Minutes of 16th RNTCP National Laboratory Committee held on 7th March 2009 at New Delhi

The 16th RNTCP National Laboratory committee was held at conference hall of New Delhi TB centre on 7th March 2009. Agenda is annexed at annexure-I. List of Participants is annexed at annexure-II.

The meeting was chaired by Dr. V M Katoch, Secretary to Govt. of India, Dept of Health research, Min. of Health & Family Welfare and Director General, Indian Council of Medical Research (ICMR). Dr. LS Chauhan, Deputy Director General, DGHS, Min. of Health and Family Welfare, Govt. of India, welcomed the participants and briefly highlighted the objectives and agenda of the meeting. The objectives of the meeting were to:

Main Agenda Items:

(1) Update on Evaluation and demonstration Projects of FIND & RNTCP for introduction of new diagnostics for TB/MDR-TB
(2) Discuss the draft RNTCP national plan for strengthening of *Mycobacterium tuberculosis* Culture & DST/ Line Probe Assay (LPA) lab capacity
(3) Update on C& DST laboratory accreditation status of IRLs, Private sectors and Medical colleges and update on the smear microscopy EQA activities-OSE visits of NRLs
(4) Discuss draft laboratory documents: (a) generic SOPs for C&DST (solid media) (b) Laboratory performance indicators (c) revised training manual for C&DST (d) revised sputum microscopy manual (e) changes in the liquid cultures in accreditation document

Committee Recommendations:

► FIND/RNTCP projects:

FIND made presentation on status of RNTCP-FIND collaborative projects in India. The committee made following recommendations/observations:

Liquid cultures

1. FIND might take some time before providing the full data supporting introduction of full-scale liquid culture systems in Indian programme conditions. Logistics need to be country based, as the experience of using liquid culture systems in the programme are minimal.
2. Meanwhile, RNTCP should initiate trainings to Lab staff of IRLs and NRLs on liquid culture systems to enhance the preparedness of laboratories as and when the Liquid culture systems are introduced.

LED-FM

1. This is pre-STAG approval demonstration study.
2. The LED-based illumination in the microscopes can also be used for transmission bright-field light microscopy with ZN stains, in addition to FM. With very less energy consumption for illumination and good battery back-up, the microscope improves TB diagnosis in India where ever power shortages and interruptions in DMCs are frequent.
3. It was decided that once the present study is completed and results evaluated favourably, the replacement of the non-functional/condemned

RNTCP microscopes should be done with LED-based illumination light microscope.

Molecular Line Probe Assay

1. For LPA discordance testing: LRS and JALMA were identified as the NRL sites for discordance testing for LPA, by solid culture LJ-DST. LRS will also undertake discordance testing by liquid culture-DST method for the existing cohort.
2. JALMA is currently undertaking DNA sequencing of cultures which had invalid results for the LPA test. DDG TB emphasised that other NRLs also need to develop capacity for DNA sequencing.
3. Secretary, Dept. of Medical Research and DG, ICMR suggested that all invalid results are to be recorded & documented and cultures preserved so that we may have a database of mutations occurring in the community not amenable to detection by the Line probe assay and for future improvements.

Other issues raised by FIND:

- Cepheid Xpert demonstration study site may be shifted from PD Hinduja to CMC Vellore as Mumbai, at present, is not a DOTS-Plus site. The CMC, Vellore is a DOTS-plus site under the programme. The protocol may be made available by FIND to Central TB and members of lab committee, and enrolment criteria or lab capacity requirements are made known. The necessary changes are to be incorporated in the MoU and approval may be obtained.

- The cost of LPA kits & custom exemption: For the non-patient management demonstration studies, CTD would provide Waiver / custom duty exemption certificate (mainly for imported kits, equipment and consumables) to FIND.

► RNTCP National Laboratory Scale-up Plan for addressing MDR/XDR TB diagnosis:

Dr Puneet Dewan, presented the RNTCP national laboratory scale up plan**.** The recommendations of the committee were:

1. Six ICMR institutions would participate in the DOTS-plus diagnostic services, after undergoing accreditation from the TRC, Chennai. The six proposed ICMR labs are situated in (a) Jabalpur (b) Jodhpur (c) Patna (d) Bubneshwar (e) Dibrugarh and (f) Port Blair.
2. All four NRLs should have capacity and proficiency in solid, liquid and Molecular LPA diagnostic technologies. NRLs need to be strengthened so that capacity is built to ensure quality accreditation of large number of C&DST labs.
3. In total 43 solid cultures labs and molecular line probe assay labs are planned (including 27 IRLs + 4 NRLs+ 12 other labs).
4. In total, 33 liquid culture labs are planned (21 IRLs +4 NRLs + 8 other labs).
5. Strengthening the lab network: Curriculum in the medical colleges for MD Microbiology course need to be updated. This need to be to be taken up with MCI and Zonal task force meetings. It can also be taken up by the NRL during the special CME workshops conducted by the medical colleges.

6. Timely establishment of labs is only possible through innovate mechanisms of funding and equipment procurement such as one being explored at present for RNTCP lab scale-up: GLI-FIND-UNITAID or through USAID/WHO.
7. Equipment procurement under GLI-FIND-UNITAID and USAID/WHO mechanism should be linked to installation and initial maintenance of equipment in the warranty period from the same vendors/supplier who should have proven ability and performance.
8. Given the constraints of establishment and maintenance of Bio-safety level 3 (BSL3) labs in the country, BSL level 2 plus labs with a containment facility of negative air pressure room would be established in the country.
9. Training of laboratory network personnel for newer technologies- liquid cultures and LPA- at national level or 'on-site' need to start well before the technologies are actually implemented, cutting short the times of standardizations in the laboratories. For this, RNTCP and NRLs need to develop training material, schedule and impart training in new technologies- Liquid cultures, LED FM and LPA- to all the lab personnel in the network IRLs.
10. DDG (TB) proposed that an advocacy group with laboratory experts should be formed at national level to further the cause of quality assured laboratory network expansion and for extracting administrative commitment from the difficult states.
11. The primary goal of RNTCP is strengthening the IRLs at state level, although interested private sector labs will also be accredited & involved as per approved schemes.
12. The lab scale up plan for MDR-TB management is approved by the lab committee (Annexure III).

► Status of accreditation of C&DST labs:

NRLs and CTD updated the lab committee with the status of C & DST labs and the EQA OSE visits. The following are committee recommendations/observations;

- A formal accreditation visit from NRL along with a representative of CTD is to be taken up for IRL Rajasthan, immediately.
- CTD representative along with NRL microbiologist would visit the labs of IRL, Haryana and PGI, Chandigrah to address issues locally for expediting accreditation process.
- **Uttarakhand** IRL needs to be visited by NRL-JALMA. Visit is planned for the third week of March, 09.
- CTD would take up issues of IRL Chattisgarh with the Health secretary, mainly regarding 'No electricity' in the lab.
- Union Territory of Pondicherry will be under TRC, Chennai due to its distance proximity to the TRC, Chennai compared to NTI Bangalore. Both the NRLs consented for the decision.
- Jabalpur ICMR lab does not need a MoU with RNTCP for providing C & DST services. Lab has passed the panel testing done by TRC and awaits formal accreditation by RNTCP, as per procedures. Subsequently, some districts for DOTS-Plus activities need to be given to them. The matter will be taken up with Madhya Pradesh to identify districts to be considered

under the Jabalpur lab for diagnosis and follow up of MDR cases. Accordingly trainings will be arranged for staff.

- For DOTS-plus services, in case Orissa, Jharkhand, UP (specially Western UP and Bundelkhand), Uttarakhand and Chattisgarh IRLs are not accredited in time, the respective NRLs would take up the C & DST for these states, under plan B.

► **DRS-activities:**

- IRL Andhra Pradesh has a big backlog for conducting DST for positive cultures. More than 500 Mtb positive cultures require to be processed for DST. Delay in the processing for DST would lead to unreliable results. CTD representatives would address this during the DOTS-Plus training in March. Meanwhile, the lab should subculture the pending cultures, in case of delays are expected due to work-load or any other management issues.

► **Second-line DST at NRLs:**

- JALMA would contact the WHO SNRL network headquarters at Antwerp, Belgium for getting included in the SNRL network for second line DST. Meanwhile, JALMA would get the PT cultures from TRC.

► **<u>Generic SOPs for C & DST (Solid media) and other lab related documents:</u>**

Generic SOPs for C & DST (Solid media) were developed by CTD and would be circulated to all NRLs for comments. Comments are to be send on or before 27th March, 09.

SOPs would also contain:

- Uniform C&DST forms and registers.
- Laboratory performance/ assessment indicators for Culture and DST
- Lab infection control and
- Bio-waste management procedures (to be provided by JALMA)
- Routine Equipment maintenance procedures
- Laboratory monthly abstracts

 The C & DST Training manual would be updated based on the SOPs and would be used as a training material by the NRL during the trainings.

 A list of suggestive indicators, which were pilot tested in New Delhi TB centre and STDC, Nagpur, were discussed and endorsed by the lab committee.

 Accordingly, States would print the laboratory registers for C & DST and SOPs for lab purposes.

 Implementation: April 1st as SOP implementation start date, and from 2nd quarter 2009 the laboratory report performance indicators to CTD and NRL. All 13 labs either accredited/or in the process of accreditation would implement SOPs and report the performance indicators.

- All the finalised laboratory documents would be hosted on the website positively before next JMM.

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RNTCP
16th National Laboratory Committee meeting
07th March 2009
New Delhi TB Centre, New Delhi

Objectives of the meeting

- Discussion on national lab plan for expansion of C&DST services
- Update the status of strengthening of C&DST labs
- Progress of SLD DST at NRLs
- Update on EQA &DRS activities

AGENDA

07th March 2009

0930 hrs	***Agenda items***	
	Introduction	**DDG(TB)**
1.	• Update on FIND projects (Liquid culture, LPA, & LED-FM) • LPA based diagnosis of MDR-TB: DST of E&S in view of Non-MDR DR cases identified in Guj & MH	FIND
2.	• Progress made in implementing decisions of 15th lab committee meeting	**NRLs, CTD**
3.	• Draft RNTCP national plan for strengthening of Culture & DST / LPA laboratory capacity	**Dr.Fraser/Dewan**
4.	• Status of accreditation of IRLs, medical college and other sector labs • Status of DRS surveys –AP,UP, Orissa • Update on capacity building for SLD DST at all NRLs • Plan B for OR, JH ,UR, CG	**NRLs**, WHO, CTD
5.	Discussions on • Generic SOPs for C & DST (Solid media) • Uniform Recording & Reporting (C&DST) in IRLs- standardized forms • Assessment of Laboratory performance (C&DST): suggestive Indicators for Culture & DST labs	CTD, NRLs, WHO,
6.	• Update on NRL EQA OSE visits (Smear Microscopy) & RBRC activities in the states	NRLs
7.	Finalization of Revised/updated guidelines • Updated Smear microscopy LT manual & EQA guideline documents (2 smear 2 week diagnosis) • Changes for the Liquid culture in the Accreditation document • Revised Training manual- C&DST (Solid media)	NRLs, CTD, WHO

Annexure-II

List of Participants

1. Dr V M Katoch, Secretary to Govt. of India, Dept of Health research, & DG, ICMR
2. Dr L. S. Chauhan, DDG (TB)
3. Dr V. Kumaraswamy, Director TRC
4. Dr D. Behra, Director, LRS
5. Dr Prahlad Kumar, Director, NTI, Bangalore
6. Dr Saxena, CMO,CTD
7. Dr Devesh Gupta, CMO,CTD
8. Dr V. P. Kalra, CMO, CTD
9. Dr N. Selva Kumar, TRC, Chennai
10. Dr Vanaja Kumar, TRC Chennai
11. Mrs Fatima Rehman, TRC Chennai
12. Dr P. Vishalakshi, LRS, New Delhi
13. Dr D.S.Chauhan,JALMA Institute,Agra
14. Dr V.D. Sharma JALMA Institute,Agra
15. Mr Anand, NTI, Bangalore
16. Ms Reena, NTI, Bangalore
17. Dr S. Sahu, NPO (TB), WHO India
18. Dr Ranjani Ramachandran, WHO-SEARO
19. Dr Puneet Dewan , MO(TB), WHO-SEARO
20. Dr Yamuna, Medical officer, FIND
21. Dr Neeraj Raizada, Medical Officer,FIND
22. Dr Sarabjit Chadha, WHO-RNTCP Consultant, CTD
23. Dr Sheena Susan George, WHO-RNTCP Consultant, CTD
24. Dr Ajay Kumar T, WHO-RNTCP Laboratory Consultant, CTD

Anneuxre III:

LABORATORY SCALE-UP PROPOSAL

OBJECTIVE:

To expand and strengthen the existing capacity of laboratories to conduct *Mycobacterium tuberculosis* Culture and Drug sensitivity testing (C & DST) to achieve access to MDR-TB diagnosis & management in the country for all smear positive cases by 2015.

LABORATORY SCALE-UP PROPOSAL

Though the modest beginning has been made, the programme intends to scale up the DOTS Plus activities rapidly across the country as:

- Access to MDR TB diagnosis and treatment is a basic 'standard of care'.
- Swelling demand for MDR TB diagnosis and treatment services by state Governments, professional medical associations, Private Practitioners, and Civil societies.
- Cost of MDR-TB diagnosis and treatment services is high, but the cost of in action is still higher.

- **Vision:**
  1. By 2012 the programme aims to provide:
     - Universal access to laboratory based quality assured MDR diagnosis for all re-treatment TB cases on entry and new cases who have failed treatment
     - Free and quality assured treatment to all MDR-TB cases diagnosed under RNTCP
     - The country plans to treat at least 30000 MDR TB Patients annually by 2012
  2. By 2015, the universal access to MDR diagnosis and treatment will be made available for all smear positive TB cases under RNTCP.

- **Scale-up Plan (by Year 2009-2012):**

  1. A total of 27 IRLs and 4 NRLs with C&DST facilities would be functional
  2. Additional C&DST laboratories would be identified and supported in Govt. medical colleges/NGOs/Private/corporate sectors.
  3. Newer technologies would be introduced after successful access/introduction demonstration studies undertaken by FIND and other partners in India.
  4. Quality assured C& DST Laboratory network of a total of 43 Solid culture and Molecular Line-probe assay labs are envisaged in the country. This includes the existing demo sites and NRLs.
  5. A subset of 33 laboratories of above envisioned 43 labs would also have liquid culture systems. Sites depend on higher MDR- TB suspects' loads, adequate bio-safety facilities, sufficiency of consumables with strong customer support plans. This includes the existing demo sites and NRLs.
  6. Two additional NRLs be developed for support & supervision of culture & DST labs

  The year wise list of laboratories to be made functional and sites where they would be placed in the country are listed in the table 1 and 2.

Table 1: Expansion of C & DST labs*: Number –Year wise

Lab Unit	2009-10	2010-11	2011-12	Total
Enhanced capacity for Solid culture / sputum processing & Human Resources	12	13	18	43
Establish Molecular unit-LPA	12	13	18	43
Establish liquid cultures system	13	9	11	33
Expected annual DST capacity	8000	35000	120000	220000

*** Explanation for table 1:**

- **Solid culture & DST**: 27 IRLs planned earlier + 4 NRLs + 12 additional solid culture labs (in the NGO/Private/Govt. med college/corporate sector labs which are already undertaking this activity)
- **Molecular LPA units** would be established in all places where solid/liquid culture is available:
  27 IRLs +4 NRLs +12 other labs (in Govt. Med colleges or other sites identified by the state including ICMR labs)
- **Liquid culture systems** would be established in 21 IRLs + 4 NRLs + 8 other labs (in Govt. Med colleges or other sites identified by the state including ICMR labs)
- **Calculation of lab units** based on minimum number of units driven by notified Sputum positive re-treatment patients from 2007 cohort
- Each lab unit needs a minimum of two microbiologists, four LTs and two assistants
- Two additional NRLs (in the reputed Govt. Institutions) are proposed to be established for year 2011-12
- **Expected annual DST capacity** is driven by phased uptake of technologies during the year whereby only a certain % of total capacity (5-50%) is initially realised depending upon the HR and equipment.
- IRL are state designated public health TB labs conducting Trainings, supervision, and EQA for sputum microscopy; in addition to Culture and DST work for MDR-TB diagnosis.
- Three LPA units and two liquid culture units are planned to be funded from GFATM round 9 proposals (as indicated in table 2) rest are planned for funding under UNITAID, USAID/WHO, World Bank.

Table 2: Expansions of C & DST labs*: Site distribution –Year wise

Lab Unit	Year 2009-10	Year 2010-11	Year 2011-12
LPA	NRL-NTI NRL-LRS Kerala Maharastra MH-1 (Nagpur) West Bengal WB-1 (Kolkata) Rajasthan RJ-1 (Ajmer) Delhi 1 -NDTB **Existing demo sites** AP-1 (Hyderabad) Gujrat- GU1 (Ahmedabad) JALMA, Agra SMS, Jaipur TRC, Chennai	TN-1 (ITM) Pondicherry Orissa GU-2 (Jamnagar) Madhya Pradesh MP-1 UP 1-Lucknow Chattisgarh-Raipur Jharkhand-Ranchi MH-2 (Pune) Haryana Chandigarh (PGI) MH-3 (Mumbai) Sikkim	Karnataka KA-1 (Bangalore) Punjab-Patiala Bihar-Patna WB-2 UP-2 (Agra IRL) AP-2 (Vizag) Assam RJ-3 KA-2 MP-2 MH-4 (Wardha) Manipur HP-1 (Dharampur) Uttarakhand-Dehradun Delhi-2 HP-2 (Tanda), NRL-5, NRL-6 } (GF)
LPA Total=43	12	13	18
MGIT	NTI JALMA Kerala MH-1 (Nagpur) Calcutta RJ-1 (Ajmer) Delhi-NDTB Hyderabad **Existing demo sites** LRS, Delhi TRC, Chennai Gujrat- GU1 (Ahmedabad) SMS, Jaipur PGI, Chandigarh	ITM(TN) Pondicherry GJ-2 (Jamnagar) MP-1 Lucknow Raipur Ranchi Haryana MH-2 (Pune)	Bangalore (IRL) Patiala Patna WB-2 UP-2 (Agra IRL) AP-2 (Vizag) Assam Cuttack Delhi-2 NRL-5, NRL-6 } (GF)
MGIT Total=33	13	9	11

***Explanation for table 2:**

1. **Solid culture & DST**: 27 IRLs planned earlier + 4 NRLs + 12 additional solid culture labs (in the NGO/Private/Govt. med college/corporate sectors)
2. **Molecular LPA units** would be established in all places where solid/liquid culture is available i.e., 27 IRLs +4 NRLs +12 other labs (in NGO/Private/Govt. Med college/Corporate sectors)
3. **Liquid culture systems** would be established in 21 IRLs + 4 NRLs + 8 other labs (in NGO/Private/Govt. Med College/corporate sectors)
4. Technology up-gradation to LPA/MGIT only after sufficient experience and obtaining validated data from the access demonstration studies of FIND;
5. **LPA consumables only**: For the exiting sites only consumables are provided: NRL-JALMA, NRL-TRC, AP-1, GU-1 and RJ-2 (Jaipur);
6. **Liquid-MGIT consumables only**: For the exiting sites only consumables are provided: NRL-LRS, NRL-TRC, GU-1 (Ahmedabad), RJ-2 (Jaipur), and Chandigarh (PGI)
7. IRL are state designated public health TB labs conducting Trainings, supervision, and EQA for sputum microscopy; in addition to Culture and DST work for MDR-TB diagnosis.

Objective of the scale-up plan are

1. To strengthen national reference laboratories (NRLs) and IRL laboratory network
    - Particularly for human resources (number of microbiologists and laboratory technical supervisors), physical infrastructure, equipment and laboratory consumables.

- Validate and demonstrate new diagnostic technologies for introduction in programme and operationalisation in IRLs – liquid culture and molecular methods.
- Capacity for second-line drug susceptibility testing
- Technical Assistance to conduct trainings, supervise and accreditation of labs, and manage lab network through laboratory information & management systems (LIMS/LIS).

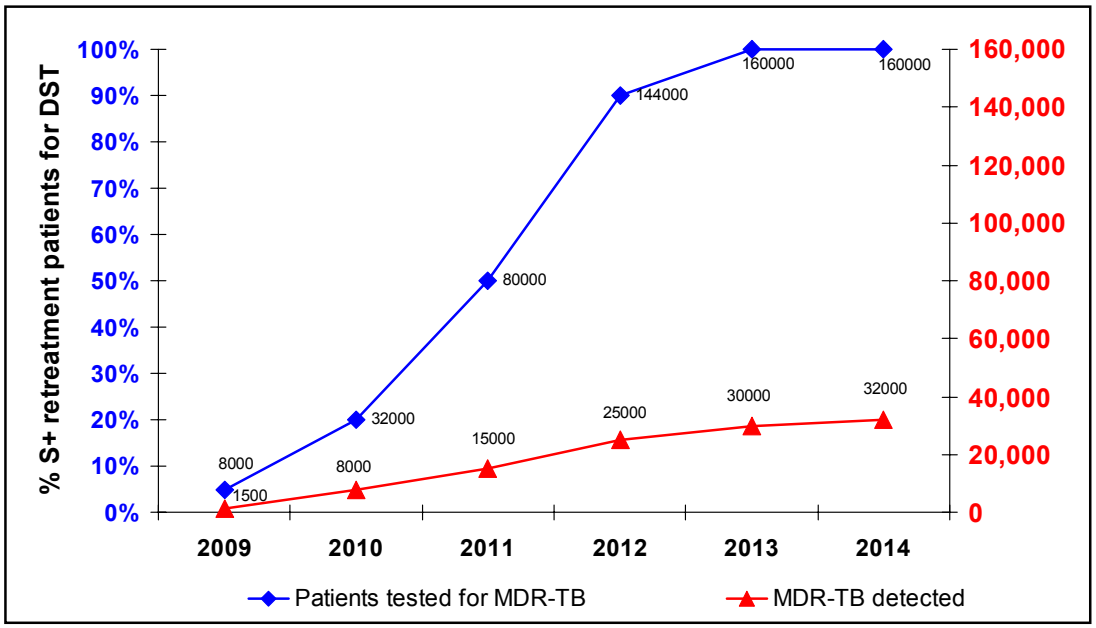
2. To enhance the individual laboratory capacity (IRLs) several fold through introduction of validated and approved newer diagnostic technologies.

3. To Increase the number of quality assured C& DST laboratories in Govt (Medical colleges and hospitals) at and Private/corporate/NGO sectors.

- **General approach for technologies** would be:
  - Initial MDR-TB diagnosis is done by rapid Line probe assay screening, further confirmed and supported by liquid culture systems and solid culture methods
  - MDR-TB follow-up patients' cultures are performed on solid media. Critical follow-up months would be through liquid cultures (where ever available).

With the above laboratory policy frame-work, implemented in a phase manner (from 2009-2014), the programme intends to enhance its ability to diagnose MDR-TB patients as detailed in fig 1.

Fig 1. Projections/Estimates for MDR-TB suspects to be tested and Patients detected (years 2009-2014) under RNTCP



As envisioned in the figure1, RNTCP plans to treat at least 32000 MDR TB Patients annually by 2014. The number of C & DST laboratories to be established/ or NRLs strengthened in the plan period are detailed in table 1.

PARTNERS / DONOR AGENCIES & PROVISIONAL FUNDING ESTIMATES:
Partners/ Donor agencies and provisional budgetary estimate for laboratory expansion plans are as follows:

Donor/funding agencies/partners:

- Government of India/RNTCP current partners for lab strengthening-World Bank, GFATM (RCC) continue to play a major role.
- Technology wise funding partners:

- Solid culture labs expansion
  - Consumables, chemicals/reagents and sterile sputum cups: Government of India/World Bank
  - Equipment in select laboratories and NRLs in 2009: USAID/WHO
  - Remaining/Additional labs, HR and additional support in 2010-11 onwards: GFATM (round 9 application)
- Molecular-LPA & liquid culture labs establishment:
  - Equipment and consumables for year 2009-11: UNITAID
  - Equipments not covered under UNITAID in 2009: USAID/WHO
  - HR, infrastructure & additional consumables, and total expenditure for years 2011-15: GFATM (round 9 application)
- Technical assistance: FIND, WHO, World Bank, PATH/ASM etc.

Provisional budgetary/funding estimates:

Overall MDR-TB diagnosis and treatment scale-up costs estimated for years 2010-14, under three heads of Laboratory scale-up costs for establishment and strengthening of new labs, laboratory running costs, and Second-line TB drug costs is given below (in US $ millions):

	2010	2011	2012	2013	2014	Totals
Lab start-up costs	2.0	3.0	3.7	-	-	8.7
Lab public sector service costs	1.8	3.6	7.0	8.1	8.7	29.2
Lab outsourced service costs	0.5	1.0	2.0	2.2	2.4	8.1
Drugs	25.5	42.5	51.0	54.4	59.5	232.9
Management costs	4.64	7.19	8.83	9.50	9.83	40.0
Technical Assistance	8	8	8	8	8	40
TOTAL ($USD m)	42.44	65.29	80.53	82.2	88.43	358.9