1st October 2013

RE: National TB Strain Typing Service

The attached summary report has been written by the National Strain Typing Project Board in collaboration with the TB Delivery Board to provide information on the key achievements and evaluation of the National Tuberculosis Strain Typing Service and its future direction.

The National Tuberculosis (TB) Strain Typing Service has been operational since January 2010 assisting in the prospective identification, rapid reporting and investigation of TB strain typing clusters to prevent further TB transmission in the UK. In March 2013 a comprehensive independent evaluation report of the National TB Strain Typing Service was published highlighting seven key recommendations for taking forward the national TB strain typing strategy.

The future direction of the service will focus on implementing the strain typing evaluation recommendations and lead towards a programme of TB genome sequencing work of every isolate initiated as part of the 100,000 Genome Project. Major highlights of the recommendations include the need to continue strain typing of TB isolates and the requirement to concentrate resources on the investigation of molecular clusters most likely to be of public health significance. We expect the implementation of these recommendations to improve the usefulness and efficiency of the National TB Strain Typing Service in providing information to support local teams and the investigation of the national epidemiology of TB and to serve as a platform for the future implementation of Whole Genome Sequencing.

The PHE TB Delivery Board and the National Strain Typing Project Board would like to thank you for providing us with the opportunity to present this report to you.

Yours Faithfully,

TB Delivery Board &
National Strain Typing Project Board
Summary report of the National Tuberculosis Strain Typing Service

This report summarises the key actions, achievements and evaluation of the National Tuberculosis Strain Typing Service since its implementation in 2010 and the future of the service.

1. National Tuberculosis (TB) Strain Typing Service

The National Tuberculosis (TB) Strain Typing Service has been operational since January 2010 assisting in the prospective identification, rapid reporting and investigation of TB strain typing clusters to prevent further TB transmission in the UK. The service prospectively types 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 which meet certain criteria are further investigated with the aim of identifying epidemiological links and transmission profiles to guide public health action.

2. Productiveness of the National TB Strain Typing Service- 2010-2012

2.1) Summary of strain typing/cluster investigation 2010-2012:

- Between January 2010 and December 2012, there were a total of 11,745 (79.9%) isolates from culture confirmed cases on which strain typing was completed for at least 23 loci; of these 6,113 cases were in 1,401 molecular clusters and 5,632 cases had a unique strain type.
- A total of 196 clusters (14%) were investigated over the last three years. By December 2012, 108 (55%) clusters remained under active investigation and 88 (45%) had been closed following investigation, because either no epidemiological links were found or links were found but no further public health action was required. Eighty six (44%) of the clusters that were investigated were national clusters; 47.7% (41) of these had at least one epidemiological link identified between individuals within the cluster.

2.2) Summary of key achievements:

- Developing professional working relationships and establishing cross-field services with the TB Reference Labs, HPA (now PHE) Local and Regional Services, TB Section Colindale, the NHS and other relevant organisations (e.g. Find and Treat, prison services).
- Producing a Strain Typing Handbook to support Health Protection teams investigate TB Clusters.
- Producing two newsletters to inform stakeholders about the Strain Typing Service and its activities
- Developing and implementing policies on the use of TB Strain Typing information.
- Developing documentation for HP Teams on ‘how to record TB clusters on HPZone’.
- Developing/facilitating a training programme for the Strain Typing Service (STS) and rolling this out throughout England.
- Producing strain typing cluster reports for all HPU’s on a monthly basis and carrying out initial risk assessment to provide recommendations for follow-up.
• Assisting with the investigation of local and regional cluster investigations/coordinating an appropriate response with stakeholders/proving epidemiological analysis of findings/interpreting data.
• Undertaking monthly preliminary review of all national clusters with new cases, and all national clusters which are under active investigation.
• Undertaking national cluster investigations/co-ordination of cross regional and national incidents/epidemiological analysis and interpretation of data/identification of possible transmission settings/recommendations on public health action.
• Contributing to initial whole genome sequencing discussions.
• Developing and promoting a ‘Cluster Investigation Outcome Form’ for HPUs to record the outcomes of cluster investigation for the Evaluation of Strain Typing
• Initiating biannual review meetings of TB clusters in England
• Establishing the Strain Typing Operational Group, the Strain Typing Biannual Review Group, the Cluster Investigators Forum and regular attendance at the HPS Regional TB Leads meeting and Strain Typing Project Board.
• Establishing a national nomenclature tool with bioinformatics team at PHE
• Developing and piloting the Strain Typing Module to prepare for national roll out of an online system to view, assess and manage clusters and cluster investigations.
• Developing and piloting the Strain Typing Module (STM) to prepare for national roll out of an online system to view, assess and manage clusters and cluster investigations
• Collaboration between other countries carrying out strain typing (e.g. Netherlands and US)
• Providing advice to countries considering establishing strain typing services (e.g. South Africa, Canada, and Norway).
• Analysis of data and reporting in national TB annual report
• Developing and running a session at HPA Annual Conference 2011 on the strain typing service including an interactive session

2.3) Presentations arising from the National TB Strain Typing Service:

• Multiple oral presentations for conferences including at the Royal Society of Medicine, New York (2012);  at The centre for disease control, Atlanta (2013); The International Tuberculosis Research Surveillance Unit, Berne, Switzerland (2013),Public Health England National TB workforce symposium (2013), British Thoracic Society (2011), HPA Annual Conference (2011) and regional conferences
• Multiple poster submissions for various conferences, International Union Against TB and Lung Disease Conference, British Thoracic Society, HPA Annual Conference

2.4) Publications arising from the National TB Strain Typing Service:

- **Tuberculosis in the UK, annual report.** Chapter on strain typing; 2011, 2012 and 2013
- **Multi-drug resistant and extensively-drug resistant tuberculosis outbreak in the UK.** M.K Lalor, N. Casali et al. Paper currently being finalised for submission
- **A football club, an internet café and a barber’s shop – hotspots for tuberculosis transmission in a Southampton Outbreak.** Anne T Black, Esther L Hamblion, Helen
3. **Evaluation of the National TB Strain Typing Service:**

At the point of service initiation in January 2010 an independent evaluation alongside the implementation of the service (2010-2012) was commissioned by PHE TB Delivery Board. In March 2013 a comprehensive evaluation report of the National TB Strain Typing Service was published. The evaluation report outlined seven key recommendations for consideration in relation to taking forward the national TB strain typing strategy which were systematically discussed by the PHE TB Delivery Board in collaboration with relevant stakeholders and all parties were in agreement with the recommendations, these included the following:

- The timely universal typing of all culture confirmed TB cases should be continued.
- The epidemiological analysis of the data should be prioritised and reported downstream.
- Cluster investigation should be reconsidered. The evaluation found no evidence to suggest that routine cluster investigations were effective or cost effective, and recommended that local cluster investigations should be initiated from the local level in response to local demand, and that national cluster investigations be limited to clusters that have been identified to be of public health importance.
- The Strain Typing Module (STM) of the Enhanced TB Surveillance System (ETS) should be released as a priority.
- Quality assurance should continue.
- A review of the human resources and capacity across the TB-STS is recommended.
- The TB service should focus on and invest in interventions and TB control strategies that will lead to the earlier diagnostic of TB.

4. **Future direction of the National TB strain Typing Service**

In response to the evaluation, the process by which molecular clusters are reported to public health teams and the recommendations for conducting cluster investigations are being modified, to ensure that resources are concentrated on investigating clusters most likely to be of public health importance. The new approach will be implemented once the Strain Typing Module of ETS is released, and Health Protection Teams will be fully informed of this process.

To enable the epidemiological analysis of the first three years of data from the Strain Typing Service, which will inform the future direction of the service, some additional data that has been collected by local Health Protection Teams on the clusters they have investigated to date will be required. The TB Section at Colindale will be contacting individual Health Protection Teams directly to request this data.

Implementing the strain typing evaluation recommendations together with PHE TB whole genome sequencing (WGS) approach, the National TB Strain Typing Service will become more efficient at
prospectively typing TB isolates with the aim of identifying epidemiological links and transmission profiles to guide public health action e.g. Once WGS becomes routine for TB typing (2014/2015) the service will move from VNTR to WGS as the core methodology for providing information to identify transmission and investigate clusters as well as identifying drug susceptibility.

**Key consideration:**

The National TB Strain Typing Service has a public health importance as it permits a collective TB strain typing database to be linked to the national surveillance database; this provides a valuable resource for research and surveillance to extend our understanding of TB epidemiology and transmission, allowing guidance for TB control policies. Furthermore the service enables the UK to contribute towards international molecular surveillance and learning for TB, which will endorse the UK’s status as a global stakeholder in scientific advancement within TB research.

1st October 2013
National Strain Typing Project Board