NATIONAL HEALTH LABORATORY SERVICE

GeneXpert MTB/RIF

Progress Report

April 2015

NATIONAL HEALTH LABORATORY SERVICE

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1. Background to Project

This project was initiated at the request of the Honorable Minister of Health, Dr Aaron Motsoaledi, in early 2011, following the World Health Organization's strong recommendation published in December 2010 which stated that "the new automated DNA test for TB be used as the initial diagnostic test in individuals suspected of MDR-TB or HIV/TB". In essence this comprises the majority of TB suspects in South Africa. A pilot study was proposed by the TB Cluster within the National Department of Health (NDoH) while a project feasibility study was being performed with due diligence.

The pilot study was initiated in microscopy centres. The NDoH requested that at least 1 instrument be placed in each province, preferably in high burden districts. Selections were made by the TB cluster, with twenty-five microscopy centres being selected and a total of 30 instruments placed.

The NDoH funded 9 GX16 and 14 GX4 instruments for the project. FIND (The Foundation for Innovative New Diagnostics) donated 6 GX4 analysers and the Infinity or GX48 was supported by PEPFAR Right to Care funds. All instruments were placed by World TB day March 242011. 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.

Since then, 309 GeneXpert instruments of varying sizes (GX4: 110; GX16:190; GX48: 1; GX80:8) have been placed in 221 sites – both urban and rural settings, by the National Priority Programmes of the NHLS and the NDoH, the progress of which is described in point 6 below.

The programme is being further expanded to directly support the annual screening for TB and HIV of a quarter of a million people in special risk populations in correctional centres and in peri-mining communities.

1.1. Correctional Services

In order to improve TB control in all 242 correctional facilities in South Africa, the NHLS is working in partnership with the Department of Correctional Services (DCS), NDoH, Aurum Institute, TB/HIV Care Association and Right to Care to ensure access to regular HIV- and TB-related screening, testing and treatment of up to 150,000 offenders through the Global Fund programme. Xpert MTB/Rif testing is being provided either on-site, or at the nearest referral laboratory. During 2014, Xpert MTB/RIF testing facilities have been established on-site at the following Correctional Facilities:

- KgošiMampuru Management Area II
- Barberton Management Area
- Johannesburg Management Area
- Groenpunt Management Area
- Pollsmoor Management Area
- St Albans Management Area
- Durban-Westville Management Area

1.2. Peri-Mining Communities

NHLS, together with the Aurum Institute, has been appointed by NDoH (under the Global Fund grant) to provide services to implement interventions aimed at improving TB and HIV/AIDS management for vulnerable peri-mining communities (estimated at around 600,000 people) in 6 main mining districts. Six staffed and GeneXpert-equipped mobile TB units will be provided within the communities to undertake Xpert MTB/RIF testing for TB. In addition, persons newly identified as HIV-infected through the clinical partner will be staged for HIV-treatment using CD4 tests provided by the closest NHLS lab in the district. The 6 districts with a high proportion of mines in South Africa that have been identified for focused attention are:

- Lejweleputswa (Free State),
- Dr K K Kaunda & Bojanala Districts (North West),
- West Rand (Gauteng)
- Waterberg & Sekhukhune (Limpopo)

2. Assays performed to date

In summary, a total of 5 793 307 specimens have been processed to date (30 April 2015). In April 191,140 specimens were processed. The total % of *Mycobacterium tuberculosis* complex (MTBC) detected in this cohort was 8.90% (17,006). As a reflection of Xpert MTB/RIF's superior sensitivity over microscopy, the average national TB positivity rate among suspects was found to be 8% using microscopy but up to 16-18% in the first year and 13-14% in the second and third year, and has remained constantly around 11% in the fourth year, after introduction of Xpert® MTB/RIF assay. To date Kwa-Zulu Natal (KZN) has performed the greatest number of tests which is probably as a result of the number of instruments placed (refer to tables 1 & 2). Average Rifampicin resistance detection rates have remained around 7% since project inception (Refer to tables 3 & 4).

Table 1: GeneXpert MTB Results by province (cumulative)

Province	Year	MTB Detected	MTB Not Detected	Test Unsuccessful	Total	% MTB Detected
EASTERN CAPE	2011	3 252	15 235	549	**19 036**	**17,08**
EASTERN CAPE	2012	15 880	84 755	2 862	**103 497**	**15,34**
EASTERN CAPE	2013	45 469	320 022	10 046	**375 537**	**12,11**
EASTERN CAPE	2014	48 900	382 950	11 369	**443 219**	**11,03**
EASTERN CAPE	2015	16 020	138 811	3 813	**158 644**	**10,10**
FREE STATE	2011	2 811	14 532	35	**17 378**	**16,18**
FREE STATE	2012	11 660	76 863	288	**88 811**	**13,13**
FREE STATE	2013	14 758	139 299	1 020	**155 077**	**9,52**
FREE STATE	2014	14 030	125 554	997	**140 581**	**9,98**
FREE STATE	2015	4 100	36 802	394	**41 296**	**9,93**
GAUTENG	2011	3 094	18 881	443	**22 418**	**13,80**
GAUTENG	2012	11 120	72 979	2 305	**86 404**	**12,87**
GAUTENG	2013	31 432	215 064	7 690	**254 186**	**12,37**
GAUTENG	2014	38 537	303 844	7 423	**349 804**	**11,02**
GAUTENG	2015	11 936	111 524	2 576	**126 036**	**9,47**
KWAZULU-NATAL	2011	7 546	30 575	896	**39 017**	**19,34**
KWAZULU-NATAL	2012	23 963	135 973	5 915	**165 851**	**14,45**
KWAZULU-NATAL	2013	42 294	293 200	15 003	**350 497**	**12,07**
KWAZULU-NATAL	2014	57 323	519 674	18 683	**595 680**	**9,62**
KWAZULU-NATAL	2015	18 284	190 800	7 206	**216 290**	**8,45**
LIMPOPO	2011	1 973	17 253	173	**19 399**	**10,17**
LIMPOPO	2012	4 004	30 924	689	**35 617**	**11,24**

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LIMPOPO	2013	13 927	188 932	6 086	**208 945**	**6,67**
LIMPOPO	2014	14 376	211 956	7 688	**234 020**	**6,14**
LIMPOPO	2015	4 085	66 665	2 335	**73 085**	**5,59**
MPUMALANGA	2011	2 629	12 683	1 100	**16 412**	**16,02**
MPUMALANGA	2012	4 035	22 226	1 133	**27 394**	**14,73**
MPUMALANGA	2013	10 406	63 030	2 210	**75 646**	**13,76**
MPUMALANGA	2014	14 650	112 752	4 210	**131 612**	**11,13**
MPUMALANGA	2015	4 317	37 744	1 654	**43 715**	**9,88**
NORTH WEST	2011	3 429	14 557	644	**18 630**	**18,41**
NORTH WEST	2012	5 499	29 977	2 052	**37 528**	**14,65**
NORTH WEST	2013	13 301	100 512	4 926	**118 739**	**11,20**
NORTH WEST	2014	17 001	150 584	6 638	**174 223**	**9,76**
NORTH WEST	2015	5 211	51 042	1 898	**58 151**	**8,96**
NORTHERN CAPE	2011	2 727	15 527	712	**18 966**	**14,38**
NORTHERN CAPE	2012	3 830	21 728	1 038	**26 596**	**14,40**
NORTHERN CAPE	2013	7 912	53 728	2 529	**64 169**	**12,33**
NORTHERN CAPE	2014	8 685	63 062	2 891	**74 638**	**11,64**
NORTHERN CAPE	2015	2 778	20 399	740	**23 917**	**11,62**
WESTERN CAPE	2011	2 173	9 897	47	**12 117**	**17,93**
WESTERN CAPE	2012	13 206	68 045	689	**81 940**	**16,12**
WESTERN CAPE	2013	28 653	155 003	2 343	**185 999**	**15,40**
WESTERN CAPE	2014	33 717	180 294	1 992	**216 003**	**15,61**
WESTERN CAPE	2015	9 007	57 450	518	**66 975**	**13,45**
TOTAL		**653 940**	**4 983 307**	**156 448**	**5 793 695**	**11,29**

Table 2: GeneXpert MTB Results by province (01-30 April 2015)

Province	MTB Detected	MTB Not Detected	Test Unsuccessful	Grand Total	% MTB Detected
Eastern Cape	3 614	34 351	824	38 789	9,32
Free State	929	8 732	88	9 749	9,53
Gauteng	2 785	27 561	544	30 890	9,02
Kwa-Zulu Natal	4 247	46 046	1 433	51 726	8,21
Limpopo	969	15 132	525	16 626	5,83
Mpumalanga	994	9 350	265	10 609	9,37
North West	1 122	11 019	295	12 436	9,02
Northern Cape	588	4 656	186	5 430	10,83
Western Cape	1 758	12 978	149	14 885	11,81
Grand Total	**17 006**	**169 825**	**4 309**	**191 140**	**8,90**

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Table 3: Provincial GeneXpert RIF Results in MTB detected cases (01-30 April 2015)

Province	Year	Inconclusive	Resistant	Sensitive	No RIF Result	Total	% RIF Resistant
EASTERN CAPE	2011	33	248	2 919	52	**3 252**	**7,63**
EASTERN CAPE	2012	213	1 077	14 456	134	**15 880**	**6,78**
EASTERN CAPE	2013	1 274	2 969	41 073	153	**45 469**	**6,53**
EASTERN CAPE	2014	1 248	2 983	44 620	49	**48 900**	**6,10**
EASTERN CAPE	2015	190	938	14881	9	**16 018**	**5,86**
FREE STATE	2011	28	155	2 626	2	**2 811**	**5,51**
FREE STATE	2012	162	755	10 717	26	**11 660**	**6,48**
FREE STATE	2013	372	800	13 564	22	**14 758**	**5,42**
FREE STATE	2014	367	816	12 843	4	**14 030**	**5,82**
FREE STATE	2015	50	227	3821	2	**4 100**	**5,54**
GAUTENG	2011	25	179	2 889	1	**3 094**	**5,79**
GAUTENG	2012	136	766	10 142	76	**11 120**	**6,89**
GAUTENG	2013	921	2 008	28 433	70	**31 432**	**6,39**
GAUTENG	2014	818	2 293	35 399	27	**38 537**	**5,95**
GAUTENG	2015	144	705	11082	5	**11 936**	**5,91**
KWAZULU-NATAL	2011	64	592	6 875	15	**7 546**	**7,85**
KWAZULU-NATAL	2012	417	2 166	21 128	252	**23 963**	**9,04**
KWAZULU-NATAL	2013	1 076	3 704	37 079	435	**42 294**	**8,76**
KWAZULU-NATAL	2014	1 512	4 962	50 646	203	**57 323**	**8,66**
KWAZULU-NATAL	2015	301	1427	16519	37	**18 284**	**7,80**
LIMPOPO	2011	25	148	1 775	25	**1 973**	**7,50**
LIMPOPO	2012	52	268	3 609	75	**4 004**	**6,69**
LIMPOPO	2013	299	715	12 803	110	**13 927**	**5,13**
LIMPOPO	2014	328	706	13 294	48	**14 376**	**4,91**
LIMPOPO	2015	36	202	3838	9	**4 085**	**4,94**
MPUMALANGA	2011	30	207	2 386	6	**2 629**	**7,87**
MPUMALANGA	2012	57	401	3 501	76	**4 035**	**9,94**
MPUMALANGA	2013	238	1 024	9 116	28	**10 406**	**9,84**
MPUMALANGA	2014	380	1 281	12 969	20	**14 650**	**8,74**
MPUMALANGA	2015	56	354	3905	2	**4 317**	**8,20**
NORTH WEST	2011	39	303	3 083	4	**3 429**	**8,84**
NORTH WEST	2012	75	414	5 000	10	**5 499**	**7,53**
NORTH WEST	2013	325	730	12 219	27	**13 301**	**5,49**
NORTH WEST	2014	504	909	15 579	9	**17 001**	**5,35**
NORTH WEST	2015	75	291	4841	4	**5 211**	**5,58**
NORTHERN CAPE	2011	28	186	2 511	2	**2 727**	**6,82**
NORTHERN CAPE	2012	50	236	3 536	8	**3 830**	**6,16**
NORTHERN CAPE	2013	175	422	7 025	290	**7 912**	**5,33**

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NORTHERN CAPE	2014	200	448	8 022	15	**8 685**	**5,16**
NORTHERN CAPE	2015	24	146	2608	2	**2 780**	**5,25**
WESTERN CAPE	2011	15	107	2 050	1	**2 173**	**4,92**
WESTERN CAPE	2012	153	653	12 397	3	**13 206**	**4,94**
WESTERN CAPE	2013	636	1 409	26 606	2	**28 653**	**4,92**
WESTERN CAPE	2014	678	1 766	31 272	1	**33 717**	**5,24**
WESTERN CAPE	2015	81	420	8504	2	**9 007**	**4,66**
Total		**13 910**	**43 516**	**594 161**	**2 353**	**653 940**	**6,65**

Table 4: Provincial GeneXpert RIF Results in MTB detected cases (cumulative)

Province	Inconclusive	Resistant	Sensitive	MTB Results	Grand Total	% MTB Detected
Eastern Cape	38	219	3 355	2	3 614	6,06
Free State	17	46	865	1	929	4,95
Gauteng	37	149	2 593	6	2 785	5,35
Kwa-Zulu Natal	51	326	3 863	7	4 247	7,68
Limpopo	7	40	919	3	969	4,13
Mpumalanga	11	66	917		994	6,64
North West	16	58	1 048		1 122	5,17
Northern Cape	7	32	549		588	5,44
Western Cape	14	73	1 670	1	1 758	4,15
Grand Total	**198**	**1 009**	**15 779**	**20**	**17 006**	**5,93**

3. Rif Concordance

Rifampicin concordance is good for both LPA and culture. The data is skewed by reporting the GeneXpert immediately, but still have to wait for MGIT and LPA results.

Table 5: Rif Concordance by LPA or DST

		GeneXpert Confirmation & Rif Concordance									
Province	Rif Resistant Cases	Cultures					LPA				
		Confirmed		Rif Concordance		Pre-analytical	Confirmed		Rif Concordance		Inderterminate
		#	%	#	%		#	%	#	%	
Eastern Cape	5 514	213	3,9%	138	64,8%	3	1 393	25%	1 290	92,6%	5
Free State	1 903	166	8,7%	95	57,2%	0	643	34%	523	81,3%	146
Gauteng	4 116	160	3,9%	109	68,1%	4	1 067	26%	968	90,7%	20
Kwazulu-Natal	9 673	2 221	23,0%	2 069	93,2%	0	2 117	22%	1 857	87,7%	80
Limpopo	1 451	85	5,9%	69	81,2%	2	335	23%	260	77,6%	9
Mpumalanga	2 369	532	22,5%	523	98,3%	0	870	37%	749	86,1%	2

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North West	2 506	143	5,7%	103	72,0%	0	799	32%	681	85,2%	31
Northern Cape	962	202	21,0%	152	75,2%	3	367	38%	281	76,6%	22
Western Cape	3 281	96	2,9%	26	0,0%	0	2 583	79%	2 403	93,0%	2
National	**31 775**	**3 818**	**12,0%**	**3 284**	**86,0%**	**12**	**10 174**	**32%**	**9 012**	**88,6%**	**317**

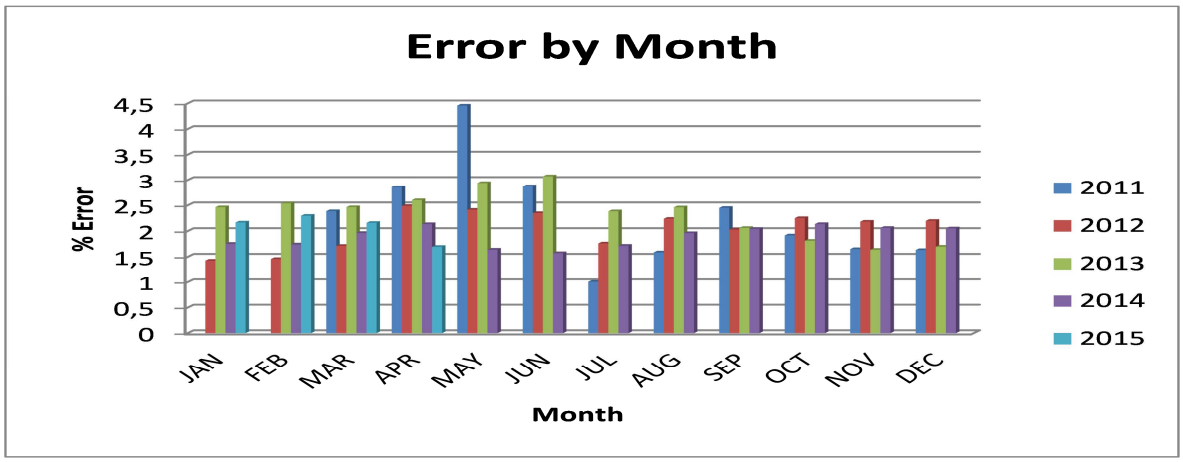
4. Errors

Average error rate has ranged consistently below 3%, however Mpumalanga reported error rates above 3% in the month of March. Details of the invalid results, which likely represent sample issues remains below 1%. These are being monitored regularly and corrective action implemented where necessary.

Table 6: Number of Unsuccessful Tests and Reasons (1-30 April 2015)

Province	Error	Invalids	MTB Results	Grand Total	% Error
Eastern Cape	633	124	37 986	38 743	1,63
Free State	56	31	9 717	9 804	0,57
Gauteng	452	75	30 489	31 016	1,46
Kwa-Zulu Natal	1 031	253	50 477	51 761	1,99
Limpopo	392	76	16 118	16 586	2,36
Mpumalanga	222	32	10 359	10 613	2,09
North West	239	49	12 161	12 449	1,92
Northern Cape	124	54	5 247	5 425	2,29
Western Cape	97	19	15 009	15 125	0,64
Grand Total	**3 246**	**713**	**187 563**	**191 522**	**1,69**

Figure 1: GeneXpert Error by Month



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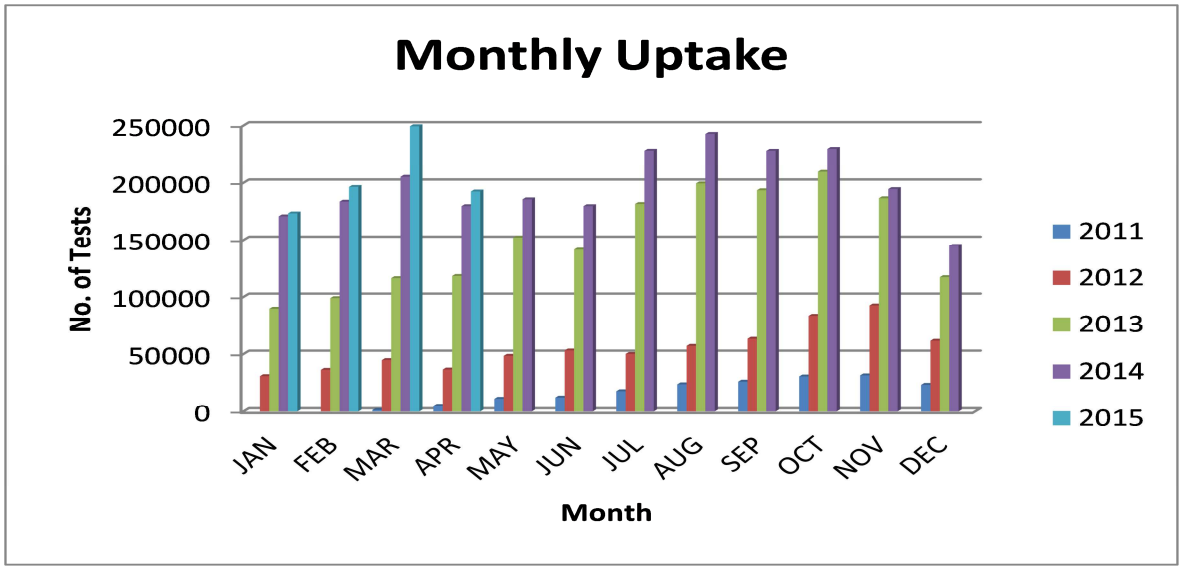
5. Monthly uptake since implementation started

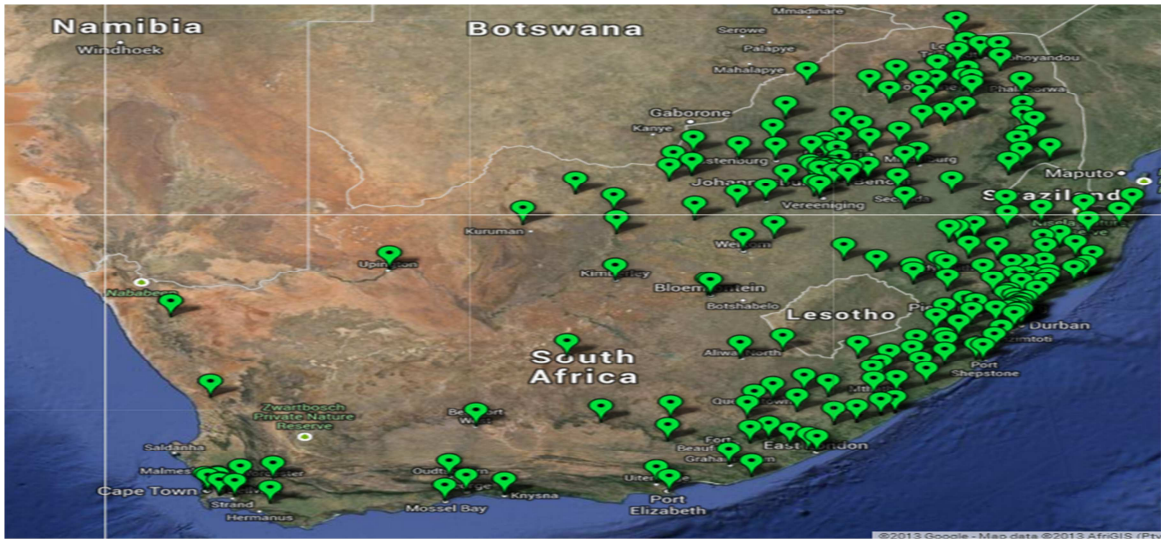
Figure 2: GeneXpert Monthly Uptake



Monthly uptake increased steadily since program inception. The main reason for interruptions is due to the variation in work practices which is expected during the December period.

6. Phased Implementation Progress

Figure 3: Current GeneXpert Placement (221 testing centers, 309 **analysers, Gx4:** 110; Gx16-8: 1**; Gx16:** 189; GX48:1; GX80-80: 8) *20 clinic placements *7 Correctional Facilities *6 Mobile Vans



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7. Training: Laboratory and Clinical

A total of 1,716 laboratory staff and 8,280 health care workers have been trained since December 2011. This will be an ongoing process to support NDoH training on clinical algorithm. Laboratory staff received both clinical and technical training.

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

- Rollout of EGK to avoid duplications
- Implementing WHO recommended guidelines for Xpert testing on EPTB and paediatric samples: being addressed
- EPTB training to be expanded to correctional facilities to ensure compliance
- Hospital staff not complying to the GXP testing algorithm because trainings has not been conducted in most of the hospitals- being addressed
- Staff rotation in hospital wards posing a challenge in the implementation and compliance to the TB algorithms resulting to delay in initiating patients on TB Treatment

9. Literature Update For GeneXpert

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

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

Manuscript	Aim/Sample population and specimen type (n=…)	Results	
		Sensitivity	Specificity
Pho et al, PloS One, 2015	Used epidemiological and operational data from Uganda (139 sites serving 87,600 individuals tested for TB) to perform a model-based comparison of the different placement strategies for Xpert device	• Placement strategies that prioritized sites with higher TB prevalence maximized Case detection rate, with an incremental rate of 6.2-12.6% compared to status quo (microscopy alone). • Diagnosis of MDR-TB was greatest when Xpert was used in place of smear microscopy. • While initial implementation costs were lowest in the Smear Volume strategy, cost per additional TB case detected was lowest in the TB prevalence strategy	

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Van Den Handel, Int J Tuberc Lung Dis. 2015	Prospective evaluation of three diagnostic approaches in the Central Karoo, South Africa: smear microscopy as the initial diagnostic, with sputum processing at centralised laboratories, and Xpert as the initial diagnostic with instrument placement at facility level or centralised laboratory	• Of 1449 individuals, 13.5% TB Positive. • The proportion positive on initial testing was: smear microscopy=8%, decentralised Xpert=20% and centralised Xpert=8% • The proportion of bacteriologically confirmed cases was smear microscopy =88%, decentralised Xpert= 99%; centralised Xpert 91% • The median time to treatment was microscopy =11.5 days, decentralised Xpert =1 day; centralised Xpert =6 days
Kim et al, Ann Clin Lab Sci. 2015	Analyzed clinical specimens from 383 patients with suspected TB who were hospitalized at a secondary hospital in Korea.	• The sensitivity of the Xpert MTB/RIF assay was 73.85% • Among 5 patients with RIF resistance determined by the Xpert, four (80%) were confirmed as suffering from multidrug-resistant (MDR) TB by DST.
Boyles, Int J Tuberc Lung Dis. 2015. Commentry	Disagree with the recommendation by the World Health Organization to use Xpert(®) MTB/RIF on cerebrospinal fluid for the initial diagnosis of tuberculous meningitis (TBM)	• Suggest a diagnostic test needs a negative predictive value (NPV) of 99% so that empirical treatment can be stopped safely. • The NPV of Xpert is around 84%, making a negative test of limited value. • While better tests are awaited, a composite score, combining Xpert with clinical variables and with high NPV, should be constructed
Mokaddas E, JCM 2015	Discordance between Xpert MTB/RIF assay and Bactec MGIT 960 Culture System for detection of rifampin-resistant Mycobacterium tuberculosis isolates in a country with a low tuberculosis (TB) incidence.	• 452 samples that were positive by the Xpert MTB/RIF (Xpert) assay and MGIT 960 system (MGIT) • 440 and 10 Mycobacterium tuberculosis samples were detected as rifampin susceptible and rifampin resistant, respectively. • Two isolates that were rifampin susceptible by the MGIT system were rifampin resistant by the Xpert assay. • rpoB sequencing identified a silent (CTG521TTG) mutation in one isolate and a missense (GAC516TAC) mutation in another.
Dharan NJ, 2015 JCM	Evaluated whether a decreased sample reagent/pellet ratio of 2:1 increased Xpert sensitivity compared to the recommended 3:1.	• Among spiked sputum pellets, the limit of detection was 1,478 CFU/ml at a 3:1 ratio and decreased to 832 CFU/ml at 2:1. • The proportion of specimens in which M. tuberculosis was detected was greater at 2:1 than at 3:1 • Among 134 concentrated sputum pellets from the clinical study, the sensitivity of

		Xpert at 2:1 was greater than at 3:1 overall (80% versus 72%)
Bansal, Ophthalmology. 2015	To compare 3 different molecular techniques to detect the Mycobacterium tuberculosis genome in vitreous fluid of eyes with multifocal serpiginoid choroiditis (MSC). N=11 patients	• The multitargeted PCR results for tuberculosis were positive for 10 eyes, the MTBDRplus assay results were positive in 6 eyes, and the Gene Xpert MTB/RIF assay results were positive in 4 eyes. • Rifampicin resistance was detected in 3 eyes by rpoB gene sequencing, in 3 eyes by the MTBDRplus assay, and in 1 eye by the Gene Xpert MTB/RIF assay.
Nikolayevskyy V, 2015, Tuberculosis	Evaluated the performance of a Propidium Monoazide (PMA) assay for the detection of viable TB bacilli in sputum specimens during anti-TB chemotherapy and its potential use as a TB biomarker. N=1937 sputum specimens	• Good sensitivity and specificity (97.5% and 70.7-80.0%) for detection of live TB bacilli was achieved using the Xpert(®) MTB/RIF test • Good correlation (r = 0.61) between Ct values and time to positivity of TB cultures on liquid media was demonstrated. • The PMA method has potential in monitoring bacterial load in sputum specimens

10. Update on GeneXpert Research projects:

11.1. *GeneXpert Verification and EQA program using Dried Culture spots (DCS)*

- TBGxMonitor™ (www.tbgxmonitor.com) upgrade specification finalized.
    - First set of developments published live and working.
    - Continued developments will be published at a later stage.
- Results for EQA panel 1 for 2015 have been submitted, analysed and released. New enrollments include sites in Austrailia, Cameroun and Kilimanjaro.
- In collaboration with CHAI, 18 news sites in India will be included as of panel 2015-2 and 2015-3.
- Additionally, a trial is being initiated to pilot the DCS EQA program on the line probe assay in collaboration with ACTG

11.2. *Connectivity solutions for the GeneXpert*

- Connectivity: Collaboration with Cepheid ongoing
    i. Cepheid RM Dashboard commercial version now available.

11.3.mHealth solutions for MDR-TB

PHC, Linkage and MDR-TB APPs (emocha)

The emocha MDR-TB mHealth project officially began its implementation on **19 March 2015**. Three facilities were implemented in the Ugu Distric of Kwa-Zulu Natal (Murchison Hospital, Kwa-Mbunde Gateway Clinic and Gamalakhe Clinic). Impemenation was conducted by the NPP (Lynsey Isherwood, Floyd Olsen and Portia Madumo), Emocha, Jphiego and Johns Hopkins University.

Training of the system was conducted on 18 March 2015 at the Ugu District offices. The training was attended by representatives from the three facilities, together with a representative from both the Port Shepstone and Murchison NHLS laboratories, as well as Mr Martin Xaba (NHLS Regional HAST Manager) and Mr Bandezi (NHLS Regional Manager).

Two monitoring visits by the NPP and Jphiego have since occurred: 25-28 March and 7-8 April 2015. During these visits, operational issues such as NHLS/emocha linkage and sputum collection re-training were addressed. Two software updates have performed to accommodate some minor technical problems. The system is now fully functional. The NPP and Jhpiego continue to monitor the progress closely, with another monitoring visit being planned towards the end of April.

- To date, 1693 patients were screened and successfully registered onto emocha between the three facilities. Thirteen of these patients were diagnosed with as RIF resistant; 12 were linked to treatment in <5 days. The other patient was an already RR diagnosed patient and was thus already on treatment

Treat-TB

An APP has been designed by the NPP to measure the turn-around-time from the diagnosis of RIF-R on GXP to the time of treatment intiation. A roll-out plan has been established between the Gauteng DOH (Dr Refilwe Mokgetle – Deputy MDR-TB Director) and the NPP. The app has been implemented in Ekhuruleni within the following facilities; Thembisa, Pholosong, Far East Rand, Natalspruit and Bertha Gxowa.

Publications/abstracts/presentations:

Title	Publication type	Authors	Journal/conference
Novel Package of Integrated Mobile Applications	Oral Presentation	Mani Naicker, Jane McKenzie-White, Sebastian Seiguer, Annatjie Peters, Lynsey Isherwood, mailto:Lynsey.Isherwood@nhls.ac.za	NDoH 90-90-90 Symposium 7th SA AIDS Conference, Durban,

Reduces Time to Treatment Initiation for Patients with MDR-TB		Floyd Olsen,, Wendy Stevens, Jason Farley	South Africa
Driving mHealth Programmes from the Laboratory	Oral Presentation	Lynsey Stewart-Isherwood	7th SA AIDS Conference, Durban, South Africa
m-Health: intervention to rapidly link Xpert MTB/RIF rifampicin resistant patients to treatment initiation in South Africa	Poster Presentation	Lynsey Stewart-Isherwood, Floyd Olsen, Portia Madumo, Lesley Scott, Leigh Berrie, Wendy Stevens[1,2]	8th IAS Conference on HIV Pathogenesis, Treatment and Prevention

11. Update on other projects

- **Evaluation of the GeneXpert to Diagnose Paediatric TB using stool specimens**: (In collaboration with David Alland and FIND). The laboratory R&D component to determine appropriate stool processing protocol has started. Phase 1a completed and involved 30 spiked TB positive and 30 TB negative specimens tested using 6 different stool processing and filtration protocols. Phase Ib completed (25 positive and 25 negative specimens processed). Phase 1c has started – 18 negative specimens have been run to date. Phase IIA (clinical phase) has started – 90 patients enrolled.
- **Longitudinal follow up of Dried Blood Spots for viral load monitoring**: Longitudinal collection of DBS from n=100 HIV-positive patients on ARV's over 72 weeks. Interim data analysis is underway and will be presented as an oral at the 7th SA HIV AIDS conference.
- **Laboratory validation of new TB diagnostics:** 1). A validation protocol is underway, for evaluation of the updated Abbott MTB-RT high throughput TB assay. The clinical study

has begun: n=239 patients have been recruited to date and tested on the new Abbott assay for comparison to MGIT culture and smear.

- **Laboratory validation of new HIV diagnostics:**
  - Pilot evaluation of Alere q VL POC instrument (Alere, Inc) on a longitudinal cohort of whole blood specimens: Performance will be compared to plasma VL on Abbott and DBS VL on Abbott to determine the place for POC. Study start June 2015.
  - Laboratory evaluation of the Cepheid HIV-1 Quantitative VL cartridge on plasma, DBS and whole blood: n=111 patients have been recruited to date; plasma, whole blood and DBS tested. Interim data analysis is underway and results will be presented at a Cepheid Symposium at the 7th HIV AIDS conference.
  - R&D is underway to investigate new materials for a molecular HIV EQA program such as Dried Plasma spots.
  - A new high throughput HIV VL platform, the Hologics Aptima HIV- 1 assay will be validated: Protocol in development

- **GCC Connectivity**
  - No specific update. The connectivity solutions are not being used at present since the study is not recruiting any further patients or performing new tests.

12. Funding

Table 9: Total and Percentage Contribution to date by Donor

Donor	% Contribution
NDoH	24.04
Bill & Melinda Gates Foundation	7.20
TB Reach	1.42
MSF	0.90
FIND	0.45
USAID	2.45
CDC NHLS 2010/11	14.78
CDC NDoH	0.72
CDC NHLS 2011/12	1.39
Dr. Niebauer	0.20
Gobal Fund NDOH	40.91
Global Fund RTC	2.78
CDC NDoH	2.77
Subtotal	**100**

CDC has contributed 19, 65% towards the program to date.

13. Recent Campaigns

None in April.