Meeting Proceedings

National Consultative Meeting on Clinical Trials

CENTER FOR INNOVATIVE DRUG DEVELOPMENT AND THERAPEUTIC TRIALS FOR AFRICA (ሲዲቲ-አፍሪካ)

COLLEGE OF HEALTH SCIENCES, ADDIS ABABA UNIVERSITY

February 8th, 2020

Intercontinental Addis Hotel, Addis Ababa, Ethiopia

ACRONYMS / ABBREVIATIONS

AAU	Addis Ababa university
AHRI	Armauer Hansen Research institute
CDT-Africa	Center for Innovative Drug Development and Therapeutic Trials for Africa
ACT	Advisory Committee on Clinical Trials
CHS	Collage of Health Sciences
CRO	Contract Research Organization
CT	Clinical Trial
CTF	Clinical Trial Forum
CTU	Clinical Trial Unit
EBTi	Ethiopian Biotechnology Institute
EFDA	Ethiopian Food and Drug Administration
EHRA	Ethiopian Health Research Agency
EHRC	Ethiopian Health Research Council
EPHI	Ethiopian Public Health Institute
FMOH	Federal Ministry of Health
GCP	Good Clinical Practice
ICTRP	International Clinical Trials Registry Platform
IRB	Institutional Review Board
MoSHE	Ministry of Science and Higher Education
MoST	Ministry of Science and Technology
NHREC	National Health Research Ethics Committee
NRERC	National Research Ethics Review Committee
PACTR	Pan African Clinical Trials Registry
SIDCER	Strategic Initiative for Developing Capacity in Ethical Review
ToR	Terms of Reference
TRAC	TB Research Advisory Committee
WHO	World Health Organization

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PREFACE

Clinical trials are not a luxury. They are key for building critical evidence base for clinical practice, policy, including rational allocation of limited resources. The current COVID-19 outbreak has demonstrated the crucial role of clinical trials. Clinical trials also contribute to health systems improvement and economic development. However, systematic planning, deliberate investment and capacity building work are essential. The Centre for Innovative Drug Development & Therapeutic Trials for Africa (CDT-Africa) is a very young institution established to build endogenous capacity for drugs, vaccines and diagnostics discovery and development. One of the major responsibilities of the centre is building clinical trials capacity in Ethiopia and Africa. In its medicinal products mapping work, the centre realized that there was an urgent need to improve the clinical trials ecosystem in the country. The establishment of the Advisory Committee on Clinical Trials (ACT) was a direct response to address this gap. In the three months of its life, the ACT had met seven times, completed a relatively largescale primary study and organized a national consultative meeting. The proceedings here come from the national consultative meeting.

Members of the ACT have worked continuously without any personal benefits other than their desire to see clinical trials flourishing in Ethiopia. I am very grateful for their important contribution. I would like to gratefully acknowledge the support of the College of Health Sciences, Addis Ababa University, the Federal Ministry of Health, the Ethiopian Food and Drug Authority and the Ministry of Science and Higher Education. I am also grateful to Professor Eyasu Makonnen, who led the ACT ably to this milestone.

We hope that this proceeding will be read widely, particularly by those who are tasked with facilitating clinical trials in Ethiopia. Those interested to conduct or sponsor clinical trials in Ethiopia would know through this document that Ethiopia is ready to be a regional hub for clinical trials.

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February 8th, 2020

EXECUTIVE SUMMARY

Clinical trials provide the highest level of clinical evidence for policy and healthcare decision making. In addition to the scientific benefits, clinical trials offer opportunities for human and infrastructure capacity building as well as economic development. In Ethiopia, encouraging steps have been taken to lay the foundations for the conduct of clinical trials. Strong frameworks and guidelines have been created for institutional, national and regulatory oversight. The Federal Ministry of Health (FMOH) introduced a clinical trials road map few years ago, an important framework to improve the clinical trials system in Ethiopia. Nevertheless, the number and extent of clinical trials in the country remains extremely low and the current clinical trials ecosystem is not sufficiently conducive to support internationally competitive clinical trials. On account of this, an Advisory Committee on Clinical Trials (ACT) was established with the aim of identifying the critical gaps and barriers for the conduct of clinical trials and explore ways to improve the clinical trials ecosystem in Ethiopia. The Centre for Innovative Drug Development & Clinical Trials for Africa (CDT-Africa), as a regional center of excellence for education and research and as a center committed to clinical trials, has taken responsibility to facilitate the establishment and the work of the ACT.

The ACT requested a study to be conducted to evaluate the existing clinical trials ecosystem to assist an informed discussion and recommendations to facilitate accelerated improvement in the clinical trials ecosystem. The ACT also recommended holding a national consultative meeting with the main goal of bringing together key national stakeholders for consultation.

The national consultative meeting thus aimed to create the platform for national level stakeholders' discussions regarding key barriers related to clinical trials; ways of strengthening the national clinical trials setup and system and finally draw recommendations for future directions to advance clinical trials in Ethiopia.

In this consultative workshop, a total of 31 stakeholders, consisting of focal representatives from the Ethiopian Food and Drug Administration authority (EFDA), National Research Ethics Review Committee (NRERC), national academic and research institutions as well as insurance company and media representatives, participated.

During this meeting, two presentations, describing the overall landscape of clinical trials in Ethiopia, and the result of the primary study, were made. The presentations were followed by a remark of the representative from EFDA. After these presentations, extensive discussion was held around the presentations and the broader clinical trials ecosystem in Ethiopia. The participants put forward actionable recommendations.

The report on the landscape of clinical trials in Ethiopia highlighted that the number of clinical trials registered from Ethiopia was small and that clinical trials registry and contract research organizations equipped with a standard infrastructure were lacking. Detailed SWOT analysis, and strategic objectives entailed in the national clinical trials road map were presented along with general observations and future prospects.

The second presentation of the results of the mixed methods study (quantitative and qualitative studies) confirmed the general observations noted in the first presentation. The quantitative study involved a total of 212 participants from three regions comparatively active in clinical trials.

Among the main findings of the quantitative study were: the time taken to get ethics and regulatory approval was unacceptably too long; most clinicians were not participating in clinical trials and, in fact, most were not aware of clinical trials that were actually happening in their institutions. Although majority of the trials were registered, publication rate was small. In view of these, awareness raising and capacity building activities; and mainstreaming of clinical trial approval are warranted.

In the qualitative study, numerous strengths of the ethics and regulatory bodies were noted. Investigators stated the relative ease of finding trial sites, patient recruitment potential and recent interest of insurance companies as main opportunities.

Three groups of key challenges delaying approval were identified:

1. Limited resources—(a) limited number and capacity of reviewers and secretariat, staff turnover); (b) infrastructural (inadequate working and archival space for reviewers, lack of space and GCP/GCLP compliant infrastructure in health facilities and stable IT set-up); (c) finance and administrative (finance-lack of designated institutional budget, inability to use budget due to bureaucracy; administrative redundancy and hierarchy of review system, absence of web-based submissions, import delays and goods handling failures at customs and institutional financial management, procurement and personnel recruitment insufficiencies).

2. Ethics and regulatory processes: weak screening system of protocol, late response of reviewers, work overload, delay in settling service fee and ambiguity of clinical trial definition;

3. Investigator related: incomplete submissions, low protocol quality, delay in responding to the reviewers' comments and engagement in risky trials

Following the presentations, the EFDA representative highlighted the recent improvements implemented by the authority. These improvements included: restructuring as a separate clinical trials directorate, permission of parallel submission with national ethics committee, working to attain higher standard regulatory maturity level and plan to improve service fee charge.

Following extensive discussion after the presentations, participants of the national consultative meeting made implementable recommendations as summarized below.

› ACT to be a national advisory committee hosted within CDT-Africa and supporting the work of the EFDA.

- Establish national clinical trials network
- Compile institutional capacity profile
- Find ways of fast-tracking clinical trial protocol approval systems
- Engage with insurance companies and provide training
- Strengthen capacity on clinical trials through short courses
- Promotion of clinical trials for health professionals and the public
- Revision of national guidelines (currently in progress)
- Finding ways of adequate clinical trials financing
- Strengthening data management centers
- Preparation of a data sharing act
- Support the update and implementation of the national clinical trials road map and
- Support preparation of the legal framework for clinical trials
- Revise the service charge for regulatory approval

The ACT was delegated to follow these recommendations up, including compiling institutional capacity and establishment of clinical trials network.

INTRODUCTION AND OBJECTIVE

Ethiopia, a country with an estimated population of 114,026,274 and ranked the 14th most populous country in the world, has the potential to be one of the leading clinical trials research hubs globally. The huge burden of communicable diseases that has not yet been addressed and the increasing burden of non-communicable diseases not only make the country attractive for clinical trials, but it also calls for new treatments and healthcare delivery innovations. Clinical trials could offer an opportunity for innovative approaches to address these problems. However, the number of clinical trials contributed by Ethiopia overall remains small. Ethiopia represents 0.38% of trials conducted worldwide and lags well behind its neighbors, Kenya, Uganda and Tanzania.

There is also underrepresentation of trials addressing specific priority health problems for developing countries: just 10 of 1556 new drugs produced in the past 30 years were targeting conditions prevalent in developing countries. Moreover, the limited number and capacity for clinical trials in Ethiopia has meant that national policy and practice has not been informed by local evidence. Most national guidelines and treatment strategies were based on international guidelines. This has significant health and economic implications.

There is now better awareness of this gap about the need to use the opportunity for conducting clinical trials in Ethiopia. There is also a growing interest of pharmaceutical industries and global trial institutions to engage Ethiopia in clinical trials owing to its enormous research potential: population, growing number of clinical scientists and researchers, diversity of diseases including cancer and non-communicable diseases (NCDs), patient recruitment potential, and lower trial costs. Although requiring further strengthening, Ethiopia also has ethics and regulatory system for safeguarding its population. Ethiopia could benefit from this opportunity in many ways. (1) The requirement for the availability of a basic standard of care would encourage improvement in the health system; (2) practitioners would receive training that improves their skills; (3) patients may have opportunity to access treatment that otherwise may not be available for them; (4) the economic potential is also untapped.

However, although tractable, there are numerous challenges that have not attracted trialists, contract research organizations and the pharma industry to take advantage of the opportunities Ethiopia offers. The low human capacity for conducting clinical trials, the efficiency of ethics and regulatory boards, the inadequacy of infrastructure, including laboratory facilities, are some of the challenges. The human capacity concern is being addressed through various training programs, one of which is the masters in clinical trials training offered through CDT-Africa. A new ethics training program is also being started by partners at Addis Ababa University. Three years ago, the FMOH initiated the clinical trials road map, an important framework to improve the clinical trials system in Ethiopia.

Prof. Asrat's presentation was titled, 'Clinical trials in Ethiopia, Bird's Eye View, and Discussion on Prospects for Transformation'.

OPENING REMARKS

The meeting was started at 9:40 AM by the welcoming address of Professor Eyasu Makonnen. He also extended the apology of H.E. Dr. Lia Tadesse, state minister, FMoH, who was expected to attend this consultative meeting and give an opening speech. Following this Professor Eyasu invited Dr. Yimtubezinash Woldeamanuel, the lead of the incubation centre, the Africa Bio-Hub and the Regulatory Affairs unit of CDT-Africa, to give an opening remark to the participants on behalf of CDT-Africa.

Dr. Yimtubezinash again welcomed the participants and briefly introduced the process of the formation and the purpose of ACT. The ACT was established, first as an initiative of CDT-Africa, together with EFDA, NRERC, Armauer Hansen Research institute (AHRI), Ethiopian Public Health Institute (EPHI), about four months earlier in recognition of the challenges of conducting clinical trials as part of its mandate for building clinical trials capacity and interactions with contract research organizations and industry with interest to conduct clinical trials in the country. The representation of these institutions in the ACT was only as a first step to facilitate the initial discussion. It was not practical to invite institutions from the region at the beginning. The consultative meeting was one of the recommendations of the ACT. Leading up to the national consultative meeting, the ACT had met seven times in the previous three months to prepare for the consultative meeting. The second recommendation by the ACT was for CDT-Africa to carry out a mixed methods study to assess the clinical trials ecosystem in Ethiopia. The purpose of the consultative meeting was to explore ways of working effectively together (at the national level) to solve the practical challenges encountered in conducting clinical trials based on a report of the findings of the study. The other recommendation was for a presentation on the background to clinical trials, including on national opportunities through conducting clinical trials.

After the brief opening remark, Professor Eyasu led the introduction of the participants, which demonstrated that most of the institutes engaged in clinical trials were represented in the consultative meeting. Then, as per the agenda set, He invited Professor Asrat Hailu, Diagnostics and Neglected tropical Diseases (NTD) lead of CDT-Africa, to present the global, regional and local landscape of clinical trial.

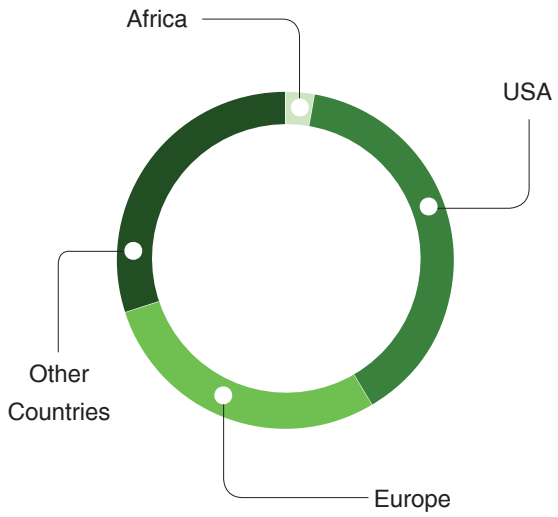
PRESENTATION I: CLINICAL TRIALS IN ETHIOPIA, BIRD'S EYE VIEW, AND DISCUSSION ON PROSPECTS FOR TRANSFORMATION

Professor Asrat started his presentation by reiterating how ACT has come to existence. He mentioned the presence of prior efforts to promote clinical trials in Ethiopia by the FMOH and that his presentation was partly based on the roadmap developed through that initiative. He also acknowledged the effort of CDT-Africa in revitalizing clinical trial promotion and creating this platform.

He then continued his presentation by giving a highlight of what clinical trial is, which in its broader sense means testing of any intervention on human beings before gaining approval for clinical use. It is the ultimate activity of discovery, innovation and translations of drug/intervention. However, countries which are economically weak tend to adopt and adapt interventions and employ interventions developed in high income countries for use in their setting, however, clinical trials are still critical to adapt the intervention to the context of the country.

Prof Asrat indicated that, as part of previous initiatives, it was recognized that there were gaps and that there was a great need for transforming the conduct of clinical trials. Then he defined the term transformation in the context of clinical trials as a "substantive change in quality and quantity of clinical trials"; quantity referring the numbers of trialists, investigators, monitors, ongoing trials, Contract Research Organizations (CROs), Clinical Trial Units (CTUs), Randomized Clinical Trials (RCT) publications, volume of funding/sponsorship, while quality may refer to accreditation, registration, publication, etc.

When referring to conduct of clinical trials, capacity required from researchers, sponsors and the industry overall are in terms of ease of recruiting patients; ease of recruiting qualified medical staff; research ethics review capability; efficiency of regulatory processes, the standards of care; medical resources/facilities; availability and applicability of data (demographic, genetic, cultural, etc.) and the market potential.



According to the percentage of registered clinical trials (clinicaltrials.gov) by region, out of 338,111 studies overall, nearly 39% are registered from the US, with only 3% originating from Africa. While Ethiopia is ranked 12th by population size in the world, its share of clinical trials is a mere 0.04%. Within Africa, the share of clinical trials contributed by Ethiopia is also comparatively small (Table 1).

Table 1: *Clinical Trials in Ethiopia in Context*

Country	Number of trials registered	Country	Number of trials registered	Country (Africa)	Number of trials registered
USA	128,383	Russia	4,787	Burkina Faso	145
France	24,203	India	3,922	Ghana	171
Canada	21,374	Philippines	965	Nigeria	173
Germany	19,337			Malawi	236
UK	17,961			Uganda	540
China	16,394			Kenya	475
South Korea	10,675			Ethiopia	150
Israel	7,477			Tanzania	343
Japan	5,775			South Africa	2,739
Netherlands	9,331			Egypt	3,735

Clinical Trials Registry

Many international and national trial registries are available (Table 2). The well-known ones are the US Clinicaltrials.gov, WHO's ICTRP and the pan African registry, PACTR. There was a plan to have Ethiopia based registry (CTRET), which has yet to materialize.

Clinical Trials (CT) Registries	
International Clinical Trials Registry Platform, ICTRP World Health organization (WHO)	Iranian Registry of CTs
Pan African Clinical Trials Registry, PACTR (Pan African)	Philippines Health Research Registry
	Sri Lankan CTs Registry
Clinicaltrials.gov (USA)	Thai CTs Registry
Health Canada CT Data Base	Brazilian Public Cuban Registry of CTs
	Peruvian Registry of CTs
EU CT Registry	
German CT Registry	Nigeria Clinical Trials Registry (NCTR)
Netherlands Trial Register	Tanzania CTs Registry of Tanzania (TzCTR)
Swiss National CTs Portal	South Africa national CTs Register (SANCTR)
ISRCTN (UK)	Egyptian?
Australian New Zealand CTs Registry	
Chinese CT Registry	
India CTs Registry	
Japan Primary Registry Network	
Clinical Research Information Service- Korea	C'TRET [Clinical Trials Registry of Ethiopia]

Prospects of Transforming Clinical Trials in Ethiopia

Prof Asrat then described the prospect of transforming clinical trials ecosystem in Ethiopia using a Strength, Weakness, Opportunity and Weakness (SWOT) analysis that was conducted as part of the Clinical Trials (CT) Roadmap work.

Strength	Weakness
1. Existence of frameworks for Institutional and national ethics review 2. Strategic Initiative for Developing Capacity in Ethical Review (SIDCER) recognized Institutional Review Boards (IRBs) (College of Health Sciences (CHS)-Addis Ababa university (AAU), ALERT-AHRI, EPHI-IRB) 3. Existence of a regulatory framework (EFDA) 4. Expanding specialty trainings in medicine and related fields 5. Improved health systems, including alternative financing/health insurance 6. Growing private health sector	1. Absence of accreditation mechanism for IRBs & CT Facilities/Institutes 2. Limited experience in CT management (CTU, CROs) 3. Limited #s and experience of investigators in CTs 4. Ineffective grant management by academic institutions 5. Sponsorship issues 6. Limited experience of the private sector (commercial IRB, CROs, insurance companies, etc.) 7. Unpredictable prospects of innovation 8. Tight curricula of medical schools limiting the space for CT module 9. Absence of laws concerning health research 10. Limited number of CT sites/facilities (Ph I – III, Labs, CTUs, etc.) 11. Funding (local)
Opportunities for transformation	**Threats**
1. Mentor institutions: CT MSc Program/PhD in Translational Medicine 2. Trainings in bioethics, ETBIN 3. Increasing interest in CTs 4. CDT-AFRICA	1. Medics staying away from medical research/CTs 2. Globalization, and competition by international CROs 3. Misinterpretation of CTs by community/media 4. Bad rapport in ethics/regulatory review and oversight processes

In relation to strategic objectives:

Prof Asrat described the strategic objectives contained in the clinical trials road map, which also has relevance to transforming clinical trials in Ethiopia.

- To re-define health research policy, and to enact laws governing health research
- To establish the Ethiopian Health Research Council (EHRC)
- To enunciate the policy and legal frameworks governing the conduct of CTs in Ethiopia; and to revise the institutional frameworks of ethics review
- To redress the ethical and regulatory processes governing CT protocol review and oversight mechanisms with the intent of mitigating hurdles and flaws of the current set-up
- To assist in upgrading the human and infrastructural set-up of tertiary level medical schools/medical research centers so as to build capability in clinical trials
- To define and outline legal and corporate business provisions guiding CT operations involving CROs and insurance companies
- To create an interactive educational and information exchange forum between actors (academia, Institutional Ethics Committee (IEC)/IRBs, regulatory bodies, sponsors, patient groups) and stakeholders (pharma industry, Product Development Partnerships (PDPs), community, mass media, lawmakers) of the CTs industry
- To put in place mechanisms that enhances transparency of CT undertakings and sharing of CT information and data through a national registry of CT protocols

Barriers to conducting clinical trials

Based on a recent systematic review prof. Asrat mentioned several barriers for conducting clinical trials

No	Barriers for conducting clinical trial	
	Thematic barriers	**Sub-themes**
1	Lack of financial and human capacity	Lack of funding Lack of skilled personnel Lack of awareness and motivation
2	Ethics and regulatory system obstacles	Delay of approval decisions Unskilled authorities Complex and strict ethical and regulatory system
3	Lack of research environment	Lack of infrastructure Lack of research materials/facilities Lack of conducive scientific atmosphere
4	Operational barriers	Unsupportive administrative system Lack of/difficult patient recruitment
5	Competing demands	Lack of time Other competing priorities

General Observations

1. Policy & statutory gaps;
   - [absence/incomplete guidelines, laws missing, directives non-existent]
     - Health Research Policy/Health Research Act needed
2. EHRC, needs establishing/strengthening
3. Questions about appropriateness of institutional framework for NHREC (National Health research Ethics Committee)
   - NRERC vs. NHREC; Ministry of Science and Technology (MoST) vs. FMoH; other options?
4. Current research ethics review and oversight mechanism is unresponsive to expanding medical research needs
   - Lacks dynamism (no possibility of cross-talk)
   - Redundancy, overlaps
   - Emphasis on review; some oversight by EFDA
   - Multiple points of entry, and reporting with different schedules
     - much of it is paper work; i.e., approvals, reports
     - no differentiation of protocols according to risk
5. Research Support Systems (administrative):
   - Public sector (CTUs in Universities/RCs, MoST, FMoH)
   - Private medical schools/hospitals (CTUs/support)
   - Commercial businesses in medical research (insurance, CROs)
6. CTs Stakeholders Forum (academia, IRBs, Others)
   - Prof Asrat acknowledged the role of CDT-Africa by stating “Thanks to CDT-AFRICA, we are here on the first meeting of the “Forum”

Policy and Regulatory Recommendations

Prof Asrat offered the following recommendations;

1. Establishment of EHRC under FMoH or under independent agency (EHRA; Ethiopian Health Research Agency)
2. FDRE’s Health Research Policy/Law/Regulations would have the following roles;

Designates & entitles authorities and agencies

- Health Research Ethics directives
- Health Research biosafety and biosecurity
- Role of public & private sector in clinical research
- Guidance on the terms of domestic & Intl CRO businesses
- Research and its ethics in herbal remedies/traditional medicine
- Health Research coordination, data base, etc.
- Health Research Insurance

3. CT ethics review: one-step rigorous review (e.g., Joint Review Schemes)
    - » embrace risk-adapted strategy
    - » CT mentors for IRB secretariat
    - » Fees for ethics review
    - » Good Clinical Practice (GCP) accreditation/certification for IRBs
    - » Guidance on patient compensations/payments
4. Establish centers of excellence (CTUs, clinical research infrastructure [Ph. I/II], etc.). Roles would include;
    - » Capacity building
    - » Post graduate curriculum/thesis
5. Domestic CT insurance schemes (Ethiopian Insurance Companies)
6. Establish C'TRET: Clinical Trials Registry of EThiopia (on-line register)
    - » Interim: CDT-AFRICA, Ethiopian Academy of Sciences (EAS), EFDA
    - » Final: EHRC (FMoH, EHRA?)
7. Public Dialogue (ethics, compensations, legal issues, consents/assents)

    (education, sensitization, engagement, etc.)

8. Endorse the formation and establishment of Clinical Trial Forum (CTF), and obtain the endorsement of the ACT by stakeholders
    - » Agree/Endorse to the suggestion that CDT-AFRICA serves as the host of CTF (seek institutional endorsement)
    - » Revise and endorse the Terms of reference (ToR) of the CTF
    - » Re-draw the agenda and strategic objectives of CTs transformation
9. Highlight future direction

Before the next presentation, Professor Eyasu re-emphasized the purpose of ACT and how it was organized to serve its purpose. He also mentioned how ACT will work in the future and what the contribution of each individual stakeholder would be. That the ACT has been established by members from institutions within Addis Ababa for practical reasons; but the intention was to include the regional partner institutions in the future. When ACT took this initiative, rapidly assessing the existing situations of the clinical trials ecosystem was believed to be an input for this consultative meeting. Following this brief emphasis, he invited Dr. Abebaw Fekadu to present the result of the rapid assessment made by ACT.

PRESENTATION II: THE CLINICAL TRIALS ECOSYSTEM IN ETHIOPIA

Dr Abebaw first offered additional background to the study he presented. He described three reasons behind the decision to conduct the study:

1. **The clear gap in clinical trials not just in Ethiopia but across the region:** CDT-Africa completed a medicinal products mapping study in 2018 (www.cdt-africa.org). This study in 9 African countries representing 25% of the population of Africa demonstrated that very few registered clinical trials were being carried out in Africa. This was particularly the case for diagnostics, vaccines and devices (Figure below taken from the report). It was then necessary to understand why this huge gap existed. Part of this exploration was understanding the opportunities, barriers and facilitators for conducting clinical trials.

	Drug	Diagnostic	Device	Vaccine	Others	Total
Burundi	1	0	0	0	0	1
Ethiopia	36	2	0	1	62	101
Kenya	91	2	16	18	228	355
Malawi	78	0	5	5	33	63
Rwanda	15	4	6	5	33	63
South Sudan	0	0	0	0	0	0
Tanzania	97	1	17	23	100	238
Uganda	140	3	12	14	192	361
Zambia	36	0	15	6	96	153
Total	**494**	**12**	**71**	**72**	**795**	**1444**

[Source: www.cdt-Africa.org; based on data from www.clinicatrials.gov]

2. **Responsibility as a clinical trials capacity building institution:** CDT-Africa was established for building endogenous capacity for medical discovery and development with clinical trials and regulation as one of the key pillars. Recognizing the clinical trials opportunity these graduates offer, the centre believed that improving the clinical trials ecosystem was necessary. CDT-Africa believed that it may need to support promotion of clinical trials as part of its responsibility in addition to building capacity.
3. **Recommendation of the ACT:**
    - The ACT recognized the need to have a better understanding of the capacity for conducting clinical trials in the country and exploring the experience of conducting clinical, the ethical and regulatory opportunities and challenges through a rapid assessment using a mixed methods approach.

» The ACT recommended holding a national consultative meeting during which findings of the rapid assessment could be presented and mechanisms on how to improve the clinical trials ecosystem, particularly strengthening the ethics and regulatory frameworks could be discussed.

Following this Dr. Abebaw presented details on the objectives, methods and results of the rapid assessment made by the ACT.

Objectives:

The main objectives of the study were to obtain a clearer understanding of the clinical trials ecosystem through:

1. A rapid assessment of the experience of (physicians) participating in clinical trials
2. Exploring the barriers, challenges and opportunities for participating in clinical trials
3. Improve understanding what should be done next to strengthen clinical trials and ethics review processes.

The study was of a mixed-methods design consisting of a cross-sectional survey and qualitative studies. In the cross-sectional study, physicians working in three university hospitals (Gondar, Jimma, Tikur Anbassa) were included through a convenience sampling approach. The hospitals were selected based on the number of clinical trials registered from these hospitals. The physicians were recruited in two ways: those who had experience of conducting clinical trials identified through registries or personal knowledge were all included. Those not in that list were approached through selected departments. A self-completed questionnaire explored participation in clinical trials, regulatory processes and interest to conduct or continue to conduct clinical trials. The initial target was to recruit 212 participants.

The qualitative study targeted four groups of participants: (1) investigators (with history of involvement in 3+ clinical trials), (2) those in ethics boards with SIDCER recognition or regulatory approval position, (3) those with responsibility to lead or facilitate research at the level of institutions and (4) insurance.

Quantitative study

Questionnaires were distributed to 354 physicians in the three institutions. 213 returned completed questionnaires with overall response rate of 60.2%, which ranged from 55.2% to 71.6%. Of these 40 (19%) had participated in clinical trials. The distribution was identical between male and female physicians. While this participation rate by physicians is acceptable (e.g., Taylor 2004), most physicians (80.0%) had participated only in one or two trials. Thus, experience and expertise are not built. While about 3 in 4 clinical trials are registered only half of the investigators had published their trials. Virtually all of physicians are interested to be involved (98%) or continue to be involved (97.5%) in clinical trials. Nevertheless, only 17% of physicians knew there was any clinical trial in their institution.

Ethics committee involvement other than the mandatory NRERC and EFDA varied between one and six, with most having reviews by one or two boards. Time to approval varied between 1 and 24 months. The longest average duration was 12.2 months.

Physicians who participated in clinical trials offered various reasons for delay in obtaining approval; the following were presented:

List of reasons given by participants for delay in approval
' Unnecessary' delays from responsible bodies and custom clearance
Capacity of staff of authorities and IRBs
Approval process at EFDA and National Committee (Ministry of Science and Higher Education (MoSHE))
Approval of study drug importation took more than a year
Approval sought from different unrelated institutions
Delay in initial review & review of response documents
Delay in IRB (office closed, no answer to phone calls, frequent change in responsible personal, not having frequent meeting they meets only once in a month)

Conclusions from the cross-sectional study

- Overall, percent of physicians participating in clinical trials is ok—generally physicians do not participate in clinical trials in large numbers. But the participation of physicians in Ethiopia seems inefficient---most do not get opportunity to acquire sufficient expertise by being part of multiple clinical trials. This needs to be encouraged.
- Proportion of female physicians participating in clinical trials is also encouraging although the overall number of female physicians in these university hospitals, at least who participated in the study was relatively small.
- Virtually all physicians would like to be involved in clinical trials. This calls for capacity building effort.
- Although most clinical trials are registered, more needs to be done to ensure all clinical trials are registered.
- Time to approval is long but was shorter than expected. Lessons may be drawn from studies with shorter approval latency These suggest that the time to approval could be substantially shortened; clinical trial approval procedures can be more mainstreamed
- Actual number of trials is very small undertaken in these three institutions is generally very small. (Measures need to be taken by institutions to change this.)
- Publication of Trial findings should be improved
- Awareness raising and capacity building work by the institutions about clinical trials being conducted is crucial.

Qualitative study

Relied on in-depth interviews of 17 participants: investigators (n=6), ethics review board members (8), regulatory authority (n=2) and insurance (n=1). Most participants have many years of experience (5+ years) in clinical trials.

Table 2: *Characteristics of participants in in-depth interviews*

Characteristics	Number	Percent
Gender		
Female	5	29.4
Male	12	70.6
Qualifications		
MD	2	11.8
MSc	6	35.3
PhD	9	52.9
Year of experience in clinical trials		
1-5	5	29.4
6-10	5	29.4
11-15	3	17.7
>15	4	23.5

Themes

Four themes were identified:

Theme 1: Motivation of investigators to conduct clinical trials

Theme 2: System of clinical trial approval

Theme 3: Challenges, strengths and opportunities for clinical trials

Theme 4: Improving the clinical trial ecosystem

Theme 1: Motivation

Motivation of participants to be involved in clinical trials in any of the roles were mostly pragmatic and were summarized in eight headings.

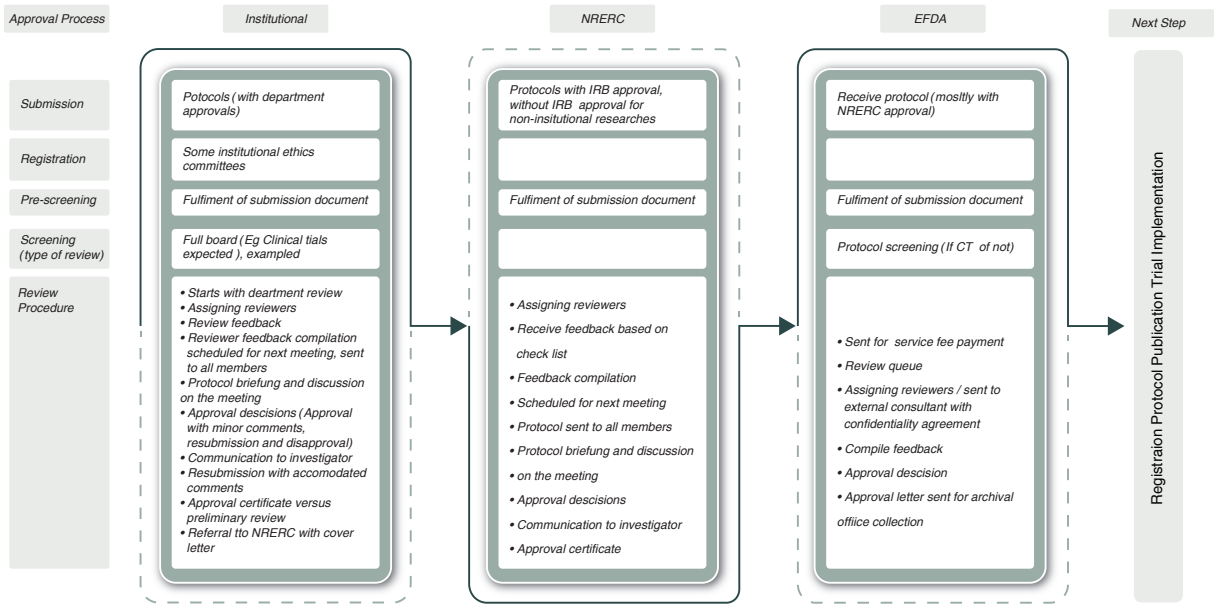
1. Impact of clinical trials in changing policy
2. The opportunity clinical trials offer for building capacity (Emphasis on Human capacity)
3. The problem-solving nature of clinical trials; ability to offer treatment opportunities where gaps existed.
4. The result ("your ability to get high level/ valuable result, gratifying")
5. Clinical trials are an intersection between research and patient care: unlike other research approaches it gives the opportunity for the clinician to combine clinical and research practice
6. Ability to produce country specific/locally relevant evidence through clinical trials

7. Opportunity for holistic knowledge (finance, patient management, administrative)
8. The challenging nature of clinical trials

Theme 2: "The System"

Was related with to the mandate of approval agencies, level of approval, procedures, strengths and opportunities in the approval system.

Approval levels and processes were represented in the diagram below.



Theme 3: Challenges, strengths and opportunities for clinical trials

Subtheme: strengths & opportunities

- Many strengths of clinical trial ethics review committees and the regulatory authority were mentioned that enabled these agencies meet the demanding nature of clinical trials
- International recognitions (e.g., WHO SIDCER recognition. Two IRBs have received such recognition and one is in the process of receiving one)
- These IRBs and agencies provide training and refreshers for members
- Guideline/ checklist and Standard Operating Procedures (SoPs) are available for submission to boards and EFDA
- Motivated and committed members to serve as ethics member irrespective of compensations
- Member composition: most committees have representation fulfilling international standard (Gender, Age, professional multi-disciplinarily) + community representative
- Generalists are highly motivated and show strong effort to build their knowledge they

feel they need to know more through area specific reading (or other mechanisms)

- Most boards have senior/experienced members in research who can answer researchers' question
- National oversight bodies were acknowledged by investigators for their openness
  - "We are following up the progress of our protocol approval using personal email and cell phone of EFDA and NRERC staff. They are okay to be contacted by telephone ...I think this is positive thing" CTI005
- Creating the opportunity to discuss with investigators for further clarifications of protocol e.g., in case of regulatory authority
- HR resources may be limited but IRBs and regulatory bodies] handle responsibilities as per mandate with the available HR resource
- One of the ethics committees has alternative committee members so that meetings will not be cancelled
- Support from institutions/general director
- Most secure grants/external funds for capacity building or work in collaboration with external projects; have established connections and working with other countries universities and ethical bodies
- Authorities buy in almost secured towards restructuring to strengthen clinical trials regulation
- Availability of advanced trainings on clinical trial (at master's level)
- Availability of online training courses
- Ease of finding trial site
- None experienced problems related with patient recruitment and consenting.
- In the past 2 years: interest from local insurance companies to provide insurance cover for clinical trials has been extremely difficult to find insurance coverage for investigator initiated clinical trials. Virtually no local company had shown interest until recently or required exorbitant amount of payment. Many such clinical trials have to purchase cover from Europe, e.g., France and recently from South Africa.

Subtheme: Challenges

Challenges were described in five subthemes:

- Human resources
- Infrastructural
- Finance related
- Administrative system
- Approval delaying factors

Subtheme 1: Human resources (challenges related to human resources for review and administration)

- All indicated that the ethics and regulatory authority offices have significant HR problem such as;
  - Limited number of reviewers for protocol review and for conducting regular monitoring/

inspection.

- + "Reviewing takes a lot of time and so … we take our spare time...for me, I always need extra time to read or review a protocol. Since I don't have a dedicated time for my IRB related duties I am always obliged to work after regular working hours ... that is the same for all reviewers." ECC001

› Lack of expertise to review some areas of clinical trials.
› Number of secretariat staff is also insufficient and not proportional to the workload
  + Weak capacity of secretariat (unattractive incentive (in government systems) and difficulty to employ experienced and competent staff)
    - "IRB without a good secretariat is weak and inefficient in a sense that you know as investigator when you visit the office there should be somebody to discuss to and provide appropriate information when you submit your protocol ....in addition, someone who is capable of communicating reviewers feedback ... ." ECC01
  + Frequent staff/secretariat turnover and inability to build the capacity responsive to the frequency of staff replacement due to other competing responsibilities of higher administration in government structures
    - "There is very high staff turnover in our IRB […] when we went to the IRB office to check the progress of our protocol review we will not get them...most of the time we will get their telephone number from the former staffs...the turnover is very high…you are supposed to explain your issue many times" CTI005

Subtheme 2: Infrastructure (challenges related to space, power and network)

› Almost all have inadequate working office space or archival space
› Unreliable electric power supply
› Erratic internet network
› Lack of space in the health facilities (trial site)
› Difficulty to get Good Clinical laboratory Practice (GCLP) compliant laboratory in the health facilities

Subtheme 3: Financial Resource (Challenge related to budget allocation and budget use)

› There are ethics committees who don't have institutional budget
› Budget is often allocated from the government but, in some cases, it is not adequate owing to shared allocation with other case teams other than clinical trials.
› There are cases where it was not possible to use budget allocated from treasury as well as revenues from service fee which is designated for the purpose of contracting external consultants.

Subtheme 4: Administrative system

› Currently there is no web-based submission system and checklist
› The sequential nature or reviews (department ethics —› institutional IRB —› NRERC

—› EFDA) or lack of harmonized approval system is indicated as daunting and time consuming. Clear procedural redundancy in ethics approval was noted. Particularly when the trial is a multi-center, approval is required from all the ethics committees and no recourse is available at the moment to cut this short.

- *" This is an important point a mixture of two things there is improvement [in the overall process of ethical approval/ authorization] for example my recent clinical trial approval process was relatively good … but the whole process of hierarchical nature or the steps of the approval process is cumbersome parallel submission is not allowed as you know getting institutional support as well as approval is mandatory and not encouraging" CTI 001*
- "To put it simply, the process is cumbersome...the ethical clearance process is challenging as well as tiresome. It is obvious that there [are] some requirements since this [clinical trial] is different due to this we have to meet the criteria and pass through complex and challenging process" CTI004
- Other investigator has also shared his experience by saying;
- "The ethical approval works at different level. As to my experience the process begins at institute level then to science and technology and finally to EFDA ...the process almost took six months...it is all about identifying the requirement and fulfilling what is needed but there are some challenges" CTI 002

› *All investigators have the experience of importing investigational products.*
  » The process was reported to be challenging by most.
  » Acquiring the pre-import permit is smooth but, the challenge is mainly at customs making sure that the cold chain and other storage requirements is maintained (One investigator mentioned that: '"Acquiring the pre-import permit was smooth but, the challenges is mainly at customs making sure that the cold chain and other requirements for the investigational product storage and transport owing to the sensitive nature of some investigational products was stressful.")
› Administrative procedures were huge challenge for participants from higher education institutions.
› Financial management,
› Procurement and
› Personnel recruitment

Subtheme 5: Approval delaying factors

A. Ethics and regulatory authority factors
  » Weak screening system of protocol and required documents which leads to incomplete submission
  » Late response of reviewers
  » Work overload
  » Delay in settling service fee
  » Investigators poor follow up of the review progress
  » Ambiguity of clinical trial definition

B. Investigator related factors
    - » Incomplete submission
    - » Protocol quality
    - » Mistimed submission (submitting close to IRB meetings when time is too short to process the review for the upcoming meeting)
    - » Delay in responding to the reviewers' comment
    - » Types of the trial (trial considered to be risky; more broadly trials considered risk irrespective of the type of trial)

Other challenges--Insurance

- › Interest of insurance companies remains low (and current initiatives are driven by company personnel rather than company itself)
- › Limited capacity of risk evaluation
- › Often risk overestimated
- › Dependent on evaluation from partner international organizations
- › "[This work] has not been promoted. Those with training, the physicians, if there are opportunities of this nature, they should push/advocate so that the industry would benefit and the country would benefit..."
- › "There is opportunity but we have not worked on it" "We are losing a big opportunity" ..." This is embarrassing as a country"

Theme 4: Improving the clinical trial ecosystem

- › Participants recommendations for improving the overall clinical trials environment was as follows.
    - » Harmonization of ethics and regulatory approvals
    - » capacity building for reviewers on emergent topics of clinical research such as genetic studies
        - + "In my opinion there is no adequate capacity to review clinical trials. I have a feeling that we need more capacity building in this area as well as update ourselves because the field of research is growing. Especially a lot now new things come in the area of genomics and so on... So there is a need for capacity building in this area." ECC01
    - » Ensuring ongoing research ethics capacity building trainings for staffs
    - » Capacitate institutional IRBs to take care of protocol approvals at their level to avoid review redundancy and the NRERC to take more of a capacity building role (check who members of the committee are, how they are doing, how many trials are being handled, solve their problems).
- › Improving physical infrastructure
    - » Designated office and archival place
    - » Better IT infrastructure
    - » Electronic submission as well as follow up platform
- › Improve stakeholder's communication/information exchange
- › Improve amount and ways of institutional budget allocation

- Incentivizing IRB members (time compensation payment, recognition of contribution and training)
- Annual internal self-auditing
- Clinical trials electronic registration
- Restructuring directorates to exclusively focus on clinical trials
- Organizing independent advisory committee, by consultants from academic institutes
- Academic institutes should provide capacity building support for different areas of research
- Need to benchmark other similar partner oversight institutions and work with them collaboratively
- Engagement with more insurance companies
  - Run a discussion platform with insurance companies asap (CDT-Africa can facilitate this with the companies that were represented)
- Build capacity
- Local risk evaluation scheme
- *"A one-week training"*
- *"Should be developed as a product"*
- *"Should be pushed as a nation, as a sector, as industry"*

Conclusion

There are strong foundations and opportunities to conduct clinical trials in Ethiopia. To harness this opportunity, stakeholders need to work on the main challenges namely

- Delay in the approval process
- Expensive regulatory service fee (individualize)
- Building clinical trials capacity,
- Awareness creation,
- Address structural issues at national and institutional level

Following Dr. Abebaw's presentation, Professor Eyasu thanked the research team members for accomplishing this task within short period of time. Then he invited Mrs Asnakech Alemu, EFDA representative, to deliver her institutes perspective.

REMARKS BY EFDA

Mrs. Asnakech in her part thanked the ACT for facilitating this consultative meeting and pointed out new developments in EFDA. GCP and clinical trial authorization guideline have been developed and implemented by EFDA. Restructuring and strengthening of the clinical trial screening system has solved previous complaints of inappropriate service fee as it allowed pre-screening and review of protocols to be handled at a single office. She thanked CDT Africa for the support it is providing with regards to human resource capacity development through its MSc Program.

On the other hand, Mrs Asnakech acknowledged the problems associated with the regulatory

approval. The problems of the regulatory approval as well as the need for the transformation of the process and procedures are already acknowledged at the level of the authority and some directions are identified. These include restructuring as a separate clinical trials directorate and is currently awaiting approval by council of ministers.

To improve the situation, EFDA has now accepted a parallel submission with that of NRERC shifting from the previous sequential approval system. The other is in terms of improvement of transparency, where discussion with applicant investigators is being entertained. As per criteria for maturity level of regulatory bodies, EFDA is currently working towards maturity level three. Regarding the review fee, she acknowledges the difficulty it poses to researchers and the draft proposal made by the ACT is being reviewed by all stakeholders and a draft including this amendment will be prepared and commented up to April for approval. Challenges encountered from applicants' side were also indicated mainly in terms of fulfilling regulatory requirements, which usually results in rounds of feedbacks. It was also indicated that clinical trials that are being conducted without regulatory authorization has emerged overtime. There is a plan to have a surveillance team under the new directorate. It was identified that it is usually from lack of awareness of the regulatory requirements. Therefore, awareness creation is one element that need to be worked out.

Promotion to fill gaps related to awareness of regulatory requirements, as well as awareness creation to clinicians/physicians to be engaged in clinical trials is proposed as a recommendation.

DISCUSSION SESSION

After the tea break the discussion was continued with question and answering session. Again, the session was facilitated by Professor Eyasu and the three presenters, Professor Asrat Hailu, Dr. Abebaw Fekadu and Mrs Asnakech Alemu, addressed the questions and comments forwarded by the participants. The major points were:

- Most participants understand the importance of such forums and thanked CDT Africa for taking the lead.
- One of the participants even considered it as historic, citing his experience with the TB Research Advisory Committee (TRAC), which started with a small group at AHRI like the ACT but became a national program later on. The establishment and achievements can also be taken as an example where TRAC is now owned by FMoH while the secretariat is hosted in AHRI. Similarly, CDT Africa could continue to host the ACT and the owner can be EFDA.
- Feedbacks to the presentations:
  - It was suggested if the survey could have a document review (of existing institutional and national guidelines) component to make the assessment comprehensive. Other sites like Hawassa, Haromaya and Mekele universities are not represented in the survey as they are actively involved in clinical trials. There are some findings

that also need further exploration such as the low rate of publication among the clinical trials. The reason why they didn't publish could have been investigated.

- » The clinical trial landscape presentation would have been more informative if it shows the trend. In the presentation, the number of clinical trials in Ethiopia was low but is it growing or reducing or stays the same over the years could be highlighted. And also need to consider if things that are presented as threats can be used as an opportunity.
- » It was pointed out that the start of parallel submission by EFDA side is good news for researchers. And it was recommended to create the awareness to all researchers and also to clarify for which ethics committees' parallel submission is permissible.
- » The rapid assessment mostly addresses the issues of human resource particularly physicians. The general clinical trials environment like infrastructure capacity and quality and attitude (of investigators and professionals) could allow understanding of the overall ecosystem and encourages local innovations related to clinical trials.

› Related to the bulky nature of clinical trials documents, a question was raised as to whether there were guidelines about the legality of certain communications, for example phone conversations.

› The capacity for clinical trials as a country was much poorer some years back compared to where we are now. There is relatively better capacity now. Through time the awareness and the capacity can be well built. But as a country, we are lagging behind in terms of clinical trials conducted, this is despite the fact that site selection and recruitment of participants were not problems.

› We need to consider if the committees even at national and other levels are able to take risks analyzing the situation to recommend directions. NRERC and EFDA need to take some calculated risk to advance clinical trial and its benefits in Ethiopia.

› The ACT needs to be more explicit in terms of what it does and how, what the structure is, which can also be sent via email for feedback. As CDT-Africa is the best hub to run this, it would enable to identify in what way the regional partner institutions can provide support.

› As previous attempts have not been successful in pushing the agenda forward, it was suggested if a focal person can be assigned who can bridge these issues, working together or seconded to EFDA, MOSHE or FMOH.

› From the EFDA part it was remarked that;

Harmonizing the national guidelines besides the parallel submission is also believed to improve the approval system. But there is also a plan to look at the overall picture as being delayed at one stage and expedited at the other may not help. This is under the plan of EFDA. And need to consider if there is a means to create a system where we can align the systems of approvals at the academic/health institutions to the national ethics approvals.

There is also a challenge where trials are being conducted without authorization. EFDA also believes the need for inspection and to find ways of facilitating the ap-

provals for those who seek approval and control those who are not adhering to the essential requirements.

Ownership of the issues is needed to facilitate and support those who are given the mandate for clinical trials. We need to take a look at what other successful programs have implemented and policy level advocacy works as well as awareness creation at lower levels needs to be done.

There is growing pharmaceutical industry interest in Ethiopia. Therefore, clinical trial capacity should also be ready for the growing demand. Most of the trials that come for approval are phase III or Phase IV. If the ecosystem is not favorable for these types of trials, how can it be inviting for the more complex earlier phase trials? This requires urgent attention.

› The NRERC representatives provided update on the development of research ethics over the past 20 years. Five guidelines have been developed and implemented. The fifth guideline has been revised in 2014. It is now planning to revise the latest version accommodating contemporary ethical issues like electronic informed consent and communications.

NRERC has been functional for about two decades and the various structural changes, including the latest restructuring that puts it under MoSHE have required adjustments.

The NRERC representative acknowledged the importance of capacity beyond the mere existence of structure. Hence, training is important for the young NRERC secretariat staffs. He also thanked the current serving members for their dedication and stressed the need for remuneration as the committee members are all volunteers. There is a national guideline to effect payment for ethics committees but not currently being implemented.

There has been no working relationship between NRERC and EFDA as such so far but there is a great need for collaboration between NRERC and EFDA.

NRERC also suggested mechanisms to mainstream ethics approval process that will be reflected upon in the new guideline revision. It was further suggested that if the stronger IRBs (such as those SIDCER recognized) can be registered and accredited by the national committee. These could be mandated to provide capacity building and supervisory support for emerging/weaker IRBs for accreditation. The experience of Uganda was shared where the national research ethics committees does not review protocols. It is the 27 IRBs (23 accredited) who conduct the protocol review and registration under the knowledge of the national committee. The IRB chairs meet every three months to discuss about the clinical trials and learning opportunities, like lectures, would be offered if necessary, to capacitate the boards.

- EFDA in principle accepted the need for delegation of ethical review process to qualified IRBs but need further discussion and working together closely.
- The promotion of clinical trials in Ethiopia was indicated to be an opportunity to the insurance industry. But little is known in Ethiopia. It is only recently that the insurance companies came to know about clinical trials. There is a great need to work on the capacity development as was a lost opportunity--there were many times where insurance coverage was sought from oversees. And high premium is requested from local insurance companies because of the knowledge gap. Therefore, awareness creation and advocacy as one product of the sector should be done. The knowledge/the information also needs to be shared with the insurance industry as well as the regulator, the national bank of Ethiopia and the Insurers association to consider clinical trials as one product of the sector.
- Following this, it was communicated that ACT may be able to facilitate a training for the insurance companies with support from the represented insurance company to create the necessary awareness.
- It was reiterated that the major challenge is seen to be one of capacity, in terms of human resource capacity and infrastructures. We need to know the existing capacity we have well to work towards the capacity issue. It is thus recommended to work institutional profile to know who has what in terms of capacity, expertise and other resources (qualification of trials, their affiliation as well as where can clinical trial unit be found.) at national level.
- Related with this, those who are engaged in clinical trials at national level are also not familiar with each other. Establishing a platform like a national investigator network (website) is suggested, which can again be linked to other networks in Africa or even global networks.
- In addition to promotion to health professionals, awareness creation is also needed for the community, for the community to consider clinical trials outcomes as public good. Celebrating clinical trials in the institutions can be one way of promotion.
- The initiative was began by CDT-Africa with the aim of creating this discussion forum. However, more needs to be done. The participants discussed whether CDT-Africa should continue to facilitate the ACT as a national entity. It was argued that since CDT-Africa was established to facilitate and create clinical trials capacity, this agenda can be pursued by the center.
- It was suggested that it would be useful if the advisory committee is inclusive of the partner universities. And if there is a way to contribute more constructive inputs. ACT should thus try to involve partners and institutions who have a stake in clinical trials.
- Even though human capacity is recognized to be crucial for clinical trials, we need to consider whether this can be fully addressed by providing long terms courses while majority of physicians who are expected to conduct clinical trials are unaware of clinical trials being conducted in their institutions. Therefore, apart from the MSc program, promotion as well as provision of short courses was needed.
- The importance of the National clinical trials network is again stressed in that it would also create the platform for experience sharing and learning from one another.

- It was recommended it would benefit to clearly recognize initial primary focus of type of clinical trials at the current capacity, whether commercial (Pharmaceutical company sponsored) or non-commercial (Hospital/research institute sponsored).
- As to the establishment of the ACT, it was clarified that the primary intention was to involve all concerned stakeholders, however, it was needed to mature it in a small group, bringing together initially members from Addis Ababa and then bringing regional partners onboard after then.
- It was requested if there is a way from the national ethics/regulatory body side to make institutions accountable to standardize their IRBs.
- It was raised that which types of studies fall under the mandates of EFDA is sometimes unclear. It was requested if trials like diagnostic kit validation trials and task shifting (health workers) trials are needed to be reviewed by EFDA. Clear awareness needs to be created as to the definitions of clinical trials as time is wasted from disagreement of the definition.
- Effort also need to be to motivate researchers in the institutions. Since institutional budget allocated for research only allows to do observational studies and makes it difficult to think of conducting clinical trials. This drives researchers to seek overseas sponsorship, which then creates a problem of data/material ownership by sponsors which poses challenges of ethical approvals.
- Recommendation was given if it was possible for NRERC to transfer its mandate to institutional IRBs. Potential reviewers list can be contributed from the institutions.
- Concern related to security of patient data was raised, if there was a national act or proclamation regarding patient data protection. How ownership of data is entertained when partnering with private companies (CROs, biotech and pharmaceutical companies) in the future needs to be well thought out including a plan on how commercialize it as a CRO.
- Regarding data sharing, it was remarked from the NRERC side that even though it is one of the important emerging issue, that we don't have clear regulation thus far. There is a plan to include this issue in a guideline by NRERC. However, it might be required at the level of legislation in the future.
- The problem of data ownership was also a shared concern among other participants where it was indicated that international guidelines support ownership of data by sponsoring industries. And thus, in addition to including it in the national ethics guideline, the need to have a national data sharing act as a country is stressed.
- Along with this, in addition to producing and capturing the data, creating the capacity for a strong data management center also needs to be given attention, as currently clinical trials data is mostly being managed and analyzed overseas.
- It was also raised that there is ongoing issue related to material transfer. The mandate for clearance is given to biodiversity institute, however, there is ambiguity of mandate on human biological samples.
- From CDT-Africa's side, it was affirmed that CDT-Africa is committed to support the basic skills that enables to understand these issues as much as possible. As, the capacity for establishing data management center required the need to work on the

fundamental human capacity development as it requires deeper capacity by itself in the areas of bioinformatics for example. Even though, the scope of this meeting is on creating on the conduciveness of the ecosystem for conducting clinical trials, it was acknowledged that a separate focus should be there in creating the capacity for knowledge generation in other areas of disciplines as well, as clinical trial is closely interlinked with other areas of capacity.

- Establishing clinical trials network has been one of the agendas of CDT-Africa. The clinical trials network can be formed with the attendees of the national consultative meeting where the investigators network can be linked with it. The national consultative meeting agenda can also be moved together with EFDA or other concerned stakeholders taking the example of TRAC. However, data sharing might emerge to be beyond control where these are driven by the industry itself where reputable journals for example have their own data sharing requirements.
- It was inquired, from the NRERC side if the system by itself is strong even if the guideline is there, it might require to conduct internal institutional assessments engaging other institutions universities.
- From Ethiopian Biotechnology Institute (EBTi) part, it was stated that expanding clinical trials given by council of ministers as one of the mandates of EBTi and expressed interest to work together with ACT. Dr Molalign taken the responsibility to follow this personally.
- In relation to the clinical trials transformations road map previously prepared by FMOH, it was raised that, to catalyze the agenda of clinical trials, creating a national clinical trial forum was among priorities recommended by the road map and CDT-Africa is acknowledged for taking this initiative. There are also other agendas indicated by the roadmap that needs to be pushed forward. ACT can be a good platform to do this. However, expectation should not be very inflated in that all agendas of clinical trials transformation might not be handled this way. The road map might also be needed to be updated and ownership has to be assumed.
- Discussion has to be there on ACT ToR or how it should operate and it was that recommended the ToR of ACT should be shared among the different parties, commented and finally endorsed
- It was reiterated that ACT was started only out of a mere concern on how to go forward and that it was not a committee organized by an establishing document. The plan/ recommendation was to endorse the existing ACT. Interested institutions can also attend ACT meetings virtually and will be open and transparent for others to join and contribute.
- Questions raised to EFDA was addressed; these includes; clinical trials involving diagnostic kit is medical device trial and needs to pass under regulatory review. International Council for Harmonization (ICH)/WHO clinical trials definition is employed by EFDA. Any study which uses human data to generate new knowledge, which is aimed at policy change is considered as a trial, however ambiguity and disagreement emerges sometimes. Related to material transfer agreement, it is being an issue at port of entries and there is a plan to prepare a guideline and it would be critical to work with

ethics committees.

- It was raised that even with increasing the capacity of NRERC, whether NRERC has to be engaged in other associated tasks (like heath research code and guidelines, data management system and transfer) or if the structure for these wholistic tasks should be under FMoH and if NRERC has to be devoted only for research ethics.

RECOMMENDATIONS/WAY FORWARD SUMMARY

- To find ways to shorten the lengthy clinical trial protocol approval (Level A and SIDCER recognized ethics review committees to be mandated to review and grant approval to clinical trials protocols)
- Provision of training to insurance companies
- Preparation of institutional capacity profile document
- Establishment of a national clinical trials networking platform
- Promotion of clinical trials to the public including using medias
- Encouraging partners to participate and CDT-Africa in best position to take the lead in engaging institutions
- Short courses should be available for physicians and other health professionals who can potentially be involved in clinical trials
- EFDA needs to have a clear guideline as to what constitutes as a clinical trial and make available to the end users.
- Identify ways of adequately financing clinical trials as they are finance intensive by nature
- Establishing strong data management center or strengthening the established ones like the data management center at EPHI.
- Preparation of a data sharing act
- Working together with FMOH to find ways to update and implement the national clinical trials road map
- Preparation of the legal framework for clinical trials which could be the mandate of EFDA.

CLOSING REMARKS

ACT was endorsed by the consultative meeting participants.

The consultative meeting was completed with a note of thanks forwarded by Dr Abebaw for all participants, thanking all who came from near and far to contribute to this important issue. He also stressed that the effort will continue and update regularly those who participate today as well as who will join ACT in the future. The meeting was adjourned at 1:00PM.

APPENDICES

List of Meeting Attendees

Name	Institution	Role
Addisu Alemayehu (Dr.)	Mekelle University	IRB Chair
Ahmed Zeynu (Dr.)	Jimma University	Dean
Amanuel Haile (Dr.)	Mekelle University	Chief Executive Director
Asefa Deressa (Dr.)	Ethiopian Public Health Association (EPHI)	R/A Advisor
Asnakech Alemu	Ethiopian Food and Drug Administration (EFDA)	PSD Director
Asrat Hailu (Prof.)	CDT-Africa	Diagnostics Program lead
Bethelhem Fekadu	CDT-Africa	Supply manager & Students' Affair coordinator
Beyene Wolde	Sheger FM	Reporter
Dawit Kebede	AAU FM 99.4	Reporter
Deborah Tilahun	EBTI	Researcher
Eyasu Makonnen (Prof.)	Center for Innovative drug development and therapeutics trials for Africa (CDT-Africa)	Deputy Head
Feleke Moges (Prof.)	University of Gondar	Institutional Review Board (IRB), Chair
Frehiwot Alemayehu	Awash Insurance	Underwriting Director
Getachew Addis (Dr.)	EPHI	IRB, Chair
Getnet Yimer (Dr.)	Ohio State University, Global One Health Initiative (O0SU-GOHi)	Director
Girmay Medhin (Dr.)	CDT-Africa	Data Management Lead
Haileleuel Bisrat	CDT-Africa	Data Manager
Hailemichael Getachew	AHRI	Researcher
Mahteme Bekele (Dr.)	Saint Paul Hospital Millennium Medical College (SPHMMC)	Director
MekonnenTeferi (Dr.)	Armaeur Hansen Research Institute (AHRI)	Researcher
Metasebia Teshome	Capital Newspaper	Reporter
Michele Joseph	CDT-Africa	Trial Nurse
Miraf Mesfin	CDT-Africa	Sr. Clinical Trial Manager
Molalegn Bitew (Dr.)	Ethiopian Biotechnology Institute (EBTI)	Health Biotechnology, Director
Sisay Yifru (Dr.)	University of Gondar	Chief Executive Director
Solomon M. Abay (Dr.)	AAU	IRB, Secretary
Tesfaye Solomon	AAU, College of Health Sciences (CHS)	External Relation
Tilahun Teka (Prof.)	Ministry of Science and Higher Education (MOSHE)	NRERC, Chair
Tsegahun Manyazewal	CDT-Africa	Scientific coordinator
Yimtubezinash W/Amanuel (Dr.)	CDT-Africa, Addis Ababa University (AAU)	Incubation Hub Head
Yodit Fikresiassie	CDT-Africa	Assistant Admin

National Consultative Meeting on Clinical Trials Schedule

Session I: Registration			
Time	**Activity**	**Moderator/Chair**	
8:30 - 9:00 AM	Registration	CDT-AFRICA Staff	
Session II: Opening and Presentations			
Time	**Activity**	**Moderator/Chair**	**Presenter/Speaker**
9:00 – 9:10 AM	Opening remark	Prof. Eyasu Makonnen, Deputy Head, CDT-Africa	Dr. Lia Tadesse, State Minister, FMOH
9:10 - 9:40 AM	Landscape of clinical trials: the global, continental, Ethiopia's context; and opportunities of clinical trials	Prof. Eyasu Makonnen, Deputy Head, CDT-Africa	Prof. Asrat Hailu, Diagnostic Lead, CDT-Africa
9:40 - 10:10 AM	Challenges and opportunities of clinical trials, ethical and regulatory review, and the capacity and practice of clinical trials in Ethiopia: results of qualitative and quantitative survey	Prof. Eyasu Makonnen, Deputy Head, CDT-Africa	Dr. Abebaw Fekadu, Head, CDT-Africa
10:10 - 10:30 AM	Remarks by EFDA	Prof. Eyasu Makonnen, Deputy Head, CDT-Africa	Ms. Asnakech Alemu, Director, Product Safety Directorate
10:30 - 10:45 AM	Coffee break		
Session III: Discussion Session			
Time	Activity	Moderator/Chair	Discussant
10:45 AM - 12:20 PM	Discussions, Recommendations, Action Plans	Prof. Eyasu Makonnen, Deputy Head, CDT-Africa	Invitees
12:20 AM - 12:30 PM	Closing and vote of thanks	Dr. Abebaw Fekadu, Head, CDT-Africa	-
12:30 PM	Lunch		

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