



Health Protection Agency

National Mycobacterium Reference Laboratory &
Regional Centre for Mycobacteriology
for South and Southeast England



User Manual

December 2011

The NMRL is a constituent laboratory of HPA Microbiology Services

The NMRL is a WHO Supranational Reference Laboratory

The NMRL is part of the Clinical TB and HIV Group, Blizard Institute,
Barts and the London School of Medicine, Queen Mary College.

Address:

Postal

HPA National Mycobacterium Reference
Laboratory
Abernethy Building
BICMS
2 Newark Street
London
E1 2AT

DX

HPA MRU
DX 6680700
TOWER HAMLETS 93 E

Tel +44 (0)20 7377 5895

Fax +44 (0)20 7539 3459

National Mycobacterium Reference Laboratory (NMRL)

The National Mycobacterium Reference Laboratory (NMRL) is a CPA-accredited constituent reference laboratory of the Microbiology Services of the Health Protection Agency (HPA). The NMRL is the HPA's National Reference Centre and the Regional (South and Southeast England) Centre for Tuberculosis.

The principal activities of the NMRL includes: a primary isolation service including microscopy and culture; Fastrack (PCR) Service for detection of *M. tuberculosis* complex and rifampicin (and multidrug) resistance; a PCR based rapid identification of *Mycobacterium* sp isolates; drug susceptibility testing for first line and second line/reserve drugs; and molecular epidemiological typing and support of outbreak investigations/contact tracing. Interferon Gamma Release Assays for detection of latent infection and diagnosis have been introduced.

The NMRL initiated the first national molecular detection and drug resistance service for patient specimens and with centres in Germany, Estonia and Russia developed and initiated new rapid liquid culture analyses for second line/reserve drugs.

The NMRL provides comprehensive molecular epidemiological typing and analyses of outbreaks. Our activities support surveillance activity for TB in the UK.

In 2005, the NMRL moved to the Blizard Institute of Cell and Molecular Sciences of Barts and the London School of Medicine, Queen Mary College where it forms the major part of the Clinical TB and HIV Group.

The Group's research interests relate to all aspects of tuberculosis and other mycobacterial diseases, respiratory infections, and HIV particularly its interaction with TB; we focus on disease diagnosis, the molecular epidemiology of TB and HIV, understanding drug resistance and disease tropisms, and broader public health problems posed by these diseases both in the UK and overseas.

We have an international staff working on collaborative national and international clinical, laboratory and public health topics relating to TB and HIV in Russia and Ukraine currently and in partnership with other institutions in Africa.

The NMRL is a WHO Supranational Reference Laboratory for *M. tuberculosis* and drug sensitivity testing (DST); together with centres in Germany, Sweden and Belgium, it co-ordinates EQA for DST across the EU and non-EU states in the WHO Euro region. It is also a member of the WHO Global Laboratory Initiative involved with the development of WHO/IUATLD strategies for management of mycobacterial diseases and participates in international EQA schemes receiving samples and dispatching to designated regions. The NMRL, with the ECDC, co-ordinates the European Reference Laboratory Network for mycobacterial disease.

Professor Francis Drobniowski
Director NMRL

NMRL contact details

Public opening hours 9 am to 5.15 pm Monday to Friday

Main numbers: Telephone 020 7377 5895; Fax 020 7539 3459

Director	Prof Francis Drobniowski f.drobniowski@qmul.ac.uk	020 7377 5895
Enquiries, Office Manager and Finance	Mrs Sheree Gustave s.gustave@qmul.ac.uk Mrs Yen Holicka y.holicka@qmul.ac.uk	020 7377 5895 020 7882 2572
Laboratory Manager	Mr Philip More p.g.more@qmul.ac.uk	020 7377 5895 020 7882 2573
Specialist, Reference and Molecular Epidemiology	Dr Ximena Gonzalo x.gonzalo@qmul.ac.uk Dr. Madeline Stone m.stone@qmul.ac.uk Dr Tim Brown t.brown@qmul.ac.uk	020 7377 5895 020 7882 2578
Quantiferon testing	Dr Vlad Nikolayevskyy v.nikolayevskyy@qmul.ac.uk	020 7377 5895 020 7882 2575
Safety Officer	Mrs Melanie Kemp m.a.kemp@qmul.ac.uk	020 7377 5895 020 7882 2575

General results enquiries are addressed by our administrative staff initially who will direct clinical and technical enquiries to the appropriate staff. There is daily cover for clinical and technical issues and asking for a specific named individual may not be the fastest option (e.g. they are on annual leave). Complex cases are discussed further internally and the advice returned will often be a product of this discussion not just the opinion of the person answering the call. We record the advice given for continuity. We must know the identity both of the patient and the caller.

Summary of Services

- **Please note that although analyses will generally be provided free to the NHS, where a patient specimen is sent a charge will be incurred. Non-NHS specimens will be charged.**
- **Identification of *Mycobacterium* sp isolates** (this is currently provided free to the NHS and is a rapid molecular DNA-amplification based identification service)
- **Drug Susceptibility Testing** (phenotypic culture based for first-line drugs on solid media and rapid liquid culture based for second-line and reserve drugs; this is provided free to the NHS).
- **Molecular Epidemiological Service** (e.g. outbreak investigations, laboratory cross-contamination, provided free to the NHS)
- **Interferon Gamma Release Assay** (latent infection and active TB diagnosis)
- **Primary Isolation Service** including microscopy and culture
- **Fastrack (PCR) Service** (molecular detection of *M. tuberculosis* complex and rifampicin resistance/MDR in primary specimens and cultures)
- **Clinical and Technical Advice**
- **Clinical Advice for case and outbreak investigation and management**
- **Computerised database on laboratory confirmed cases**
- **Archived collection** of *Mycobacterium* isolates for epidemiological analysis
- **Training**
- **Research and Development**

For further information concerning services or matters of interest visit the HPA web-site at www.HPA.org.uk.

Services Available

For further information and advice on these services please call 020 7377 5895.
Samples/cultures cannot be received after 17:15.

Reference Service

Turnaround times are dependant upon the receipt of a pure culture containing sufficient bacteria for analysis

Identification of cultures of AFB

Rapid identification of M. tuberculosis complex and some common non-Tuberculous Mycobacteria using PCR-based techniques.

For cultures received before 9.30 am results are available at 4.45pm. All other cultures are processed the following day.

DNA sequencing and phenotypic tests are performed when identification is not possible by the above method.

A printed report sent out within 2 working days of culture receipt

M.tuberculosis first line Sensitivities

Isoniazid, rifampicin, ethambutol, streptomycin, pyrazinamide.

A report sent out within 2-3 weeks of culture receipt

Reserve Drugs

**Ofloxacin, moxifloxacin
Amikacin, kanamycin, prothionamide, capreomycin**

A report sent out within 2-3 weeks of request for these sensitivities or after identification of rifampicin resistance or MDRTB in referred cultures.

Additional Reserve Drugs

PAS, linezolid

A report sent out within 2-3 weeks of request for these sensitivities or identification of XDRTB

Primary Service

Microscopy performed within 1 working day of sample receipt.

Decontamination and culture of clinical samples on liquid and solid media.

Culture of blood and bone marrow.

Incubation of inoculated cultures

Microscopy report sent out within 1 working day.

Final Negative result reported after 6 weeks (or 8 weeks for blood cultures and CSF samples)

NB. Incubation will be continued for up to 12 weeks, but a further report is not issued unless culture becomes positive

Molecular Epidemiology Service

VNTR- MIRU analysis

Confirmation of rapid fingerprinting by further VNTR-MIRU analysis (or other appropriate methodology)

Preliminary analysis within 5 working days of receipt of a suitable culture.

Report telephoned (or final written report) within 6 weeks of receipt of a suitable culture.

Fastrack Service

Rapid PCR service for the detection of TB and rifampicin/Isoniazid resistance.

Rapid PCR service for TB and rifampicin resistance detection in pulmonary & CSF samples

Rapid PCR service for TB and rifampicin detection in non-pulmonary samples (except CSFs)

Appropriate cultures received by 9:30 am, analysed daily and results telephoned within 1 working day.

Appropriate pulmonary & CSF samples received by 9:30 am, analysed daily results will be telephoned within 1 working day.

Samples received before 9:30 am Wednesday, results telephoned to sending laboratory by Thursday pm

Interferon Gamma Release Assay

Quantiferon Assay

Reports sent out within 10 working days of receipt of sample.

Clinical and Technical Advice

Incoming calls for clinical and technical advice available Monday-Friday 9.00 to 17.00. Please note that clinical advice calls may be returned up to 22.00.

Key factors affecting specimen performance

If a specimen is received at the NMRL, which is unsuitable for examination, we will endeavour to contact the sender to discuss the problem.

If a specimen is submitted to NMRL for an investigation that we do not offer we will temporarily archive the sample/isolate and issue a report to the sender explaining the reasons for the sample's rejection.

Reference service

The time taken to perform bacterial identification and drug susceptibility tests is dependent on the receipt of pure cultures. Cultures that require purification or that cannot be retrieved because they are no longer viable and necessitate a second isolate may increase turnaround time significantly. Our approach is to assist you wherever possible by not rejecting contaminated cultures; however submitting a second culture is usually the best strategy. If an aliquot of a liquid culture is to be sent then a concentrated sample is best; i.e. remove 5-10 mls of the liquid culture and centrifuge. Decant the supernatant leaving about **2 ml** in the container to re-suspend the deposit. Either leave this in a sterile plastic universal container or transfer to a 2ml sterile cryovial/ microcentrifuge tube for transport

Primary Service

The specimens to be sent should be as fresh as possible. Nothing should be added to the sample except in the following cases:-

- When the specimen is a small piece of tissue in which case sterile saline or sterile water should be added. ***Do NOT use formalin as this will kill the mycobacteria.***
- Blood samples (and Bone Marrow) for culture should be sent in a vacutainer containing lithium-heparin. (***Mycobacterial survival is lower in EDTA tubes.***)
- We strongly recommend that specimens are refrigerated if any delays in submission to the NMRL are likely.
- We do not usually perform microscopy on urine specimens, only culture of early morning urine specimens.

Fastrack Service

The ideal specimen is a smear positive sputum or a positive cultures. All other specimens have lower sensitivities for detection although the detection sensitivity for non-formalin fixed tissue biopsies and a proportion of smear-negative sputa specimens are reasonably good (see Sam et al Emerging Infectious Diseases, (2006) 12: 752-9)

In general, dilutional fluid samples (eg CSF, pleural fluid, ascites etc) have much lower sensitivities; the minimum amount of CSF that will be examined is 0.5ml. However submitting the largest possible volume of CSF and other fluids will increase the sensitivity. Please submit as much of these fluids as possible-you can never submit too much!

Lysed blood or heavily bloodstained samples can interfere with PCR based reactions.

DNA in specimens requesting molecular tests may degrade if stored for too long before referral.

Paraffin waxed blocks can be examined but sensitivity is lower than that for fresh tissue. In these cases the whole wax block must be sent along with a diagram/slide indicating the area where AFB /granuloma were seen to aid sampling. This will be returned to the sender on completion of the Fastrack.

Interferon Gamma release Assay

Blood should be collected in the tubes provided (follow instructions) and incubated for 16-20 hours before sending. If sent before incubation please indicate as such on the form.

Contact tracing/case meeting

We are frequently asked to attend case meetings (or via teleconference) for complex patients and larger contact tracing investigations in institutions such as schools, prisons and health care institutions. We will try and assist where possible but requests with less than 1-2 working days notice of the meeting are unlikely to be feasible.

Referral of Specimens/cultures

No specimens or cultures are referred to other laboratories. If other investigations are required at another laboratory then it is strongly recommended that a further specimen/culture is sent by the sending laboratory directly.

NMRL Price List

April 2011-2012

* = Internal Recharging (NHS/HPA)

** = External Recharging

*** = Outside of outbreak investigations we do not analyse non NHS/HPA cultures without prior agreement.

METHODS	REQUEST	NHS/HPA PRICE * (per isolate/sample)	NON-NHS PRICE ** (per isolate/sample)
Identification of submitted cultures and first line drug testing on solid media (no charge if within the remit of HPA).	ID and Sensitivity	£0	£80
Reserve drugs for DST.		£0	£60
Molecular epidemiology of TB cultures. ***	MIRU/RFLP	£0	£50
Primary specimen receipt and inoculation into standard solid and rapid liquid culture medium.	Standard Culture & Rapid Liquid Culture	£33	£45
Blood/bone marrow inoculated into rapid culture vial by sending laboratory or at the NMRL.	Rapid Culture	£30	£40
<u>Fastrack</u> : PCR identification of <i>M. tuberculosis</i> complex and molecular rifampicin testing (includes culture of residential material & identification of resulting culture).	Fastrack	£130	£160
Quantiferon Gold for diagnosis of latent infection and active tuberculosis (based on purchase of 10 tests at a time)	IGRA	£45	£45

SPECIMEN AND SAMPLE SUBMISSION GUIDELINES

All Specimens **MUST** be labelled with the following:-

Surname/Forename or other Unique Patient Identifier
Sender's Sample Number

Request Forms MUST match and include the above information on the sample
Plus Name and contact information of requester (telephone number vital for urgent requests)

Tests required
Specimen type and site
Sender's Sample Number
Consultant or GP (if applicable)
Date of dispatch
Sex
Date of Birth
Relevant clinical information
NHS number
Date and time of collection of specimen

Please complete the forms in BLACK or BLUE pens (NOT RED or any other colour).

Please ensure that the correct telephone number is included particularly for Fastrack requests-in our annual audits approximately 15% of request forms do not have the correct telephone number)

The space marked "For NMRL Use only" is intended to record the date and time of receipt at the NMRL. Please do not write in this space.

The HPA NMRL laboratory encourages the proper completion of request forms by advising users if they are inappropriately completed; however, the NMRL supports its users by not rejecting referred specimens and cultures wherever possible.

GUIDANCE ON PACKAGING SAMPLES

The HPA has produced a short film clip to provide guidance for referring laboratories on how to package samples to the required standard.

 [How to package samples video \(Quicktime Movie, 3.4 MB\)](#)

A small but significant proportion of samples received by the HPA Microbiology Services are poorly or inappropriately packaged. This often leads to samples leaking or being damaged during transport, therefore posing a serious risk to HPA staff handling them. HPA hopes to eliminate this risk by helping laboratories to understand basic packaging requirements.

The following guidelines are intended to cover the transport of clinical samples from humans, or cultures of micro-organisms isolated from such samples to another laboratory for diagnostic or other clinical testing within the U.K. where the micro-organisms suspected of causing the disease are all either Hazard groups 2, 3 or 4.

The terms Category A and Category B are limited to classifying samples / microbial cultures being transported to another laboratory.

Sample Description	Packaging Requirement
Category A samples are known or suspected to contain a microbial agent with the following definition "an infectious substance which is transported in a form that if exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease to humans or animals" (see indicative list) The majority are Hazard Group 3 or 4	Assign to UN2814 (Humans) Packaging Instructions PI620 Supporting documentation as per ADR Transport as category A ADR licensed courier
For practical reasons to allow referral / reference services to continue a limited number of Category A agents have exempted from being transported as Category A. These are Verocytotoxin producing Escherichia coli (VTEC), Mycobacterium tuberculosis and Shigella dysenteriae 1	Assign UN3373 Packaging instruction PI650 Send by courier Royal mail will NOT accept
Category B samples are those that do not meet the definitions of Category A	Assign UN3373 Packaging instruction P1650 Post or courier Royal mail WILL accept

These guidelines are not intended as a substitute for reading the advice given by DfT and DoH. Use the links below for further information.

http://www.dft.gov.uk/stellent/groups/dft_freight/documents/page/dft_freight_611600.pdf

http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_07543

<http://www.icao.int>

<http://www.unece.org>

Reporting incidents during transportation that may affect the safety of personnel.

The NMRL will report to users any leaking containers and improperly packaged parcels. Repeated offences will be referred to the HPA Safety Committee who may refer to the Health and Safety Executive.

Labelling and Packaging (NMRL)

All specimens/cultures sent to the NMRL must be packed in accordance with IATA regulations 650/602.

Label the specimen/culture bottle with the name of the patient (or unique identifier) and the laboratory number.

The top of the specimen/culture bottle must be fixed on firmly so that there is no chance of leakage. It may be necessary to use parafilm to ensure that the top remains on tight during transport. This will also prevent desiccation of the specimen/culture in transit which will compromise successful culture. Wrap the bottle in absorbent material and seal inside a minigrip bag. (The NMRL will endeavour to process the material if leakage occurs but this is likely to compromise the chance of successful culture (if a primary specimen) and we will request the user to send us an additional specimen)

Place the specimen/culture inside a leakproof plastic container with enough absorbent material to be able to absorb all the contents of the bottle in case of leakage.

Place the plastic container inside a fibreboard box.

Place the form between the plastic container and the outer cardboard box. DO **NOT** PLACE IT INSIDE THE PLASTIC CONTAINER. In the event of leakage/breakage the whole shipment will be destroyed without opening.

Specimens may be sent by Royal Mail or Courier. We recommend that to minimise delays specimens are sent by routine courier e.g. DX or other specialised courier. Please ensure that the courier is likely to be able to reach the NMRL before 1700h.

Cultures can only be sent by courier.

Reporting incidents during transportation that may affect the quality of the specimen or the safety of personnel. The NMRL will report to users any leaking containers and improperly packaged parcels. Repeated offences will be referred to the HPA Safety Committee who may refer to the Health and Safety Executive.

Faxing and emailing reports containing patients' data.

It is our policy that reports containing patient data should not be sent by routine E-mail.

E-mails cannot be relied on to guarantee security of patient data because they can be intercepted by a third party on route (unless encrypted).

In some circumstances NMRL can send results by fax. In this case the following conditions must be adhered to (refer also to the document "HPA recognition of Caldicott recommendations"):

The report must be sent to a "safe haven" fax machine. This means that, if the location is in general use, consideration must be given to ensuring that unauthorised personnel are unable to read reports, accidentally or otherwise. Also, the room housing the fax machine must be in a secure location, which is locked if it is likely to be unattended at the time the fax is sent.

Assurance must be sought from the intended recipient of the faxed report, preferably in writing, that the receiving fax machine is a safe-haven. If it is essential to fax patient identifiable information to NMRL please speak to the administration office at NMRL who will arrange for someone to receive the fax.

Confirmation must always be sought from the intended recipient that the fax is expected and has been received.

Compliance with the Human Tissue Act

Submitting tissue samples from deceased people

The HPA Microbiology Services is licensed by the Human Tissue Authority (HTA) (Licence number 12459) to store tissues from deceased people for scheduled purposes. Post mortem samples are submitted to HPA Microbiology Services by coroners or pathologists for examination to help them determine the cause of death.

As part of our public health remit, we sometimes need to retain these samples for the purpose of public health monitoring which is defined as a scheduled purpose within the [Human Tissue Act 2004](#). Further analysis of these samples may help determine the cause of an outbreak due to an infectious disease or may allow identification of new strains of infectious agents at a later date.

Obtaining consent to remove, store and use human tissues for a scheduled purpose is one of the underlying principles of the Human Tissue Act. HPA Microbiology Services receives post-mortem samples from Coroners' post-mortems or from NHS establishments across the UK and therefore we are not in a position to either seek consent ourselves or have arrangements in place to confirm that the requirements of the Act have been complied with by the sender.

We would ask coroners and pathologists who send post mortem samples to HPA Microbiology Services to provide us with details of consent, and would also ask that consent includes retention of the samples for the purpose of public health monitoring.

When tissue samples from deceased people are received at the HPA Microbiology Services they are retained securely and confidentiality is maintained in compliance with [Caldicott principles](#) as are all samples received at this centre. It is normal practice for tissue samples from the deceased to be disposed of in the same way that all other clinical samples we receive are disposed of. However, we will adhere to any specific requirements regarding disposal or returning tissue samples if requested by the sending coroner or pathologist.

HPA Microbiology Services recognition of Caldicott recommendations

The recommendations of the Caldicott report (1997) have been adopted by the Health Protection Agency (HPA) as by the national Health Service as a whole. These recommendations relate to the security of patient identifying data (PID) and the uses to which they are put. The HPA observes Caldicott guidance in handling PID and has appointed its own Caldicott Guardian. Who advises the Director of Microbiology Services on confidential issues and is responsible for monitoring the physical security of PID in all parts. This also applies to the transfer of results of investigations to and from HPA Microbiology services whether by mail services; telephone or fax. The value of 'safe haven' arrangements or other means of the sender and receiver information identifying themselves to each other before data is transferred is emphasised (see attached HPA Policy on faxing and emailing reports containing patient data).

The HPA is anxious to audit the security of its PID in collaboration with its customers. Customers are invited to review our arrangements in conjunction with individual laboratory directors and/or the Caldicott Guardian. Customers are also asked to draw to the Caldicott Guardian's attention any instances where PID security has been threatened or has broken down. Uses that PID are put to outside clinical diagnostic services generally allow patient identifiers to have been removed before hand, and when PID is used for research purposes the proposals are considered first by the appropriate Ethics Committee. All enquiries about the security and use of PID should be addressed to the Caldicott Guardian of the Microbiology Services David Carrington (email: David.Carrington@HPA.org.uk).

Forms to accompany specimens/cultures

The following forms can be downloaded from the HPA website (www.hpa.org.uk) and are designed to be easy to photocopy.

- **Reference culture submission form (N1)**
- **Fastrack form (N2)**
- **Molecular epidemiology request form (N3)**
- **QuantiFERON[®]-TB Gold test (N4)**

Key References

- Wright, A, Zignol, M, Van Deun, A, Falzon, D, Ruesch Gerdes, S, Feldman, K, Hoffner, S, Drobniewski, F, Barrera, L, van Soolingen, D, Boulabhal, F, Paramasivan, C.N, Kam, KM, Mitarai, S, Jaramillo, E, Nunn, P, Raviglione, M for The Global Project on Anti-Tuberculosis Drug Resistance Surveillance Anti-tuberculosis drug resistance in the world, 2002-2007. *Lancet* 2009 May 30;373(9678):1861-73.
- Ojo, O, Sheehan S, Corcoran GD, Okker M, Gover K, Nikolayevsky V, Brown T, Dale J, Gordon SV, Drobniewski F, Prentice MB. *Mycobacterium bovis* strains causing smear-positive human tuberculosis, Southwest Ireland. *Emerg Infect Dis.* 2008 Dec;14(12):1931-4
- Drobniewski, FA, V Nikolayevskyy, S Hoffner, O Pogoryelova, D Manissero, AJ Ozin. The added value of a European Union tuberculosis reference laboratory network – analysis of the national reference laboratory activities. *Euro Surveill* 2008;13(12).
- Kruijshaar, ME, Watson JM, Drobniewski F, Anderson C, Brown TJ, Magee JG, Smith EG, Story A, Abubakar I. Increasing antituberculosis drug resistance in the United Kingdom: analysis of National Surveillance Data. *BMJ.* 2008 May 31;336(7655):1231-4. Epub 2008 May 1.
- Drobniewski, F, Cobelens F, Zellweger JP; and KNCV/EuroTB Workshop. Use of Gamma-interferon assays in low- and medium-prevalence countries in Europe: a consensus statement of a Wolfheze Workshop organised by KNCV/EuroTB, Vilnius Sept 2006. *Eurosurveillance* 2007; 12 (7) E070726.2
- Dinnes, J, Deeks J, Kunst H, Gibson A, Cummins E, Waugh N, Drobniewski F, Lalvani A. A systematic review of rapid diagnostic tests for the detection of tuberculosis infection. *Health Technol Assess.* 2007 Jan;11(3):1-314.
- Shah NS, Wright A, Bai GH, Barrera L, Boulabhal F, Martín-Casabona N, Drobniewski F, Gilpin C, Havelková M, Lepe R, Lumb R, Metchock B, Portaels F, Rodrigues MF, Rüsche-Gerdes S, Van Deun A, Vincent V, Laserson K, Wells C, Cegielski JP. Worldwide emergence of extensively drug-resistant tuberculosis. *Emerg Infect Dis.* 2007 Mar;13(3):380-7.
- Drobniewski F, Rüsche-Gerdes S, Hoffner S and Subcommittee on Antimicrobial Susceptibility Testing of *Mycobacterium tuberculosis* of the European Committee for Antimicrobial Susceptibility Testing (EUCAST) of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). Antimicrobial susceptibility testing of *Mycobacterium tuberculosis* (EUCAST document E.DEF 8.1)-- report of the Subcommittee on Antimicrobial Susceptibility Testing of *Mycobacterium tuberculosis* of the European Committee for Antimicrobial Susceptibility Testing (EUCAST) of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID).. *Clin Microbiol Infect.* 2007 Dec;13(12):1144-56.
- Nikolayevskyy, VV, Brown TJ, Bazhora YI, Asmolov AA, Balabanova YM, Drobniewski FA. Molecular epidemiology and prevalence of mutations conferring rifampicin and isoniazid resistance in *Mycobacterium tuberculosis* strains from the southern Ukraine. *Clin Microbiol Infect.* 2007; 13: 129-38.
- Drobniewski FA, Hoffner S, Rusch-Gerdes S, Skenders G, Thomsen V. Recommended standards for modern tuberculosis laboratory services in Europe. *Eur Respir J.* 2006 28(5):903-909.
- Drobniewski F, Balabanova Y, Zakamova E, Nikolayevskyy V, Fedorin I. Rates of Latent Tuberculosis in Health Care Staff in Russia. *PLoS Med.* 2007 Feb 13;4(2):e55.
- Gopaul, KK, Brown, TJ, Gibson, AL, Yates, MD and Drobniewski, FA Progression towards an improved DNA- amplification based typing technique in the study of *Mycobacterium tuberculosis* epidemiology. *J Clin Microbiol.* 2006; 44: 2492-2498.
- Kruuner A, Yates MD, Drobniewski FA. Evaluation of MGIT 960-based antimicrobial testing and determination of critical concentrations of first- and second-line antimicrobial drugs with drug-resistant clinical strains of *Mycobacterium tuberculosis*. *J Clin Microbiol.* 2006 Mar;44(3):811-8.
- Sam, IC, Drobniewski, F, More, P, Kemp, M and Brown, T. *Mycobacterium tuberculosis* and rifampin resistance, in the United Kingdom.. *Emerging Infectious Diseases* 2006; 12:(5):752-9
- Drobniewski F A. , Balabanova, Y, Nikolayevsky, V, Ruddy, M, Kuznetzov, SI, Zakharova, SM, Melentyev, AS, Fedorin, IM. Drug resistant tuberculosis, clinical virulence and the dominance of the Beijing strain family in Russia. *JAMA* 2005; 293:2726-2731.
- N. Seoudi, S. Mitchell, T. Brown, F. Dashti, A.K. Amin, F. A. Drobniewski Rapid molecular detection of tuberculosis and rifampicin drug resistance: retrospective analysis of a national UK molecular service over the last decade *Thorax* (2012) in press.

- Bamford AR, Crook AM, Clark JE, Nademi Z, Dixon G, Paton JY, Riddell A, Drobniewski F, Riordan A, Anderson ST, Williams A, Walters S, Kampmann B. Comparison of interferon- γ release assays and tuberculin skin test in predicting active tuberculosis (TB) in children in the UK: a paediatric TB network study. *Arch Dis Child*. 2010 Mar;95(3):180-6. Epub 2009 Oct 8.
- Brown T, Nikolayevskyy V, Velji P, Drobniewski F. Associations between Mycobacterium tuberculosis strains and phenotypes. *Emerg Infect Dis*. 2010 Feb;16(2):272-80.
- Reddy S, Brown T, Drobniewski F. Detection of *Mycobacterium tuberculosis* from paraffin embedded tissues by INNO-LiPA Rif.TB assay: retrospective analyses of HPA Mycobacterium Reference Unit data. *J Med Microbiol*. 2010 May;59(Pt 5):563-6. Epub 2010 Feb 4.
- Anderson C, Story A, Brown T, Drobniewski F, Abubakar I. Tuberculosis in UK prisoners: a challenge for control. *J Epidemiol Community Health*. 2010 Apr;64(4):373-6. Epub 2010 Mar 15
- Mitchell SL, Seoudi N, Hutchison DCS, Drobniewski FA, Multidrug –resistant tuberculosis: resistance dates to first and second line antituberculosis drugs in the UK in 2008/2009 and the role of rapid molecular tests for drug resistance. *Thorax* 2010 Sep 29
- Moore, JE, Kruijshaar, ME, Ormerod, P, Drobniewski, F, Abubakar, I. Increasing reports of non-tuberculous mycobacteria in England, Wales and Northern Ireland, 1995-2006. *BMC Public Health* 2010 Oct 15;10:612
- Martineau, AR, Peter M. Timms Graham H. Bothamley, Alleyna P. Claxton, Geoffrey E. Packe, John C. Moore-Gillon, Mathina Darmalingam, Robert N Davidson, Thomas C. Stokes Heather J. Milburn Lucy V. Baker Stefan Lozewicz Richard D. Barker Nicholas J Woodward, Yasmeen Hanifa, Kamrul Islam, Timothy R. Venton, Korina E. Barnes Christopher J. Mullett Anna K. Coussens, Clare M. Rutterford Charles A. Mein, Geraint R. Davies Robert Wilkinson Vladyslav Nikolayevskyy, Francis A. Drobniewski Sandra M. Eldridge, Christopher J Griffiths. High-dose vitamin D3 during intensive phase treatment of pulmonary tuberculosis: a double-blind randomised controlled trial. *Lancet*. 2011 Jan 15;377(9761):242-50.
- Stone MJ, Brown TJ, Drobniewski FA. Human Mycobacterium bovis infection in London and southeast England. *J Clin Microbiol*. 2011 Nov 9.
- Mironova S, Pimkina E, Kontsevaya I, Nikolayevskyy V, Balabanova Y, Skenders G, Kummik T, Drobniewski F. Performance of the GenoType(R) MTBDRPlus assay in routine settings: a multicenter study. *Eur J Clin Microbiol Infect Dis*. 2011 Oct 25.
- Balabanova Y, Tchernyshev V, Tsigankov I, Maximova S, Mikheeva N, Fedyukovitch L, Kuznetsov S, Fedorin I, Drobniewski F. Analysis of undiagnosed tuberculosis-related deaths identified at post-mortem among HIV-infected patients in Russia: a descriptive study. *BMC Infect Dis*. 2011 Oct 18;11:276.
- Faksri K, Drobniewski F, Nikolayevskyy V, Brown T, Prammananan T, Palittapongarnpim P, Prayoonwiwat N, haiprasert A. Epidemiological trends and clinical comparisons of Mycobacterium tuberculosis lineages in Thai TB meningitis. *Tuberculosis* (Edinb). 2011 Nov;91(6):594-600. Epub 2011 Sep 14.