



NATIONAL HEALTH
LABORATORY SERVICE

GeneXpert MTB/RIF

Progress Report

March 2012





GeneXpert Implementation Report Update

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1. Background to Project

This project was initiated at the request of the Honorable Minister of Health in early 2011. A pilot study was proposed by the National Department of Health (NDoH) (particularly the TB cluster) while due diligence was being done with respect to project feasibility. This was further prompted by the World Health Organization's strong recommendation in December 2010 that "the new automated DNA test for TB be used as the initial diagnostic test in individuals suspected of MDR-TB or HIV/TB (i.e. all SA TB suspects).

The pilot phase was initiated in microscopy centres in high focus TB areas. The ministry requested that at least 1 instrument be placed in each province, preferably in a district that had a high burden of TB (Selections were made by TB cluster). Twenty-five microscopy centres were selected and a total of 30 instruments placed. The NDoH funded 9 GX16 and 14 GX4 instruments for the project. FIND donated 6 GX4 analysers and the Infinity or GX48 was supported by PEPFAR RTC. All instruments were placed by World TB day March 24th. This placement represented about 10% of national coverage. The basis for the calculations was an assumption that 2 smears at diagnosis would be replaced by 1 Xpert MTB RIF assay. All instruments were interfaced to the NHLS Laboratory Information System (LIS) allowing for troubleshooting and data collection.

2. Assays performed to date

In summary, a total of 311,117 specimens have been processed to date (27 March 2012). The total % of MTB detected in this cohort amounted to 16.74% (52,068 new TB cases). The percentage positivity has remained on average between 16-17% monthly nationally. To date KZN has performed the largest number of tests which is probably as a result of the throughput of the GX48 analyzer (Refer to table 1). Average Rifampicin resistance detection rates have remained around 7% since project inception (Refer to table 2)



Table 1: GeneXpert MTB Results by province

Province	MTB Detected	MTB Not Detected	Test Unsuccessful	Total	MTB % Detected
Eastern Cape	5,936	28,135	987	35,058	16.93
Free State	5,006	27,534	64	32,604	15.35
Gauteng	4,461	28,181	601	33,243	13.42
Kwa-Zulu Natal	17,999	68,338	2,343	88,680	20.30
Limpopo	2,776	23,271	284	26,331	10.54
Mpumalanga	3,468	16,799	1,335	21,602	16.05
North West	3,292	16,376	753	20,421	16.12
Northern Cape	4,032	20,158	751	24,941	16.17
Western Cape	5,098	23,067	72	28,237	18.05
Total	52,068	251,859	7,190	311,117	16.74

Table 2: Provincial GeneXpert RIF Results in MTB detected cases

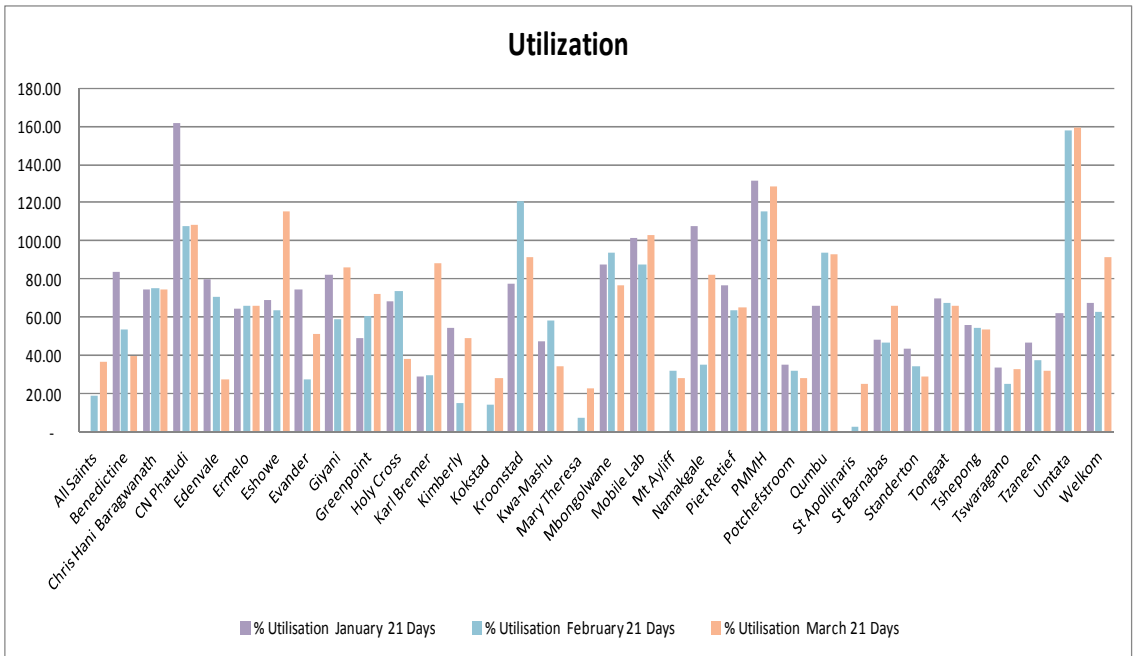
Province	Inconclusive	No Result	Resistant	Sensitive	Grand Total	RIF % Resistant
Eastern Cape	70	97	454	5,315	5,936	7.65
Free State	64	8	278	4,656	5,006	5.55
Gauteng	45	1	270	4,145	4,461	6.05
Kwa-Zulu Natal	222	107	1,405	16,265	17,999	7.81
Limpopo	40	26	203	2,507	2,776	7.31
Mpumalanga	50	32	281	3,105	3,468	8.10
North West	39	7	264	2,982	3,292	8.02
Northern Cape	38	3	252	3,739	4,032	6.25
Western Cape	47	1	240	4,810	5,098	4.71
Grand Total	615	282	3,647	47,524	52,068	7.00

Errors have ranged consistently below 3%. Details of invalid results, which likely represent sample issues remains below 1%. These are being monitored regularly and corrective action implemented where necessary.

Table 3: Number of Unsuccessful Tests and Reasons

Province	Error	Invalid	No Result	MTB Result	Grand Total	Error %
Eastern Cape	891	80	16	34,071	35,058	2.54
Free State	56	8		32,540	32,604	0.17
Gauteng	520	71	10	32,642	33,243	1.56
Kwa-Zulu Natal	1,594	697	52	86,337	88,680	1.80
Limpopo	227	47	10	26,047	26,331	0.86
Mpumalanga	1,230	96	9	20,267	21,602	5.69
North West	703	43	7	19,668	20,421	3.44
Northern Cape	575	159	17	24,190	24,941	2.31
Western Cape	56	12	4	28,165	28,237	0.20
Grand Total	5,852	1,213	125	303,927	311,117	1.88

3. Utilization rates of instruments within the field



Instrument utilization remains variable over the months and is dependent on requests from various the health care facilities that refer samples to the laboratories.

4. Further project phases as defined in the NTCM model

Phase I has been completed and has been reported on in the section above.

Phase IIa involves full capacitation of existing labs: Completed October.

Phase IIb: Full capacitation of high burden districts.

Phase IIIa and b: Gates funded study (Gauteng, EC and Free State)

Phase IIIc: ensuring all districts have a minimum of 1 instrument per district

Phase IIId: Completion of all current microscopy and clinic sites

5. Specific GeneXpert Progress

- **Phase 2a:** Completed
- **Phase 2b:** Global Fund funding for phase 2b has been approved. Singing of contracts between the primary recipients and sub-recipients is underway. Phase 2b is projected to roll-out in April 2012. 19 Instruments have been installed at 12 sites. Training, verification and LIS interfacing of the instruments are completed.

Table 4: Phase 2b

Province	District	Lab	GX4	GX16	Capacity Per Day	Comment
GP	City of Johannesburg	NJH ROUTINE	1		16	From Edenvale
KZN	eThekwini	Hlengisizwe MC	1		16	Installation Completed
KZN	eThekwini	Clairwood	1		16	Installation Completed
EC	O.R. Tambo	ST LUCY	1		16	Instrument Delivered. Installation Pending
KZN	eThekwini	Catherine Booth	2		16	Instrument Delivered. Installation Pending
KZN	eThekwini	Osindisweni	1		16	Installation Completed
KZN	eThekwini	Manguzi	2		32	Installation Completed
KZN	eThekwini	Verulam MC	1		16	Installation Completed
LP	Mopani	SEKORORO	1		16	Installation Completed
EC	O.R. Tambo	ST ELIZABETH		1	64	Global Fund DOH
EC	O.R. Tambo	ZITULELE		1	32	Global Fund DOH
KZN	eThekwini	Addington		1	32	Global Fund DOH
KZN	eThekwini	RK Khan		1	64	Global Fund DOH
KZN	eThekwini	Wentworth		1	32	Global Fund DOH
KZN	eThekwini	Mahatma Ghandi		1	48	Global Fund DOH
KZN	Zululand	Benedictine		1	48	Global Fund DOH



KZN	eThekweni	Dbn Chest Clinic MC		1	64	Global Fund DOH
KZN	eThekweni	Inanda C MC		1	32	Global Fund DOH
KZN	eThekweni	Charles James MC		1	32	Global Fund DOH
KZN	eThekweni	KwaDabeka MC		1	32	Global Fund DOH
KZN	eThekweni	PineTown MC		1	48	Global Fund DOH
KZN	Sisonke	RIETVLEI	2		48	Installation Completed
LP	Mopani	KGAPANE		1	32	Global Fund DOH
LP	Mopani	PHALABORWA		1	32	Global Fund DOH
MP	Gert Sibande	EMBHULENI		1	32	Global Fund DOH
NC	Siyanda	UPINGTON		1	64	Global Fund DOH
WC	City of Cape Town	GROOTE SCHUUR		1	48	Global Fund DOH
KZN	Sisonke	Kokstad	1	1	16	Installation Completed. GX16 Pending Global Fund
GP	City of Johannesburg	CENTRAL TB	1	1	80	GX4 from Baragwanath + Global Fund DOH
			14	19	1040	

Table 5: Phase 3a Progress

Installations, training and instrument verifications using dried culture spots completed.

Table 6: Phase 3b

The remaining 10 machines will be placed in July 2012 in the following laboratories:

Serial	Province	District	Lab	GX4	GX16	GX48	Capacity Per Day	Status	Donor
25	EC	Chris Hani	COFIMVABA		1		64	Pending	Gates Foundation
29	EC	Chris Hani	QUEENSTOWN	1	1		80	Pending	Gates Foundation
33	EC	Nelson Mandela Bay Metro	UITENHAGE		1		64	Pending	Gates Foundation
57	FS	Thabo Mofutsanyane	MANAPO		1		48	Pending	Gates Foundation
68	GP	City of Tshwane	JUBILEE		1		48	Pending	Gates Foundation
69	GP	City of Tshwane	MAMELODI		1		64	Pending	Gates Foundation
77	GP	Ekurhuleni	NATALSPRUIT		1		64	Pending	Gates Foundation
85	GP	West Rand	CARLETONVILLE		1		64	Pending	Gates Foundation
46	EC	Ukhahlamba	TAYLOR BEQUEST	1	1		80	Pending	Gates Foundation
133	MP	Ehlanzeni	NELSPRUIT		2		128	Pending	Gates Foundation

Phase 3c and 3d remain on further release of funding

Pelonomi, Edendale, Christ the King and St. Appolinaris laboratories were fast tracked. This was made possible through a partnership between TB/HIV Care Association who donated two GX4s and PEPFAR CDC (4 GX16 machine).

6. Training: Laboratory and Clinical

A total of 73 laboratory staff and 139 health care workers have been trained since December 2011 as summarized in table 7 and 8. This will be an ongoing process to support NDoH training on clinical algorithm. Laboratory staff will receive both clinical and technical training.



Table 7: Laboratory Training

Venue	DATE	Trainer	TOTAL # OF DELEGATES	Outcomes
Christ the King	12 December 11	Veeresh	2	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry
Kokstad	15 December 11	Trevor	2	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry
St. Apollinaris	13 December 11	Veeresh	3	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry
Thembisa	15 December 11	Sebaka/Sheila	7	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry
Pretoria West	10 January 12	Sebaka/Sheila	4	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry
Mary Theresa	11-12 January 12	Maxine	4	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry
Mt Ayliff	10 January 12	Trevor	4	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry
All Saints	11 January 12	Trevor	4	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry
St Patrick	13 January 12	Maxine	3	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry
Bethlehem	23 January 12	Trevor	3	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry
Helen Joseph	23 January 12	Sheila	11	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry
Witbank	16 January 12	Sheila	10	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry
Tembisa	20 January 12	Sheila	5	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry
Tambo Memorial	12 January 12	Sheila & Sebaka	11	GeneXpert Operation, Maintenance, Troubleshooting and Data Entry



Table 8: Clinical Training

Venue	Date	Trainer	Total # of Delegates	Outcomes
Manapo Dept. of Social Services	08 & 09 Feb	Sebaka	28	Background to GeneXpert, TB Testing Algorithm, Recording and Reporting
Siphosensimbi CHC	17 Feb 12	Linda	18	
Phola CHC	20 Feb 12	Linda	8	
eThafeni CHC	23 March 12	Linda	4	
Tembisa Main Clinic	23 March 12	Linda	5	
Voslorus Poly Clinic	30 March 12	Linda	12	
Dawn Park Clinic	02 April 12	Linda	11	
Mpumalanga District	25 March 12	Elizabeth	40	
Emalaheni Sub-District	12 April 12	Elizabeth	13	

7. Challenges identified during the course of the project to date

- Finalization of request forms: Incorporate TB testing in the CCMT from if we are to bill using existing channels
- Delay in training health care workers on clinical algorithm
- Lengthy time between training and going live with testing,
 - Pretoria West and Helen Joseph due to shortage of staff
 - Tambo Memorial due to problems with power supply
- LIS downtime impacting on TAT(Witbank)

8. Literature Update For GeneXpert

There has been an expansion of the literature with respect to the assay performance. The highlights are summarized in table 9 below:



Table 9: Recent publications (GeneXpert for pulmonary TB and extrapulmonary TB)

Manuscript	Sample population and specimen type (n=...)	Results	
		Sensitivity	Specificity
Rachow et al , Clin Inf Dis, 2012	164 children with suspected TB. Twenty-eight of 164 children (17.1%) had confirmed tuberculosis	Vs Smear: Xpert detected 100% (95% confidence interval [CI], 59.0%-100%) of smear-positive cases and 66.6% (95% CI, 43.0%-85.4%) of culture-positive but smear-negative cases. Vs Culture: Xpert displayed a similar sensitivity (54.7% [95% CI, 42.7%-66.2%]) compared with culture methods.	Xpert = 100%
Safianowska, Pneumonol Alergol Pol. 2012	1875 samples for AMPLICOR MTB (104 were inhibited), and 213 samples for Xpert MTB/RIF	The assay sensitivities was 81.9% for AMPLICOR MTB and 81.8% for Xpert MTB/RIF, as compared to culture on Lowenstein-Jensen medium.	The assay specificities were 97.2% for AMPLICOR and 99.5% for Xpert,

9. Update on GeneXpert Research projects:

- DCS Verification – all phase 2a instruments verified.
- Cepheid Liquid EQA pilot prepared for 20 sites with questionnaire: awaiting return of results from sites
- DCS EQA panel and additional liquid EQA panel (Vircell) to be piloted at selected NHLS labs.
- DCS EQA & verification program development - ACTG (3 sites) and MSF included in program: first batch of verification and pilot EQA material ready for shipment to ACTG sites.
- Flow cytometry on raw/processed sputum still under development
- Alternative specimen preparation protocols:



- i. Protocols developed for Pediatric TB diagnosis and Extra-pulmonary TB diagnosis
 - ii. Paediatric study at Rahimma Moosa Mother and Child Hospital: n=305 TB suspects have been recruited to the study for comparison of Xpert MTB/RIF assay to smear and culture on paed specimens.
 - iii. Protocols under development for solid tissue, gastric aspirates etc
 - iv. Sputum heat inactivation: to determine whether heat inactivation can be used prior to Xpert testing to render it safe for further manipulation – study complete. Analysis underway.
- Evaluation of G4 cartridge:
 - G4 Cartridge evaluation against G3 completed. Results showed no significant difference in the performance of the assays but reported reduced 5011 error rates. Publication in process.
 - TBGxMonitor™ (www.tbgxmonitor.com) automated GeneXpert Verification and EQA reporting platform has been upgraded to include full EQA report processing. Both Verification and EQA components have been completed. Next development phase to include EQA qualitative and quantitative evaluation and reporting of sites.
 - Connectivity: Collaboration with Cepheid ongoing
 - i. Remote connectivity – Remote connectivity pilot protocol approved. System to be piloted within the NHLS with Cepheid. Pilot to begin upon finalization of the NHLS sites.
 - ii. Remote Calibration – Tentative release of remote calibration cartridges to pilot from Cepheid to the NHLS is 3rd quarter of 2012.

10. HIV/TB Integration

- Grand Challenges Canada: Multiple POC HIV/TB integration project
 - Phase I complete
 - Phase II: Evaluation of nurse operated POC versus routine lab completed at HJH Themba Lethu clinic (n=326) has been completed and analysis of results are underway.



- Site visits completed (n=12) and selection of first site (Grace Mokgomo, North West Province) for randomized controlled trial (RCT) has been finalized.
- RCT: A study coordinator and POC nurse has been recruited. Both will be trained on respective platforms for the study start by end of April.
- Connectivity:
 - Conworx (POCcelerator) and LDS (AegisPOC) to be trialed in 2 sites during RCT
 - HemoCue project at CMJAH – network installation for the Hemocue’s has been completed. Awaiting installation of offline version of TrakCare by NHLS.

11. Grants submitted

None

12. Funding issues

Additional funding totaling 4.4 million ZAR was received from URC-USAID for procurement of 11 GeneXpert machines.