



WGS in England

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UK WGS service

- Started in 2017 – North and South reference lab
- Cultured isolates only
- All drugs predicted S (or only pyrazinamide for M.bovis / BCG) – no further testing
- Phenotypic pyrazinamide testing for lineage 1
- Turnaround time 7 days
- Isoniazid resistance alone predicted – isoniazid phenotypic testing
- Isoniazid resistance plus any first line / fluoroquinolone – first line phenotypic testing
- Pyrazinamide / ethambutol resistance predicted - first line phenotypic testing
- Rifampicin resistance predicted – full phenotypic testing
- Unknown mutations / failed predictions – complicated!
- Turnaround time for phenotypics 40 days

Date	Culture	GeneXpert	Whole genome sequence identification	Whole genome sequence mutations and resistance prediction	Phenotypic susceptibility testing
September 2021	Positive	No <i>rpoB</i> mutations	<i>M.africanum</i>	<i>KatG</i> mutation – predicted isoniazid resistance	Isoniazid resistance only
December 2021	Positive	No <i>rpoB</i> mutations	<i>M.africanum</i>	<i>KatG</i> mutation – predicted isoniazid resistance	Isoniazid resistance only
July 2022	Positive	<i>rpoB</i> mutation present	<i>M.africanum</i>	D435Y <i>rpoB</i> mutation – uncertain rifampicin prediction, has been associated with low-level resistance <i>KatG</i> mutation – predicted isoniazid resistance	Isoniazid resistance only
December 2022	Positive	<i>rpoB</i> mutation present	<i>M.africanum</i>	<i>KatG</i> mutation – predicted isoniazid resistance	Isoniazid resistance only
February 2023	Negative	Not tested	Not applicable		
March 2023	Negative	Not tested	Not applicable		
May 2023	Negative	Not tested	Not applicable		
September 2023	Positive	<i>rpoB</i> mutation present	<i>M.africanum</i>	S450L <i>rpoB</i> mutation – predicted rifampicin resistance <i>KatG</i> mutation – predicted isoniazid resistance Rv0678 mutation – uncertain prediction for bedaquiline and clofazimine	Rifampicin and isoniazid resistance Bedaquiline and clofazimine testing in Milan

Ethambutol, Rifampicin, Pyrazinamide +/- Moxifloxacin

Bedaquiline, Moxifloxacin, Linezolid, Clofazimine, Cycloserine, Pyrazinamide

Rifampicin, Ethambutol

Rifampicin, Pyrazinamide, Ethambutol, Moxifloxacin, Linezolid, Terizidone

Bedaquiline, Linezolid, Moxifloxacin, Terizidone, Clofazimine, Pyrazinamide, Prothionamide, Meropenem with co-amoxiclav -> delamanid

Thoughts

- Definite advance in clinical care
- Relatively laborious to update catalogue
- Expertise required for administration of the service and feedback to clinicians
- Real life turnaround times more complicated
- Does not remove the requirement for phenotypic DST capability
- Perhaps less impact on real-time investigation of clusters
- Is this the model for other settings?