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Technical Report

Brazilian Response to *Global End TB Strategy*: The National Tuberculosis Research Agenda

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INTRODUCTION

The *Global End Tuberculosis (TB) Strategy*, endorsed by the World Health Assembly in May 2014, aims to reduce TB deaths and incidence in all countries to levels currently observed in high-income countries. This can be achieved via reducing mortality, improving early diagnosis, providing more effective treatment, monitoring possible mycobacterial resistance, and expanding contact tracing and infection control[1] [2]. The strategy is based on three pillars: integrated, patient-centered care and prevention (Pillar 1); bold policies and supportive systems (Pillar 2); and intensified research and innovation (Pillar 3)[3]. Achieving these ambitious goals within countries currently devastated by TB-in other words, whose citizens suffer significant morbidity and mortality from TB-will require substantial expansion of TB-related research (i.e., Pillar 3) within these countries[3] [4] [5].

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In November 2014, the World Health Organization (WHO) designated Brazil as one of the few *model* countries that already have substantial TB research capacity and could achieve these goals rapidly. Furthermore, it highlighted the importance of the existing Brazilian TB Research Network (Rede TB), which has been working closely with the National TB Program (NTP) of the Ministry of Health (MoH) over the last 10 years. Rede TB is a non-governmental non-profit organization (www.redetb.org) that aims to improve TB control via focusing on integrated research activities through collaborative actions involving researchers, students, health professionals, industry, civil society, and the government[6] [7] [8]. At present, 320 members working at 65 institutions throughout 16 out of the 27 Brazilian states are affiliated with Rede TB. TB research activities carried by Rede TB members have received support from both state [state research councils (FAPs)] and national funding agencies [the Brazilian National Council for Scientific and Technological Development (CNPq)], under the Ministry of Science, Technology and Innovation (MCTI); the Coordination for the Improvement of Higher Education Personnel (CAPES), a project under the Ministry of Education (MEC); and the Department of Science and Technology (DECIT) and NTP of the MoH]. International funding agencies (the National Institutes of Health (NIH), Centers for Disease Control and Prevention,

Canadian Institutes of Health Research, European Union, and Bill and Melinda Gates Foundation) have also provided funding via competitive selection.

Using the *Global Action Framework for TB Research – the Third Pillar of 'End TB Strategy* document as the basis and following discussions coordinated by Rede TB and the MoH [including the NTP, DECIT, and the Oswaldo Cruz Foundation (FIOCRUZ)] and other initiatives (e.g., the BRICS Plan and Brazil/China Initiatives for TB Research[9], Global Plan to End TB[10]), we reviewed the National TB Research Agenda. The aim of this technical report is to present the results of the actions that led to the establishment of the National TB Research Strategy Plan, which was launched in November 2015.

METHODS

On April 28, 2015, a workshop was carried out to review the *Results on TB Research Gaps and Priorities* survey conducted by Rede TB (from February to April 2015, see Annex 1). A consensus was reached on the need to develop a National TB Research Agenda through various research platforms covering a number of disciplines, and include it in the National TB Research Strategy Plan.

In June 12, 2015, a summary of the key ongoing activities, gaps, and priorities in TB research established for each research platform were presented in a meeting organized by Rede TB, FIOCRUZ, and the NTP in Rio de Janeiro. The general recommendations and priorities for each platform noted in this meeting were consolidated as key steps for developing and implementing a National TB Research Strategy Plan, which are here further disseminated for use by national and international stakeholders.

GENERAL RECOMMENDATIONS

Considering that the "Global End TB Strategy" does not merely attempt to address a biomedical public health problem, but also a development challenge, achieving it must go beyond mere development of TB programs. The following recommendations have been made towards achieving the *Global End TB Strategy*:

1. Promote the creation of a national TB research committee that will foster the inclusion of Pillar 3 (research) of the *Global End TB strategy*[2] and Stop TB Partnership's Global Plan (2016–2020)[10] in the National TB Strategic Plan as well as build its framework and monitor its implementation.
2. Include other stakeholders beyond the MoH, such as the MCTI, MEC, Ministry of Development, Industry and Commerce (MDIC), Ministry of Justice (MJ), Ministry of Social Development (MDS), Ministry of Foreign Relations (MRE), various universities, research institutions, industries, NGOs, biomedical associations, parliamentarians, and advocates for greater TB research investments.
3. Incorporate the National TB Research Agenda into both the National TB Plan and National Health Research Plan.
4. Launch a Strategic Science and Technology Innovation Plan for TB, using funds from the Brazilian government to leverage international funding and thereby foster research and innovation.
5. Develop an operational framework for research to be included in the National TB Strategic Plan.
6. Pursue actions to promote a favorable environment and appropriate strategies to bring national key players from the research arena to work together with NTP managers on Pillar 3 and facilitate their effective interaction with those working on Pillar 1 (TB control) and Pillar 2 (bold policies).
7. Coordinate with the NTP to monitor the National TB Research Agenda implementation and help coordinate support for Pillar 3.
8. Mobilize and prioritize resources according to research priorities and track their application.
9. Establish country-level process indicators for the roll out of new diagnostic, drug, and health management policies to measure research progress.
10. Identify best practices and share them with other countries, initially with Latin/Central America and African countries wishing to improve their national TB research platforms.

The working groups for each of the research platforms identified gaps, established strategies to correct those gaps, and created research priorities for their platforms, as presented below.

FUNDAMENTAL RESEARCH PLATFORM

Strategies to correct gaps

1. Enhance knowledge of the immunopathogenesis of the disease and *Mycobacterium tuberculosis* (Mtb) biology at different stages of TB.
2. Create a coordination research group on fundamental and translational research that pursues increased collaboration among labs to better utilize the available knowledge of different groups.
3. Promote exchange experience between junior and senior scientists from international research groups
4. Provide training courses for fundamental and translation scientists pursuing interaction between academia and industry.
5. Improve the interaction between Brazilian groups carrying out translational studies, especially those performing cohort studies or clinical research.

Research priorities

1. Develop new vaccines using new biotechnologic methods such as knockouts, knockdown, or the CRISPR-Cas-9 (clustered regularly interspaced short palindromic repeats–CRISPR-associated nusclease 9) approach.
2. Investigate host–pathogen interaction targeting new genetic, molecular, immunological, or metabolic markers, through the following:
    - Large-scale approaches using omics techniques such as genetic epidemiology (e.g., evaluate single nucleotide polymorphisms (SNPs) in candidate genes or genome-wide associated studies).
    - Projects with a large-scale population with the disease phenotype or well-characterized endophenotypes.
    - Gene expression studies of molecular markers in the blood or other clinical samples, which can result in identification of molecular signatures and gene maps that can be used to define a risk score for progression to disease in contacts.
    - Developing a robust database of clinical data, including metabolomic and proteomic analyses of serum or urine samples and data on the activation (or deactivation) of the immune response (e.g., interferon gamma release assay [IGRA] with new specific mycobacterial antigens).
    - Studies on the genetics of the pathogen useful for epidemiological surveillance aimed at infection control, evolution of resistance, or monitoring the virulence states of specific strains.
    - Large-scale experimental model studies of pathogen growth in specific culture conditions or infections that assist in the understanding of pathogenesis mechanisms, such as ESX-1, which surrounds protective immune cells and reprograms host cells or enzymes (Zimp) that control the tissue physiology of the patient.
    - Collecting data that consolidates the studies mentioned above, and evaluating how different strains can activate the immune response or jointly evaluating the genetics of the host and pathogen.

DRUG DEVELOPMENT AND PRODUCTION PLATFORM

Strategies to correct gaps

1. Create a coordination research group on drug development that pursues increased collaboration among labs to better utilize the available knowledge of different groups.
2. Provide training courses for fundamental and translational scientists pursuing effective interaction between academia and industry.
3. Create collaborations with Brazilian research groups to provide highly representative and well-evaluated isolate lineages of drug-sensitive and drug-resistant Mtb. These activities should pursue the molecular characterization and creation of a reference biobank of mycobacterial strains using genomics and sequencing for use in the testing cycle for the development of new molecules.
4. Evaluate possible technology transfer for large-scale chemical synthesis with countries such as India or China.
5. Increase the interaction of Brazilian research groups with recognized foreign centers for chemical synthesis and toxicological assays in animal models with rodents and (especially) non-rodents.
6. Create collaborations with international groups with experience in pharmacokinetics and toxicokinetics pursuing joint proposals and exchanging of senior and junior scientists.
7. Increase international collaboration pursuing the production of fixed-dose combinations of drugs for TB among children.
8. Improve the interaction between Brazilian groups that are carrying out translational studies, especially those performing cohort studies or clinical research.

Research priorities

1. Develop pre-clinical studies evaluating new drugs against specific molecular targets for drug-sensitive and drug-resistant Mtb.
2. Amplify the screening for target compounds in different environments (e.g., sea, soil).
3. Identify new targets through screening, including high throughput screening (HTS) with natural products and high content screening (HCS) with relevant enzyme assays.
4. Develop fixed-dose combinations of drugs for pediatric TB in collaboration with the Global TB Alliance.

DIAGNOSTIC DEVELOPMENT AND PRODUCTION PLATFORM

Strategies to correct gaps

1. Create a coordination research group on diagnostic development that pursues increased collaboration among labs to better utilize the available knowledge of different groups.
2. Provide training courses for fundaemtal and translational scientists pursuing effective interaction between academia and industry.
3. Encourage co-financing with national and international companies in the development and validation of new diagnostic tests/biomarkers

Research priorities

1. Validate prototypes of diagnostic tests developed by FIOCRUZ-Parana, IBMP-Tecpar-UFPR, Scientific and Technology Development Center, and State Foundation for Health Science and Production [e.g., QuantStudio 3 real-time polymerase chain reaction (PCR) system, Xpert MTB/RIF to detect multidrug-resistant (MDR) TB] in different laboratories [research or the provision of services from state reference laboratories (LACENS)].
2. Finish the laboratory validation of antibiotic susceptibility kit SIRE Nitratase® produced by the domestic company Plastlabor (POC technology transfer made by the Federal University of Minas Gerais (UFMG). Validation will be carried out at research laboratories and LACENS in Brazil and reference laboratories in Portugal.
3. Validate the recombinant purified protein derivative [PPD; no cross-reactivity with Bacillus Clamette-Guérin vaccine or non-mycobacterial tuberculosis (NMT)] developed by FIOCRUZ-PR and Tecpar-UFPR in different regions of the country compared to traditional PPD (PPD RT23) and to newer immunological tests (e.g., IGRA provided by Qiagen).
4. Large-scale recombinant PPD production to meet the needs of Brazil and other high-burden countries.
5. Research aimed at identifying TB diagnostic biomarkers that can aid in the development of point-of-care non-sputum-based tests.
6. Harmonize laboratory criteria for drug susceptibility testing (DST) of NMT in reference laboratories.
7. Assess the prevalence of NMT in certified laboratories and validate pathogenicity criteria in humans, whether suspected of having TB or not.

CLINICAL RESEARCH PLATFORM

Strategies to correct gaps

1. Creation of an inter-group support system to develop capacity for clinical research coordination at different sites.
2. Increase the number of clinical research sites qualified to perform clinical research and capable of participating in multicenter projects, aiming to include those that are conducting well-characterized cohort studies of TB cases and their contacts.
3. Implement quality management system aiming for accreditation via the National Institute for Metrology, Quality and Technology (INMETRO) for identified sites.
4. Designate training sites for clinical research (human research and biosafety).
5. Develop and validate clinical and therapeutic protocols for specific populations-for example, severe TB cases attending tertiary-level facilities.
6. Identify international partnerships, with a focus on co-financing strategies.
7. Improve investment in infrastructure including renovation of laboratory spaces and equipment.

Research priorities

1. Implement the STAND Phase 2b trial at four Brazilian site for a drug regimen called PaMZ (PA 824, Moxifloxacin and Pyrazinamid). This proposal resulted from a partnership between the Brazilian government [i.e., Science Technology Strategies Supplies (SCTIE)] and the TB Alliance, and led to a shorter treatment regimen (i.e., 2 months for standard treatment and 6 months for MDR-TB)].
2. Promote clinical trials that evaluate the safety and tolerability of anti-TB drugs and their interaction with new anti-retroviral drugs for patients with TB and HIV.
3. Promote clinical studies with new regimens for latent TB infection.
4. Promote clinical trials for new regimens for severe TB patients with or without HIV.

OPERATIONAL, HEALTH SYSTEM, AND EPIDEMIOLOGIC RESEARCH PLATFORM

Strategies to correct gaps

1. Create an inter-group support system to develop capacity of operational and health system research coordination at different sites.
2. Increase number of research sites qualified to perform operational research and capable of participating in multicenter projects.
3. Implement quality management system for identified sites.
4. Designate training sites for operational research (human research and biosafety)
5. Identify international partnerships, with a focus on co-financing strategies
6. Improve the investment in infrastructure including renovation of laboratory spaces and equipment.

Research priorities

1. Evaluate the services and health care system performance at different health care levels (primary, secondary, and tertiary) in TB control in the general and vulnerable populations (i.e., those with HIV/AIDS, diabetes, or other chronic comorbidities; inmates; people living in international border regions; indigenous people; drug users; and health professionals) focusing on the following topics:

- Analysis of more effective access strategies for TB diagnosis and treatment in vulnerable subjects.
- Impact analysis of direct and indirect costs for TB patients and for the National Health System in different regions.
- Impact of latent TB treatment on disease incidence, both regionally and locally.
- Comparison of the performance of innovative approaches to pulmonary TB triage using signs and symptoms.
- Impact of diabetes, smoking, and drug addiction on TB, TB/HIV, and MDR-TB control activities.
- Analysis of the health unit adoption of the TB Infection Control Recommendations described in the National TB Guidelines[11] .
- Analysis of the clinical impact, cost-effectiveness, and economic impact of different TB infection control strategies in health units at different levels of health care.
- Analysis of cultural aspects of programs for TB control.
- Evaluation of different approaches to retreatment of TB and its drug-resistant forms [including drug-resistant (DR), MDR, and excessively drug-resistant (XDR)] on maintenance of the TB transmission chain.

2. Evaluate performance of health services and systems at different health care levels (primary, secondary, and tertiary) and promote user-oriented strategies for TB control (self-care, self-monitoring, and adherence), focusing on the general and vulnerable populations (people with HIV/AIDS, diabetes, or other chronic comorbidities; inmates; people living in international border regions; indigenous peoples; drug users; and health professionals).
    - Evaluate impact of provision of directly observed treatment in the organization of TB services and follow-up of vulnerable TB cases.
    - Identify the most effective strategies used by services that result in a positive impact in adherence to TB treatment.
    - Analyze TB patients' access to secondary and tertiary referral centers.
    - Analyze hospital needs (e.g., beds, complexity of workups, intensive care units) for TB cases with and without social deprivation.
    - Analyze the quality of care of TB services in primary care.
    - Evaluate the contribution of traditional healers and the role of traditional medicine in the strengthening and contextualization of TB control actions in the native and culturally differentiated communities.
3. Spatial analysis of avoidable hospitalizations and mortality from TB and social inequalities in various territories.
    - Identification of TB distribution considering environmental aspects and social inequalities.
4. Evaluation of policy transfer, technologies, and care practices in the health system for TB control.
    - Evaluate the factors that contribute to the development and expansion of new diagnostic technology: Who is involved and affected by innovation and change? How they are bound? Who supports and who opposes or resists innovations?

IMPACT OF THE INCORPORATION OF NEW TECHNOLOGIES PLATFORM

Strategies to correct gaps

1. Increase number of research sites qualified to perform impact assessment of the incorporation of new technologies and are capable of participating in multicenter projects.
2. Implement quality management system for identified sites.
3. Create training research programs to evaluate the impact of new technologies in the unified health system (Tripartite will help in the development of the TB Research Agenda within the National Health Agenda).
4. Improve investment in infrastructure including renovation of laboratory space and equipment.
5. Acquire financial support via state and national funding agencies.
6. Identify a transfer mechanism such that states and municipalities that incorporate technology assessment in their budgets receive more funds from the central government.
7. Identify international partnerships, with a focus on co-financing strategies.

Research priorities

1. Perform a clinical impact and economic analysis (cost-effectiveness and budget impact) on the following:
    - Recombinant PPD in the diagnosis of latent TB in different regions of the country.
    - Xpert MTB/RIF or INH assay, the upcoming Alere q assay, and other molecular tests developed domestically (e.g., QuantStudio 3 real-time PCR system) for use at different health care levels (primary, secondary, and tertiary).
    - Phenotypic methods (using liquid culture or not) in the detection of MDR and XDR TB in Brazil (i.e., MGIT 960 with TB eXiST software, kit SIRE Nitratase®, TB Scott/Ogawa-Kudoh swab cultures).
    - Xpert MTB/RIF assays in Brazil that consider different populations (mainly the general population, health professionals, people living with HIV/AIDS, children, persons deprived of liberty, and indigenous populations living in urban areas).

- TB control decentralization for primary care in Brazil.
- Use of bedaquiline for treating pre-XDR or full-blown XDR TB on a national scale.
- New treatment regimens for latent TB in different regions of Brazil.
- Implementation of quality management system in the research laboratories (collaborating centers) and services (LACENS).
- Digital health approaches for TB control, such as use of mobile phones or Skype to support TB screening, diagnosis, and treatment.
- Incentives provided for anti-TB treatment.
- Use of TB-Web/SINAN/SIM/SITE-TB systems for TB, TB/HIV, and DR-TB surveillance.

2. Analysis of:
   - The clinical and economic impact of the directly observed treatment for TB in vulnerable populations.
   - The impact of communication interventions, advocacy, and social mobilization carried out by forums, networks, committees, and NGOs working to fight TB in Brazil.
   - The impact of actions developed through coordination between civil society and management of states/provinces and municipalities.
   - Impact on TB control of the relationship between leadership activists and health services managers, locally, regionally, and nationally.
   - The association between the health care services characteristics and the successful treatment of TB patients.
   - The association between the characteristics of health care services and TB case detection.
   - Incorporation of a fixed-dose combination of a drug named 4:01 (RHZE) in Brazil.

COMMUNITY ENGAGEMENT PLATFORM

Strategies to correct gaps

1. Promote a national discussion among TB/TB-HIV activists on research engagement and generate a legitimate community research agenda.
2. Create a permanent educational and incentive platform for community engagement to promote community participation in research based on the following:
   - Permanent education (diagnostics, treatment and research literacy) and
   - Funding to establish and support community advisory boards (CABs) and ethics committee participation.
3. Create and maintain a platform and accessible database on research for common users.
4. Promote regular consultation among the various sectors, including the community, academia, health services, and the government and congressmen (e.g., TB Front on National Congress), on research development and the TB agenda.

Research priorities

1. Evaluate strategies to increase interaction between community advocates, researchers, and health professionals on topics such as access to services, quality of service delivery, patient support, and adherence issues.
2. Evaluate the efficacy of different strategies against stigma and discrimination against people with TB from the view of people affected.
3. Assess and document communication interventions, advocacy, and social mobilization carried out by forums, networks, committees, and NGOs working in the fight against TB.
4. Evaluate policy relations between community organizations and TB programs at the three levels of health care (primary, secondary, and tertiary).
5. Evaluate the efficacy of compulsory hospitalization for TB in Brazil by engaging patients' perspective.

QUALITY MANAGEMENT SYSTEM PLATFORM

Strategies to correct gaps

1. Perform an inventory of public health laboratories and collaborating centers conducting TB activities of the established capacity and existing quality management activities.
2. Review policy for public health laboratories and collaborating centers (linked to universities and research institutes) seeking allocation of financial and human resources to implement the much-needed quality management system.
3. Conduct courses and continued training on quality management.
4. Perform laboratory accreditation by INMETRO (ISO 15189 or ISO 15015) at least for the reference laboratories and collaborating centers that agree to focus on the National TB Research Agenda.

Research priorities

1. Evaluate the laboratory impact of the implementation of quality management system on TB activities in the four reference laboratories and four collaborating centers.

2. Evaluate strategies that promote behavior change relating to current cultural values and habits in public and research laboratories towards the adoption of a quality management system in order to provide better services in the SUS and appropriate incorporation of new technologies.

CAPACITY BUILDING OF HUMAN RESOURCES FOR TB RESEARCH PLATFORM

Current gaps

1. Committed mentors' promotion and follow-up of research projects developed by trainees.
2. Help by mentors with trainees' funding applications to grant sustainability to the projects.
3. Support by mentors for paper publications and results presentation at national and international meetings.

Strategies to correct gaps

The platform should use the successful experiences from the International Clinical, Operational and Health Services Research Training Award project and those strategies presented above, along with others not until now:

1. Shared funding between agencies in Brazil and abroad will allow new collaborations, including research capacity building.
2. More intensive use of the Science without Borders (SwB) program from the Brazilian government. The main goals of the SwB are to increase the presence of students and scientists in international institutions, encourage young talents and highly qualified researchers from abroad to work in Brazil, and facilitate the internationalization of universities.
3. Extension of the Brazilian experience in research capacity building in African Lusophone countries and in Latin American countries.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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ABBREVIATIONS

ANVISA	National Agency for Sanitary Surveillance
BMGF	Bill and Melinda Gates Foundation
BRICS	Brazil-Russia-India-China-South Africa
CABs	Community advisory boards
CDCT	Scientific and Technology Development Center
CIHR	Canadian Institute for Health Research
CNPq	National Counsel of Technology and Scientific Development
CONEP	National Commission on Ethic and Research
CPGM	Research Center Gonçalo Muniz
CRPHF	Helio Fraga Reference Center
DECIT-SCTIE	Department of Science & Technology/Science Technology Strategies Supplies
DST	Drug susceptibility testing
EBA	Early bactericidal studies
ENSP	National School Public of Health
FEPPS	State Foundation for Health Science and Production
FIC	Fogarty International Center
FINLACEN	Financing System for Public Health Laboratories
FIOCRUZ	Oswaldo Cruz Foundation
FM	Medical Faculty
FMT-AM	Amazon State Tropical Medicine Foundation
FUNASA	National Health Foundation
FURGS	Foundation of Federal University of Rio Grande
GEOTB	Tuberculosis Epidemiological and Operational Research Group
GWAs	Genomic Wide Association Studies
HCS	High Content Screening
HTS	High Throughput Screening
IAL	Adolf Lutz Institute
ICC	Carlos Chagas Institute
ICOHRTA	International Clinical, Operational, and Health Services Research and Training Award
IGRA	Interferon gamma release assays
INI	National Infectology Institute Evandro Chagas
INMETRO	National Institute for Metrology, Quality and Technology
IOC	Oswaldo Cruz Institute
LACENS	State Reference Laboratories
LNBIO	National BioScience Laboratory
LNN	National Reference Laboratories
LRN	Regional Reference Laboratories
LTBI	Latent TB infection
NDI	Infectious Diseases Nuclei
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NTM	Non-mycobacterial tuberculosis

NTP	National Tuberculosis Program
MCTI	Ministry of Science, Technology and Innovation
MDIC	Ministry of Industry Development
MDR-TB	Multidrug-resistant tuberculosis
MDS	Ministry of Social Development
MEC	Ministry of Education
MJ	Ministry of Justice
MoH	Ministry of Health
Mtb	Mycobacterial tuberculosis
PAHO	Pan American Health Organization
PPD	Purified protein derivative
PUC	Catholic Pontificy University
Rede TB	Brazilian Tuberculosis Research Network
REPORT	Regional Prospective Observational Research in Tuberculosis
RP-USP	Ribeirao Preto State University of São Paulo
SAR	Structure activity relationship
SBMT	Tropical Medicine Brazilian Society
SBPT	Pneumology and Tuberculosis Brazilian Society
SES	State Health Secretary
SINAN	National Notifiable Diseases Information System
SISLAB	Public Health Laboratories National System
SITE TB	Information System of Special Treatment for Tuberculosis
SMS	Municipality Health Secretary
SNPs	Single Nucleotide Polymorphisms
StopTB	Stop Tuberculosis Partnership
SUS	Unified Health System
SVS	Surveillance Health Secretary
TecPAR	State Technology Foundation of Parana
Tripartite NHP	Tripartite National Health Plan
UFBA	Federal University of Bahia
UFC	Federal University of Ceará
UFGDO	Federa University of Grande Dourados
UFES	Federal University of Espirito Santo
UFMG	Federal University of Minas Gerais
UFPR	Federal University of Goias
UFPR	Federal University of Parana
UFRGS	Federal University of Rio Grande do Sul
UFRJ	Federal University of Rio de Janeiro
UNB	National University of Brasilia
União Européia	European Union
UNION	International Union Against Tuberculosis and Lung Diseases
USAID	United States Agency for International Development
USP	State University of São Paulo
WHO	World Health Organization
XDR-TB	Extensively drug-resistant tuberculosis

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ANNEX 1 – 2015 SURVEY ON GAPS AND PRIORITIES FOR TUBERCULOSIS RESEARCH IN BRAZIL

This survey was carried out by Rede TB between March and April 2015. The questionnaire was administered to 114 participants and covered the following main topics:

- Main research activity carried out: public universities (n = 63) and research institutions (n = 21)
- Main research area of expertise: operational (n = 71), basic (n = 47), and translational (n = 42)
- Perceptions on what research arena has been used most by policymakers in the last 10 years: impact of new technologies (n = 56) and operational research (n = 39)
- The most effective inter-sectorial activity identified: Decit-CNPq-FAPs (n = 48), NTP-universities (n = 41)
- Major shortages according to the research platforms:
  - Drugs: Development, preclinical studies, and distribution
  - Vaccines: Management distribution and clinical studies
  - Diagnostic: Interaction between university/research institute and industry (product creation) and lack of accredited laboratory for validation/proof of concepts
  - Clinical Research: Research training, interaction with regulatory agencies (CONEP and ANVISA), and interaction between research groups
  - Operational Research: Research training, lack of funding and infrastructure, and little interaction between research groups
  - Impact of Incorporation of New Technologies: Research training, lack of funding and infrastructure, and little interaction between research groups
  - Health System Research: Research training, lack of funding, and little interaction with civil society
  - Research Priorities: Impact of the incorporation of new technologies (n = 59), operational research (n = 63), clinical research (n = 60), development and production of new diagnostic tests (n = 60), health system research (n = 55), and drug development (n = 45)