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Regulatory System Opportunities and Barriers for Conducting Clinical Trials in Ethiopia: A Descriptive Qualitative Study

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SIGNATURE FORM

This thesis paper is prepared under my supervision by Mehiret Maru entitled '**Regulatory system opportunities and barriers for conducting clinical trials In Ethiopia: A descriptive qualitative study'** and submitted in partial fulfillment of the requirement of the degree of Masters of Science (MSc) in Clinical trials.

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ABBREVIATIONS/ACRONYMS

ALERT	All Africa Leprosy, Tuberculosis and Rehabilitation Training
CDT Africa	Center for Innovative Drug Development and Therapeutics Trials for Africa
CROs	Clinical Research Organizations
EFDA	Ethiopian Food and Drug Authority
EQA	External Quality Assessment
ERC	Ethics Review Committee
IPs	Investigational Products
IRB	Institutional Review Board
MENA	Middle East/Northern Africa
NHRERC	National Health Research Ethics Review Committee
NRA	National Regulatory Authorities
PIs	Principal Investigators
SAE	Serious Adverse Effect
SOP	Standard Operating Procedure
SPC	Statistical Process Control
SSA	Sub-Saharan Africa
TB	Tuberculosis

ABSTRACT

Introduction: A clinical trial is a research method used to provide evidence on the safety and effectiveness of interventions for specific medical conditions. In contrary to the disease burden, most of the clinical trials were conducted in developed countries and the share of Africa as of 26 June, 2020accounts only around 2.98% of clinical trials done worldwide. Among the 10,249trials conducted in Africa only 1.53% has been done in Ethiopia. Different factors have been identified as a barrier for trial development in Africa and challenges associated with Ethical and regulatory system has been stated as the second most common barrier. The regulatory body is the one who authorizes and inspect clinical trials in Ethiopia. However, no study has been done so far on the opportunities and challenges of clinical trial regulation which affect trial development.

Objective: In this study the enablers and barriers of the regulatory system on clinical trial development in Ethiopia is studied.

Method: In this descriptive qualitative study, a total of 15 participants, who had experience in conducting clinical trials in Ethiopia and staffs working in Ethiopian Food and Drug Authority(EFDA) clinical trial team were identified from https://ClinicalTrials.gov, http://apps.who.int/trialsearch/default.aspx, from a data obtained from EFDA and by snowball sampling and involved in the study. Then data was analyzed in the thematic way of analysis.

Result: The presence of a specific team within EFDA with a guideline, and staffs initiation to regulate clinical trials are mentioned as an opportunity for clinical trial implementation. Different barriers such as lack of human resource and capacity, financial, infrastructure, regulatory guideline and directives, and trial site follow-up inspection are stated as a bottleneck for the researchers to do clinical trial in Ethiopia. Moreover, not having a feedback for reports, not taking part in the trials closeout and unreasonably stringent regulatory system also mentioned as a barrier.

Conclusion and recommendation: In Ethiopia, clinical trial researchers face substantial up and downs starting from clinical trial authorization to trial completion. We recommend that there is a need to strengthen the capacity of regulatory body and develop efficient system in order to improve clinical trials regulation in Ethiopia.

Keywords: *Clinical Trial, Ethiopian Food and Drug Authority (EFDA)**,** opportunity, barrier, challenge.*

1. INTRODUCTION

1.1 Background

A clinical trial is a study of testing effectiveness and safety of intervention, and it is the foundation for development of new medical products and used as a gateway for the conversion of research to useable products for public health (1,2). According to Ethiopian Food and Drug Authority (EFDA) proclamation, clinical trial is defined as "Any systematic study on medicine or medical devices in volunteer human subjects to discover or verify the effects of, and/or identify any adverse reaction to the products, and or to study its absorption, distribution, metabolism, and excretion to ascertain their efficacy and safety"(3). Clinical trials are crucial for the development of new medical treatments and diagnostic tests. Without clinical trials, we cannot properly determine whether new treatments developed in the laboratory or by using animal models are effective or safe or whether a diagnostic test may work properly. Computer simulation and animal testing can only tell us so much about how a new treatment might work, and are no substitute for testing in a living human body. Most modern medical treatments are a direct result of clinical research. New treatments for all diseases and conditions including cancer, heart disease, high blood pressure and asthma have been developed through clinical research (23). Data generated from clinical trial helps to add medical knowledge, make health care decision, and revise or develop treatment guidelines. Clinical trials can provide valuable information regarding the cost-effectiveness of a treatment, the clinical value of diagnostic test, and how treatment improves quality of life (4).

Four decades ago clinical trials were largely restricted to industrialized nations and only limited number of clinical trials used to be conducted in developing countries. However, over the past few years the involvement of developing nations is increasing (1). Clinical trial implementation in developing countries differs in numerous ways from that of developed countries. For instance, in developed countries clinical trial is budget intensive which requires stringent regulations, extensive safety consideration, and compensation. Also the small patient populations have made it challenging for researchers to conduct trials in these countries (1). The African continent offers conductive environments for conducting clinical trials, such as minimal costs for implementation, a diverse population of potential patients, and populations who may not have been previously exposed to any kind of modern medicines (5). Despite these advantages, the

number of clinical trials conducted in African countries is still a small proportion compared to that of clinical trials conducted in other parts of the world (6). According to the clinicaltrials.gov database, from a total of 343,835 trials done worldwide Africa accounts only 2.98% up to June 26, 2020.Among 10,249 trials implemented in Africa, the share of Ethiopia is very scanty, which is 1.53%, as compared to Egypt (41.93%) and South Africa(27.24%) (6).

Different factors have been identified as a barrier that forced Africa to have a little contribution of clinical trial for the world. The challenges vary from individual level to institutional level as shown in some literatures. The most commonly cited barriers in Africa include lack of expertise, lack of budget and infrastructure, lack of suitable research environment, ethical and regulatory challenges, language and culture barriers, and socio-political (2,7–15)(16,17). In Ethiopia different stakeholders are involved in clinical trial implementation and regulation. From those stakeholders EFDA is a governmental institution who had legally supported mandate to regulate clinical trials which are conducted in Ethiopia. In the Ethiopian food and medicine administration proclamation No. 1112/2019, the role of EFDA and different legal issues on clinical trials are clearly stated on article 27, sub article 1-11 (22).

It is therefore important to understand the role of all stakeholders and identify different factors that encourage and hinder clinical trial implementation. From those responsible institutions, EFDA is one of the governmental organizations that had a role in clinical trial regulation. However, no study done in identifying problems associated with EFDA which hinder the implementation of clinical trial in Ethiopia. Hence, the objective of this study is to investigate regulatory authority system opportunities that encourage clinical trial development and regulatory authority barriers which hinder clinical trial implementation and development in Ethiopia. Moreover the different challenging factors are prioritized and possible solution to improve the regulatory system is proposed.

1.2 Statement of the Problem

Clinical trial is a research tool which provides a new medical knowledge and intervention. It helps the community get a better way for the treatment of medical conditions, disease prevention and method of diagnosis(1).Despite the importance and advantages of conducting clinical trial in Africa, different factor should back its implementation. Previous studies have identified a lot of factors that hinders trial execution in Africa(7–9). And regulatory system barriers were identified

as the second most important factor which acts as an obstacle for the development of clinical trials in developing countries(7). In different countries, clinical trials are regulated by different governmental organizations operating in different ways. Effective regulatory system should be stablished in each country to maximize the opportunities and minimize the challenges to promote clinical trial development. To achieve this regulatory system opportunities and challenges should be identified.

In Ethiopia to our knowledge there is no previous qualitative study which identified regulatory system opportunities and obstacles in the development of clinical trial.

1.3 Significance of the Study

Clinical trial is regulated by different stakeholders and EFDA is one of those which plays significant role in the authorization and supervision of clinical trials from its initiation up to completion. Identifying the regulatory opportunities and barriers for conducting clinical trials will be useful in the implementation of clinical trials in Ethiopia. Data generated from this study will, therefore, help the regulatory body improve its regulatory system by implementing corrective actions in order to promote conduct of clinical trials in the country. The findings will also help investigators and trial sponsors understand the existing regulatory system and contribute to the improvement of the system to create enabling environment for the conduct of clinical trials.

2. LITERATURE REVIEW

The health care system of Ethiopia with its primary focus on prevention and primary care has shown a remarkable improvement in recent years(18). However, health research, especially in the form of clinical trials has not been done sufficiently. According to Clinicaltrias.gov until June 26, 2020, the registered number of clinical trials conducted in Ethiopia made up only 1.53% of all clinical trials done in Africa which account for only 2.964% of trials conducted worldwide (6). Trial development in Ethiopia is limited compared to other African countries like Egypt and South Africa. Even though doing a clinical trials with limited capacity have its own risk, no conducting clinical trials will also makes Ethiopia to lose a lot of opportunities that the country should gain from conducting clinical trial. Such opportunities include exploring traditional remedies from the natural resource the country has, addressing country specific diseases condition and evidence based treatments.

Different barriers for conducting clinical trials in different part of the world have been mentioned in many literatures (7).Most studies aiming to identify the factors which hinder the conduct of clinical trials are carried out by collecting qualitative and quantitative data from experienced researchers and different stakeholders.

A systematic review conducted in 2015 found that regulatory system obstacles to be the second most important barrier for conducting clinical trials in developing countries. In the same review delay of approval decisions, unskilled authorities, and complex and strict ethical and regulatory system were identified as a major regulatory barriers in developing countries (7).

2.1 Time Taken for Regulatory Review

In developing countries regulatory review process takes longer time to start clinical trials which is leading to frustration of investigators and sponsors, and forcing sponsors to look for other countries who have shorter review process. On the top of delayed approval, regulatory bodies are not able to predict the time they need to clear the application (7).

Lengthy regulatory approval time has been a challenge for conducting vaccine trials in Africa (8). A review on the Impact, Challenges, and Future Projections of Vaccine Trials in Africa showed that there is a time lag between the time of budgeting and the actual initiation of the studies because of the period required to get regulatory approvals and import licenses (9).

A study on issues surrounding the conduct of the Cameroon Mobile Phone SMS (CAMPS) trial showed that delays can make the trial meaningless or out of date by the time the study is allowed to start (10). A commentary reflected during the celebration of International Clinical Trials Day, the status and opportunities for conducting clinical trials, and the way forward for facilitating clinical trials in Ethiopia and Africa showed that; regulatory frameworks and processes were lengthy, slow and bureaucratic(11).

A qualitative study that investigated the barriers and enablers to the implementation of local investigator-initiated clinical trials in Ethiopia showed that regulatory and ethical review times introduced delays and it was not uncommon for grants to expire before all approvals were in place (12).

2.2 Skill and Resources

In developing countries, the presence of unskilled authorities in the review process posed a barrier to conducting clinical trials (7). Poor quality of scientific and ethical review processes, sub-optimal regulatory processes for new drugs and clinical trials, and unfamiliarity with clinical trial regulation are identified as challenges for conducting clinical trials in low and middle-income countries (13).

In practice, many committees in developing countries have insufficient resources and expertise to perform their function adequately. More than 50% of the Ethical Review Boards in the developing nations (such as Uganda, Turkey, Sudan, Granada, India, etc.) lack a proper quorum and standard operating procedures, and members often have inadequate training to perform their functions satisfactorily (1).

The regulatory authorities have limited experience with novel vaccines and are often reluctant to take responsibility for novel trials being conducted in the country (8). According to a review of regulatory oversight of clinical trials in Africa, staff from National Regulatory Authorities (NRA) and members of Ethics Committees need basic academic and professional development (14). The regulatory agencies in countries where Tuberculosis (TB) is more prevalent, may be relatively inexperienced in the regulation of “first in human” products, or may lack the resources and regulatory framework to guide the development of a new TB vaccine product (15).

In a review on opportunities and challenges of cardiovascular clinical trials in Africa, the possible inadequacy with regards to regulatory and ethical control and overview is frequently

cited as problems in developing countries(16). The article that describes the challenges in designing and conducting a phase III intermittent preventive therapy in pregnancy clinical trial stated that the suboptimal regional regulatory infrastructure to evaluate a novel treatment is the key issue that must be overcome before initiating any study in Sub-Saharan Africa (SSA) (2). In SSA there is a lack of capacity of NRAs and many committees are not yet fully functional due to lack of funding, infrastructure, training, standard operating procedures, and sometimes simply lack of political commitment from the governments (17).

During the implementation of an Ebola vaccine trial in Sierra Leone, a limited experience of regulatory authority on trials conducted during an epidemic was one of the challenges encountered while setting up a clinical trial during and after an epidemic (19). A prospective, qualitative study that investigated the barriers and enablers to locally-led clinical trial conduct in Ethiopia, Cameroon, and Sri Lanka showed that regulatory and ethical bodies lacked sufficient capacity to govern research (20).

2.3 Bureaucracy

The legislation in most African countries do not assign a clear mandate for regulation and oversight of clinical trials to a specific body within the health authorities (14). Over complex and unreasonably strict ethical and regulatory systems were reported as a barrier in developing countries (7). Ill-defined approval process and a significant bureaucracy of the regulatory authority are the challenges for conducting vaccine trials in Africa (8).

The multiple layers of local and national regulatory review/ approvals process are difficulties in conducting clinical trials for AIDS-associated Kaposi's sarcoma in SSA (21). A review that identifies the various challenges and opportunities for the expansion of clinical trials in the Middle East/Northern Africa (MENA) region stated that Clinical Research Organizations (CROs) and trial sponsors need to constantly monitor regulatory change to avoid delays or disruptions in ongoing trials (5). According to a qualitative study conducted in Ethiopia, respondents reported that; for investigator initiative trials complex and strict government regulations made it very difficult to investigate novel interventions and recruit vulnerable populations (12). Another article stated that in Ethiopia regulatory frameworks that are underdeveloped or imported directly without consideration of the local context are also a barrier for conducting clinical trials in Ethiopia (11).

2.4 Other Factors

In addition to the factors mentioned, there are also some factors like language barriers that are encountered and the approval process varies from country to country and it is often required to prepare separate documents and dossiers for submission in the countries (8). In Ethiopia, Cameroon, and Sri Lanka, most regulatory procedures lacked legal backing (20). One study stated that a regulatory body with different standards is one of the difficulties that may be encountered during multi countries trials (10).

3. OBJECTIVES

3.1 General Objective

Identify regulatory opportunities and barriers for conducting clinical trials in Ethiopia.

3.2 Specific Objectives

→ Identify regulatory opportunities that encourage clinical trial implementation in Ethiopia.

→ Identify regulatory barriers for conducting clinical trials in Ethiopia.

→ Prioritize regulatory barriers for conducting clinical trials in Ethiopia.

4. METHOD AND PARTICIPANTS

4.1 Study Area and Period

Data for this study was collected from clinical trial experts who have conducted and/or are currently engaged in a clinical trial, in different hospitals, universities, and clinical trial sites in Ethiopia. The study areas were selected based on the involvement of the institutions in clinical trial implementation as a sponsor or as a clinical trial site in Ethiopia. Information about the study areas were collected from EFDA, https://ClinicalTrials.gov, and http://apps.who.int/trialsearch/default.aspx. Based on the number of clinical trials previously conducted or currently ongoing in the Universities, hospitals, and trial sites, the first top-five Universities or hospitals or trial sites were selected as a study area. Based on this criteria, the study was conducted at Addis Ababa University (AAU), College of Health Sciences (CHS) (Addis Ababa); All Africa Leprosy, Tuberculosis and Rehabilitation Training (ALERT) Hospital (Addis Ababa); Jimma University Referral Hospital (Jimma); University of Gondar (Gondar); Hawassa Hospital (Hawassa) and Arba Minch university (Arba Minch). And data was collected from January 01, 2020 – April 25, 2020.

4.2 Study Approach

The study was conducted using, a qualitative descriptive study approach.

4.3 Population

4.3.1 Source population

All individuals who were involved as Principal Investigators (PIs) or as Co-PI or trial coordinator with a delegation from the PI, on clinical trials conducted in Ethiopia and require authorization from EFDA. And also EFDA staff who are working in clinical trial team were taken as source population.

4.3.2 Study Participants

All individuals who were involved as PIs or as Co-PI or trial coordinator with a delegation from the PI to handle administrative and regulatory issues, on clinical trials which conducted in Ethiopia and requires authorization from EFDA and who meet the eligibility criteria of this study. In addition EFDA staffs working in clinical trial team were also participated in the study.

4.4 Eligibility Criteria

Clinical trial researchers who meet the following criteria were included in the study

- → Individuals who were conducting /conducted clinical trials authorized by EFDA at least once as PIs in Ethiopia;
- → Individuals who were conducting /conducted clinical trials authorized by EFDA at least once as Co-PIs in Ethiopia with a delegation from PIs to handle regulatory issues;
- → Clinical trial coordinators who had experience in processing trial authorization and other issues related to EFDA;
- → Those who were volunteer and gave informed consent to participate in the study;
- → Those who were available at the study areas during data collection;

EFDA staffs who meet the criteria listed below were included in the study

- → Individuals who are working in EFDA clinical trial team and had experience on clinical trial regulation;
- → Those who were volunteer and gave informed consent to participate in the study;
- → Those who were available at the EFDA office during data collection.

4.5 Participants Recruitment

Eight clinical trial researchers and one EFDA clinical trial team staff were identified from trial registration database and the list from EFDA clinical trial team using eligibility criteria. Then snowball sampling methods were used during data collection. Then each participant was requested to recommend other clinical trial experts who could articulate their view about clinical trial regulation. Individuals who had experience in doing clinical trials in Addis Ababa, Jimma, Hawassa, Arba Minch and Gondar as PIs, Co-PIs or trial coordinators and had experience in obtaining trial authorization from EFDA, and took part in overall trial regulation by EFDA were invited to participate in the study. In addition staffs of EFDA who were working in the clinical trial team at the time of the study also invited to participate in this study.

A total of eighteen individuals were invited to take part in the study out of whom 15 individuals (13 clinical trial experts and 2 EFDA clinical trial team staffs) were participated. Two of the researchers and 1 EFDA staff were not able to take part in the study because they were busy by other duties during data collection period. As there is no general agreement on sample size

determination for qualitative studies, which involve key informants, the sample size was determined by theoretical saturation for this study.

4.6 Data Collection Procedure

For data collection a semi structured interview guide was prepared in English and translated to Amharic. In-depth interview was conducted by the main researcher and the first two interviews were in Amharic as per the protocol but when it was realized that English was the working language for the experts the remaining interviews were conducted in English after getting protocol amendment. Because it will save time which is going to be used for translation. All interviews were conducted in person. For participants who were in Addis Ababa the interview was conducted in A.A and the main researcher traveled to the selected regional institutions and conducted the interview with regional researchers. The interview took 36 min to 92min and all interviews were recorded with the permission of the respondents. The overall aim of the interview was to get insight about the clinical trial regulation system in the EFDA. The interview was carried in the place convenient for the participants.

4.7 Data Analysis Procedure

After conducting each interview the recorded interviews were transcribed to word file and care was taken by anonymizing some information to assure the respondents would not be identified from the reports. The Amharic transcriptions were translated to English. The principal investigator read the transcription repeatedly to become familiar with the data and the thematic data analysis method was implemented using open code 4.03 software. The thematic analysis was approached in an inductive way of coding in which coding and theme developments were directed by the content of the data. The first 4 transcribed data were imported to the open code and coded by the principal investigator and another person independently. Then the two individuals discussed on the codes and the code list were prepared. After 4 transcriptions were coded based on the listed codes a code-book was then developed and the mutual exclusiveness of each code was checked and minor changes were made on the codes. The remaining data were coded and the newly emerged codes were included in the codebook. The identified codes were grouped into sub-themes, themes and categories.

4.8 Quality Assurance

The interview guide was pretested to practice interview questions and to get feedback on the interview method, by taking a sample of two volunteer individuals who had experience with clinical trial and who had a chance to visit EFDA to get service. After this interview, all necessary minor corrections were made on the interview guide.

After conducting the interview the principal investigator transcribed the data before conducting the next interview and did the necessary corrections on the interview guide when it was needed. A person who can speaks both Amharic and English was consulted to validate the Amharic interview translation to English. The transcribed Amharic sample and its translation were given to the individual and asked to trace and compare the translated data with the original interview. In addition the individual was asked to provide any other possible translation for the same data.

4.9 Ethical Considerations

The study was approved by the Scientific and Ethics Review Committee of the Center for Innovative Drug Development and Therapeutic Trials for (CDT Africa), CHS, AAU. Informed consent was obtained from each participant before starting the interview. The recorded audio were copied to the main researcher's personal computer and deleted from the tape-recorder. Both the voice and the transcribed data were kept with the main researcher's personal computer by locking it with password. Participants were interviewed in the place that they selected and also makes the interview confidential.

4.10 Data Presentation and Dissemination

The output of this study will be prepared both in soft copy and hard copy and submitted to CDT Africa and AAU CHS. Besides, it will be presented to all stakeholders and other concerned bodies and submit for publication.

5. RESULT

From our data, a total of 4 categories 7 themes and 21 sub-themes were identified and listed in Table 1. The findings of this study is presented in to three main sections. The first part describes the characteristics of the study participants, the second section briefly introduce clinical trial regulation, mandate of EFDA, and the protocol authorization process at EFDA. The last and the main part of the result contains detail of the research findings per our objectives.

Table 1. Identified categories, themes and sub-themes

Category	Themes	Sub-themes
Regulatory system	Mandate	Trial related EFDA responsibility
		EFDA approval procedure
	Communication	Means of information exchange
Opportunity and Strength	Opportunity	Opp. from EFDA to researcher
		Opp. from EFDA to the staffs of EFDA clinical trial team
	Strength	Regulatory system strength
Challenges	Resource related challenge	Challenges related to human resource
		Challenges related to financial resource
		Challenges related to infrastructure
		Challenges related to guideline/ criteria
	System-related challenge	Challenges related to authorization
		Challenges related to service fee
		Challenges related to trial materials import/export
		Challenges related to site inspection
		Challenges related to report and feedback
		Challenges related to materials disposal
		Challenges related to communication
		Challenges related to trial regulation
Prioritized problems	Factors based on their impacts on clinical trial	Primary challenging factor
		Secondary challenging factor
		Tertiary challenging factor

5.1 Study Participant Characteristics

In the present study a total of 15 participants; 13 trial experts with experience in conducting trials and 2 EFDA staffs working in clinical trial team with experience of 4-6 years as a clinical trial regulator were involved. The respondents were 2 females and 13 males and the researchers are engaged in clinical trial as PIs (n=13), Co-PIs (n=9), as a trial monitor and Drug Safety Management Board member and chairperson (n=1), trial coordinator (n=1), supervisor (n=1), sub-investigator (n=1) and collaborator (n=1). From 13 researchers 6 of them are from Addis Ababa; 3 of them are from Jimma; 2 of them are from Gondar; and 2 of them had an experience on working in different regions of Ethiopia (Hawassa, Gondar and Arba Minch).(Table 2).

Table 2. Participant characteristics

Academic level/ Number		**Engagement in clinical trials/ Number**		**Number of trials being involved/ Number**	
MD	2	1-5 years	3	1-3	5
BSc	2	6-10 years	8	4-6	6
MSc	1	11-15 years	3	7-9	1
PhD	10	16-20 years	1	10-12	1

5.2 Clinical Trial Approval Procedure

It was noted from EFDA trial authorization guideline, before launching clinical trials in Ethiopia they had to be approved first by Ethics Review Committees (ERC)/ Institutional Review Boards (IRBs) and then by the National Health Research Ethics Review Committee (NHRERC) and authorized by the national regulatory body. It was also noted that clinical trials conducted to evaluate new drugs, or new combinations of drugs, vaccines, new therapeutic regimens, food supplements, herbal products and other biological products as well as invasive diagnostic procedures and bioequivalence/bioavailability studies would need to be authorized by EFDA (3). These trials would have to be submitted to EFDA simultaneously with the NHRERC or after having the NHRERC approval. The authorization of EFDA would, however, be obtained after getting approved by the NHRERC, and the trial could be implemented in compliance with Good Clinical Practice (GCP) standards thereafter.

5.2.1 Trial authorization process at EFDA

The findings of this study showed that the clinical trial team from Product Safety Directorate of the EFDA would be responsible for all issues related to clinical trials. To obtain EFDA authorization the investigator would need to fulfill regulatory requirements and submit trial protocol and other related documents both in hard and soft copies with evidence of IRBs approval if it had already been obtained. Then the investigator needs to pay the service fee and provide the receipt to the directorate, which is a prerequisite to start the review process. The process is shown in Figure 1.

It was noted that the EFDA clinical trial authorization guideline did not indicate a clear time line for clinical trial authorization (3); though in the citizen charter it had been stated that the review process would take 6 days to give the first response. However, according to the response given by the staffs of EFDA who worked at clinical trial team, the practical review duration mainly depended on how much of the criteria got fulfilled during submission, trial complexity, risk level, phase of the study, number of protocols submitted within that period, presence of other prioritized staffs responsibility, number of staff in the team and the timely response of the investigator to the provided feedback. As per the staff response, the longest time taken to review and provide the first feedback for a low and high risk trials might be 1 month and 2 to 3 months, respectively. It was noted that it might take 2-4 months to give trial authorization.

It was also noted that communication between the investigator and regulatory staff was needed to facilitate the approval process. The staffs also stated that the EFDA website was used to introduce EFDA's roles and responsibilities and to avail various guidelines available for the public. One of the staff indicated that Clinical trial team used to introduce their roles and responsibilities in workshops organized for guidelines development by the authority and in similar workshops organized by other stakeholders. The staff also revealed that the trial team had its own email in addition to personal work email used for Serious Adverse Effect (SAE) reporting, feedback/information exchanges, and to communicate any trial related issues.

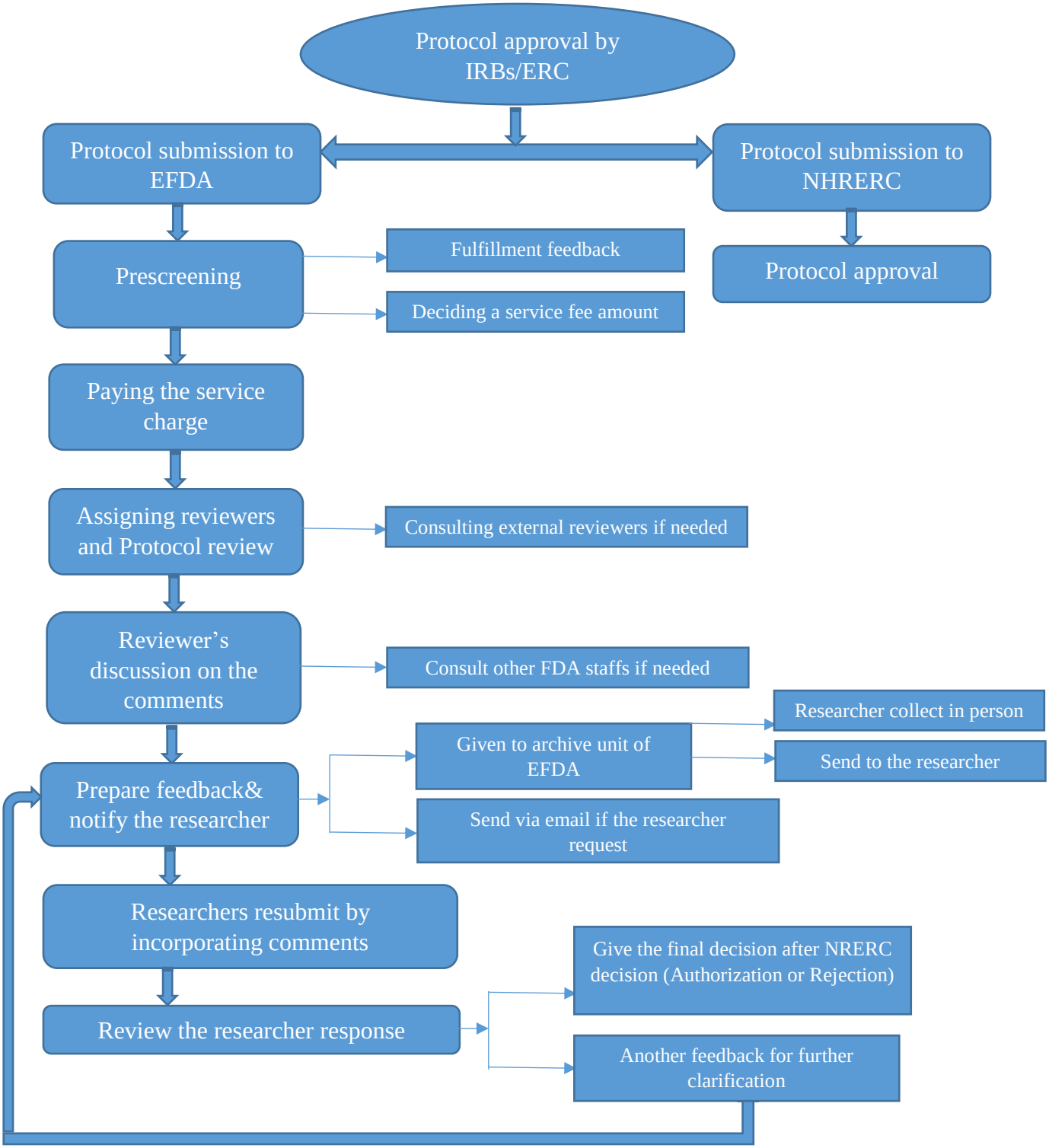

Figure1. Clinical trial authorization process at EFDA

5.2.2 Mandates of EFDA on clinical trial

The role of EFDA and different legal issues on clinical trials are clearly stated on article 27, sub article 1-11 of the food and medicine administration proclamation No. 1112/2019 (22).Clinical trials should, therefore, be conducted in accordance with this proclamation and regulations issued to implement the proclamation. EFDA would take part during clinical trial pre-initiation, implementation and completion (Figure 2), (3 and 22).

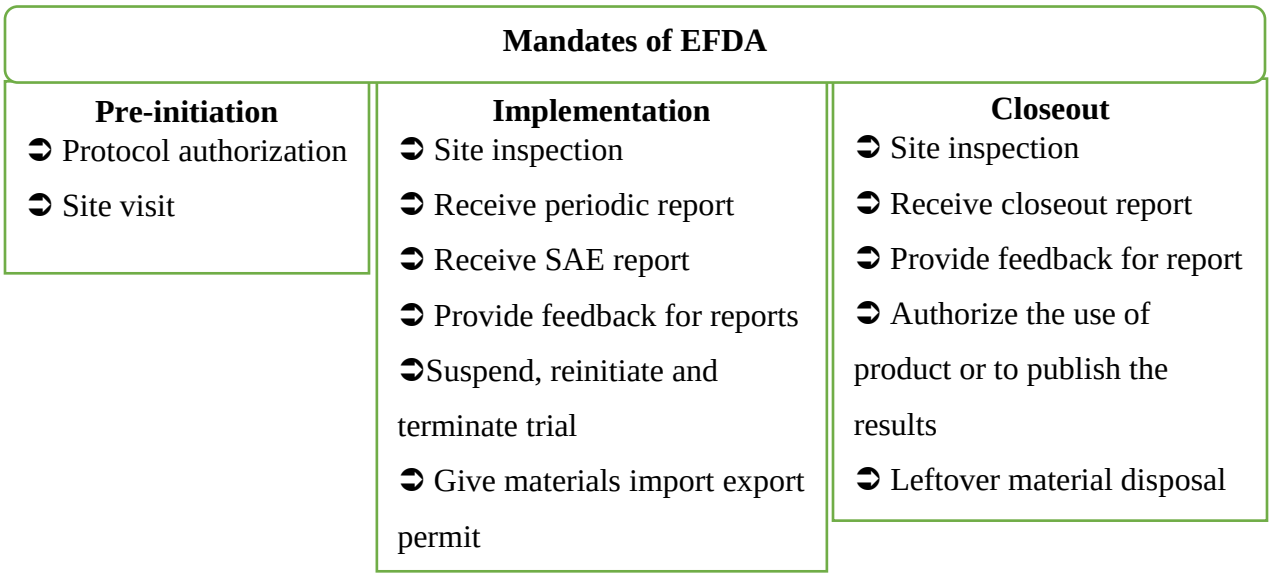

Figure2. Mandates of EFDA on clinical trials

5.3 Opportunity and Strength of Regulatory System

Under this category, the regulatory system opportunities for both researchers and EFDA staff are discussed in detail. In addition the strength of the regulatory system in regulating clinical trial are also stated below.

5.3.1 Opportunity of the regulatory system

The researchers have mentioned the EFDA's staffs and management initiation and commitment to regulate clinical trials as an opportunity. The staffs are interested to learn and improve themselves, do their routine activity like reviewing protocols and trial sites inspection, cooperative in service provision and participate in joint meeting with research institutions. The management also work on staff capacity building by giving chance for graduate studies and short term trainings. Having country specific trial authorization and inspection; online accessible GCP

guidelines; parallel submission of trial application to NHRERC for review were also mentioned by the researchers as opportunities that the regulatory provides.

As one of the EFDA staff said the initiative taken by the authority to resolve payment related issues and to re-structure the clinical trial team in an attempt to improve trial regulation can be considered as an opportunity which helps to develop trial regulation system. Participation of the staff in national and international conferences and workshops; having dedicated office and internet access were also other opportunities mentioned by EFDA staff which improve trial regulation.

In contrast to the other individuals, 3 of the researchers felt that the regulatory system did not bring opportunity which helps to facilitate trial implementation, as respondent said *"No, no opportunity at all"* RSOB GU001.

5.3.2 Strength of the regulatory system

Four of the respondents among clinical trial experts felt that the presence of EFDA to regulate clinical trials which are conducted in Ethiopia and to safeguarding trial participants and the public at large from unethical research practice as one of the strengths of the regulatory system.

"… so the good thing is just we have the structure, the institutions, the mechanisms … that is the strength by itself." RSOB JU003

Another respondent had pointed EFDA's concern for participants' safety as a good side. Others responded that the regulatory system's strength included the in-depth protocol review which could assure both the scientific and ethical merits of the trial; and online application for trial material importation which facilitated the import permit of investigational products in a short period.

Two of the respondents believed EFDA being the only stakeholder responsible for GCP inspection could be considered a strength of the regulatory system. The commitment of the regulatory body to do its job was also considered as a strength by other 2 respondents. One respondent expressed confidence in the system, and said *"I always have confidence in what EFDA does if the EFDA approve a clinical trial that clinical trial would have had appropriate scrutiny. The drugs I mean would have had appropriate evaluation or assessment."*

The existence of nationally recognized and legally bind proclamation for trial regulation and GCP guideline which could help guide researchers how to conduct trial in the country were also perceived as strengths of the regulatory system both by researchers and EFDA staff.

Trial experts pointed out presence of a clinical trial team within EFDA responsible for trial authorization and inspection, the upfront communication of the staff during site inspection, willingness and ability to learn from its routine activities through time, the interest shown to improve institutional capacity and the progress made through time were the strength of the regulatory system.

Staff of clinical trial team of the EFDA also pointed out that showing a progress on the trial regulation system, setting a plan to improve staff profile and working to upgrade the trial team to a directorate could be considered as the strength of the system.

Another respondent believed that providing trial authorization within short period of time to be as the strength of the regulatory system and responded that *"Maybe I am lucky I saw that others have contradictory feelings, the time we spent for approval was far from what I expected I see this strength."*

From all participants, 3 of the researchers were not able to mention any strength or good thing about the clinical trial regulation of EFDA.

"It was mostly difficult and it's hard to think of some good things. So I'm trying to think of good things really. Long silence *…… there weren't really any good things yeah." RSOBC003*

5.4 Challenges of the regulatory system

Under this category different types of challenges at different levels of trial implementation were described by the respondents. These include resource and system related challenges as described below.

5.4.1 Resource related challenges

Resource related challenges included poor staff profile of the clinical trial team, small financial resources, weak infrastructure and unsuitable working documents were described under this theme.

A. Challenges related to human resource

Within EFDA clinical trial team there are 4 staffs who are responsible both for clinical trials regulation and for doing activities related with pharma co-vigilance. Even though some of the researchers did not have exact data on the number of the staff of the clinical trial unit, they pointed out from their experience that the inadequate number of staff to provide trial related service and absence of delegating practice while one was not in the office were considered as barriers for implementation of clinical trial.

"I think the challenge is they don't have enough staffing so if that person is on meeting your issue will be suspended. There is only one or two individuals who are responsible and you have to wait literally beg. Instead of being your right it is rather begging for your document to be reviewed" RSOBC001

Challenges related to staff's capacity included: limited training on clinical trials, lack of capacity to review protocols and to regulate clinical trials (N=8); lack of experience on protocol review and trial regulation (N=6); most of the staffs having only first degree and so that not being able to understand researcher and not having practical experience on trial implementation (N=4). As one of the respondents mentioned there was also a language barrier and lack of capacity to write review feedback and site visit reports as well as lack of understanding and experience on some types of clinical trials which hindered trial development. The ideas about the lack of training in trial-related issues were also shared by EFDA staff.

"So the problem was I think the EFDA is very much structured towards medication trials and for a sort of device trials and has very limited experience and expertise in the area of health service trials and complex interventions." RSOBC003

Limited professional mix within the trial regulation team like not having physicians (N=2), not having a committee to do protocol review (N=1), having double responsibility and being busy by other activities like going field with multiple activities, attending meeting and not being in the office to do the review and to meet investigators (N=3) and staffs turnover after getting the experience on trial regulation and upgrading their academic level (N=2) were also mentioned to be some more barriers for trial development. As 3 of investigators from regions within the country indicated getting the staff in offices was so difficult that it created inconvenience in terms of time wastage and economic loss while staying in Addis Ababa.

"Most of the time those who review the protocol also go field visit…… sometimes we come back with the protocol or with the letter that we take to the regulatory." RSOBAH001

Some more barriers such as poor understanding on the importance of clinical trial misunderstanding as if the trial benefits only investigators; not realizing that regulating clinical trials was their duty rather assuming as if the staff was doing favor the investigators; misunderstanding of the staff about the current global situations of clinical trial and not considering the country and global need of medical innovation were mentioned as challenges by the 3 of the respondents.

"... The most important thing is their attitude for a clinical trial, for them clinical trial is a thing that only beneficial for PIs but not for the country, and they didn't know that trial review and authorization is the duty of regulatory authority. Rather they think that there is somebody who is going to be benefited from that trial… "RSOBC001

Three respondents indicated that though the proclamation allowed to involve vulnerable groups in clinical trial with justification the staff tended to reject trials involving vulnerable population which was a barrier to conduct such types of trials in Ethiopia; and the automatic rejection of trials on vulnerable groups without even writing a formal letter was also mentioned as a challenge by 1 respondent.

Difficulty to identify a responsible directorate, not knowing where to go and whom to talk during the first time visit to submit application were mentioned as challenges for the new investigators. As 3 of the respondents pointed out the frequent change of the staff and office location within the authority and difficulty to identify the right person for specific issues which need discussion or clarification were also consider challenges even for senior investigators.

Staffs like having dual or other prior responsibilities, insufficient staff number and lack of professional mix were also mentioned by the EFDA staffs as factors which contributed for inefficient trial regulation. Six of the respondents mentioned that they did not have information about number of staff, their profession, level of education and trial reviewing experience.

B. Challenges related to financial and infrastructure resource

Challenges related with financial resources mentioned by EFDA staff included: lack of budget to organize or attend trial related trainings organized by other stakeholders; having only

governmental budget for trial regulation which was not sufficient; and lack of support from partners of EFDA who were working in other units of the regulatory body. As one of the researchers, lack of laboratory capable to test the quality of imported products for clinical trial was also indicated as a barrier for trial implementation. Not having enough, lockable and separate spaces for archival and substandard office setup were also mentioned by one of the staff as infrastructures related challenge.

C. Challenges related with guidelines and criteria

Criteria

Having the same criteria for all types of trials and not contextualized requirements with the country's situation and with the type of product to be investigated were mentioned by 5 respondents as barriers to conduct trial on some areas of national need and traditional medicine.

As one of the respondents mentioned, having the same criteria for trials conducted by university students as partial fulfillment of their trainings and trials conducted on new drugs were barriers to encourage new investigators to conduct clinical trial.

One of the investigators mentioned that some criteria were included only for the sake of completing the form leading to extra pressure on investigators rather than protecting trial participants. However, 7 respondents involved mainly in clinical trials funded by international funders responded that there is no unnecessary criterion requested for trial authorization.

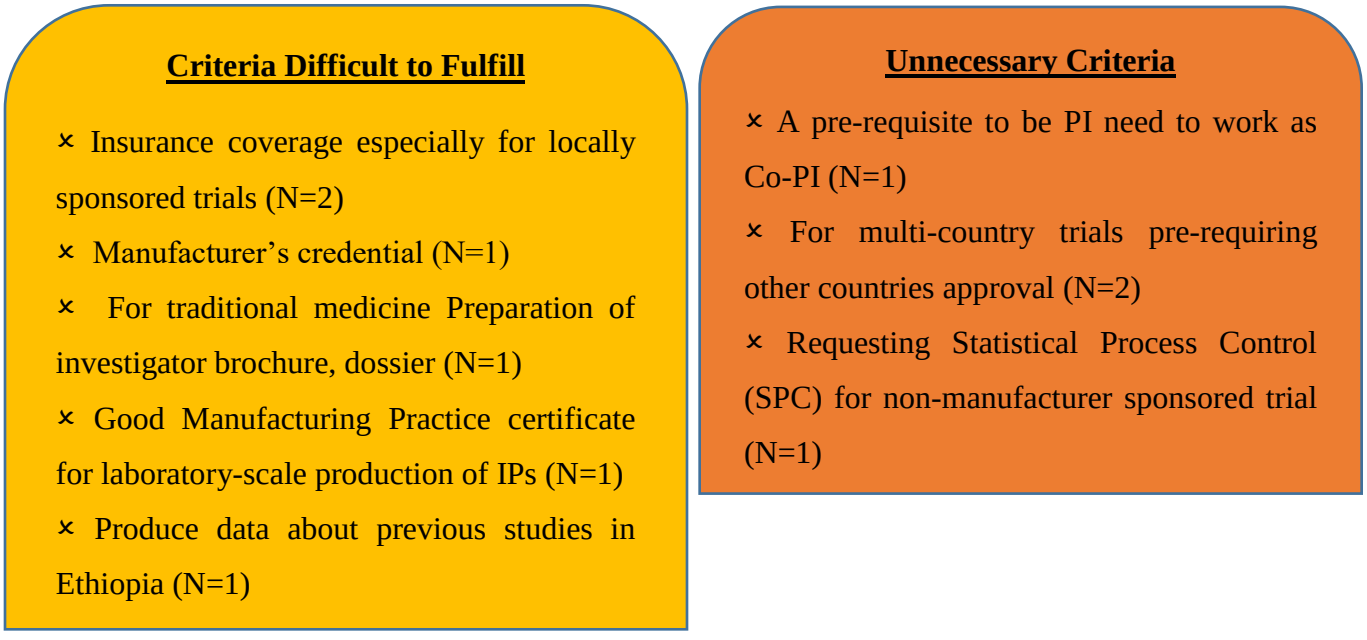

Figure 3. Criteria difficult to fulfill and unnecessary

Guidelines

In relation to guidelines, many barriers were raised both from the researchers and the regulatory staff which hindered trial development and make trial implementation difficult. Most commonly mentioned challenges by 6 of the respondents were, lack of detailed information on the guidelines with specification and pre-question for involvement of vulnerable groups in research. Not having clear procedure and timetable for each activity undertaken during protocol authorization. (N=6) was also mentioned as a barrier.

"It is the process that it takes you to get your approval. When should you expect your comments? When should you respond? Within what period you should respond to those comments. And after you submitted your comment when do you expect the approval. Those things should be kept clear." RSOBAH003

Other challenges reported both by researchers and EFDA staff as barriers were the guideline not being practical (N= 2), not having a separate guideline for different types and phases of trials like trials on traditional medicine (N= 3), lack of Standard Operating Procedures (SOP) for protocol review (N= 2).

The nature of the guideline which led to make a personal decision (N= 1), ambiguous definition of clinical trial and investigational product (N= 2), lack of detail information about specific issues (N= 1), not having case specific directives (N= 2), lack of specific guideline for trial materials importation (N= 1), taking much time to revise and apply regulation (N= 1) were considered barriers. Not updating the guideline regularly (N= 1), not uploading the updated part of the guideline in their website (N= 3), were also additional barriers.

Some guideline related challenges such as not having detail about vulnerable group exclusion, not having trial type-specific guidelines, ambiguous definition of clinical trial and investigational product, lack of specific guidelines for trial materials importation, and lack of activity-specific SOPs were also mentioned by participants from EFDA.

5.4.2 System-related challenges

Challenges related with trial authorization, service fee, product import and exportation, follow-up inspection, report and feedback provision, product disposal, means of communication and overall trial regulation system were discussed in this theme.

A. Challenges related to authorization

Challenges on the process of trial protocol authorization were reported both by investigators and the regulatory staff. Prolonged approval process was the challenge reported by mostof the respondents (N=10) for trial implementation. The approval process took 2 month up to 2 years as reported by investigators. As the EFDA staff indicated that providing the first review response might take 1 to 4 months and to review query responses it might take 1-4 weeks. One respondent said *"In a multi-country trial, when we got the approval and starts the recruitment the study get completed in other countries."* RSOBJU001.

Unnecessary protracted protocol review, detailed review comments and comments disagreement with other review committees were mentioned as barrier by 4 of the respondents. Not having a clear platform for approval steps and procedures was mentioned as a challenge by 3 respondents. Requiring hard copy submission of documents and poor documentation or archiving system for trial related documents were also barriers. Other challenges mentioned for trial authorization were reviewing protocols in a way of faultfinding; not having a joint review system with ethics committees; not involving external reviewers and lack of system to consult experts in protocol review process were mentioned by 2 of the respondents.

Not having a clear guide where to go and how to apply and no protocol prescreening during submission were pointed as challenges which extended the approval by 2 respondents. One of the respondents reported that not providing letter of receipt of application mentioning date and number of documents submitted made the review follow-up difficult.

Lack of streamlined approach for amendment (N=1), not having a system to handle researcher complaint (N=2), lack of clear guideline for approval or rejection of trials (N=1) and lack of a system to notify investigators when the review is completed (N=2) were stated as challenge by many investigators.

B. Challenges related to service fee

Not differentiating self-initiated or locally sponsored trials from external or industry sponsored trials, charging the same amount for all trials and requesting fees to be paid in dollar both for authorization and protocol amendment were reported by 8 of the respondents as barriers which hinder the involvement of national researchers in clinical trials and trial development in Ethiopia.

"The biggest complication was when they needed payment in dollars…. We need to submit the amendment and they refused to process because we weren't able to pay in the dollar because the money for the trial was in Ethiopia. We couldn't convert it into a dollar." RSOBC003

The amount of the service fee was too much even for sponsors (N=6) and for self-initiated and/or locally funded trials (N=4). Eight of the respondents, however, felt that the fee was fair and reasonable for trials funded by industries or profitable companies. Bureaucratic and time taking payment process which delayed approval and hindered trial implementation was identified (N=6).

One of the participants stated that the need for payment and the amount is not being announced on the website and require a service charge for amendment as a regulatory system barrier.

"……..but the number of amendments should be determined by what is needed scientifically not what can be afforded by the project. Otherwise, you know that is a real danger or pushing unsafe practice underground." RSOBC003

Paying service charge being a pre-requisite for protocol review (N=2), not getting good service compared to the amount paid (N=3), deciding service charge related issues without consulting other stakeholders (N=1) and unwillingness of the sponsors to pay this much amount of money for trial approval were also stated as barriers which affect trial development. On the contrary one of the EFDA staff mentioned that the service fee was cheaper than other countries and not too much compared with the regulatory services given. One of the respondents did not have any information about the service charge.

The regulatory staff also stated not posting the updated issues on payment on the website and guideline, like starting to receive in birr for nationally sponsored trials were also considered to create information gap.

C. Challenges related to trial materials import/export

Though the online product import application system was commendable the delay to get product import permission from EFDA and became difficult to follow the application progress were mentioned as barriers (N=5); not having complaint handling system for issues related with online application was mentioned as a challenge (N=1) and 2 of the researchers in the regions stated in person application for sample export permit and time taking to obtain the permit were also barriers which cause loss of money and time.

Time taking paper work at custom, staff of EFDA at airport not working for 24 hours and not doing or delayed product inspection by EFDA staff at port of entry were pointed out to be challenges (N=4). Lack of knowledge of EFDA staff at the port on Investigational Products (IPs)was also identified as a challenge (N=1). In addition, when trial participant sample is needed to be sent to another country for laboratory analysis not giving an export permit for all trial samples at one time and requiring to apply each time was mentioned as a challenge by 5 participants and also requiring to apply for product importation each time when trial materials or IPs are needed were stated as a barrier by one of the researcher. Frequently changing the importation requirements was stated as a barrier for trial material importation (N=3).

".....after preparing a list of things required for the importation of things …… just all of a sudden changes the new expectation, so it's very challenging to keep track of changes …"

RSOBJU003

Not having a separate custom system for trial-related materials import and export, lack of infrastructure to maintain product storage condition at custom, zero level flexibility on custom requirements, or not consider the situation was mentioned as a challenge concerning EFDA custom system were mentioned by 2 of the participants.

D. Challenges related to site inspection

Lack of regular site inspection and follow-up was mentioned as a barrier (N=12); only one of the respondents mentioned that there was regular site inspection from EFDA.

"I hadn't had a chance of having a regular visit from their side. Even if they say in the approvals they would have a regular visit at times even they might not come on demand from the project side." RSOBAH003

Not being inspected timely, doing only checklist based inspection, not conceptualizing with the trial type, not doing further investigation, not doing a supportive inspection or onsite support for the investigators and inspecting in the way of faultfinding were pointed out as a challenge.

By the staff of EFDA, not doing site inspection as planned and not having Standard Operating Procedure (SOP) to prioritize trials for conducting site inspection were also stated as a gaps.

E. Challenges related to report and feedback

As 2 of the researchers mentioned unless the researcher could provide the reports there was no proactive request of reports from EFDA and they did not even acknowledge on time reporting. One of the respondents mentioned that not providing response for the requested justifications as a challenge, and not giving exact and not getting clear response about the progress of protocol review was also stated as a challenge (N=2). Challenges related with the feedback provision were described on Figure 4.

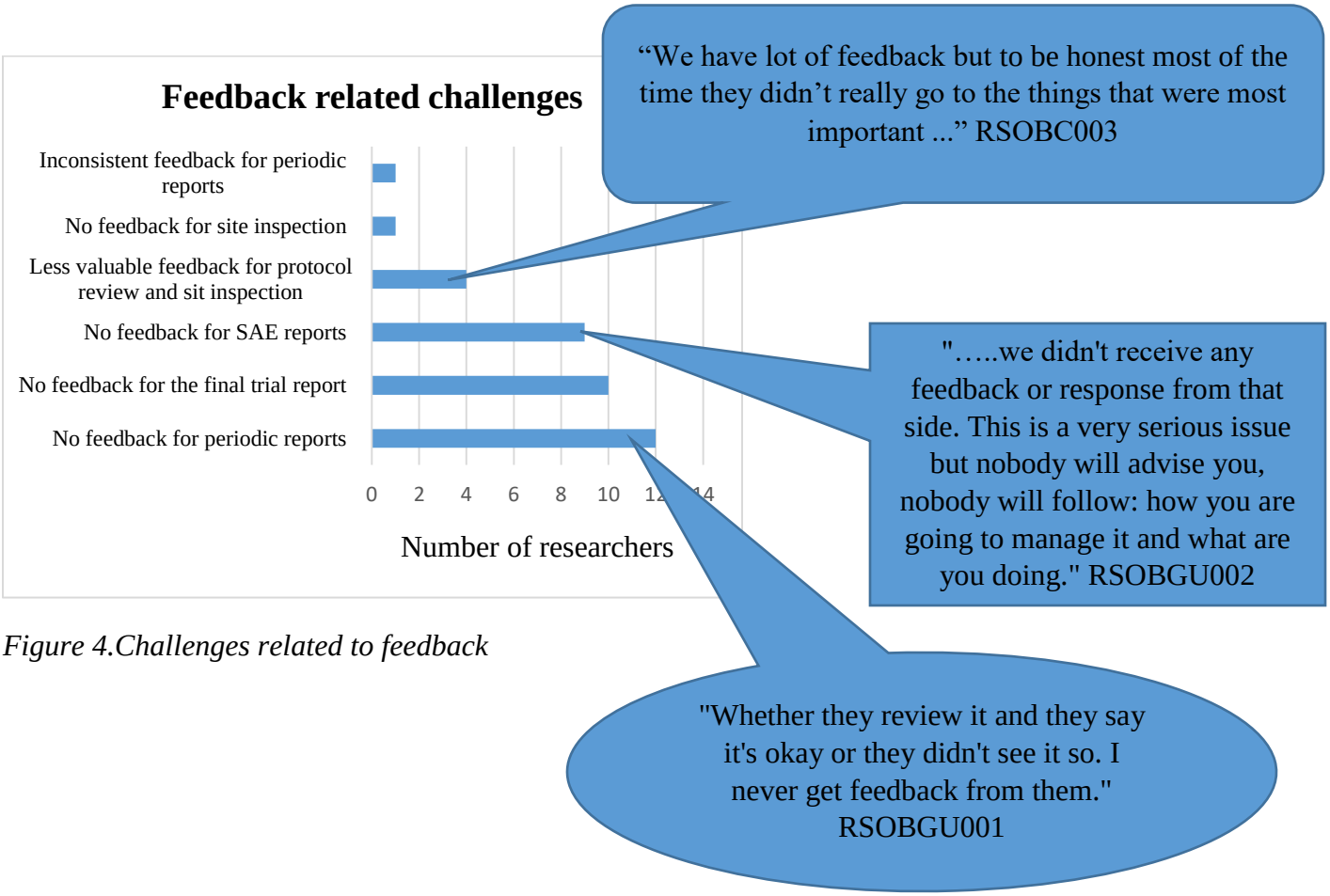

Figure 4.Challenges related to feedback

F. Challenges related to materials disposal

According to 3 of the respondents, the process of investigational product destruction was time taking and not properly handled by EFDA, and one of them also mentioned that the products would occupy space for storage at trial site. Not having a separate drug disposal system for trial

products and not timely providing a disposal certificate were also mentioned as challenges (N=2).

"They will not come even after repeated application. They don't even consider drug disposal as their responsibility so you have to beg for this also, write a letter, and later there are also issues to get disposal certificate." RSOBC001

Three of the participants mentioned that not having specific drug disposing company in the country licensed by EFDA was a challenge to destroy trial products. Lack of clear system for application of drug disposal and difficulty to identify the responsible directorate were mentioned as a challenge by one of the respondent. In contrast to others two of the researchers stated that the disposal process was facilitated.

G. Challenges related to communication

In the communication between the researcher and EFDA staff, there are different factors mentioned as a challenge by trial experts. According to 8 of the respondents, personal visit to the office to have clear and up to date information or to give some clarification, not having electronic means of authorization application; lack of communication via email; requiring hard copy submission of protocol and periodic reports are challenging factors which will cause loss of money and time of the researchers. As the 3 of regional researchers this factors will have a high impact on them.

*"… when you go in person you can access it but for someone like us who work out of the center Addis Ababa it is very difficult to have a communication with them.*RSOBGU001

Not responding office phone, posting email address on website and guideline which is not functional, and using staff's personal phone to get information about protocol review progress or other issues were also stated as communication challenge (N=7).

One of the respondents mentioned that lack of clear information on the website about where to go, what to do and when to get responses on trial authorization and not having information about changes made on trial regulation system are challenges especially for new researchers.

Other challenges were: not having online system to send review feedback (N=1) and not having documentable means of communication showing the progress of protocol review (N=2) were

also pointed out by respondents. One of the researchers mentioned that in person visit would have a positive impact by shortening approval process.

H. Challenge related to trial regulation

Having a rigid system and not trying to understand the researcher's condition (N=4) and being conscience and unreasonably stringent without considering the current global science level (N=1) were mentioned as factors which hindered trial development in the country though they could protect the public from trial related damages. Being too stringent on trials approval process which comes to EFDA, not having a system to control trials conducted without regulatory authorization and not being vigilant to identify unauthorized trials were also pointed out to be factors affecting participants' safety (N=3).

"So even at the time we were straggling to get that ethical clearance, there were researchers and research that going around doing clinical trial without getting authorization and any ethical clearance in Ethiopia. So I mean that type of situation that type of partiality you know or inequity in terms of being treated unfairly also calls lots of frustration and grievance." RSOBJU002

As of the 2 respondents regulatory system being unfavorable for international researchers and having a locked system not attractive to external researcher to conduct trial in Ethiopia and not collaborating with researchers and other stakeholders to develop clinical trial regulation were stated to be other barriers for trial development.

As a country implementing hierarchical trial approval system and the EFDA being another layer for the review process, barriers to get information about the mandate of EFDA on clinical trials, not having a system to regulate and to follow the trial result implication, not controlling the expected benefit of the trial for the country, and being unnecessarily stringent due to wrong understanding of the regulatory body to be the only responsible body for the safety of trial participants were mentioned as challenges for trial development.

"I could be completely wrong but that is my understanding, sometimes their orientation is you know they assume they are the once to protect the society. They are there to defend from the evils of the researchers." RSOBJU002

As one of the regulatory responsibility not giving a focus for clinical trial regulation, giving less attention to regional research institutions and mainly focusing on research done in A.A, not attending meetings organized by researchers or other stakeholders and not participating in international trainings organized by sponsors or researchers and not showing improvement on trial regulation systems were also mentioned to be challenges.

5.5 Prioritized Problems

After identifying the challenges, respondents were asked to prioritize the challenging factors based on their impact they have on trial implementation and development. The participants prioritized the problem based on their personal experience, because of that one factor can be a primary challenge for some researchers and it can be secondary or tertiary for the others (Figure 5).

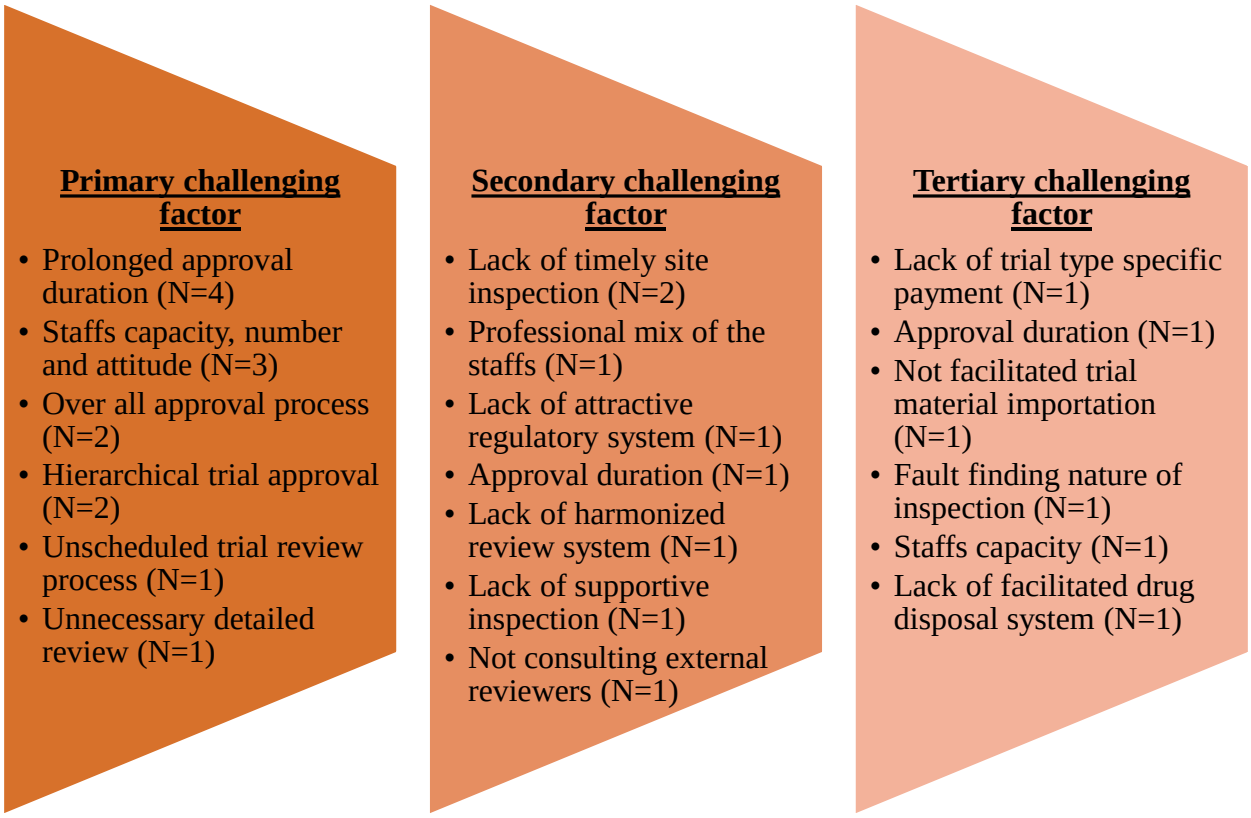

Figure 5. Prioritized problems

6. DISCUSSION

The study was designed to identify regulatory system opportunities which enhanced clinical trials implementation and development and regulatory barriers that hindered clinical trial implementation in Ethiopia, by interviewing clinical trial investigators and EFDA clinical trial team.

Researchers who had experience in conducting clinical trials explained that there were some opportunities of the regulatory system which enhanced trial development. Meetings organized by EFDA to have a discussion with researchers were mentioned as an opportunity which helped researchers raise issues which need improvement of trial regulation and have information on some updated issues. The ability of EFDA to do protocol review and site inspection were also pointed as an opportunity which facilitated legal way of trial implementation. Willingness of the management and staff of EFDA to improve the regulatory system, availability of guidelines for trial authorization and inspection and the online accessibility of the guidelines were also stated as opportunities which encouraged researchers' involvement in clinical trial.

The EFDA clinical trial team expressed the interest of EFDA management to address the regulatory challenges such as trial service fee, short and long term trainings, to be opportunities to boost the interest of the clinical trial team within the EFDA and improving the regulatory system for trial development in the country at large. There is no difference between researchers from Addis Ababa and other parts of Ethiopia to be beneficial from regulatory system opportunities.

Clinical trial researchers expressed the barriers they faced at all stages, starting from trials authorization to completion.

In trial pre-initiation phase there were a number of barriers in getting trial authorization on time from EFDA. The challenges started from lack of appropriate information on the role of EFDA regarding clinical trials.

Though the EFDA staff stated that there was a help desk to provide appropriate information to newcomers most of the researchers disagreed for the existence of such help.

As has been indicated on reviews of successes and challenges to do clinical trials in low and middle-income countries (13) and conduct of clinical trials in developing countries (1), in our

study not having a capacity to review trial protocols due to lack of expertise, trainings and experience in the area, delayed the approval process leading to frustration of researchers on the conduct of clinical trials in Ethiopia. The findings of the present study are in agreement with those obtained from a similar study done on a review of regulatory oversight of clinical trials in Africa (14), which identified barriers like the limited number of staff with limited mix of professions within the clinical trial team which called upon a need for academic improvement to affect protocol review process and the final decision made by the regulatory system.

Automatic rejection of trials involving vulnerable groups without requesting justifications for their inclusion, lack of clear criteria to exclude vulnerable groups in trials and not considering the global experience were pointed out to be barriers to generate local data which helps to address nation specific conditions. These findings are in agreement to those of another study conducted in Ethiopia to identify challenges for self-initiated trial which reported the difficulty of involving vulnerable group in trials(12).

The other major factor mentioned as a barrier by almost all researchers was associated with the service fee for trial authorization including protocol amendment such as: payment to be effected in dollar and non-discriminatory amount irrespective of the differences in trial types, trial complexity, trial phase and sponsor type (e.g., same amount requested for nationally sponsored trials)as well as the prepayment requirement with the long bureaucratic payment process were mentioned to be serious barriers for researchers to conduct self-initiated and locally sponsored trials. The requirement to pay service fee for protocol amendment in dollar might force investigators not to apply for every amendment they made leading to the possibility of unethical practice which might harm trial participants. The high service fee requested for locally initiated trials might encourage investigator to conduct clinical trials with requesting for trial authorization leading to illegal practices which will add a challenge to the strength of the regulatory system.

Absence of specific criteria for different types, natures and phases of trials in the regulatory guideline and also lack of activity-specific directive were hindering development of traditional medicines through clinical trials. Comparable with the systematic review conducted in 2015 (7), participants in this study also mentioned that absence of clear schedule for each activity on the

guideline became a barrier to implement trials as planned by the researchers resulting in sponsors loss of interest to conduct trials in Ethiopia.

Consistent with the findings of a qualitative study carried out in Ethiopia to investigate barriers and enablers to the implementation of local investigator-initiated clinical trials (12), most researchers in the present study pointed out that long time taken to issue trial authorization leading to delayed trial initiation to be a barrier for involvement of Ethiopia in multi-national, externally funded and international companies sponsored trials and the sponsors and funders will lose interest to conduct trials in Ethiopia. The stringent review process carried out sequentially at various levels of ethics committees and irreverent feedbacks which had no relation to participants' protection and data credibility discouraged investigators to conduct clinical trials. Lack of coordination between ethics committees and the regulatory body to harmonize trial protocol review process which delay trial approval resulting in loss of researchers' interest to be engaged in clinical trials.

Product importation for trial purpose also identified as another challenging factor for trial implementation. The time taking process to obtain import permit of trial materials and frequent changes of the required documents for importing products lead to additional cost and waste time of researchers as well as sponsors. A review on the impact, challenges, and future projections of vaccine trials in Africa also showed that a delay to obtain product import permit caused budget stress due to value depreciation of local currency (9).

After having the permit; custom clearance and product inspection at port of entry by EFDA staff also took longer time. As the staff are not working for 24 hours, i.e., work only for fixed time to conduct product inspection, there will be delay product importation. Furthermore absence of temperature regulated storage area at the port of entry, the imported products will be liable for damage and premature decomposition before use resulting in loss of budget and interest of sponsors to work in Ethiopia. That is why most of the trials are conducted in countries with efficient regulatory system and custom clearance. This means Ethiopia cannot be competitive to approve and to attract externally and companies sponsored trials. Researchers working in regions within Ethiopia are discouraged to conduct clinical trials as they are required to apply for material transfer permit for each sample in person at EFDA headquarters which incurs extra expense and time of the researcher. Lack of a separate custom system for trial materials

importation also discourages researchers to be involved in clinical trials as this also incurs extra expense and wastage of time.

During trial implementation, absence of a regularly scheduled or consistent site visit will be a barrier to conduct GCP compliant trials, participant protection and data credibility will be serious problems. Even in scenarios where site inspections were conducted, the staff had no experience of inspection and they did not achieve the objectives of the inspection instead they were faultfinding. This could rather be frustrating for investigators and will not contribute to fill the implementation gap. Most of the researchers stated that even if they were reporting every SAE and sending progressive reports as required there was no feedback from the regulatory body for any of their reports nor acknowledgment for the receipt of the reports. This will forfeit the purpose of reporting. Unless the SAEs are not reviewed properly, they may not be able to serve as signal detection and contribute for labeling information as well as taking corrective measures on the trial conduct. There was also absence or delay in providing feedback for trial closeout reports which could prolong trial completion period unnecessarily as to have regulatory approval is a requirement to complete clinical trials. Not getting feedback on time, requiring long time for the disposal of the remaining investigational products and not providing a disposal certificate on time were also barriers to complete trial document compilation on time. Moreover, lack of a separated drug disposal system for trial materials, not having its own disposal site or not identifying licensed drug disposing organizations were pointed out as factors which contributed for delayed destruction of the remaining investigational products. This might be hazardous to the environment.

In contrast to a qualitative study investigating the barriers and enablers to locally-led clinical trial conduct in Ethiopia, Cameroon, and Sri Lanka (20), our study participants mentioned having a regulatory body with legally stated role and responsibility to be one of regulatory strength. In a country where there are no larger number of trials conducted, many published qualitative work designed to identify regulatory system opportunities and clinical trial regulation barriers for trial implementation and development in Ethiopia may not be expected. So we believe that our descriptive study will be used as important input to improve clinical trial regulation system and to intervene accordingly on challenging factors.

7. CONCLUSION

Clinical trial regulation is a multi-sectorial activity and EFDA is one of the stakeholders. The results of our study suggested that the capacity of EFDA will have a direct impact on clinical trial development in the country. Not having a strong, well organized and capable regulatory authority will have a negative impact on clinical trial development in the country and act as a bottleneck for researchers and sponsors to conduct clinical trials. According to our study result in addition to the existence of EFDA trial regulatory team to do trial authorization and site inspection there are only limited regulatory system opportunities mentioned as factors which enhance trial development in the country.

Researchers faced different challenges in relation to the EFDA trial regulatory system starting from trial authorization to the completion or closeout of the study. Challenges like prolonged approval duration, unscheduled activity for trial authorization, the amount and being in dollar of service fee, not doing a regular site visit, not providing feedback for periodic and conditional reports and staffs lack of capacity are mostly denoted regulatory system barriers for doing trials in Ethiopia. From the identified factors most of them were believed to have a direct impact on trial development and mentioned by more than one of the participants as factor which hinder the researchers' involvement on clinical trial. On top of the challenges faced by researchers in Addis Ababa, those from regions face additional challenges like in person application for trial authorization and product export permit which incur additional cost and time consumption. From this study it can be concluded that all factors have direct or indirect negative impact on clinical trial growth in Ethiopia. To measure the level of impact of each factor and to prioritize the impacts on trial development it needs quantitative study.

8. RECOMMENDATION

To improve the clinical trial regulation system all stakeholders of clinical trials need to work together with EFDA to discharge their responsibilities and needs to support the system in all aspects. The EFDA need to work hard to strengthen the regulatory system of clinical trials in Ethiopia. The collaborative efforts of researchers, local and international sponsors, universities, research institutions, ministry of health and NHRERC are highly needed. The following corrective measures needs to be taken to overcome challenges, to improve the regulatory system and to encourage clinical trial development in Ethiopia.

- Enrich EFDA manpower in number, qualification, professional mix and trial related trainings. The staffs also need to understand the benefit of clinical trial for the public.
- Online systems should be developed to authorization application, review feedback provision, response submission, follow Protocol approval progress and to have documentable track record.
- Within EFDA there should be well organized and secured archival for trial documents and the office needs to well equipped.
- There should be prescreening during protocol submission and clear platform which shows the overall procedures of protocol approval process which is time bounded and duration of trials authorization needs to be shortened.
- EFDA and ethical committees in collaboration need to have a clinical trial registration platform and there should be nationally harmonized protocol review system and guideline.
- The prerequisites for protocol authorization need to be reviewed and contextualized.
- EFDA should establish a system to acknowledge clinical trial experts for their contribution, to encourage new researcher involvement and to have a feedback from the researchers about their regulation system.
- To encourage clinical trial on traditional medicine and to regulate trials as required EFDA need to have guidelines which are specific for clinical trial type and phase of the study.
- Regulatory authority needs to develop directives and SOPs for specific issue.

- Guidelines need to be updated regularly and/ or as needed and need to be uploaded on the website.
- The amount of service fee needs to be categorized based on the trials nature/ complexity, funders, trial phase and types of investigational product.
- EFDA needs to have a clear system to consult external reviewers and to pay for their time compensation
- Based on the risk level of the trials there should be regularly scheduled site inspections or follow-up visits and feedback need to be provided for site inspection and reports (periodic, SAEs and final).
- Need to have a separate import and exportation and custom system for clinical trial related materials.
- The regulatory authority need to work in collaboration with drug disposing companies.
- In addition to trial regulation EFDA need to involve on clinical trial development activities and work on awareness creation about the role and responsibility of the institution.
- To make change on the regulatory system and to overcome the identified challenges EFDA needs to acknowledge the existence of those problems or challenges.
- In addition to governmental budget EFDA needs to work with collaborators to have a financial support for clinical trials regulation.
- EFDA requires a system which helps to identify illegal clinical trial practices within the country.

9. LIMITATION OF THE STUDY

To conduct this study we have a limited time and resource because of that only researchers who had an experience on doing clinical trials were taken as a study participant but it would have been good that if we were include researchers who are doing other types of studies, because it give us an information about the factors which act as a barrier for the researchers to engage in clinical trials.

To complete the study within the specified period of time, in addition to restricting types of participants we were also mainly focus on the current experience of the researchers and it lacks a data about the progress of the regulatory system overtime.

In this study assuring participants confidentiality may not be 100% successful, because the numbers of clinical trial researchers within the country were limited and their experience in relation to EFDA Is easily identifiable by the staffs of EFDA at clinical trial team.

REFERENCE

1. *Devasenapathy N, Singh K, Prabhakaran D. Conduct of clinical trials in developing countries: A perspective. Curr Opin Cardiol. 2009;24(4):295–300.*
2. *Chandra RS, Orazem J, Ubben D, Duparc S, Robbins J, Vandenbroucke P. Creative solutions to extraordinary challenges in clinical trials: Methodology of a phase III trial of azithromycin and chloroquine fixed-dose combination in pregnant women in Africa. Malar J. 2013;12(1):1–8.*
3. *Food , Medicine and Healthcare Administration and Control Authority of Ethiopia.Second Edition Addis Ababa , Ethiopia. 2017;(June).*
4. *Nichols, Hannah. How do clinical trials work and who can participate?Medical News Today. 2014*
5. *Nair SC, Ibrahim H, Celentano DD. Clinical trials in the Middle East and North Africa (MENA) Region: Grandstanding or Grandeur? Contemp Clin Trials [Internet]. 2013;36(2):704–10. Available from: http://dx.doi.org/10.1016/j.cct.2013.05.009*
6. *https://ClinicalTrials.gov.*
7. *Alemayehu C, Mitchell G, Nikles J. Barriers for conducting clinical trials in developing countries- a systematic review. Int J Equity Health. 2018;17(1):1–11.*
8. *Kochhar S. Challenges and impact of conducting vaccine trials in Asia and Africa: New Technologies in Emerging Markets, October 16th-18th 2012; World Vaccine Congress, Lyon. Hum Vaccines Immunother. 2013;9(4):924–7.*
9. *Idoko OT, Kochhar S, Agbenyega TE, Ogutu B, Ota MOC. Review: Impact, challenges, and future projections of vaccine trials in Africa. Am J Trop Med Hyg. 2013;88(3):414–9.*
10. *Mbuagbaw L, Thabane L, Ongolo-Zogo P, Lang T. The challenges and opportunities of conducting a clinical trial in a low resource setting: The case of the Cameroon mobile phone SMS (CAMPS) trial, an investigator initiated trial. Trials. 2011;12:1–7.*
11. *Fekadu A, Teferra S, Hailu A, Gebre-Mariam T, Addissie A, Deressa W, et al. International Clinical Trial Day and clinical trials in Ethiopia and Africa. Trials. 2014;15(1):1–6.*
12. *Franzen SRP, Chandler C, Enquselassie F, Siribaddana S, Atashili J, Angus B, et al. Understanding the investigators: A qualitative study investigating the barriers and enablers to the implementation of local investigator-initiated clinical trials in Ethiopia.*

BMJ Open. 2013;3(11).

13. *Grover S, Xu M, Jhingran A, Mahantshetty U, Chuang L, Small W, et al. Clinical trials in low and middle-income countries — Successes and challenges. Gynecol Oncol Reports [Internet]. 2017;19:5–9. Available from: http://dx.doi.org/10.1016/j.gore.2016.11.007*
14. *Maïga D, Akanmori BD, Chocarro L. Regulatory oversight of clinical trials in Africa: Progress over the past 5 years. Vaccine. 2009;27(52):7249–52.*
15. *Brennan MJ, Fruth U, Milstien J, Tiernan R, Nishioka SDA, Chocarro L. Development of new tuberculosis vaccines: A global perspective on regulatory issues. PLoS Med. 2007;4(8):1299–302.*
16. *Terblanche M, Burgess L. Cardiovascular clinical trials in Africa: opportunities and challenges. SA Hear. 2017;8(2):114–21.*
17. *Kuepfer I, Burri C. Reflections on clinical research in sub-Saharan Africa. Int J Parasitol. 2009;39(9):947–54.*
18. *Africa WR office for. Who Country Cooperation. Who. 2015;*
19. *Mooney T, Smout E, Leigh B, Greenwood B, Enria L, Ishola D, et al. EBOVAC-Salone: Lessons learned from implementing an Ebola vaccine trial in an Ebola-affected country. Clin Trials. 2018;15(5):436–43.*
20. *Franzen SRP, Chandler C, Siribaddana S, Atashili J, Angus B, Lang T. Strategies for developing sustainable health research capacity in low and middle-income countries: A prospective, qualitative study investigating the barriers and enablers to locally led clinical trial conduct in Ethiopia, Cameroon and Sri Lanka. BMJ Open. 2017;7(10):1–16.*
21. *Manuscript A. NIH Public Access. 2014;23(5):461–2.*
22. *Gazette Federal Negarit. Federal negarit gazette Scanned with CamScanner. 2019;*
23. https://www.australianclinicaltrials.gov.au/why-do-we-need-clinical-trials

ANNEX 1. STUDY PARTICIPANT INFORMATION SHEET

Consent Form

Regulatory System opportunities and Barriers for Conducting Clinical Trials in Ethiopia: A descriptive qualitative Study

I confirm that I have read and understood the participant information sheet for the above study and have had the opportunity to ask question. I understand that my participation is voluntary and even if I agree to participate now, I can withdraw at any time or refuse to answer any question without any consequences. I understand that participation involve deep interview and I understand that I will not benefit directly from participating in this research. I recognize that all information I provide for this study will be treated confidentially and in any report on the results of this research my identity will remain anonymous. I understand that I am free to contact any of the people involved in the research to seek further clarification and information.

Name of Participant Signature_____ Date _____

Signature of Principal Investigator:_____ Date _____

You will be given a copy of this form to keep for your records. This consent form will be kept by the researcher and was approved by the IRB on [26/12/19].

Mehiret Maru…….Phone number [09 10 00 79 42]

Email: [Mehiretmaru2019@gmail.com]

Dr. Yemtubezinash W/Amanuel.....Phone number [09 11 22 58 32]

Email: [yimtuwa@gmail.com]

Prof. Eyasu Makonnen……..Phone number [09 11 24 75 56]

Email: [eyasumakonnen2yahoo.com]

ANNEX 2. STUDY PARTICIPANTS CONSENT FORM

Participant Information Sheet

Study title: Regulatory System opportunities and Barriers for Conducting Clinical Trials in Ethiopia: A descriptive qualitative Study

Investigator: Mehiret Maru (Pharmacist, MSc student in clinical trial)

You are invited to take part in this research project. Before you decide to do so, it is important you understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

What is the Purpose of the Study?

As we know in Ethiopia there are so many opportunities to conduct clinical trials but there are also obstacles at different levels which can hinder the initiation and implementation of trials. The purpose of this research is to investigate the regulatory factors which can be an opportunity to conduct clinical trials and to identify a barrier/challenge for the implementation of clinical trials in Ethiopia and to specify some solutions to overcome this challenge. We believe this research will contribute to generate relevant data for regulatory authority and policy makers to improve regulatory system and make an amendment on policies to enhance the conduct of clinical trials in Ethiopia.

Why Have I Been Chosen?

You have been chosen because as a PI or co-PI with full delegation from PI you had experience on conducting Clinical Trials (CT) in Ethiopia, and you will have knowledge about the service provided by EFDA for the initiation and implementation of CT and you can easily identify the regulatory challenging factors which can hinder the conduct of CT in Ethiopia.

Do I Have to Take Part?

It is up to you to decide whether or not to take part. You are kindly asked to go through this information sheet, which we will hero you understand your participation in this study. If you do

decide to take part you will be asked to first sign a consent form. However, you are free to withdraw at any time, without giving an explanation without any consequences on your clinical trial approval process.

What is Expected of Me if I Take Part?

You will be asked to have a deep interview and your voice will be recorded during the interview. The recorded voice will be transcribed to written form for further analysis.

Please answer the questions with good and brief explanation during deep interview. There are some very quick short questions and some which take a little more time and thought to answer. Please answer all questions applicable to you, however if there are any questions you do not wish to answer just tell the interviewer to pass it over.

What are the Possible Discomfort and Risks of Taking Part?

Participating in this research is not anticipated to cause any discomfort on you.

What are the Possible Benefits of Taking Part?

There is no direct benefit to you in participating in the study, but the information we collect from you will help improve regulatory approval process for investigators who will be involved in the conduct of clinical trials in the future.

What about Confidentiality?

All of your voice records will be kept confidential and the transcript are anonymous, so no one will have knowledge concerning your identity, or about which responses you gave. Your voice recorded and anonymous transcript will only be accessed by the research team conducting the study. The hard copy of transcript and the original tape record will be kept in a locked drawer and the soft copy of voice record and anonymous data will be kept in a password protected computer. The responses you provide will be used in the researcher's final year thesis; direct quotes may be taken from the material but will remain completely anonymous.

Will I be Recorded, and How Will the Recorded Media be Used?

Your voice will be recorded during the interview and the voice will be transcribed to written form and used for further data analysis.

Who Has Reviewed the Study?

The study was approved by the IRB of CDT Africa, AAU.

Whom Can I Contact for Further Information?

If you have any questions regarding the study you may contact:

Mehiret Maru…….Phone number [09 10 00 79 42]

Email: [Mehiretmaru2019@gmail.com]

If you have any questions about your rights as study participants, you can contact:

IRB-CDT Africa Phone number [09 11 24 75 56]

ANNEX 3. ENGLISH VERSION KEY INFORMANT INTERVIEW GUIDE

Interview Guide for Clinical Trials Principal Investigators

I. Background

1. Please tell me about yourself

   Probes: → Gender

   →Academic background

   →Year of experience

   →Institution

2. Tell me about your clinical trial experience

   Probes: → For how long have you been engaged in clinical trials?

   →In how many clinical trials have you ever participated as a PI?

   →When was your last time involvement in clinical trial as a PI?

II. Regulatory system opportunities

3. Please tell me about the strengths of FDA regarding

   Probes: →Clinical trials authorization

   →Clinical trials inspection

   →All services related to clinical trials

4. What are the opportunities provided from FDA for the execution of clinical trials Ethiopia?

   Probes: →Any types of support which helps to conduct clinical trials easily.

   →Starting from application for authorization up to the end of the trial.

III. Challenges to Get clinical trials Authorization

5. How do you know about the importance of FDA trial authorization?
6. What was the challenge to know about the role/ mandate of FDA in CT?

   Probes →Please explain

7. What was/are the challenge you face during your visit to FDA as a customer to get trial related service?

   Probes →Please explain more

8. How can it be a challenge for you as investigator to conduct trials in Ethiopia?
9. How do you know (get the information) about the criteria that you need to fulfill to get trial authorization

   Probes → What was the challenge you faced to get this information

10. Which criteria /document was difficult to provide/ fulfill?

    Probes → What is your thinking about its importance?

11. How can it be a challenge/barrier to conduct trials in Ethiopia?
12. Tell me your opinion about the **number** and **qualification/ experience** of FDA staffs in comparison with the mandate they had.

    Probes → How can it be a challenge/ barrier to conduct trials in Ethiopia?

13. From your experience what was the longest time does it take to get trial authorization from FDA?

    Probes → How can it be a challenge/ barrier to conduct trials in Ethiopia?

14. What is your thinking about the authorization service charge/payment requested by FDA?

    Probes → How can it be a challenge/ barrier to conduct trials in Ethiopia?

15. What is your thought about the FDA Guidelines and directives used for clinical trial?

    Probes → How can it be a challenge/ barrier to conduct trials in Ethiopia?

16. Tell me about any barrier/ challenge you faced to get trial authorization?
17. Is there any trial that you applied and not authorized by regulatory authority (EFDA)?

    Probes → If yes, what was the reason?

IV. Challenges During Implementation

18. After getting the authorization, what are the barriers/ challenges you faced during the trial implementation?

    Regarding

    - Inspection time
    - Inspection feedback
    - Regulatory measures
    - SAE reporting system
    - Others

19. Have you ever participated in a trial which required sample export for analysis?
    - If yes, what were the regulatory challenges you faced
20. Have you ever initiate a clinical trials by yourself?
    - If yes, how can it different from other trials initiated by sponsors?
21. Tell me all about the challenge/ barriers you faced to implement this trial in Ethiopia.

V. Challenges After Completion

22. After conducting the trials, what are the barriers/ challenges you faced during the trial completion?

VI. Problem Prioritization

23. From the challenges you discussed previously can you prioritize them based there negative impact on trial implementation in Ethiopia?

VII. Recommendations

24. What are the areas which needs an improvement?
25. What type of support does FDA required to overcome the challenges?
26. From whom the support should be provided?
27. Can you propose some solutions/way outs for the above regulatory system barriers?
28. Have we missed something you think is important? / What else should we talk about regarding this issue?

ANNEX 4. AMHARIC VERSION KEY INFORMANT INTERVIEW GUIDE

ከህክምና ማኅራጥና ትሃላፊዎችጋርየ ሚደረግቃለ ማኪይቅመመሪያ

I. ዳራ

1. እባክዎንስለራስዎይንገሩኝ?

ምሪ ሚራዎች →፬ታ

→ትምህርታዊዳራ

→የ ሚሰሩበት ተቋም

→የ ስራል ምድ

2. በህክምና ማኅራስራላይስላሎትየ ስራል ምድንገሩኝ?

ምሪ ሚራዎች →ለ ምን ያህልጊዜበህክምና ማኅራዎችጥና ት ውስጥሲሰሩቆይተዋል?

→እንደዋና የ ጥና ትሃላፊበ ምን ያህልየ ህክምና ማኅራዎችላይተሳትፈዋል?

→በ ህክምና ማኅራዎችላይእንደዋና የ ጥና ትሃላፊለ ሚጨፈሻ ጊዜየ ተሳተፉትመቼነ በር?

II. የ ቁጥጥር ስር አቱየ ሚፈጥራቸውመልካ ምአ ጋጣሚዎች

3. እባክዎን ስለ ምጣብእና መድሃኒት ጠንካራጎኖች ይንገሩኝ?

ምሪ ሚራዎች →የ ህክምና ማኅራ ጥና ቶችን የ ማኅራት ፈቃድ ከ ማኅጠት አኳያ

→የ ህክምና ማኅራ ጥና ቶችን ከ ማቆጣጠር አኳያ

→ከህክምና ማኅራ ጥና ቶች ጋር የ ተዛ ማዱ ሁሉም አገ ልግሎቶች ላይ

4. የ ህክምና ማኅራ ጥና ቶችን ለ ማኅራት ከ ምጣብ እና መድሃኒት ባለስልጣንየ ሚ ኙመልካ ምአ ጋጣሚዎች ምን ድን ና ቸው?

ምርመራዎች →ክሊኒካዊ መካራዎችን በቀላሉ ለማካሄድ የሚረዳ ማንኛውምዓይነት ድጋፎች

→የማስራት ፈቃድ ለማግኘት ከማመልከት ጀምሮ ጥናቱን ሰርተውእስከሚያጠናቅቁበት ጊዜ ድረስ

III. የህክምና መካራ ጥናቶችን የማስራትፈቃድለማግኘትተፈታታኝሁኔታዎች

5. የህክምና መካራጥናት ለማካሄድየምግብእናየመድኃኒትባለስልጣን ሚጋገጩማግኘትአስፈላጊ ሚሆኑንእንዴትአወቁ?
6. የምግብእናየመድኃኒትባለስልጣንበህክምና መካራ ጥናቶችውስጥያለውን ሚና/ተልእኮለማወቅየነበሩትፈታኝሁኔታዎችምንነበሩ?
7. ከህክምና መካራ ጥናቶችጋርበተገናኘየተለያዩአገልግሎቶችንለማግኘትወደምግብእና መድኃኒትባለስልጣንሲሄዱምንተግዳሮቶች/ፈታኝነገሮችነበሩ?
8. እንደተመራማሪነትዎእኚህፈታኝሁኔታዎችበኢትዮጵያውስጥየህክምና መካራ ጥናቶችለማካሄድእንቅፋትሊሆንየሚችለውእንዴትነው?
9. የህክምና መካራ ጥናት ፈቃድለማግኘትለማመልከትስለሚያስፈልጉትመመዘኛዎችእንዴትሊያውቁቻሉ (በምን መንገድ መረጃውን አገኙ)

ምርመራዎች →ይህንንመረጃለማግኘትምንተግዳሮቶችነበሩ

10. የትኛውን መመዘኛ /ሰነድለማቅረብ/ለማሟላትአስቸጋሪሆኖበትነበር?

ምርመራዎች →ስለአስፈላጊነቱእርሶያሎትአመለካከትምንድነው?

11. ይህ መመዘኛ/ ሰነድማጠየቁበኢትዮጵያየህክምና መካራ ጥናቶችን ለማካሄድእንቅፋትሊሆንየሚችለውእንዴትነው?
12. የምግብእናየመድኃኒትባለስልጣንሰራተኞቹን ብዛት፣ ልምድእና ብቃትካለበትሃላፊነትጋርሲነፃፀርያሎትንአስተያየትይንገሩኝ፡ ፡

ምር ሚራዎች

→ይህ ሁኔ ታበ ኢትዮጵያ የ ህክ ምና ማካ ራዎችን ለ ማ
ካ ሄ ድፈ ታኝ / እ ን ቅፋ ትእ ን ዴትሊ ሆን ይች ላ ል ?

13. ካ ሎት ል ምድበ ማ ሳ ትየ ህክ ምና ማካ ራጥና ትማካ ሄ ጃ ፈ ቃድ ከ ምግ ብ እ ና
ሞድሃ ኒ ት ባ ለ ስ ል ጣን ለ ማግ ኘ ትየ ወሰ ደ በ ትረ ዝሞ ዚ ሜ ምን ያ ህ ል ነ ው?

ምር ሚራዎች

→ይህ ሁኔ ታበ ኢትዮጵያ የ ህክ ምና ማካ ራዎችን ለ ማ
ካ ሄ ድፈ ታኝ / እ ን ቅፋ ትእ ን ዴትሊ ሆን ይች ላ ል ?

14. በ ምግ ብእ ና ሞድሃ ኒ ትባ ለ ስ ል ጣን ስ ለ ሚከ የ ቀ ውየ ፍ ቃድአ ገ ል ግሎ ትክ ፍ ያ የ እ
ር ስ ዎ ሀ ሳ ብምን ድ ነ ው?

ምር ሚራዎች

→ይህ ሁኔ ታበ ኢትዮጵያ የ ህክ ምና ማካ ራዎችን ለ ማ
ካ ሄ ድፈ ታኝ / እ ን ቅፋ ትእ ን ዴትሊ ሆን ይች ላ ል ?

15. ለ ህክ ምና ማካ ራ ጥና ት
የ ሚከ ቅመ ምግ ብእ ና የ ሞድ ታ ኒ ትባ ለ ስ ል ጣን መሚ ያ ዎች ላ ይየ እ ር ስ ዎ ሀ ሳ ብ
ምን ድ ነ ው?

ምር ሚራዎች

→ይህ ሁኔ ታበ ኢትዮጵያ የ ህክ ምና ማካ ራዎችን ለ ማ
ካ ሄ ድፈ ታኝ / እ ን ቅፋ ትእ ን ዴትሊ ሆን ይች ላ ል ?

16. የ ህክ ምና ማካ ራ ጥና ት
ፈ ቃድለ ማግ ኘ ትስ ላ ጋ ጠመ ዎ ትማን ኛ ውን ምኡ ይ ነ ትማ ና ክ ሎች /
ተ ግ ዳ ሮ ትይ ን ገ ሩ ኝ ?

17. የ ህክ ምና ማካ ራ ጥና ት
ፈ ቃድለ ማግ ኘ ትአ ሜ ል ክ ተ ውሳ ይፈ ቀ ድሎ የ ቀ ረ ማን ኛ ውም ኡ ይ ነ ትማ ካ ራአ ለ ?

ምር ሚራዎች →ሜ ል ሶ አ ዎ ከ ሆ ነ ፣ ምክ ን ያ ቱ ምን ድ ን ነ በ ር ?

IV. በ ሞ ተ ግበ ር ጊ ዜ የ ሚ ጥ ሞ ች ግ ሮ ች

18. የ ማህ ራትፈ ቃድካ ገ ኙበ ኋ ላ በ ትግበ ራወቅ ትያ ጋ ጠመ ቻትማህ ና ክ ሎች / ተግዳ ሮቶ ችምን ድና ቸው?

እ ኚን በተ ጣ ለከ ተ

→የ ቁ ጥጥር ጊ ዜ

→የ ምር ሚራ ግብረ ሜ ል ስ

→የ ቁ ጥጥር እ ር ም ጃ ዎች

→የ ከ ባ ድ ማ ጥፎ ክ ስ ተ ት ሪ ፖር ት ማድረ ጊ ያ ሥር ዓ ት

→ሌ ሎች

19. ለ ምር ሚራና ማ ኛ ከ ሃ ገ ር ውጪ ም ላ ክ በ ሜ ፈ ል ግየ ህ ክ ምና ማህ ራ ጥና ት ውስ ጥተ ሳ ትፈ ውያ ውቃ ሉ?

- ሜ ል ሶ አ ዎከ ሆነ ፣ የ ቁ ጥጥር ተግዳ ሮቶ ችምን ነ በ ሩ?

20. በ ራሶ ሃ ሳ ብአ ማን ጪ ት የ ህ ክ ምና ማህ ራ ጥና ቶ ችን ለ ማህ ሄ ድአ ሜ ል ክ ተው/ አ ካ ሂ ደ ውያ ውቃ ሉ?

- ሜ ል ስ ዎአ ዎከ ሆነ ፣ በ ስ ፖን ሰ ሮ ችከ ተ ነ ሳ ሱ ሌ ሎች ማህ ራ ዎች እ ን ዴት ሊ ለ ያ ይ ይ ችላ ል?

21. ይህ ን ን የ ህ ክ ምና ማህ ራ ጥና ት በ ኢ ትዮ ጵ ያ ውስ ጥለ ማ ት ግበ ር ያ ጋ ጠ ማ ት ን ፈ ታ ኝ ሁኔ ታ/ ማህ ና ክ ሎች ሁሉ ን ገ ሩ ኝ ፡ ፡

V. ከ ተ ጠ ና ቀ ቀ በ ኋ ላ ያ ሉ ፈ ተ ና ዎ ች

22. የ ህ ክ ምና ማህ ራ ጥና ቶ ች ን ካ ካ ሄ ዱ በ ኋ ላ በ ማ ጠ ና ቀ ቁ ወቅ ት ያ ጋ ጠ መ ቻ ት ማህ ና ክ ሎች / ተግዳ ሮቶ ችምን ድና ቸው?

VI. የ ች ግ ሮ ች ቅ ደ ም ተ ከ ተ ል

23. ቀደምሲል ከተወያየንባቸውተግዳሮቶች ውስጥ በኢትዮጵያ የህክምና ሜካራ ጥናት ትግበራ ላይ አሉታዊ ተፅእኖ ከሜጭጡር አንፃር ችግሮቹን በቅደም ተከተል ሜክቀሜጥከቻሉቢገልፁልኝ?

VII. የሜጭትሄሀሳቦች

24. ሜሻሻልየ ሜያስፈልጋቸውዘርፎችየ ትኞቹናቸው?
25. የምግብእናሜድኃኒትባለሥልጣንተፈታታኝሁኔታዎችንለሜሸነፍምንዓይነት ድጋፍይፈልጋል?
26. ድጋፉከማንሜሳጡትአለበት?
27. ከላይለተጠቀሱትየቁጥጥርስርዓትሜሳናክሎችየ ተወሰኑሜጭትሄዎችን / ሜክተካከያመንገዶችንሜቅረብይችላሉ?
28. አስፈላጊነውለውየ ሜያምኑትእናሳናነሳየቀረነውዛሳብካለእንወያይበት? / ይህንጉዳይበተሜላከተሌላምንሜ ጋገርአለብን ብለውያስባሉ?