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24–27 OCTOBER 2018. THE HAGUE, THE NETHERLANDS
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Clinical trial capacity building to address MDR-TB: challenges and the way forward

Ethics and regulatory capacity building

Abraham Aseffa

Armauer Hansen Research Institute (AHRI), Ministry of Health, Ethiopia

Federal Democratic Republic of Ethiopia
Ministry of Health

The Union

Outline

- The context
- The practice and challenges
- Capacity building efforts

Acknowledgements

- Yohannes Sitotaw – ex-National Health Research Ethics Review Secretary (NERC), MoST, Ethiopia
- Zenebe Akalu and Tesfamariam Mebrahtu, AHRI STREAM Trial Team
- Liya Wassie, vice-Chair, NERC, Ethiopia

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Ministry of Health

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Conflict of interest disclosure

- I have **no**, real or perceived, direct or indirect conflicts of interest that relate to this presentation.

Affiliation / financial interest	Nature of conflict / commercial company name
Tobacco-industry and tobacco corporate affiliate related conflict of interest	
Grants/research support (to myself, my institution or department):	
Honoraria or consultation fees:	
Participation in a company sponsored bureau:	
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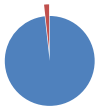
The Context

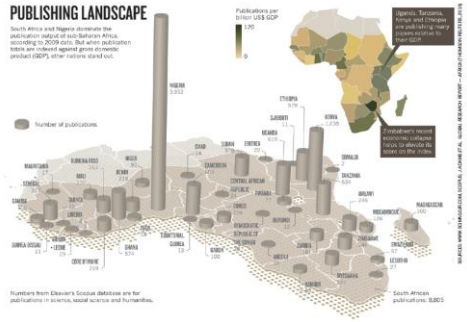
Research: Africa contributes 2% of publications



Africa: 2% of world production of 3 768 434 scientific papers in 2001 and 2004: Africa: 67831 (1.8%). Pouris and Pouris (2009)

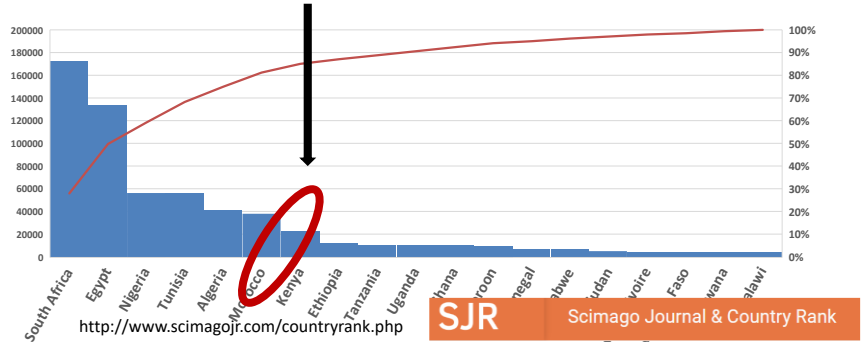
AU–NEPAD: African Innovation outlook 2010

Sub-Saharan Africa's share of global research spending rose from 0.7% in 2007 to 0.8% in 2013 (UNESCO Science Report Towards 2030)



Vivienne Irikefe Nature 2011;474:556-559

Top 20 African publications in 2015



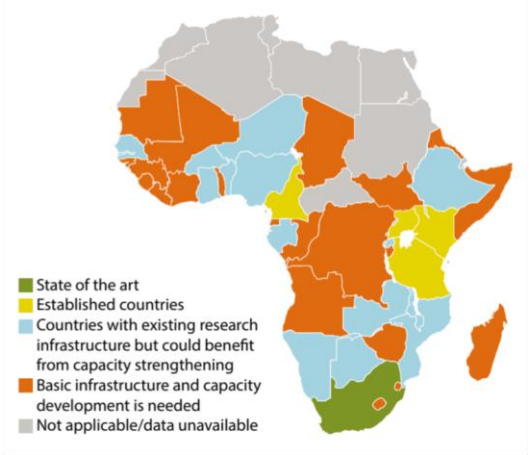
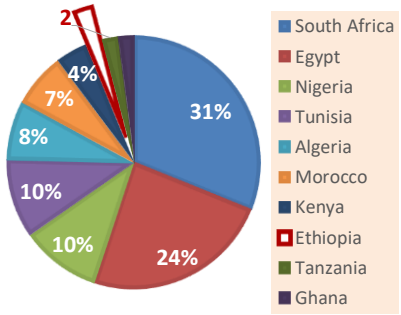
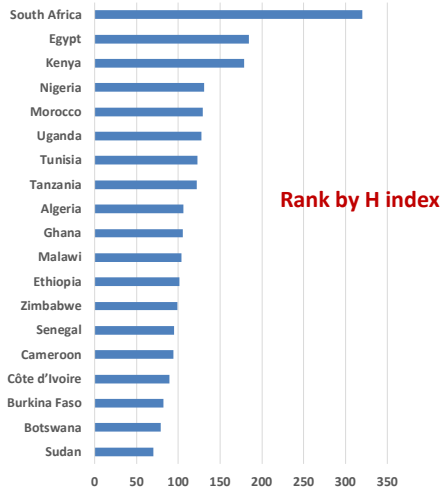


Figure 11 Categorisation of countries into research capacity for PRNIDs tiers

Ethiopia : 2015 publications



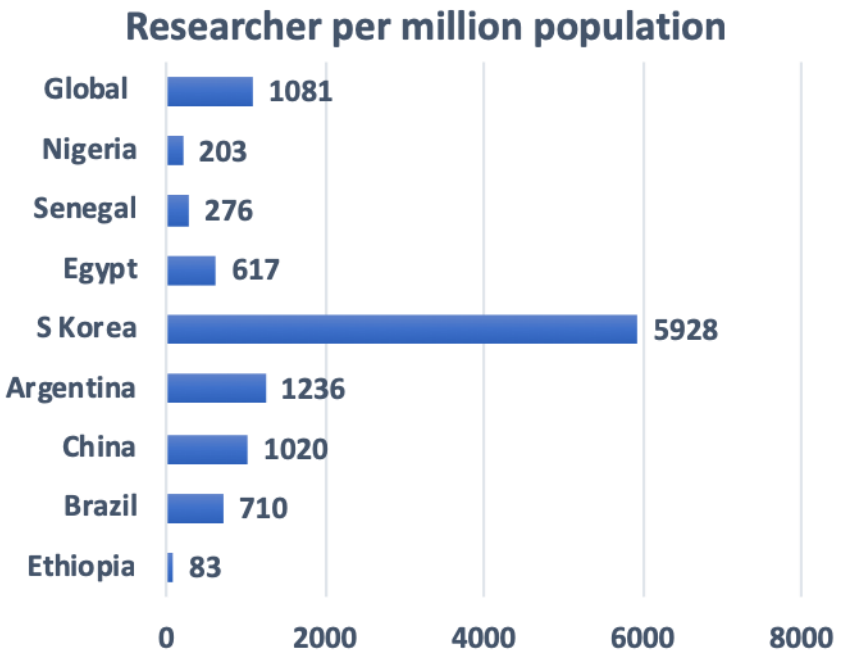
2% of top 20 African publications

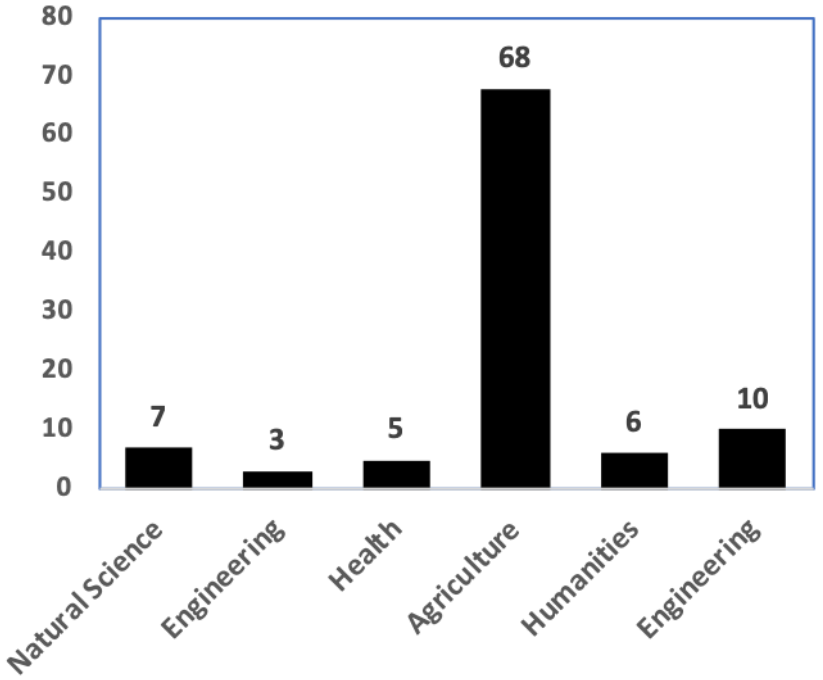


Rank by H index

http://www.scimagojr.com/countryrank.php

Example Ethiopia: number of researchers



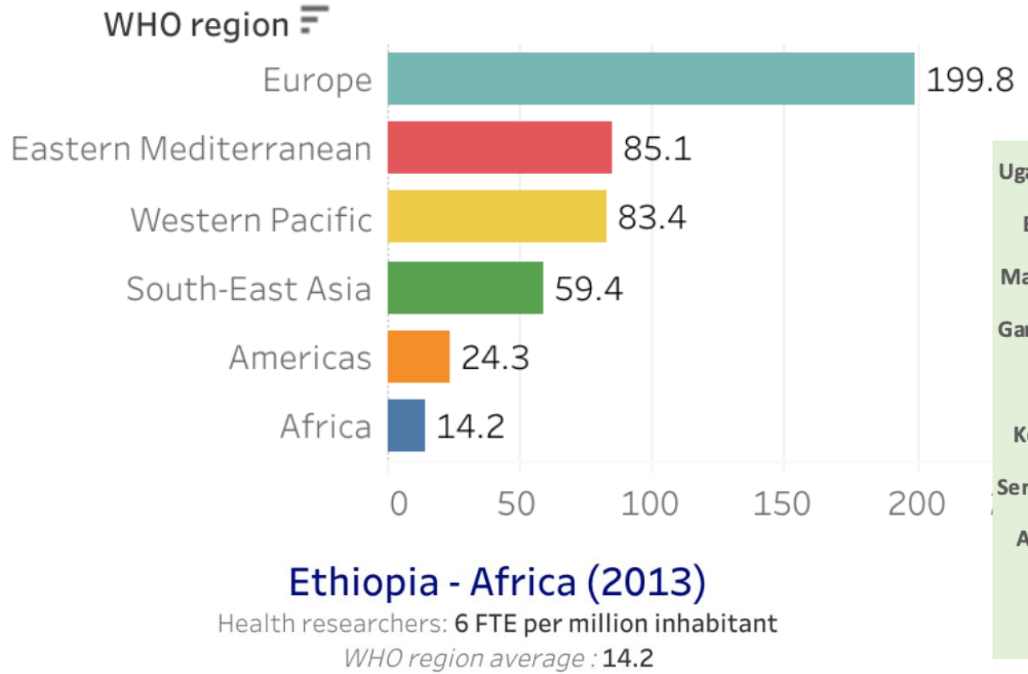


Source: MoST, Ethiopia: indicators, 2015

Health researchers by WHO region

(FTE per million inhabitants)

based on 61 countries



Ethiopia - Africa (2013)

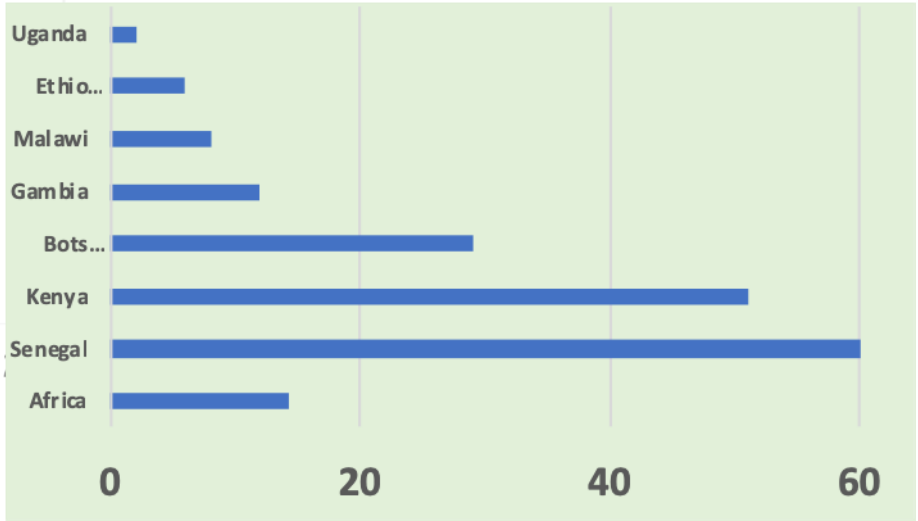
Health researchers: **6 FTE per million inhabitant**

WHO region average : **14.2**

Global Observatory on Health R&D

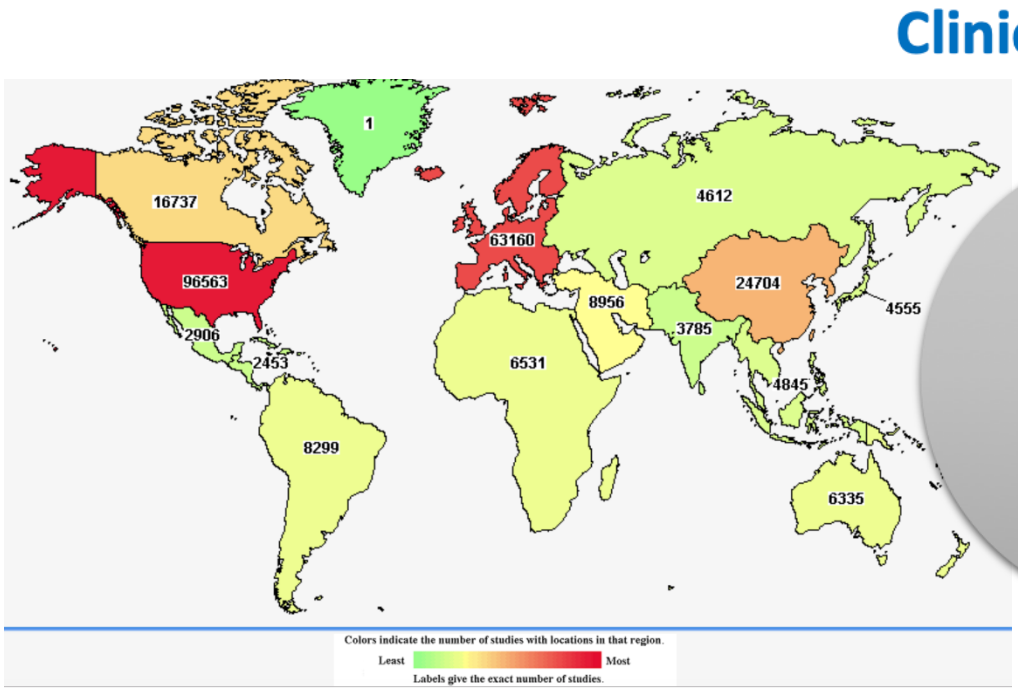
Health researchers (in full-time equivalent) per million inhabitants, by WHO Region (first set of charts)

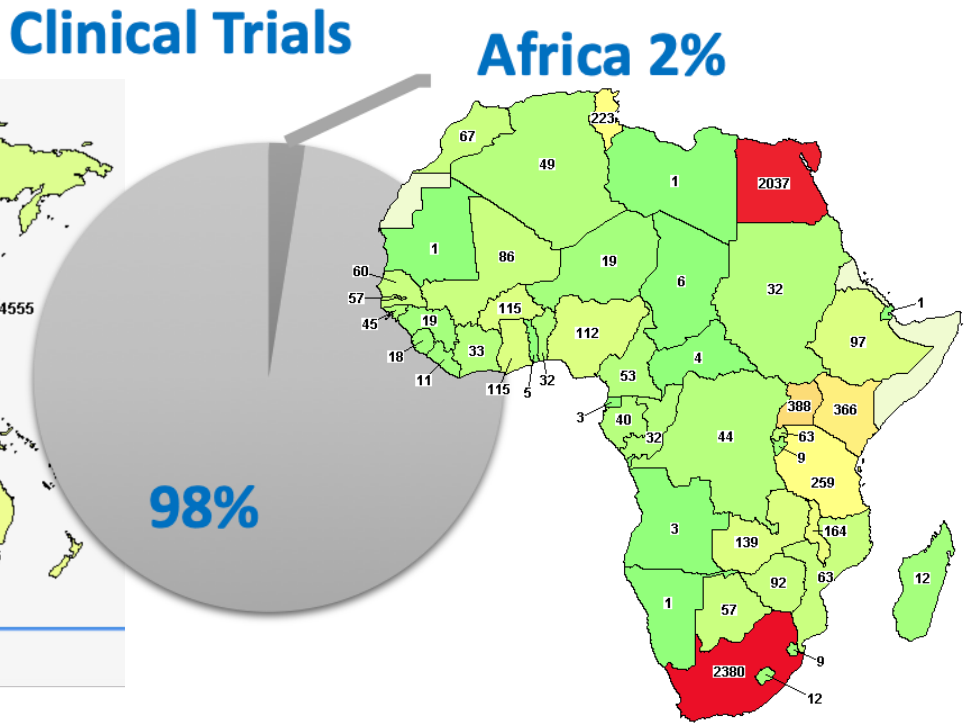
Published: January 2018



http://www.who.int/research-observatory/benchmarking/researchers_whoreg/en/

Clinical trials in Africa





Source: ClinicalTrialsGov, category intervention – www.clinicaltrials.gov

Clinical Trials in Africa. Trials.Gov 2018

Africa: a fast growing economy

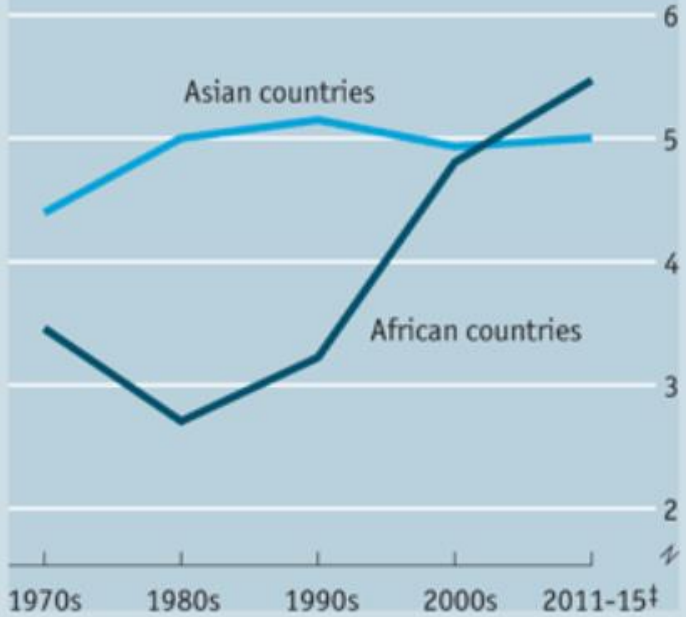
World's ten fastest-growing economies*

Annual average GDP growth, %

2001-2010†		2011-2015‡	
Angola	**11.1**	China	9.5
China	10.5	India	8.2
Myanmar	10.3	**Ethiopia**	**8.1**
Nigeria	**8.9**	**Mozambique**	**7.7**
Ethiopia	**8.4**	**Tanzania**	**7.2**
Kazakhstan	8.2	Vietnam	7.2
Chad	**7.9**	**Congo**	**7.0**
Mozambique	**7.9**	**Ghana**	**7.0**
Cambodia	7.7	**Zambia**	**6.9**
Rwanda	**7.6**	**Nigeria**	**6.8**

Sources: *The Economist;* IMF

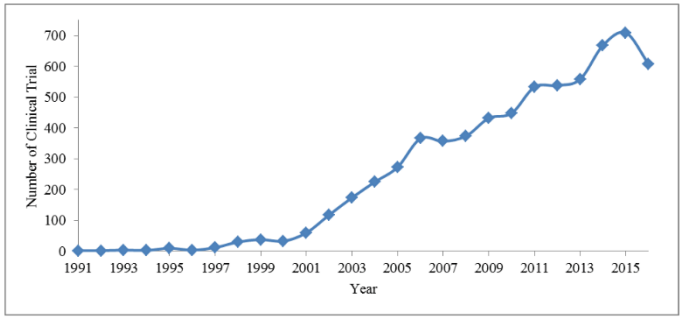
GDP growth, unweighted annual average, %



*Excluding countries with less than 10m population and Iraq and Afghanistan †2010 estimate ‡Forecast

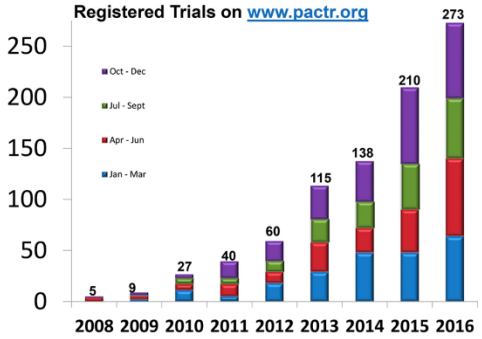
Growing number of clinical Trials in Africa

Need for matching growth in capacity building
for credible data and participant safety and wellbeing

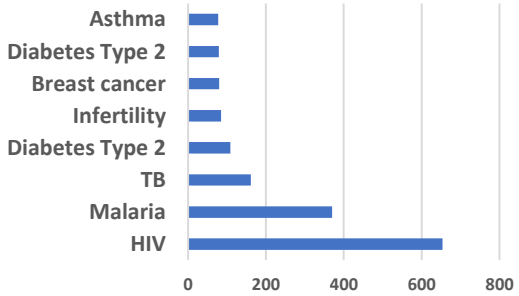


Source: Adapted from Clinical TrialsGov March 2017

Kumar S, Muchie M. Asian Biotechnology and Development Review Vol. 19 No. 3, pp 3-23 © 2017, RIS.



http://www.who.int/ictrp/network/pactr2/en/



Source: Adapted from Clinical TrialsGov March 2017

The practice - and challenges

Experience in Ethiopia – system

Challenges – Ethiopia and other

system

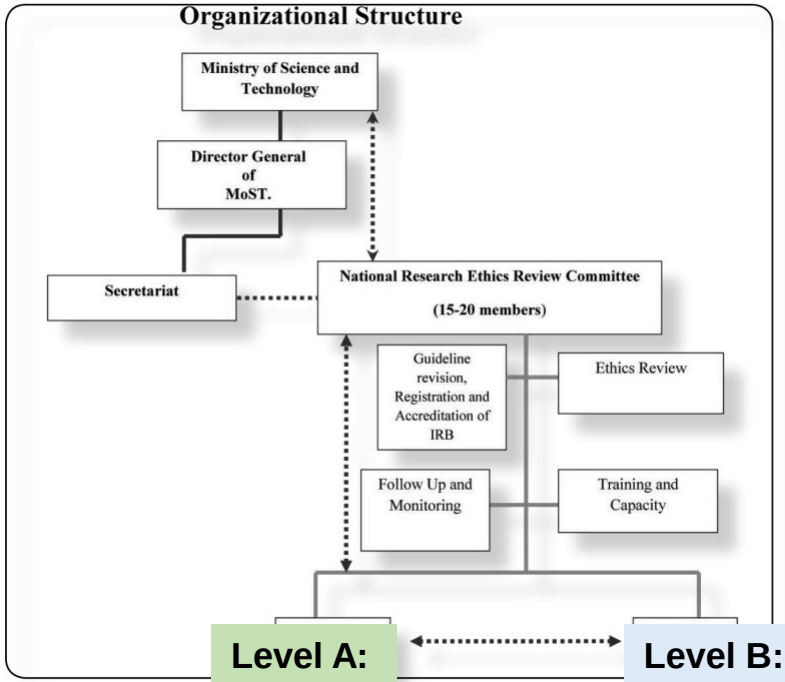
specific

National Research Ethics Review Guideline

FDRE Ministry of Science and Technology

September 2014

Fifth Edition



Level A:

5.3.2.5. Review and approve research protocols similar to the NRERC except:

- Genetic research, stem cell research
- Research involving human biological material transfer outside of Ethiopia provided that the IRB notifies the NRERC Multicenter international collaborative research of experimental nature
- Investigation of new devices, drugs or vaccines not registered for use in Ethiopia
- Review of trials that are funded by manufacturers and pharmaceutical companies

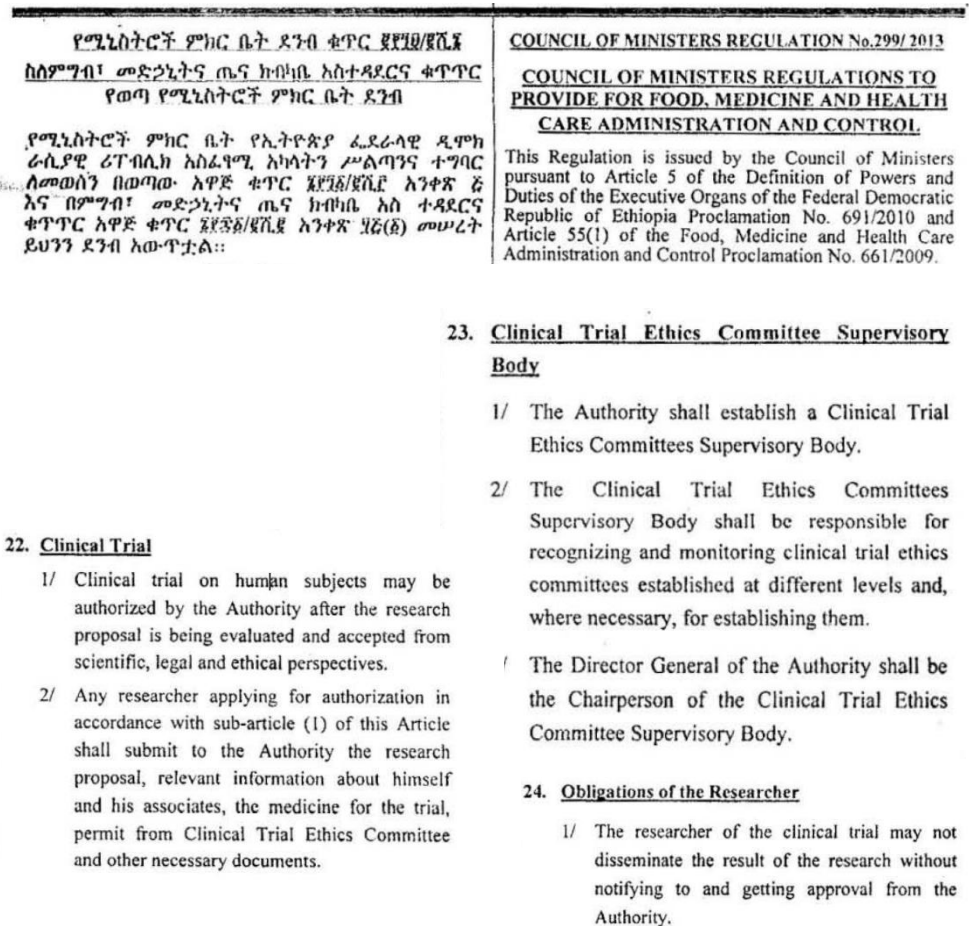
Level B: Review and approve research protocols that involve minimal risk

8.1.7. All applications should be submitted to the IRBs depending on the location of the research site.

8.1.8. The IRBs shall give final official approval for studies under their mandate. However, if an applicant has a complaint(s) against the decision of the IRBs, the study should be reviewed by the NRERC.

Regulatory oversight

Institutional ERC
National Ethics Review Committee
Drug Regulation Authority



የሚኒስትሮች ምክር ቤት ደንብ ቁጥር ፮፻፺፱/፪ሺ፮

ስለምግብ፣ መድኃኒትና ጤና ክብካቤ አስተዳደርና ቁጥጥር የወጣ የሚኒስትሮች ምክር ቤት ደንብ

የሚኒስትሮች ምክር ቤት የኢትዮጵያ ፌደራላዊ ዲሞክራሲያዊ ሪፐብሊክ አስፈፃሚ አካላትን ሥልጣንና ተግባር ለመወሰን በወጣው አዋጅ ቁጥር ፮፻፺፩/፪ሺ፫ አንቀጽ ፶ እና በምግብ፣ መድኃኒትና ጤና ክብካቤ አስ ተዳደርና ቁጥጥር አዋጅ ቁጥር ፮፻፷፩/፪ሺ፪ አንቀጽ ፶፫(፩) መሠረት ይህንን ደንብ አውጥቷል።

COUNCIL OF MINISTERS REGULATION No.299/ 2013

COUNCIL OF MINISTERS REGULATIONS TO PROVIDE FOR FOOD, MEDICINE AND HEALTH CARE ADMINISTRATION AND CONTROL

This Regulation is issued by the Council of Ministers pursuant to Article 5 of the Definition of Powers and Duties of the Executive Organs of the Federal Democratic Republic of Ethiopia Proclamation No. 691/2010 and Article 55(1) of the Food, Medicine and Health Care Administration and Control Proclamation No. 661/2009.

22. Clinical Trial

1/ Clinical trial on human subjects may be authorized by the Authority after the research proposal is being evaluated and accepted from scientific, legal and ethical perspectives.

2/ Any researcher applying for authorization in accordance with sub-article (1) of this Article shall submit to the Authority the research proposal, relevant information about himself and his associates, the medicine for the trial, permit from Clinical Trial Ethics Committee and other necessary documents.

23. Clinical Trial Ethics Committee Supervisory Body

1/ The Authority shall establish a Clinical Trial Ethics Committees Supervisory Body.

2/ The Clinical Trial Ethics Committees Supervisory Body shall be responsible for recognizing and monitoring clinical trial ethics committees established at different levels and, where necessary, for establishing them.

3/ The Director General of the Authority shall be the Chairperson of the Clinical Trial Ethics Committee Supervisory Body.

24. Obligations of the Researcher

1/ The researcher of the clinical trial may not disseminate the result of the research without notifying to and getting approval from the Authority.

Challenges:

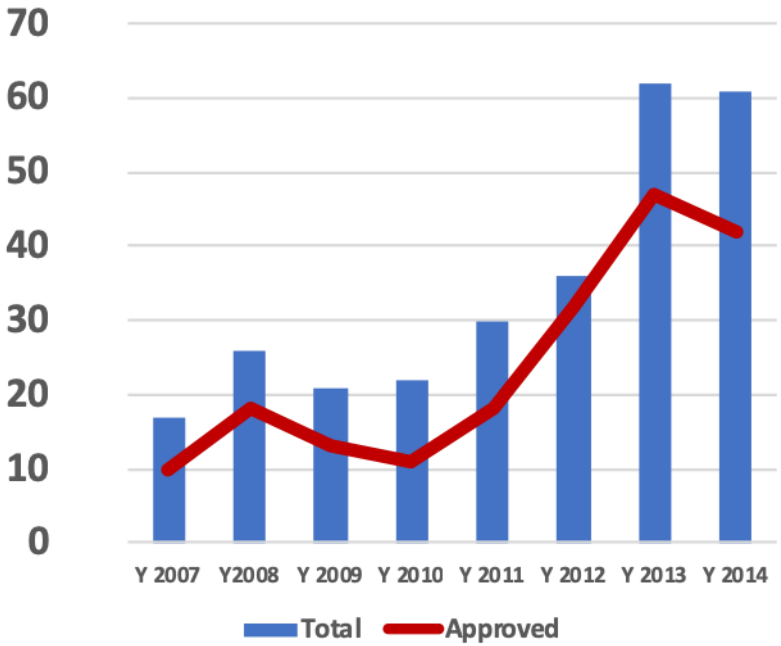
Ethics Review Committee perspective

- Increasing workload overtime
  - Voluntary panels
  - No time for monitoring
- Poorly prepared submissions
- Weak institutional support
  - Not in the organogram
  - Weak Secretariat
  - Delayed communications
  - Incomplete documentation
- Growing complexity of protocols
- No unified legislation on clinical trials

Liya Wassie, Yimtubezinash Woldeamanuel , Senkenesh Gebre-Mariam, Yeweyenhareg Feleke, Fuad Temam, Abebe Hailu, Hiwot Abay, Zeyin Zerihun, Solomon Bussa, Lensa Aberra, Geremew Tarekegne, Asfawessen Gebre-Yohannes, Abraham Aseffa. *Ethiop Med J, 2015, Vol. 53, Supp. 1*

ORIGINAL ARTICLE

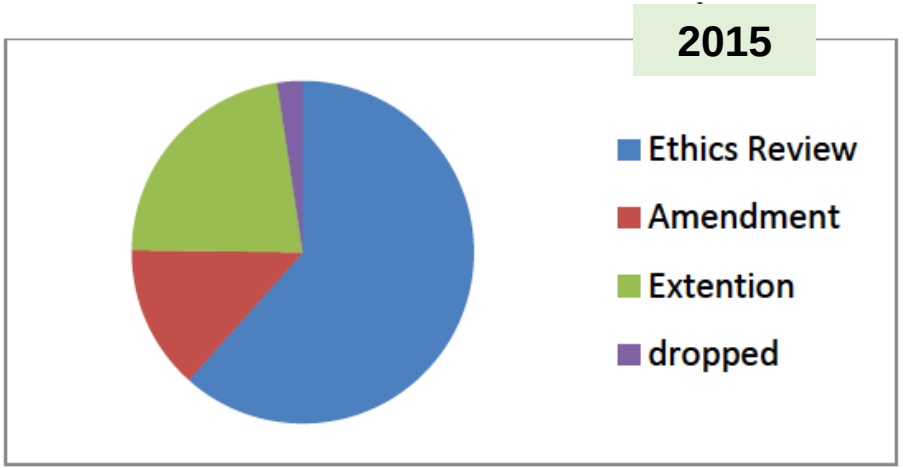
RESEARCH ETHICS REVIEW PRACTICES: EXPERIENCES OF THE ARMAUER HANSEN RESEARCH INSTITUTE/ ALL AFRICA LEPROSY AND TUBERCULOSIS REHABILITATION AND TRAINING CENTER ETHICS REVIEW COMMITTEE, ETHIOPIA



AHRI AAERC trend of approved proportion Wassie L et al EMJ 2015

Ethiopian National Research Ethics Review Committee

Ethics Review	77
Amendment	17
Extension	28
Dropped	3



15 members
Voluntary
Monthly meeting quorum

40% reviewed by external experts

6.4 External Reviewers

- If a protocol requires expertise that is beyond the competence of the IRB members or the IRB need additional opinion in the review process, the IRB may engage independent experts to review and give their opinion.

47 clinical trials between 2010-2018

Courtesy of Yohannes Sitotaw, MoST HRE Directorate

Challenges:

Researcher perspective

- Multiple review requirements
- Delayed approval
- Poor quality comments
  - Focus on science than ethics

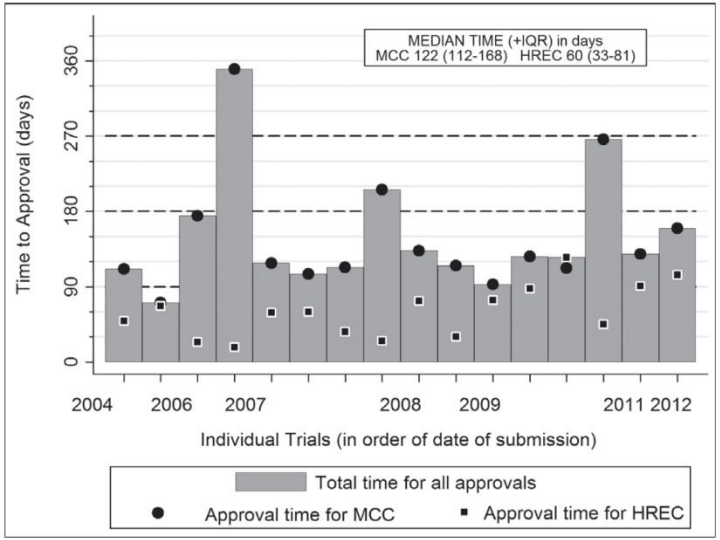


Fig. 2. Time to approval for first submissions per individual trial. Total time to final approval is shown, as well as individual times for MCC and HREC. MCC and HREC approval submissions were made simultaneously.

Geldenhuys H *et al*. S Afr Med J 2013;103(2):85-89. DOI:10.7196/SAMJ.6390

Delayed time to approval

Ethiopia:

- 60-90 days for AAERC
- 80—180 days for NRERC
- >180 days for FMHACA

STREAM Trial Stage 2 - 294 days total for final approval

AAERC:	**120 days** (8 Apr 2015 – 07 Aug 2015)
NRERC:	**70 days** (12 Oct 2015 – 21 Dec 2015)
FMHACA:	**169 days** (11 Aug 2015 – 27 Jan 2016)

Identifying reasons for delays in ethics approval: Experience of an institutional ethics review committee

- Chandanie Amila Wanigatunge, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka Email: caw@sjp.ac.lk, (Corresponding author)
- Shamini Prathapan, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka
- Gizelle Malinka Warnacula:, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka
- Rochelle Shanika Tanner, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka

Eubios Journal of Asian and International Bioethics 26 (November 2016)

(ERCs). There is no local mechanism to evaluate or accredit ERCs resulting in inequalities in the quality of ethics review provided by different ERCs where some committees are perceived as being "more rigorous" and "strict" than others. In the absence of a national mechanism for accredit ERCs, many are now seeking recognition by the Forum for Ethics Review Committees in the Asia and the Western Pacific (FERCAP) under its Strategic Initiative for the Development of Capacity in Ethical research (SIDCER) [5]. In the absence of a legal framework, ERC remains a major form of research oversight.

Quality of review

- "Some committees are more rigorous than others"
- "Some focus more on scientific methods than ethics"

6.2.2 Applying to Establish an IRB

An institution that needs to establish an IRB shall apply in writing for approval and registration at the National Secretariat at MoST, and include the following requirements:-

- Statement that the IRB will follow the guidelines as stipulated in this document, law, relevant regulations.
- A list of IRB members identified by name, qualifications, profession, current

5.9 Registration and Accreditation

5.9.1. All IRBs in Ethiopia have to be accredited by the NRERC, and registered and licensed by the Secretariat of the NRERC at MoST.

5.9.2. Registration and renewal of all IRBs shall be done every two years from the date of registration or renewal of the IRB.

Quality of work with the community

Need for accreditation and monitoring and continuous improvement

Capacity building efforts

Examples

- Systems – review quality

Efforts at capacity building

- National ethics review system
- Ethics training
  - Researchers - Reviewers
  - Postgraduate curriculum
  - *Research ethics review committees*

Multi-stakeholder engagement

National forum for health research ethics
Pan-African Forum for Bioethics

Recognition of ERCs

Pan African Bioethics Initiative
PABIN
Réseau Panafricain de Bioéthique

la Vie la Santé la Justice

CAMBIN

Ethiopian Bioethics Initiative
የኢትዮጵያ የሔና ምርምር ስነምግባር ማህበር

Forum for Ethical Review Committees in the Asian & Western Pacific Region
www.fercap-sidcer.org

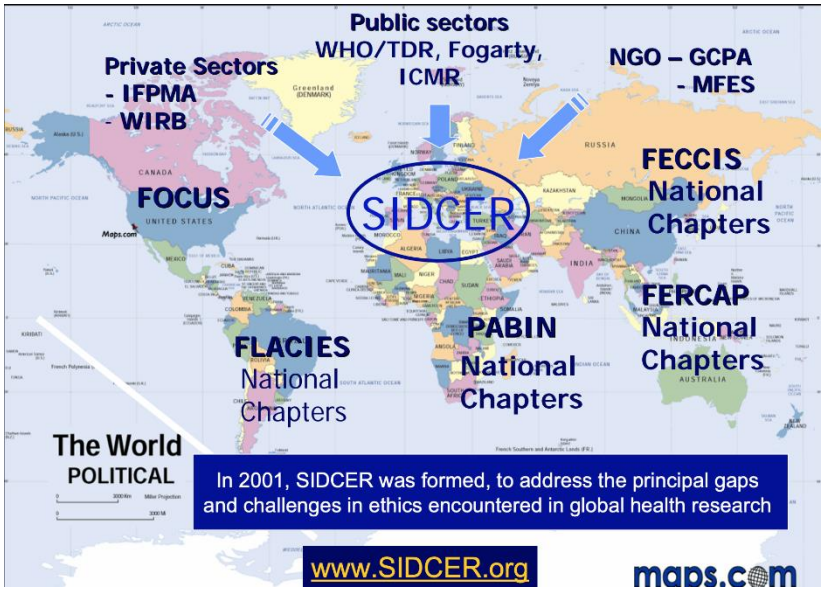
Fostering **team work and strategic partnerships** at the national, regional, and international levels with human research stakeholders sharing common values and common goals

Promoting **quality culture in ethical review** of health research

Facilitating training and providing education opportunities for health research stakeholders

Establishing **monitoring and evaluation programs** for continuous quality improvement of ethical review systems

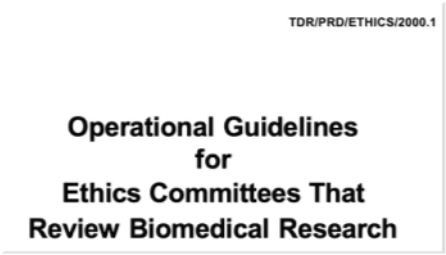
http://www.fercap-sidcer.org/recog.php

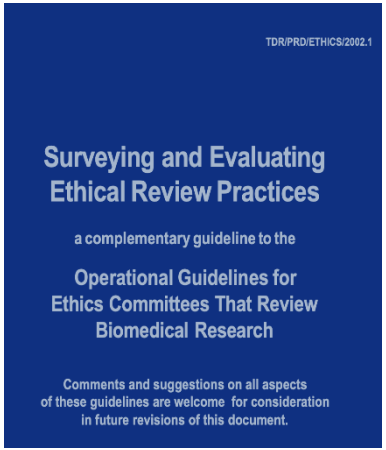


http://www.unicri.it/special_topics/clinical_research/round_table/presentations/19_KARBWANG.pdf

Recognition program tools

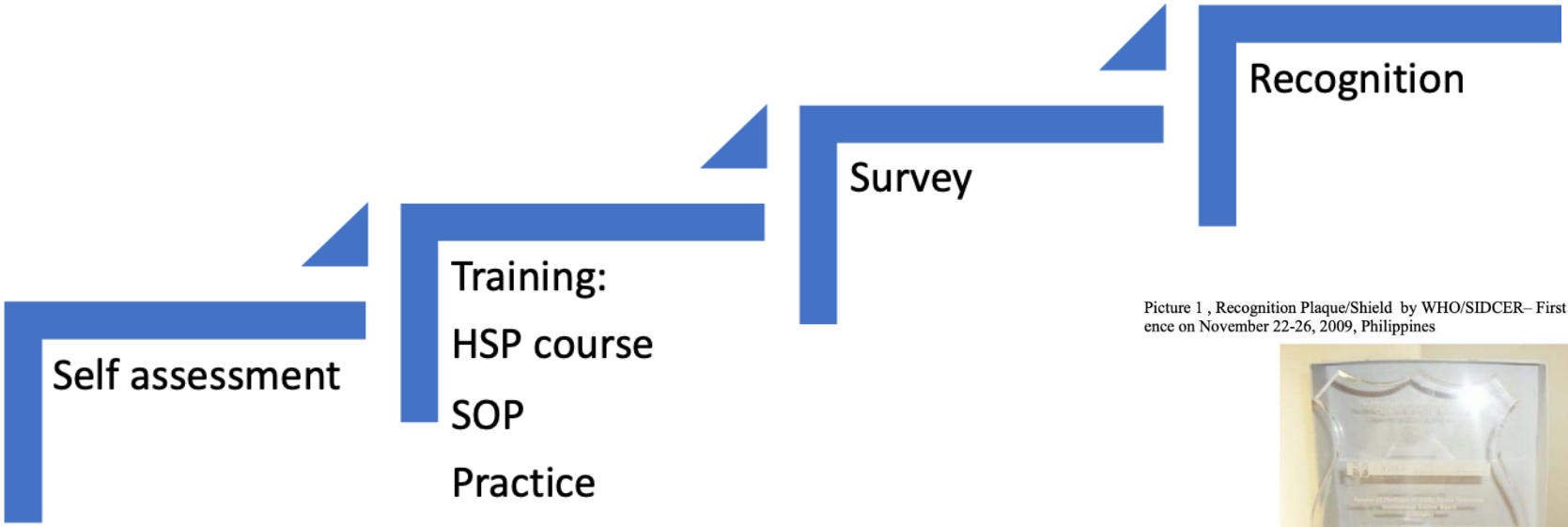
- Operational Guidelines for Ethics Committees That Review Biomedical Research (2000) by World Health Organization (WHO)
- Surveying and Evaluating Ethical Review Practices (2002) by World Health Organization (WHO)
- SIDCER Self-Assessment Tool
- FERCAP Standard Operating Procedures (SOPs) for Ethics Committees





http://www.fercap-sidcer.org/recog.php

SIDCER Recognition Program



Picture 1 , Recognition Plaque/Shield by WHO/SIDCER– First IRB from Africa
ence on November 22-26, 2009, Philippines

Activities That Support EC/IRB Recognition Program

Community engagement

- **Culture of science – community knowledge**
- **Negative rumors – suspicion or lack of trust**
- **Exploitation – fear or suspicion of exploitation**
- **Lack of interest – does not affect me or will not benefit me**
- **Media**

Community advisory Board

Rapid Ethical Appraisal

Adamu Addissie, Gail Davey , Melanie Newport, Bobbie Farsides, Yeweyenhareg Feleke. *Ethiop Med J, 2015, Vol. 53, Supp. 1*

ORIGINAL ARTICLE

FEASIBILITY OF RAPID ETHICAL ASSESSMENT FOR THE ETHIOPIAN HEALTH RESEARCH ETHICS REVIEW SYSTEM

Understanding of research, genetics and genetic research in a rapid ethical assessment in north west Cameroon

Jonas A. Kengne-Ouafo[a,c], James D. Millard[b,*], Theobald M. Nji[c,d], William F. Tantoh[d], Doris N. Nyoh[e], Nicholas Tendongfor[a,c], Peter A. Enyong[a,c], Melanie J. Newport[b], Gail Davey[b] and Samuel Wanji[a,c]

Published in final edited form as:
J Empir Res Hum Res Ethics. 2012 February ; 7(1): 37–52. doi:10.1525/jer.2012.7.1.37.

Tailoring Information Provision and Consent Processes to Research Contexts: The Value of Rapid Assessments

Susan Bull

Tailoring Consent to Context: Designing an Appropriate Consent Process for a Biomedical Study in a Low Income Setting

Fasil Tekola[1,2,3*], Susan J. Bull[4], Bobbie Farsides[2], Melanie J. Newport[2], Adebowale Adeyemo[3], Charles N. Rotimi[3], Gail Davey[1]

Wellcome Open Research

Check for updates

RESEARCH ARTICLE

Rapid Ethical Appraisal: A tool to design a contextualized consent process for a genetic study of podoconiosis in Ethiopia [version 1; referees: awaiting peer review]

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Summary of tasks

- Mobilize researchers to work with policy makers to build research ethics ***systems*** in countries
  - Legal framework
  - Within country and regional forums
  - Academic and research centres – training on research ethics
- Establish/strengthen national accreditation systems and regional recognition mechanisms
  - Within country and regional teams (including surveyor teams)
- Strengthen community engagement
- Secure funding for health research ethics and regulatory capacity building

Thank you for your attention!

Federal Democratic Republic of Ethiopia
Ministry of Health

Examples of time to approval - Ethiopia

- Oral Cholera vaccine trial
  - AAERC: 73 days (10 July – 21 Sept 2011)
  - NRERC: 74 days (25 Sept – 08 Dec 2011)
  - FMHACA: 359 days (15 Dec 2011-09 Dec 2012) (3 recommendations)

- TB drug regimen shortening trial (SimpliciTB, TB Alliance)
  - AAERC: 99 days (27 Mar -04 July 2018)
  - NRERC: 104+ (10 July 2018 – pending….)
  - FMHACA: 89+ (25 July 2018 – pending…)