemiological links are recorded in the STM by the cluster investigator.

4. On-going transmission considered - cluster investigator and HPT roles
If no epidemiological links are identified the cluster investigator closes the investigation.

Any potentially linked cases with previously unidentified epidemiological links should be added to the cluster by the cluster investigator. 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.

If evidence of a potential epidemiological link is identified, the national cluster investigator should consider if there is the possibility of an on-going risk of transmission and if so, inform the HPT(s) of the findings. Findings will be summarised and where appropriate will include cluster diagrams, a summary of cases in the cluster and a summary of the risk of transmission with suggestions for public health actions. A national level Incident Control Team may be required.

The HPT(s) should take the appropriate public health actions (eg initiating an outbreak investigation, conduct expanded contact tracing and screening, in line with existing guidelines and best practice). During this time the HPT(s) and the national cluster investigator should be in regular contact.

3.3.2 Expanded contact tracing (widening the search)

The aim of expanding contact tracing is to ensure that all contacts of a patient with infectious TB are identified, appropriately screened and treated as required. The goals of standard contact tracing and expanded contact tracing are similar. Expanded contact tracing involves applying greater resources to identify and evaluate contacts including those not yet traced and screened, as well as those outside the immediate close household group, since the possibility of recent transmission to known contacts has been established from strain typing information.

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.
Figure 1: Flow chart for cluster investigation

A] Local Investigations

Legend/Explanatory Notes

1. Risk factors: The cluster includes cases who belong to the following groups or have the following characteristics:
   - Child (under 16 years)
   - Health care workers
   - The cluster includes a drug-resistant case
   - Known HIV infection
   - Currently homeless or history of being homeless 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
B] National Investigations

1. National Cluster report generated on STM
   - Preliminary Strain Type Cluster Review of National Clusters
   - Commence full cluster investigation if national cluster is of public health importance
   - No further action
     - Review if cluster expands

2. Update STM/National cluster database/Tick which questionnaires to be completed by nurses on STM
   - Complete cluster investigation questionnaire
   - Review investigation questionnaires and any other information gathered for evidence of epidemiological association

3. No epidemiological links identified
   - No further action - update STM record, national cluster database and cluster monitoring database
   - Review if cluster expands

4. Possible or definite epidemiological links identified
   - Consider if there is potential for ongoing transmission
   - If yes: feedback findings to HPTs
   - If no: Update STM record, national cluster database, cluster monitoring database

5. Consider expanded contact tracing, convening outbreak control team
   - Feedback any public health action taken, and new cases identified and any additional epi links identified to National Cluster Investigator
   - When investigation concluded update STM record, national cluster database, cluster monitoring database
   - Review if cluster expands

Legend/Explanatory Notes:
- HPS Cluster Investigators Role
- NHS TB Team
- HPT Role
3.4 Possible outcomes following a cluster investigation

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

3.4.1 No epidemiological links identified

If a full cluster investigation fails to identify any recent epidemiological links between cases in a cluster then it becomes less clear if any of the cases are involved in the same chain of recent transmission. The possible explanations for such a situation include:

- chance occurrence that members of the cluster have the same strain
- the MIRU-VNTR strain typing method is not discriminatory enough and strains may have genetic differences that are undetected by this method
- imported cases, where the cases have been infected by endemic strains acquired abroad
- 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
- difficulty engaging the patient(s) or with interpretation
- investigators may not have asked the right questions to elicit an epidemiological link or patients 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 which several years later may reactivate and become active TB. Interviews may fail to establish a recent epidemiological link between patients if the actual links between these patients occurred several years in the past.

The cluster status on the STM should be updated at this stage.

3.4.2 Epidemiological links are identified between SOME but not ALL members of the cluster

If a full cluster investigation identified definite or possible epidemiological links in some cases, but not all cases in the cluster then as in 3.4.1 it is not clear if cases with no links identified are involved in the same chain of recent transmission as other cases in the cluster. The possible explanations for this are outlined in 3.4.1. For cases which have definite or possible epidemiological links, there is good evidence they are involved in the same chain of recent transmission and therefore public health action may need to be taken if there is a risk of on-going transmission.
3.4.3 Epidemiological links are identified between ALL members of the cluster

If definite or possible epidemiological links (see definitions in section 2.4) are identified linking members of the cluster, this is good evidence that they are involved in the same chain of recent transmission and therefore public health action may need to be taken.
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 the STM as well as HPZone by the team leading the cluster investigation.

The detail of all cluster investigations should be recorded on HPZone as recommended for all incidents. Detailed instructions for recording cluster investigations on HPZone are shown in Appendix 4.

Summaries of actions, epidemiological links (known prior to or due to the investigation) and outcomes should be recorded on STM.

4.2 Recording cluster investigations on the STM

In addition to the cluster reporting function, the STM will be used as a management tool to aid the active investigation of a cluster and to record outcomes of the investigation.

In order to maximise the full potential of the STM, information should be recorded by the HPT Lead for the cluster under investigation.

After logging on to the ETS system and entering the STM, recording information should be completed by following the ‘Enter Cluster Details’ facility and filtering on the cluster of interest. Core information that should be recorded on the STM for each cluster report includes;

- **cluster Status** - see Section 3.2.2 - update if and when required
- **notes on cluster** - In this section the following information should be included
  - a summary of the cases in the cluster after risk assessment
  - any information already known that may be relevant to the investigation eg “active investigation not required at present as epi links already well known”
    - HPZone number
    - actions taken during the investigation - e.g Cluster questionnaires sent out, screenings undertaken
    - any information obtained during the course of the investigation that cannot be entered into the questionnaires- eg “investigated whether new cases since 2012 have ever been to ‘The Red Lion pub’ (where outbreak investigation was conducted in 2010), they have not, so no further investigation of the ‘The Red Lion pub’ is required at present”
    - reason if cluster status changed
- **actions recommended by investigator** - eg “Additional screening of hostel should be considered as two cases reside in the same hostel (this information should be recorded by the HPT if discussion or advice is sought from cluster investigators).” It should be noted that this text box should be completed by those leading the cluster investigation at local level
- questionnaire - questionnaires should be completed where possible by NHS TB case managers on STM, but if this is not possible or paper forms are returned, the HPT should enter the information into the questionnaire on STM. The summarised results of these are illustrated in the (yellow) ‘Summary’ table. The information is also shown in the download of the cluster information to enable analysis of the cluster. If additional information about a case is identified after the questionnaire has already been completed, the questionnaire can be updated so that the information will appear in the summary and download.

- epidemiological links eg FRED is linked to JOHN as follows POSSIBLE EPI LINK through type of contact FRIEND at contact setting EDUCATION at Postcode of setting XX5 1XX. Comments can also be added such as Fred and John were in Waverley College in Form 3A from September 2012 to March 2013 when Fred was symptomatic.

- add case eg if a case is highly suspected to belong to the cluster they can be added to the cluster by entering their respective ETS number (please see section 3.2.1)

After entering/updating information on the cluster details page save the data by clicking the following buttons ‘Save Cluster Details’, ‘Add notes’, ‘Add actions recommended’, ‘Add link’. All information added will be saved with the date and the user name of the individual who entered the details. For more specific guidance on the recording of data in the STM, please see the separate Strain Typing Module user manual.

### 4.3 Recording cluster investigations on HPZone

If all the cases in a cluster are within a single HPT, and that cluster has not been recorded on HPZone then that HPT should record the cluster on their HPZone system. Please check carefully and thoroughly before entering the VNTR or cluster number as a new context to avoid duplication.

If cases within a cluster occur in more than a single HPT area, then the CCDC investigators from those areas should agree which HPT will hold the core HPZone record following discussions with the HPT TB leads. The HPZone record host could be either:

- the HPT with the greatest number of cases
- the HPT with the most recently identified case
- the HPT in which the suspected source / exposure occurred (where known)

HPTs with cases forming part of a multi-HPT 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.

In order to support effective management of clusters and full evaluation of the national universal TB Strain Typing Service, it is essential that all cluster investigations are recorded systematically and consistently.

HPZone is an integrated case management and support tool designed to facilitate best practice and case recording for health protection professionals.

Appendix 3 gives step by step instructions on how to record TB strain type cluster investigations on HPZone. HPZone screen shots from a fictitious entry have been included in the appendix for clarity and are referred to in the text following.
4.4 Reporting the outcomes of cluster investigations

The actions and outcome of all cluster investigations should be recorded in the STM for public health quality assurance as recommended in the evaluation of the Strain Typing Service.

In addition it is recommended that a **TB cluster investigation outcome reporting form** is completed to summarise the investigation and its outcomes and that this is uploaded to the HPZone record after an investigation has been completed. Please see appendix 5 for the **TB cluster investigation outcome reporting form**.

4.5 Sharing Strain Typing Data with the NHS

Strain typing and cluster data have been seen to be beneficial for NHS colleagues. It is therefore recommended that strain typing data is regularly shared by HPT colleagues with their NHS colleagues dependant on local situations and need. Examples of this can be through providing information to TB clinics for multi-disciplinary team meetings (MDTs) or through the cohort review process.

The report in the STM can be used for this purpose, data can be downloaded into an excel spreadsheet and filtered by clinic before sharing, whilst following appropriate data sharing protocols, see STM user guide for technical guidance.
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 HPT and NHS primary laboratory via agreed local mechanisms for onward dissemination to TB clinical teams
- strain typing data should be transferred into the Enhanced Tuberculosis Surveillance (ETS) database within one working day of results being available by the typing centre
- 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

Health Protection Teams

- determine if local strain typing clusters need investigating and identify a local lead for the investigation
• responsible for collaborating with NHS and taking the lead in the investigation of potential local clusters based on information provided by reference laboratories, working in collaboration with the NHS
• provide a timely response to investigation of clusters
• record all cluster investigations on HPZone and on the STM
• complete a Cluster Investigation Outcome Reporting Form and upload to HPZone

CIDSC TB Section, TB Cluster Investigator

• responsible for generating cluster reports on STM, and regenerating reports on a weekly basis
• responsible for running national cluster reports through red flags check and undertaking monthly Preliminary Cluster Reviews of any red flag national clusters
• lead the review and investigation of national clusters working with the HPS TB cluster investigators, regional TB leads and HPT TB leads and NHS staff (i.e. gathering information by phone, sending out questionnaires, collating information and summarising it, generating cluster diagrams)
• maintain the repository national cluster database with all information relating to national clusters that were investigated prior to STM
• record information on active national clusters led by CIDSC TB section on STM
• lead on development and maintenance of STM by liaising with the Software Development Unit
• in collaboration with FES, provide technical support for users of the STM
• in collaboration with FES, continue to provide training on cluster investigation process and the use of STM as required
• liaise with HPT TB leads when public health action is required on a national cluster
• undertake analysis of epidemiological data linked to strain typing data at a national level to improve the understanding of the epidemiology of tuberculosis in the UK to inform future public health policy and action, including writing the strain typing chapter in the UK TB annual report
• prepare for, and ensure a response to, the likely changing demands of strain typing and WGS

Field Epidemiology Services, TB Cluster Investigators

• provide support to PHE Centre staff across England investigating clusters
• provide support for investigations of clusters that cross PHE Centres or, if requested, that cross former HPU boundaries, within former HPA regions
• ensure that support and advice is available to HPTs, and PHE Centres where needed for any cluster investigations and undertake epidemiological analysis of cluster information as required
• ensure continued analysis of epidemiological data/strain typing data/outcome data
• periodically review cluster reports at former HPA regional level, usually quarterly, with the objective to enable prioritisation for example of serious, or large and rapidly growing clusters of public health concern that might otherwise not be recognised as such, in order to assist colleagues at HPT level within the region in their own reviews and investigations
• in collaboration with CIDSC, provide technical support for users of the STM
• in collaboration with CIDSC, continue to provide training on cluster investigation process and the use of STM as required
• prepare for, and ensure a response to, the likely changing demands of strain typing and WGS
NHS TB Services

- responsible for collecting and reporting information to PHE relating to individuals who are identified to them as being in clusters or outbreaks and requiring active investigation that have been identified by the HPT
- involved in local Outbreak Control Teams 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 are able to support any additional public health activity (eg expanded contact tracing) 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 Outbreak Control Team be convened to manage significant clusters or outbreaks (in line with usual local practice)
Appendix 1: Cluster investigation Questionnaire

TB Cluster Investigation Questionnaire

<table>
<thead>
<tr>
<th>Cluster ID</th>
<th>Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case ID</td>
<td>HPU</td>
</tr>
<tr>
<td>Patient Forename</td>
<td>Region</td>
</tr>
<tr>
<td>Patient Surname</td>
<td>Source Lab</td>
</tr>
<tr>
<td>Patient DOB</td>
<td>MIRU/VNTR</td>
</tr>
<tr>
<td>Case Manager</td>
<td>Mycobacteriology Reference Unit</td>
</tr>
</tbody>
</table>

Dear Colleague,

There are currently _____ TB cases in this cluster.
The other cases are in the following HPTs/Regions/Towns/Cities: ________________________________
Cluster characteristics of interest:
____________________________________________________________________________
____________________________________________________________________________
____________________________________________________________________________

To investigate transmission of disease, could you please provide the following information and ask extra questions in relation to the information given above on this cluster (eg did the patient visit or have visitors from these areas). Please provide postcodes of places visited/frequent contacts where possible.

Please return this form to: _________________________
Thank you very much for your help and co-operation.

Patient specific questions:

__________________________________________

---

2 Available to be completed electronically on the STM or for download from STM as a stand-alone word document
### Did patient regularly attend the following in the 2 year before diagnosis:

<table>
<thead>
<tr>
<th></th>
<th>Yes/ No/ Don’t know</th>
<th>If yes, please specify type and provide name, address and dates</th>
<th>Other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Childcare/ Education</strong></td>
<td>☐ Y ☐ N ☐ DK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Nursery, Pre-school/Play group, Primary School, Secondary School, College/sixth form, University, Child minding service/Baby sitter, After school clubs, Adult education, religious learning centre, Language learning centre, Private tutoring)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Work place</strong></td>
<td>☐ Y ☐ N ☐ DK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Office, Factory, Warehouse, Outdoors, Hospital/Medical centre, Recreational centres, Catering, Sports and Health clubs, Home maker, Farming, Driving, Construction, Retail, Pub/Bar/Club, Restaurant/Café, Trades, Armed forces, Emergency services, Education, Other)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Place of worship</strong></td>
<td>☐ Y ☐ N ☐ DK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Church, Synagogue, Mosque, Multi-faith centre, Community centre, Hindu Temple, Derasar, Fanums, Hof, Jinja, Gurdwara, Biddhist Temple, Taoist temple, Other)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Regular place of socialising</strong></td>
<td>☐ Y ☐ N ☐ DK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Pub/bar, Club, Sports/leisure centre, Restaurant, Private Members Club, Womens Club, Crack house, Shisha parties, Gym, Health club/spa, Dance classes, Yoga centre, Choir, Music classes, Karaoke, Community Activity Club, Cinema, Community centre, Arcade house, Shopping centre, Religious gathering (social), Friends house, Volunteer, Other)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Did patient regularly attend the following in the 2 year before diagnosis:

<table>
<thead>
<tr>
<th>Detention (eg Prison) (Prison, Immigration centre, Youth detention centre, Terror Detention)</th>
<th>Yes/ No/ Don’t know</th>
<th>If yes, please specify type and provide name, address and dates</th>
<th>Other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Y</td>
<td>☐ N</td>
<td>☐ DK</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment /Rehab Centre (Alcohol rehabilitation centre, Drug rehabilitation centre, Medical/Physical rehabilitation centre, Mental health rehabilitation centre, Healthcare/Clinic)</th>
<th>Yes/ No/ Don’t know</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Y</td>
<td>☐ N</td>
<td>☐ DK</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other places of interest (Public transport, Air travel, Hospital, Elderly home, Nursing home, Hospice, Hall of residence, Retreat (spiritual/health), Pharmacy, Other)</th>
<th>Yes/ No/ Don’t know</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Y</td>
<td>☐ N</td>
<td>☐ DK</td>
<td></td>
</tr>
</tbody>
</table>

### In the 2 year before diagnosis:

<table>
<thead>
<tr>
<th>Was the patient in hospital as an inpatient?</th>
<th>Yes/ No/ Don’t know</th>
<th>Please provide details:</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Y</td>
<td>☐ N</td>
<td>☐ DK</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Did they have previous history of exposure to TB (e.g. invited for screening as a contact)</th>
<th>Yes/ No/ Don’t know</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Y</td>
<td>☐ N</td>
<td>☐ DK</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Did they live or work overseas for more than 3 months?</th>
<th>Yes/ No/ Don’t know</th>
<th>(If yes, please specify name of countries and cities.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Y</td>
<td>☐ N</td>
<td>☐ DK</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Did they regularly have friends/family visiting from overseas or elsewhere in the UK?</th>
<th>Yes/ No/ Don’t know</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Y</td>
<td>☐ N</td>
<td>☐ DK</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Did they regularly visit friends/family overseas or elsewhere in the UK?</th>
<th>Yes/ No/ Don’t know</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Y</td>
<td>☐ N</td>
<td>☐ DK</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Is/was the patient known by any other names or nicknames?</th>
<th>Yes/ No/ Don’t know</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Y</td>
<td>☐ N</td>
</tr>
<tr>
<td>Further Information</td>
<td>Details</td>
</tr>
<tr>
<td>------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Addresses in the previous two years</td>
<td></td>
</tr>
<tr>
<td>If patient was born in the UK, please specify place of birth</td>
<td></td>
</tr>
<tr>
<td>Please list all the names the patient listed as close contacts</td>
<td></td>
</tr>
<tr>
<td>Please ask patients if they have been to, or had visitors from any of the following places in the two years prior to diagnosis. Please provide postcodes of contacts and places visited.</td>
<td></td>
</tr>
<tr>
<td>Please give details of any known or possible epidemiological links this patient may have with others that you know of</td>
<td></td>
</tr>
</tbody>
</table>

Case manager’s signature                                                                 Case manager’s name printed                          Date form completed
Appendix 2: Examples of useful cluster investigation tools

The examples below demonstrate some of the tools that can be used when investigating a TB cluster to aid visualisation.

**Example 1: Cluster diagram**

The diagram below can be created in MS Excel. Each TB case is placed on the timeline based on the case report date. The shapes and colours of the individuals indicate the site of disease and the tails behind each individual display the length of time from onset of symptoms to case report date. Risk factors are also indicated on the diagram and additional information on age and sex are shown in the table on the left hand side.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>26</td>
<td>F</td>
</tr>
<tr>
<td>2</td>
<td>33</td>
<td>F</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>M</td>
</tr>
<tr>
<td>4</td>
<td>31</td>
<td>F</td>
</tr>
<tr>
<td>5</td>
<td>52</td>
<td>F</td>
</tr>
</tbody>
</table>

**Example 2: Representation of cases and their contacts**

The diagram below can be created in MS Word or MS Powerpoint. It is a representation of four cases with the same strain type and the results of the screening that had previously been undertaken. This is a useful tool to identify gaps in screening.
Example 3: Time, Person and Place Analysis

Epidemic curve
An increase in the number of cases in a cluster may be indicative of transmission. This can be presented as a standard epidemic curve created in MS Excel.

Person
The demographic, clinical and social risk factor information can be summarized for the cluster by calculating numbers and proportions for each characteristic out of the total number of cases in the cluster.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (25-35 yrs)</td>
<td>35</td>
<td>88</td>
</tr>
<tr>
<td>Sex (Female)</td>
<td>35</td>
<td>88</td>
</tr>
<tr>
<td>UK born</td>
<td>15</td>
<td>38</td>
</tr>
<tr>
<td>Site of Disease</td>
<td>30</td>
<td>75</td>
</tr>
<tr>
<td>Sputum Positive*</td>
<td>24</td>
<td>80</td>
</tr>
<tr>
<td>Previous TB</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Risk Factors</td>
<td>22</td>
<td>55</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>100</td>
</tr>
</tbody>
</table>
Place
It is useful to view the cases in the cluster in terms of geographical proximity to either each other or to potential suspected transmission settings. Maps can be created in Geographic Information Systems (GIS) such as ArcMap.

GIS mapping of clustered TB cases by place of birth

Example 4: Social networking tools
Diagrams can be created illustrating the epidemiological links between cases and links to transmission settings in a cluster. The diagram below is created in i2analyst (http://www-03.ibm.com/software/products/us/en/analysts-notebook/). Relevant demographic or clinical information is displayed underneath each case. Epidemiological links between cases or between cases and settings are shown by lines. This diagram is useful for indicating who might have the greatest number of links or be at the centre of the outbreak.
Appendix 3: Creating an HPZone record

Start by creating a **NEW SITUATION** and selecting **CLUSTER**

<table>
<thead>
<tr>
<th>HPZONE OPTIONS</th>
<th>ACTION / INFORMATION TO RECORD</th>
</tr>
</thead>
</table>
| **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 known)  
(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). |

<table>
<thead>
<tr>
<th>ASSESSMENT</th>
<th>SCENARIO</th>
<th>Leave blank</th>
</tr>
</thead>
<tbody>
<tr>
<td>INFECTIOUS AGENT</td>
<td>Select ‘Mycobacterium tuberculosis complex’</td>
<td></td>
</tr>
<tr>
<td>CONFIDENCE</td>
<td>Select ‘Laboratory confirmed’</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>KEY DETAILS</th>
<th>CLUSTER NUMBER</th>
<th>Record the CLUSTER Number as issued by the reference laboratory / STM eg E1069</th>
</tr>
</thead>
</table>
| LOCATION | See screen shot 1  
Record the CLUSTER NUMBER, prefixed with ‘TB CLUSTER’  
(This will determine the title of the HPZone record).  
eg E1638 |
| POSTCODE | Leave blank as cases are likely to have multiple postcodes. First part of the postcode may be recorded if all the same eg 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. |

<table>
<thead>
<tr>
<th>AUTOMATICALLY GENERATED ACTION LIST</th>
<th>Manage the automatically generated action list as per the usual approach in your HPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CURRENT RISK ASSESSMENT</td>
<td>Complete as normal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ADMINISTRATION</th>
<th>MANAGER</th>
<th>Record name of agreed investigation lead</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCT</td>
<td>If all or majority of the cases are within one PCT select that PCT, otherwise leave blank.</td>
<td></td>
</tr>
</tbody>
</table>

| 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 shot 1) |
### HPZONE OPTIONS

<table>
<thead>
<tr>
<th>SPECIFIC CONTEXT</th>
<th>ACTION / INFORMATION TO RECORD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>See screen shot 3 – 6</td>
</tr>
<tr>
<td></td>
<td>1. Always add TWO contexts for a cluster - the full VNTR number and the Cluster Number</td>
</tr>
<tr>
<td></td>
<td>2. Select <strong>ADD A NEW CONTEXT</strong></td>
</tr>
<tr>
<td></td>
<td>3. Select <strong>CONGREGATION</strong> from the list of options. This will bring up a list of all relevant contexts nationally.</td>
</tr>
<tr>
<td></td>
<td>4. If your cluster is part of a cluster already being investigated elsewhere, the VNTR number or cluster number will appear in the list of contacts and can be selected.</td>
</tr>
<tr>
<td></td>
<td>N.B. check for both the full VNTR number and the Cluster Number.</td>
</tr>
<tr>
<td></td>
<td>5. <strong>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).</strong></td>
</tr>
<tr>
<td></td>
<td>6. The next section (see screen shot 6) can be left blank and saved.</td>
</tr>
<tr>
<td></td>
<td>7. In addition to recording the VNTR number as a ‘context’ always create a 2nd CONTEXT for the Cluster Number.</td>
</tr>
<tr>
<td></td>
<td>This is an important step as it allows us to link all cases that form part of any cluster at HPT, regional and national level.</td>
</tr>
</tbody>
</table>

### ASSOCIATED CASE

Record all case details as usual by creating a ‘case’ on HPZone and linking it to the ‘cluster situation’. Complete a cluster investigation form for each case (appendix2) & upload

### ASSOCIATED CONTACT

You may wish to enter the details of known close contacts of each TB case in the cluster here (optional)
Appendix 4: Cluster Reporting Form

TB STRAIN TYPING CLUSTER INVESTIGATION OUTCOME REPORTING FORM

Please complete at closure of cluster investigation

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

<table>
<thead>
<tr>
<th>CLUSTER NUMBER</th>
<th>HPZone NUMBER</th>
<th>MIRU VNTR PROFILE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of reporter</td>
<td>Email Address</td>
<td></td>
</tr>
<tr>
<td>Position</td>
<td>Telephone</td>
<td>Fax</td>
</tr>
<tr>
<td>HPT</td>
<td></td>
<td>dd / mm / yyyy</td>
</tr>
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</table>

Details of Lead Cluster investigator

<table>
<thead>
<tr>
<th>Name</th>
<th>Email Address</th>
<th>Telephone</th>
<th>HPT</th>
<th>Region</th>
</tr>
</thead>
</table>

CLUSTER DETAILS at date of report

Total number of cases in the cluster (include cases without matching strain type data where an epidemiological link identified)

No. of cases in 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 HPTs with cases in this cluster

List the HPTs involved and no. of cases in each

Date investigation commenced dd / mm / yyyy

Reason for beginning investigation

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):

Available as a stand-alone document
Please summarise your findings from the cluster investigation. Please tick all options that apply and provide details

<table>
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<th>Option</th>
<th>Please comment:</th>
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<td>No epidemiological links found</td>
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</tr>
<tr>
<td>Epidemiological links known prior to VNTR result and no additional public health action taken</td>
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</tr>
<tr>
<td>New epidemiological links found following VNTR cluster identification</td>
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</tr>
<tr>
<td>Additional contacts identified and screened following VNTR cluster identification</td>
<td>If yes, how many:</td>
</tr>
<tr>
<td></td>
<td>If additional contacts identified and screened:</td>
</tr>
<tr>
<td></td>
<td>• How many new cases of active TB identified and treated?</td>
</tr>
<tr>
<td></td>
<td>• How many new cases of latent TB infection identified?</td>
</tr>
<tr>
<td></td>
<td>• How many new cases of latent TB infection given prophylaxis</td>
</tr>
<tr>
<td>Other</td>
<td>Please explain:</td>
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Please indicate which factors you believe may have contributed to this cluster

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<tr>
<td>Inadequate identification of and screening of contacts of early cases: See note below</td>
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<tr>
<td>Delayed diagnosis of early cases</td>
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<tr>
<td>Lack of cooperation from early cases</td>
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<tr>
<td>Other. (Please explain ):</td>
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<tr>
<td>No factors identified</td>
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</table>

Public Health Outcome at date of report

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<td>Probable or definite chain of transmission identified and actions taken to interrupt further transmission</td>
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</tr>
<tr>
<td>No apparent chain of transmission identified, no further action deemed necessary</td>
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</tr>
<tr>
<td>Investigation inconclusive; to maintain a watching brief</td>
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</tr>
<tr>
<td>Investigation ongoing (active investigation):</td>
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<tr>
<td>Other (Please explain ):</td>
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</table>

Is a full incident report available?  

Yes  
No  

General comments

Was the strain typing information useful to you / has knowing the VNTR been helpful?  
Yes  
No  

The strain typing information disproved suspected links and provided reassurance  
Yes  
No  

Any other comments:

THANK YOU FOR COMPLETING THIS CLUSTER REPORT

TB Cluster Investigators:

National clusters: Maeve Lalor, CIDSC, maeve.lalor@phe.gov.uk
London & South East: Esther Hamblion, FES Victoria, esther.hamblion@phe.gov.uk
Rest of England: Andy Burkitt, FES North East, andy.burkitt@phe.gov.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.

<table>
<thead>
<tr>
<th>TERM / ACRONYM</th>
<th>DEFINITION</th>
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</thead>
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<tr>
<td>Cluster</td>
<td>A cluster in this handbook will refer to two or more <em>M. tuberculosis</em> isolates that share indistinguishable strain types.</td>
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<tr>
<td>Cluster investigation</td>
<td>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.</td>
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<tr>
<td>Endemic strains</td>
<td>A strain of <em>M. tuberculosis</em> 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 (ie within the previous 2 years) even though the strain type of the isolates from the patients are indistinguishable</td>
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<tr>
<td>Epidemiological cluster</td>
<td>Two or more persons with TB who share definite epidemiological links.</td>
</tr>
<tr>
<td>Epidemiologically confirmed strain type cluster</td>
<td>Strain typing clusters that contain patients with known or definite epidemiological links.</td>
</tr>
<tr>
<td>ETS</td>
<td>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.</td>
</tr>
<tr>
<td>FES</td>
<td>Field Epidemiology Services</td>
</tr>
<tr>
<td>HPZone</td>
<td>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</td>
</tr>
<tr>
<td>Indistinguishable strain types</td>
<td>Two or more <em>M. tuberculosis</em> isolates that share the same strain type. Indistinguishable strain types may include missing data/loci</td>
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<tr>
<td>HPT</td>
<td>Health Protection Team</td>
</tr>
<tr>
<td>LTBR</td>
<td>London Tuberculosis Register is a web-based system surveillance and case management used in every tuberculosis clinic across London</td>
</tr>
<tr>
<td>Loci / Locus</td>
<td>The specific location of a DNA sequence on the <em>M. tuberculosis</em> chromosome. Usually denoted by a number/letter for each VNTR</td>
</tr>
<tr>
<td>Matching strain types</td>
<td>Same as indistinguishable strain types, but fully identified, no missing data / loci</td>
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<tr>
<td>MIRU-VNTR</td>
<td>Mycobacterial Interspersed Repetitive Unit – Variable Number Tandem Repeats. MIRU is a PCR based strain typing assay.</td>
</tr>
<tr>
<td>MIRU-VNTR strain type</td>
<td>Finger printing designation that results from MIRU-VNTR analysis</td>
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<tr>
<td>Non-traditional setting</td>
<td>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.</td>
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<tr>
<td>PCR</td>
<td>Polymerase chain reaction is a method of amplifying small quantities of DNA up to amounts suitable for further analysis</td>
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<tr>
<td>PHE</td>
<td>Public Health England</td>
</tr>
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### 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 - 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.

### STM

Strain Typing Module - a strain typing cluster identification and management tool used primarily by the Health Protection Teams for the investigation of strain typing clusters that may pose a threat to public health.

### 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: Key Contacts

<table>
<thead>
<tr>
<th>Role in service</th>
<th>Name</th>
<th>Region covered</th>
<th>Base</th>
<th>Email</th>
<th>Tel / Fax</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB Cluster Investigator</td>
<td>Maeve Lalor</td>
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<td>T: 020 8327 7154</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>F: 020 8327 6112</td>
</tr>
<tr>
<td></td>
<td>Esther Hamblion</td>
<td>London &amp; South East</td>
<td>Field Epidemiology Services, Victoria</td>
<td><a href="mailto:esther.hamblion@phe.gov.uk">esther.hamblion@phe.gov.uk</a></td>
<td>T: 020 7811 7228</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>F: 020 7811 7757</td>
</tr>
<tr>
<td></td>
<td>Andy Burkitt</td>
<td>All other English regions</td>
<td>Field Epidemiology Services, North East</td>
<td><a href="mailto:andy.burkitt@phe.gov.uk">andy.burkitt@phe.gov.uk</a></td>
<td>T: 0844 225 3550</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>F: 0191 2212584</td>
</tr>
<tr>
<td>Head of TB Section, CIDSC</td>
<td>Ibrahim Abubakar</td>
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<td>020 8327 6165</td>
</tr>
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<td>020 8327 7499</td>
</tr>
<tr>
<td>CCDC National Programme Lead</td>
<td>Philip Monk</td>
<td>National</td>
<td>HPS East Midlands South HPT</td>
<td><a href="mailto:philip.monk@phe.gov.uk">philip.monk@phe.gov.uk</a></td>
<td>0844 2254524</td>
</tr>
<tr>
<td>HPS TB PHEC Lead Director</td>
<td>Stephen Morton</td>
<td>National</td>
<td>HPS Yorkshire and the Humber</td>
<td><a href="mailto:stephen.morton@phe.gov.uk">stephen.morton@phe.gov.uk</a></td>
<td>0113 3860315</td>
</tr>
<tr>
<td></td>
<td>Gina Radford</td>
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<td>HPS Anglia and Essex</td>
<td><a href="mailto:gina.radford@phe.gov.uk">gina.radford@phe.gov.uk</a></td>
<td>0303 444 6694</td>
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<td>Helen Maguire</td>
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<td>020 781 17205</td>
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<tr>
<td>HPS TB Leads</td>
<td>Peter Acheson</td>
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<td>North East HPT</td>
<td><a href="mailto:peter.acheson@phe.gov.uk">peter.acheson@phe.gov.uk</a></td>
<td>0844 2253550</td>
</tr>
<tr>
<td></td>
<td>Marko Petrovic</td>
<td>Greater Manchester</td>
<td>Greater Manchester HPT</td>
<td><a href="mailto:marko.petrovic@phe.gov.uk">marko.petrovic@phe.gov.uk</a></td>
<td>0161 786 6717</td>
</tr>
<tr>
<td></td>
<td>Evdokia Dardamissis</td>
<td>Cheshire &amp; Merseyside</td>
<td>Cheshire &amp; Merseyside HPT</td>
<td><a href="mailto:evdokia.dardamissis@phe.gov.uk">evdokia.dardamissis@phe.gov.uk</a></td>
<td>07979 508 267</td>
</tr>
<tr>
<td></td>
<td>Kenneth Lamden</td>
<td>Cheshire &amp; Lancashire</td>
<td>Cheshire &amp; Lancashire HPT</td>
<td><a href="mailto:kenneth.lamden@phe.gov.uk">kenneth.lamden@phe.gov.uk</a></td>
<td>07967 194296</td>
</tr>
<tr>
<td></td>
<td>ebere.okereke</td>
<td>Yorkshire &amp; the Humber</td>
<td>West Yorkshire HPT</td>
<td><a href="mailto:ebere.okereke@phe.gov.uk">ebere.okereke@phe.gov.uk</a></td>
<td>01133 860300</td>
</tr>
<tr>
<td></td>
<td>Sophia Makki</td>
<td>East Midlands</td>
<td>East Midland HPT</td>
<td><a href="mailto:sophia.makki@phe.gov.uk">sophia.makki@phe.gov.uk</a></td>
<td>0844 2254 524</td>
</tr>
<tr>
<td></td>
<td>Nic Coetzee</td>
<td>West Midlands North</td>
<td>West Midlands North HPT</td>
<td><a href="mailto:nic.coetzee@phe.gov.uk">nic.coetzee@phe.gov.uk</a></td>
<td>0844 2253560</td>
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<tr>
<td></td>
<td>Roger Gajraj</td>
<td>West Midlands East</td>
<td>West Midlands East HPT</td>
<td><a href="mailto:roger.gajraj@phe.gov.uk">roger.gajraj@phe.gov.uk</a></td>
<td>0844 225 3560</td>
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<tr>
<td></td>
<td>Naveed Syed</td>
<td>West Midlands West</td>
<td>West Midlands West HPT</td>
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<tr>
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<td>Mike Lilley</td>
<td>South Midlands and Hertfordshire</td>
<td>South Midlands and Hertfordshire HPT</td>
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<tr>
<td></td>
<td>Giri Shankar</td>
<td>Anglia</td>
<td>Anglia HPT</td>
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<td>0844 2253546</td>
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<tr>
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<td>Sultan Salimee</td>
<td>Essex</td>
<td>Essex HPT</td>
<td><a href="mailto:sultan.salimee@phe.gov.uk">sultan.salimee@phe.gov.uk</a></td>
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<td>Name</td>
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<td>Sarah Anderson</td>
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<td>Sudy Anaraki</td>
<td>North East &amp; North Central London</td>
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<td><a href="mailto:sam.perkins@phe.gov.uk">sam.perkins@phe.gov.uk</a> 0203 0494338</td>
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<td>Anita Roche</td>
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<td><a href="mailto:anita.roche@phe.gov.uk">anita.roche@phe.gov.uk</a> 0844 3262052</td>
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<td>Muhammad Abid</td>
<td>Thames Valley</td>
<td><a href="mailto:muhammad.abid@phe.gov.uk">muhammad.abid@phe.gov.uk</a> 0845 279 9879</td>
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<td>Bernadette Purcell</td>
<td>Sussex, Surrey &amp; Kent</td>
<td><a href="mailto:bernadette.purcell@phe.gov.uk">bernadette.purcell@phe.gov.uk</a> 0845 894 2944</td>
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<tr>
<td>Catherine Southwood</td>
<td>Sussex, Surrey &amp; Kent</td>
<td><a href="mailto:catherine.southwood@phe.gov.uk">catherine.southwood@phe.gov.uk</a> 0844 225 7968</td>
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<tr>
<td>Anand Fernandes</td>
<td>Wessex</td>
<td><a href="mailto:anand.fernandes@phe.gov.uk">anand.fernandes@phe.gov.uk</a> 0845 055 2022</td>
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<tr>
<td>Anne Black</td>
<td>Wessex</td>
<td><a href="mailto:anne.black@phe.gov.uk">anne.black@phe.gov.uk</a> 0845 055 2022</td>
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<tr>
<td>Mark Kealy</td>
<td>South West</td>
<td><a href="mailto:mark.kealy@phe.gov.uk">mark.kealy@phe.gov.uk</a> 0844 225 3557</td>
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</tr>
<tr>
<td>Sarah Harrison</td>
<td>Devon, Cornwall and Somerset</td>
<td><a href="mailto:sarah.harrison@phe.gov.uk">sarah.harrison@phe.gov.uk</a> 0844 225 3557</td>
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<tr>
<td>Mark Evans</td>
<td>South West</td>
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<td></td>
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<tr>
<td>Lika Nehaul</td>
<td>Wales</td>
<td><a href="mailto:lika.nehaul@nphs.wales.nhs.uk">lika.nehaul@nphs.wales.nhs.uk</a> 01495 332219</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Francis Drobniewski</td>
<td>London, South East, East of England, South West, Gloucestershire</td>
<td><a href="mailto:francis.drobniewski@phe.gov.uk">francis.drobniewski@phe.gov.uk</a> 020 7811 7228</td>
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<tr>
<td>Tim Brown</td>
<td></td>
<td><a href="mailto:tim.brown@phe.gov.uk">tim.brown@phe.gov.uk</a> 020 7377 5895</td>
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<td>Madeline Stone</td>
<td></td>
<td><a href="mailto:madeline.stone@phe.gov.uk">madeline.stone@phe.gov.uk</a> 020 7377 5895</td>
<td></td>
<td></td>
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</tr>
<tr>
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<td>West Midlands, East Midlands, North Lincolnshire, South Yorkshire</td>
<td><a href="mailto:grace.smith@phe.gov.uk">grace.smith@phe.gov.uk</a> 0121 424 3247</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sarah Gardiner</td>
<td>Birmingham Microbiology Reference Unit</td>
<td><a href="mailto:sarah.gardiner@phe.gov.uk">sarah.gardiner@phe.gov.uk</a> 07585401324</td>
<td></td>
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</tr>
<tr>
<td>Jason Evans</td>
<td></td>
<td><a href="mailto:jason.evans@phe.gov.uk">jason.evans@phe.gov.uk</a> 0121 424 0250</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>John Magee</td>
<td>North West, North East, North Yorkshire, West Yorkshire &amp; the Humber</td>
<td><a href="mailto:john.magee@phe.gov.uk">john.magee@phe.gov.uk</a> 0191 2138783</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anne Barrett</td>
<td></td>
<td><a href="mailto:anne.barrett@phe.gov.uk">anne.barrett@phe.gov.uk</a> 0191 213 8784</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Deborah Osborne</td>
<td></td>
<td><a href="mailto:deborah.osborne@phe.gov.uk">deborah.osborne@phe.gov.uk</a> 0191 2138784</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Michael Ruddy</td>
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<td><a href="mailto:michael.ruddy@wales.nhs.uk">michael.ruddy@wales.nhs.uk</a> 029 20 716408</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lewis White</td>
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