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**Understanding constraints and enablers of turnaround time for ethics review:
The case of institutional review boards in Tanzania**

Mwifadhi Mrisho

Student number:

216074142

Supervisor:

Dr Zaynab Essack

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Declaration

I declare that this dissertation is the result of my own work except for those where due acknowledgment is made. This work has not been included in a thesis dissertation or report submitted to this university or any other institution for a degree, diploma or other qualifications.



Signed:

Mwifadhi Mrisho, PhD

ABSTRACT

Background

Independent ethics review is one of the fundamental principles of research ethics. The body of literature has documented increasing bureaucratic delays associated with ethics review, which has impacted the start of research activities. This study aimed to determine the extent of variability in turnaround times for protocol review among different institutional review boards (IRBs) within Tanzania. It also assessed the challenges and experiences of submitting and reviewing protocols after introducing the tablet PC, from the perspectives of Ifakara Health Institute IRB (IHI-IRB) members and investigators.

Methods

This cross-sectional study employed a mixed-methods approach which consisted of qualitative and quantitative approaches. The quantitative data were obtained retrospectively from databases of seven selected IRBs in Tanzania. Purposive sampling was used to select seven IRBs for inclusion in the study. Seven IRB secretaries and their assistants from five institutions were interviewed to respond to the research questions. In addition, 19 in-depth interviews were conducted with IRB members and investigators to explore their experiences of using tablet PCs in reviewing protocols and in submitting electronic proposals, respectively. This study was conducted in mainland Tanzania and Zanzibar. Quantitative secondary data were analysed using Stata software (quantitative data analysis software, version 10). Qualitative data were categorised in an Excel spreadsheet and analysed using thematic analysis.

Results

The median time for ethics review across the visited sites was 32 days and ranged from 1 to 396 days. Qualitative results found that eleven thematic issues emerged from in-depth interviews with IRB members and the secretariat in the visited study areas. Generally, looking into the procedures for submission of protocols to the secretariat of the IRB, these were more or less the same across IRB institutions in Tanzania. However, investigators sometimes failed to adhere to the submission checklist and guidelines which resulted in delays in the timeous review of protocols. Most of the IRB members and investigators preferred electronic submission for its ease of use and reduced burdens associated with paper-based submissions, such as printing, distribution and misplacing of protocols.

Conclusion

Data from this study suggest that there is an urgent need to address the issues raised in order to improve the turnaround time of protocol review in Tanzania. Investigators should adhere to the submission checklist and guidelines to avoid delays in the ethics approval process. Ethics review boards need to invest in technology and system strengthening to facilitate timeous processing of ethics applications.

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CHAPTER 1

INTRODUCTION AND BACKGROUND

1.1 History of research abuses

Independent ethics review is one of the fundamental principles of research ethics. Ethics review of a research proposal involving human participants is a procedure that starts with the submission of a proposal to the institutional review board (IRB), research ethics committee (REC), or ethics review board (ERB) (as referred to in some countries) for critical review of the proposal, data collection tools, informed consent documents, data-sharing plan, investigator CVs, and any other relevant documents related to the study (Kruger, Ndebele & Horn, 2014; Page & Nyeboer, 2017).

The aim of research ethics is to minimise the possibility of exploitation and research fatigue by ensuring that research participants are not merely used but are treated with full respect and dignity while contributing to the improvement of society or knowledge. Ethics review of research proposals became established after a long history of unethical research that happened during the Second World War, as well as the Tuskegee Syphilis Study conducted in the United States (US) (Thomas & Quinn, 1991). In the Tuskegee study, researchers did not inform participants adequately about the study, and even when treatment became available, participants were denied the right to get medication; this led to the general mistrust of public health research still apparent today (Thomas & Quinn, 1991; Wassenaar, 2006). Ethics violations in research still persist. For example, as recently as 2014, Facebook employees performed an experiment titled “Massive-scale contagion via social networks” without their research participants’ knowledge or consent (Kramer, Guillory & Hancock, 2014).

1.1.1 Obligation to obtain ethical approval

According to the World Medical Association (2013), the declaration of Helsinki (1964) stipulated two major requirements prior to the implementation of clinical trial. Firstly all research participants must understand the risk, benefits and alternatives of the experiment so that they can participate voluntarily, that is, provide informed consent. This requirement mandates the importance of the investigator ensuring that potential participants have understood the research (WMA, 2013). Secondly, the declaration stipulated that there should be a committee disconnected from the research to independently review the proposed research prior to implementation. This committee should be located in the country where the research will be conducted. The ethics committee should be independent and transparent in its functioning, and must be comprised of qualified people. Likewise, ethical committees have the authority to approve or reject research protocols depending of the scientific and ethical merit of the research (Silaigwana & Wassenaar, 2019). The committee is expected to monitor ongoing research,

taking into account laws and regulations of the country where the research is implemented (WMA, 2013).

1.2 Prominent guidance documents

The Nuremberg Code was published in response to the abuses of the Nazi research during the Second World War and marked an important foundation of contemporary medical ethics in the contexts of both research and treatment (Arras, 1991). The trial of several Nazi doctors in Nuremberg was followed by the publication of the Nuremberg Code in 1948 (Amdur & Bankert, 2010). The Nuremberg Code's ethical guidelines reaffirmed the legitimacy of clinical experiments, while providing certain safeguards for research participants (Faden, Lederer & Moreno, 1996). This code emphasised the importance of individual informed consent in all research with human participants, so as to prevent a recurrence of abuses by scientists in the name of research (Leach, Stevens, Lindsay, Ferrero & Korkut, 2012).

The Nuremberg Code is relatively restrictive concerning persons competent of consenting to research, and thus the World Medical Association published the more detailed Declaration of Helsinki in 1964 (Williams, 2008). The Helsinki Declaration, among other statements, stipulated the health priority of the trial participants (World Medical Association (WMA), 2013). The Helsinki Declaration states that:

It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research participants. The responsibility for the protection of research participants must always rest with the physician or other health care professionals and never with the research participants, even though they have given consent. (WMA, 2013, p. 2191)

Likewise, the Helsinki Declaration underscored that research with patients or healthy volunteers should be conducted with the supervision of qualified researchers (WMA, 2013). In addition, the Helsinki Declaration stated that research protocols should be submitted for ethics review and approved by IRBs before the study begins. These committees should be transparent in their functioning and must be independent of the researcher, the sponsor and any other undue influence (WMA, 2013). The main obligation of IRBs is to protect potential research participants, but they must also take into account potential risks and benefits for the community in which the research will be implemented. The ultimate goal of ethics review is to promote high ethical standards in research (World Health Organization (WHO), 2009).

The ethics committee should also follow the laws and regulations of the particular country or countries in which the research is to be performed. In addition, the committee must follow international norms and standards, where applicable (WMA, 2013). Review is also essential if the researchers plan to

publish the results of their study, as most medical journals do not publish the findings of research that has not received ethics approval (WHO, 2009).

Over time, the authors of the Helsinki Declaration were concerned that the Nuremberg Code did not provide adequate guidance for many research activities carried out by medical doctors with human participants and therefore added provisions for authorisation by proxy consent for the participation of children in research (Levine, 1996). As with other guidelines, the Helsinki Declaration has several editions and is updated periodically.

The regulations for the protection of human subjects developed by the Department of Health and Human Services (DHHS), published in 1974, also included a requirement for ethics review (Grady, 2015). Therefore, the term ‘institutional review board’ was introduced at that time. Hence, the World Medical Association also introduced review by an independent committee for oversight of science and ethics into the 1975 revision of the Declaration of Helsinki (Riis, 1977). These regulations were published in response to violations in research, especially during the second world war. For example, the NAZI regime was widely known in the US by 1946. So, these regulations are relevant as they aimed at protecting participants from harm. Local regulations are being informed by the international regulation to protect human subjects (Mashalla et al., 2019).

Another important guiding document in research ethics is the Belmont Report of 1979, which provided a framework to guide the resolution of ethical problems in research with human participants (Amdur & Bankert, 2010). This report identified three fundamental ethical principles, namely, respect for persons, beneficence, and justice (Cassell, 2000). Hence, this provided a basis for the conduct of ethical research involving human participants (Beauchamp, 2003; Cassell, 2000). The report also highlighted three important principles, namely, informed consent and protecting vulnerable groups, risk-benefit considerations and fair selection of the study participants (Cassell, 2000). These are basic principles, and they are recognised as universal as they apply all over the world. These principles will be discussed further in section 1.3.

Other important guidelines in the history of ethics include the *International ethical guidelines for health-related research involving human subjects* developed by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with World Health Organisation (WHO) (CIOMS & WHO, 2016) and the Nuffield guidelines (Levine, 1996). These guidelines are considered a progression, with each succeeding document superseding its predecessors (Levine, 1996).

It has been argued that the CIOMS guidelines were more successful than their predecessors in reaching global applicability (Levine, 1996). In addition, the author argues that the CIOMS guidelines, unlike

the Nuremberg Code and Helsinki Declaration, recognised certain behaviours that were ethically acceptable in one cultural context which may be unacceptable in another (Levine, 1996). Furthermore, in comparison to other guidelines, CIOMS outlined specific conditions related to the avoidance of exploitation particularly in underprivileged communities; for example, research should not be undertaken except when the research is responsive to the health requirements of the people, and it should be well conducted (Levine, 1996). The CIOMS guidelines also highlighted another important issue about the responsibility of sponsors post-trial; that is, whenever an effective product is identified as a result of a study, it should be made available to that particular community where the research took place (CIOMS & WHO, 2016).

Another board governing research was established in the United Kingdom. This is known as the Nuffield Council on Bioethics which was established in the early 1990s as a response to the rising concerns regarding genetics research (Shapiro, 1995). The Nuffield Council on Bioethics raised important issues related to the use of human tissues and genetics. This guideline was published in response to public concern regarding securing informed consent to export genetic samples for research (O’Neil, 2003; Shapiro, 1995). It further mentioned that when externally sponsored research is proposed and falls outside the national priorities, its relevance must be justified to the appropriate research ethics committees (RECs) (McMillan & Conlon, 2004). The major role of these committees is to safeguard the interest of participants involved in research. The guidelines therefore emphasise that committees must consider relevance of the proposal to priorities in healthcare within the country, scientific validity and ethical acceptability of the proposed research (McMillan & Conlon, 2004).

1.3 Fundamental ethical principles

The three widely accepted philosophical principles governing research are 1) respect for autonomy, which puts emphasis on the rights of an individual, 2) respecting an individual and 3) protecting those who are incapable and vulnerable such as children and incapacitated persons (Beauchamp, 2003; Cassell, 2000). The principles of non-maleficence and beneficence are closely related. These principles require that potential research participants should not be harmed, and that benefits to participants or society are maximised. It is therefore important to ensure that all efforts are made to mitigate risks. The principle of justice entails that those who bear the burdens of research should receive the benefits (Cassell, 2000; Beauchamp, 2003). These principles require informed consent, risk-benefit determinations, and fair subject selection (Beauchamp, 2003), respectively.

Most of the IRBs rely on these principles for their decision-making (Nolen & van der Putten, 2007; Wassenaar & Mamotte, 2012). However, due to the growing realisation that the above-mentioned principles may not be universally applicable across the world, there was a need to identify appropriate principles in relation to the context, history, culture, politics, gender, and social and economic status of

participants (Molyneux & Geissler, 2008). Recent works by Emanuel and colleagues have attempted to spell out the ethical obligations in a simplified way (Emanuel et al., 2008; Wassenaar & Mamotte, 2012).

1.4 The role of ethics review boards

IRBs are charged with providing an independent assessment that the proposed research is ethically acceptable, scrutinising clinical investigators' potential biases, and assessing compliance with guidelines and regulations intended to safeguard human participants (Grady, 2015). IRBs have a significant role to play in ensuring the ethical standards and scientific value of studies involving human participants. According to Gelling (1999) and WHO (2009), IRBs must ensure that the rights of research participants are protected. This is partly accomplished by ensuring participants receive appropriate information about the research. The information must be well packaged to promote understanding. Likewise, there should be good mechanisms in place to protect participants from any potential adverse consequences of the research (Gelling, 1999; WHO, 2009).

In addition, IRBs have an obligation to provide guidance and ensure compliance in terms of the ethical conduct of research. IRBs are also obligated to the investigator, by making sure that the submitted protocol is treated with confidentiality, respect and due consideration. Likewise, all investigators must support the contribution made by IRBs to ensure that research meets the high ethical and scientific standards expected by the community (Gelling, 1999; WHO, 2009). Review by IRBs is required by international ethical standards governing research involving human participants, as well as by local laws, in many jurisdictions (WHO, 2009). The advantage of IRBs that operate within research institutions, universities and hospitals is that they are familiar with the local environments and can be involved in closer monitoring of ongoing research (WHO, 2009).

It is within this context that IRBs are positioned to assist research investigators to comply with all forms of ethical standards, while generating new knowledge which can be implemented for the benefit of the targeted community and without compromising the welfare and dignity of the potential participants involved in the research.

In Tanzania, the responsibility to promote research integrity falls within the mandate of the Commission of Science and Technology (COSTECH) (Diyamett, Szogs & Makundi, 2010); however, currently there is an ongoing effort to develop a National Framework for Research Integrity. In the absence of a national framework to guide the conduct of research in Tanzania, IRBs, where they exist, have been serving that purpose (Tanzania Commission for Science and Technology, 2015). With regard to health research, in the mid-1970s, this was managed under the umbrella of the East Africa High Commission, through the East African Medical Research Council (Magesa, Mwape & Mboera, 2011). However, after the collapse

of the East African Community, the National Institute for Medical Research (NIMR) was established by an Act of Parliament (No. 23 of 1979) (Magesa, Mwape & Mboera, 2011; United Republic of Tanzania, 1979).

According to Ikingura, Kruger and Zeleke (2007, p. 154), the “national research ethics committee in Tanzania was established in 2002” to function “under the auspices of the Medical Research Coordinating Committee (MRCC)” which is “an overall coordinating body for health research in Tanzania”. The MRCC established the National Health Research Ethics Committee (NatHREC) to oversee ethics review, and approve and monitor health research in the country (Ikingura et al., 2007). This committee is hosted by and functions under the NIMR.

Like many other countries, the NIMR standard operating procedures follow the international guidelines such as the Nuremberg Code, Declaration of Helsinki, CIOMS and WHO’s *International ethical guidelines for health-related research involving human subjects*, WHO and ICH (International Council on Harmonisation) *Guidelines for good clinical practice* which outline the ethical and scientific standards for biomedical research (National Institute for Medical Research (NIMR), 2007). The NIMR guidance states that compliance with the above-mentioned guidelines helps to ensure that the dignity, rights, safety, and well-being of research participants are promoted, and that the results of the research are trustworthy (NIMR, 2007).

1.4.1 Composition of IRB members

Generally, an IRB is composed of scientist and non-scientist individuals who convene to review and approve or reject proposals for research studies that involve human participants (Schwenzer, 2008). Members of these IRBs have diverse backgrounds, including for example, bioethics, clinical trials, biomedical science, paediatrics, epidemiology, entomology, public health, religion, law, social science and biostatistics (Ifakara Health Institute (IHI), 2010). These individuals are either from within or outside the institution hosting the IRB. The community representatives also play multiple roles in terms of representing the interests and concerns of the community. IRBs have an important role in protecting human research participants from possible harm and exploitation that may result during the conduct of research (Frankel & Siang, 1999; Schwenzer, 2008; Seidman, 2013).

1.4.2 Independence of IRBs

Any system of ethics review has to prevent undesirable research practices and promote good ethical research that protects participants (Bridges et al., 2011; Hesse-Biber & Leavy, 2010; Shamoo & Resnik, 2009). IRBs should be independent in such a way that they protect research participants by ensuring that ethical principles are followed by researchers so as to safeguard the welfare of the participants and

at the same time contribute to the body of knowledge through rigorous research (Grady, 2015; Millum, Wendler & Emanuel, 2013; Schwenzer, 2008). Apart from reviewing and approving protocols, IRBs are also responsible for monitoring the already approved research involving human participants (Schwenzer, 2008).

1.4.3 Decision-making of IRBs

Although there are no ideal models of the deliberative process of the IRBs in the literature, more general theories of group decision-making processes can provide a framework which IRB can adapt for decision making (Candilis, 2006). Most of the IRBs incorporated the ethical issues as per international and local guidelines to make deliberations. For example, according to WHO guidelines, the process by which decision making is reached is reported as an important outcome (WHO, 2009). The decision must be transparent and inclusive taking into account the views of all members with different backgrounds. Most IRBs makes decisions through a process of consensus, whereby instead of taking a vote and following the decision of the majority, members attempt to make decisions that most members would feel comfortable with (WHO, 2009). In Tanzania, most IRBs use this approach in reviewing research proposals. After the review, the committee's decision is communicated to the principal investigator. The decision may be categorised as: presented, if the proposal is scientifically and ethically sound whereby approval certificate is issued; minor revision, whereby the proposal is missing some minor but important issues that need to be attended to; major revision, whereby the proposal is not scientifically or ethical sound; not recommended, the proposal is not scientifically or ethical sound; and outright rejection whereby the protocol lacks scientifically and ethical sound (NIMR, 2014). The decision-making processes are documented in the local guidelines (NIMR, 2014; ZAMREC, 2012).

1.5 Challenges with ethics review identified in the literature

Turnaround time refers to the total time taken between the submission of a protocol to the IRB secretariat for review until the full approval is provided to the investigator. There have been reported delays in reviewing protocols submitted for approval, both in developed and developing countries (Millum & Menikoff, 2010; Page & Nyeboer, 2017). The body of literature has documented an increasing bureaucratic delay associated with ethics review (Angel et al., 2008; Clarke 2014; Cleaton-Jones, 2010; Jamrozik, 2004; Schwenzer, 2008; Wald, 2004; Warlow, 2004). For example, A study conducted in the United States Department of Veterans Affairs by Petersen et al. (2012) found that the median time for IRB approval at 43 sites in the US was 286 days, with a minimum of 52 days and a maximum of 798 days (Greene & Geiger, 2006; Petersen et al. 2012).

These slow turnaround times have impacted on commencement of research activities (Gold & Dewa, 2005). For example, a study conducted by Mamotte and Wassenaar (2009) revealed the experience of

South African social scientists by pointing out the undesirable “pragmatic reasons such as slow turnaround time, inadequate review and problems associated with the centralisation of ethics review” (p. 70). The slow turnaround time of IRBs affects researchers’ satisfaction with the ethics review process and their ethics compliance (Ashcraft & Krause, 2007; Liddle & Brazelton, 1996). Time delays may also impact on both the timeline and budget of the research – and negatively affect researcher-funder relationships. Time delays can also weaken investigator interest in researching a rapidly emerging problem (Nolen & vander Putten, 2007; Silberman & Kahn, 2011).

Researchers in the US and elsewhere believe that IRBs hinder their research, citing difficulties in seeking approval to implement their protocols (Silberman & Kahn, 2011). Reports from various sources have also highlighted a number of constraints and enablers related to IRBs during review. These may include issues such as being a slow, cumbersome and inconsistent process (Straight, 2009), excessively delaying research (Marsh, McMaster, Parvizi, Katz & Spindler, 2008), demotivating investigators (Infectious Diseases Society of America, 2009), and lack of capacity to review protocols (Emanuel, Wendler, Killen & Grady, 2004; Silberman & Kahn, 2011). For example, Silberman and Kahn (2011) documented long delays in the approval process, which nevertheless varied from one IRB to another.

According to Grady (2015, p. 1), “some researchers are complaining that IRB review is time-consuming and burdensome without clear evidence of effectiveness at protecting human participants”. Additionally, “IRBs operate inconsistently and inefficiently, and focus their attention on paperwork and bureaucratic compliance” (Grady, 2015, p. 6). Mamotte and Wassenaar (2009) recommended further research to verify and explore the element of turnaround time so as to distinguish between pre-review delays, post-review and pre-approval delays.

There are numerous plausible explanations regarding why there is divergence in turnaround times of ethics review (Clarke, 2014). According to Gold and Dewa (2005) the process of ethics review at several sites can be an overwhelming task, time-consuming, and costly (e.g. money for printing documents). In Tanzania, for example, if an investigator works with an external collaborator, the protocol must be submitted to the local investigator’s institution prior to the submission to the national IRB. In addition, the effectiveness of IRBs has been undermined because of the IRB system’s failure to adapt to the changing research environment (Christian et al., 2002). The current practice for research ethics review, which involves seeking ethics approval from each institution’s IRB, is not very conducive to collaborative, multicounty research due to the delays as a result of the need for a protocol to be reviewed in different countries (Gold & Dewa, 2005). Hence, there is a need to understand the nature of these constraints and enablers arising from reviewing protocols in order to address the problems encountered (Barchi, Kasimatis Singleton & Merz, 2014; Kuyare et al., 2014).

Among the challenges highlighted by Silaigwana and Wassenaar (2015), in their review of literature from 23 empirical studies, was the inadequate capacity to review and monitor studies, which hinders the effective functioning of IRBs. Dada and Moorad (2001) also pointed out that long turnaround times could be attributed to the high workload of IRBs and that most members who serve on committees work on a part-time voluntary basis. In addition, the use of excessive paper and bureaucracy has been reported as a barrier to the review process (Grady, 2010). Changes from the current paper-based ethics review system are necessary not only to facilitate the conduct of multi-site research but also to preserve the integrity of the ethics approval process in general. For example, the use of technology as a means of handling multisite ethics review has already been proposed (Gold & Dewa, 2005), and new technology such as the Internet and tablet PCs can help members receive and review protocols more timeously.

Delays in processing submissions due to paper-based submissions are frustrating for both researchers and sponsors (Oder and Pittman, 2015; Whitney et al. 2008). Due to the competitiveness of research environments, it is important that institutions continuously improve their administrative support processes in order to support investigators to effectively accomplish the requirements associated with their research activities (Kakande & Namirembe, 2012; Liberale & Kovach, 2017;). Efforts have been made by different institutions to overcome the reported challenges through introduction of technological advancement. For this case, the use of computerized systems has been implemented in several industries or institutions in order to increase efficiency and eradicate process bottlenecks that can lead to employee or customer dissatisfaction. For example, the Mayo Clinic increased the quality of the services offered by its research administration offices by implementing a new pre-award and IRB system (Oder and Pittman, 2015; Smith & Gronseth, 2011). In this era, it is therefore important for the institutions to invest in technology such as electronic tools in order to reduce the burden and increase efficiency (Glenn & Sampson, 2011).

1.5.1 Problem statement

The research ethical processes are not well understood and it is reported that there is no gold standard against which to measure (Nicholls et al. 2015; Turner, 2004). Therefore, little information is available on how IRB may systematically improve their turnaround time (Page & Nyeboer, 2017). In efforts to improve efficiency of IRB review, specifically turnaround times, electronic review processes through tablet PCs were implemented. However, there is little data on whether this electronic system improves review turnaround time, or the perspectives of REC members who use tablet PCs. Moreover, there is a dearth of information on constraints and enablers of turnaround times of IRBs in Tanzania. The current available literature contains practically no significant studies on the enablers and turnaround times of IRBs or the usefulness of tablet PCs in reviewing protocols. This study aimed to determine the extent of variability in turnaround times for protocol review among different IRBs within Tanzania, as well as assess the experience and challenges of submitting and reviewing protocols after introducing tablet PCs,

from the perspectives of IHI-IRB members and investigators. The study also aimed to identify the key factors that enable or constrain turnaround times of protocol review, in order to inform appropriate interventions.

1.6 Ethical review process in Tanzania

In Tanzania, the NIMR through the MRCC has been mandated to grant ethical approval to conduct research in the country (Ikingura et al., 2007; Mashalla et al., 2009). In order to improve efficiency and reduce delays in issuing approvals, NIMR has permitted organisations authorised to conduct health research to form IRBs (Ikingura et al., 2007). Their main function is to review research proposals for health research intended to be conducted within or by the institution. If the research team is composed of local researchers (Tanzania citizens only), the research is implemented as soon as possible (Mashalla et al., 2009). However, if it involves external researchers, it has to be submitted to NIMR for clearance (Mashalla et al., 2009).

According to the standard operating procedures (SOP) of these local IRBs (research institutions, universities and hospitals), they are supposed to perform the following roles:

- safeguard the dignity, rights, safety, and well-being of all actual or potential research participants;
- defend the principles of justice, beneficence and respect for persons;
- provide independent, competent and timely review of ethics of proposed studies;
- be responsible for acting in the full interest of actual or potential research participants and concerned communities;
- take into account the interests and needs of researchers, having due regard for the requirements of relevant regulatory agencies and applicable laws;
- provide ethical oversight of approved projects; and
- ensure that only qualified investigators are allowed to conduct proposed studies.

Any research or proposal dealing with human participants is submitted and reviewed in these review boards. According to the National Health Research Ethics Committee (NatREC) guideline, there is a client service charter (2014), stipulating the turn-around time for ethical approval (NIMR, 2014). The charter has stipulated that the timeline for the whole review process and ethical clearance would take 6 to 8 weeks from the date of receiving a complete initial/ revised submission. However, for the expedited submission the review process is accomplished within four weeks after receiving the complete applications (NIMR, 2014).

1.7 Conceptual framework

In this study, we adapted the IRB review process framework developed by Liberale and Kovac, (2017) summarised in Table 1 below. This framework consisted of five components including suppliers, inputs, process, outputs and customers (SIPOC) (Liberale & Kovach, 2017). The suppliers included investigators and IRB secretariat from the seven institutions visited. Secondly, the input was another component which included research protocols, checklist, guidelines, tablet PC and platform for the submission of protocols. Thirdly, the review process included: receiving of proposal by different IRBs, assigning of proposal to reviewers, reviewing proposals, analysing proposals in the meeting, decision making and sharing comments with the investigators. Fourthly, once the decision is made, it may be categorised into 4, approved as presented, minor revisions, major revision or outright rejection. Finally, the framework composed of customers which are the investigators, research participants and the IRB secretariat. Using the review process framework developed by Liberale and Kovac, (2017), this study determined the extent of variability in turnaround times for ethics review of proposals among different IRBs and highlighted the key factors that can enabled or contained the turnaround time. The study also assessed the reported challenges and experience of using tablet PC (input) in reviewing protocols.

Table 1: The IRB review process framework developed by Liberale and Kovac (2017)

Suppliers	Input	Process	Outputs	Customers
IRB secretariats	Protocols	1.Receive research protocols	1. Approved as presented	Investigators
IRB 1	Checklists	2.Assign to IRB Committee	2. Approved with minor revision	Research participants
IRB 2	Guidelines	3.Assign to reviewers	3. Approved with major revision or	and the IRB secretariats
IRB 3	IRB systems	4.Review research protocol	4. Outright rejection	
IRB 4	Tablet PC	5.Analyse research protocol in the IRB meeting		
IRB 5		6.Decision making		
IRB 6		7.Send decision to investigator		
IRB 7		8.Modify protocol if need arise		
Investigators		9.Repeat steps 4-8 if need arise		

1.8 Objectives and research questions

This study was guided by an overall aim, specific aims and research questions.

1.8.1 Aims

The overall aim of this study was:

1. To identify key factors that enable or constrain turnaround times for the ethics review of protocols in Tanzania.

Specific aims:

1. To determine the extent of variability in turnaround times for ethics review of protocols among different IRBs within Tanzania.
2. To assess reported challenges and experiences of Ifakara Health Institute IRB members and investigators regarding submitting and reviewing protocols after the introduction of tablet PCs.

1.8.2 Research questions

This study was guided by the following research questions:

1. What are the key factors that enable or constrain turnaround times for reviewing protocols in different local IRBs in Tanzania?
2. What is the variability in turnaround times for reviewing protocols among different IRBs in Tanzania?
3. What are the challenges and experiences of reviewing protocols at Ifakara Health Institute IRB after the introduction of tablet PCs?

CHAPTER 2

METHODOLOGY

This chapter explains the general methodology used to address the research questions. It will start with study location, research methods, sample size and data collection processes and conclude with sections on rigour and ethical considerations.

2.1 Location of the study

This study was conducted in mainland Tanzania and Zanzibar. Zanzibar is a semi-autonomous region within the United Republic of Tanzania. However, due to financial limitations, the focus of the study was limited to IRBs located in Dar es Salaam, Kilimanjaro, Mwanza, Mbeya and Zanzibar. These are the major cities where most of the IRBs are located. Likewise, Ifakara Health Institute (IHI), Muhimbili University of Health and Allied sciences (MUHAS) and NIMR, which are the major IRBs, are all located in Dar es Salaam. The selection of the study sites and IRBs was done purposively to reflect a diversity of institutions (universities, research institutions, hospital-based institutions) and determined by willingness to participate.

2.1.1 Brief description of study areas

Dar es Salaam is the former capital and largest city in Tanzania. It is one of the largest cities in East Africa by population, as well as a regionally important business centre. Dar es Salaam is one of Tanzania's 31 administrative regions, and consists of five districts namely: Kinondoni in the north east, Ilala in the centre, Ubungu in the north, Temeke in the south and Kigamboni in the south-east. Specifically, this study was conducted in Ilala and Kinondoni districts where most of these IRBs and research institutions are located. The region had a population of 4,364,541 as of the official 2012 census (United Republic of Tanzania, 2013).

The main public health facilities in Dar es Salaam include: Muhimbili Referral Hospital, Amana Regional Hospital, Mwananyamala Hospital, Mnazi Mmoja Hospital, Ocean Road Hospital and Lugalo Military Hospital. Likewise, the major private hospitals include: Agakhan Hospital, Rabinsia Memorial Hospital, Regency Medical Centre, Hindu Mandal Hospital and TMJ Medical Centre. However, it is the duty of the municipality to provide preventive, promotive, rehabilitative and curative health care services in the Dar es Salaam. According to Parsa, Nekanda, McCluskey, and Page (2011), about 70% of the population in Dar es Salaam lives in poor and unplanned settlements.

Mbeya region is located in the south-western corner of the southern highlands of Tanzania. Administratively, the region is divided into ten district councils including Mbeya City, Kyela, Rungwe,

Mbarali, Ileje, Mbozi, Chunya, Mbeya DC, Busokelo and Momba. Busekelo and Momba are new district councils. Mbeya IRB is located within the Mbeya Referral Hospital in Mbeya City. This region is further sub-divided into 28 divisions, 214 wards, 832 villages and 181 streets. The region has 415 health facilities including hospitals, health centres and dispensaries. Of these, 82% provide maternal, newborn and child health (MNCH) services. In Mbeya region, HIV prevalence at 9% is higher than the national average (Tanzania Demographic and Health Survey (TDHS), 2015/16).

Kilimanjaro region is another of Tanzania's 31 administrative regions. The regional capital is the municipality of Moshi. According to the 2012 national census, the region had a population of 1,640,087 (United Republic of Tanzania, 2013). The region is administratively divided into seven districts: Hai, Moshi Rural, Same, Mwanga, Rombo, Moshi Municipality and Siha. The Kilimanjaro Christian Medical Centre (KCMC) IRB is located in Moshi municipality. Mawenzi is a regional hospital in Kilimanjaro region with a 300-bed capacity. Kilimanjaro Christian Medical Centre (KCMC) is the main private hospital and serves as a zonal referral hospital. This hospital has more than 450 beds.

Mwanza region is also one of Tanzania's 31 administrative regions. The regional capital is Mwanza, which is the second largest city in Tanzania. Administratively, the region is divided into seven districts: Misungwi, Sengerema, Ukerewe, Nyamagana, Magu, Kwimba and Ilemela. The Bugando IRB is located in Nyamagana municipality. According to the 2012 national census, the Mwanza region had a population of 2,772,509 (United Republic of Tanzania, 2013).

Zanzibar is a semi-autonomous region of Tanzania in eastern Africa. It consists of many small islands and two large ones: Unguja (the main island, referred to as Zanzibar) and Pemba. The capital is Zanzibar City, located on the island of Unguja. According to the 2012 census, Zanzibar has a population of 1,303,569 people (United Republic of Tanzania, 2013). Administratively, Zanzibar is divided into five administrative regions, three in Unguja and two in Pemba. Each region is subdivided into two districts, which make a total of ten districts for the islands. The lowest government administrative structure at the community level is Shehia. The ZAMREC IRB is located in Zanzibar, Unguja Island.

The geographical health infrastructure in Zanzibar is distributed into primary, secondary and tertiary levels of health care services. The distribution allows good access to primary services, with 95% of the population living within at least five kilometres of the nearest public health facility. Health facilities at this level provide preventive, treatment and care services for diseases and health conditions including malaria, upper respiratory tract infections, injuries, and water- and food-borne diseases (Zanzibar Ministry of Health, 2013). The capacity for the secondary level to serve as a referral centre for primary level facilities is, to some extent, inadequate. The upgrading of all cottage hospitals to become district hospitals has been necessary and hence Mkoani and Wete District Hospitals serve as regional hospitals.

In addition, Chake Chake Hospital will become a referral hospital for Pemba while Mnazi Mmoja Hospital will be transformed into a national referral centre for Zanzibar

2.2 Research methods

This was a descriptive cross-sectional study which employed a mixed-methods approach, that is, it used both quantitative and qualitative methods. This method is scientifically rigorous, driven by the inductive theoretical drive which is the generation of new theory emerging from data (Morse & Niehaus, 2009). It comprises qualitative and quantitative supplementary components. A mixed-method design, if conducted carefully, is stronger than one that uses a single method, as it enhances the validity of the study by corroborating the results from another perspective (Silverman, 2013; Tashakkori & Teddlie, 2003; Onwuegbuzie & Johnson, 2006; Morse & Niehaus, 2009).

The quantitative data were obtained retrospectively from databases of the NIMR, IHI and other selected IRBs in Tanzania (appendix 6). This methodology was selected due to the nature of the study, which seeks to understand the time variability and factors that enable or constrain turnaround time for ethics review of protocols. Furthermore, qualitative methods were also applied in triangulation, incorporating the advantages of each research approach because one data source may be insufficient to address the issues explored (Creswell & Plano Clark, 2007). For example, in-depth interviews were conducted with selected investigators and members of the IHI-IRB to assess the experiences and challenges of submitting and reviewing protocols after the introduction of tablet PCs, from the perspectives of the investigators and IRB members, respectively.

In-depth interviews provide much more detailed information than what is available through other data collection methods. Furthermore, in-depth interviews offer insight into the context and hence present a more comprehensive picture of what transpired (Boyce & Neale 2006). Likewise, with in-depth interviews, one can learn from someone with experience in a particular topic and thereby broaden understanding in that area (Arthur, Coe, & Hedges, 2012). For this reason, key informant interviews were carried out with relevant stakeholders from Muhimbili University of Health and Allied Sciences (MUHAS) and NIMR to explore their perspectives on how to improve ethics review processes in the country. Table 2 summarises the objectives and data collection methods.

2.3 Sample size and data collection process

Purposive sampling was used to select IRBs for inclusion in the study (see Table 2). Purposive sampling is the deliberate selection of participants due to characteristics the participant possesses (Etikan et al., 2016). It is a non-random approach that does not need fundamental theories or a set number of participants. The researcher decides what needs to be known and sets out to find people who can (and

are willing to) provide the information by virtue of their knowledge or experience (Bernard et al., 2002; Tongco, 2007; Etikan, Musa, & Alkissim, 2016). This method is useful when seeking out experienced individuals (Etikan et al., 2016) and involves identification and selection of individuals or groups of individuals who are expert and knowledgeable in terms of the phenomenon of interest (Creswell & Plano Clark, 2011).

The PI of this study ensured that all types of IRBs, such as those belonging to universities, research institutions and hospitals, were included in the sample. The following IRBs were selected: NIMR, MUHAS, KCMC, Bugando, Mbeya Medical Research and Ethics Committee and Zanzibar Medical Research Committee (ZAMREC) (see Table 3). Usually, protocols that are submitted through university IRBs mainly comprise students' proposals. However, there are a few proposals submitted by individual investigators, in the form of consultancies.

In terms of the qualitative sample, seven secretaries and five deputy secretaries of the visited IRBs were involved as key informants. In addition, nine members of IHI-IRB were involved in this study, as well as ten IHI investigators. Only one of the approached IHI-IRB members refused to participate. IHI project leaders at the time of the study who had submitted protocols in the previous year were listed and the leader of every fifth application was randomly selected to participate in the study. From that list, those who agreed to participate were consulted for an interview. Almost all the respondents were English speakers, for this case English tool (appendix 1) was applied in data collection exercise. Each objective is linked with an appropriate research method, targeted population, tool and number of respondents, as shown in Table 2.

Table 2: Objectives and data collection methods

Number	Objective	Method	Targeted population	Tool	Data sources
1	To identify key factors that enable or constrain turnaround time of reviewing protocols in different ethics review boards	In-depth interviews with key informants	IRB secretariat in Dar es Salaam (IHI, NIMR & MUHAS) Kilimanjaro (KCMC), Mwanza (Bugando), Mbeya (Mbeya Medical Research and Ethical Committee) and Zanzibar (ZAMREC)	Appendix 1/2: In-depth interview guide	7 IRB secretaries 5 IRB deputy secretaries
2	To determine the extent of variability of turnaround time of reviewing protocols among different IRBs within Tanzania	Retrospective data from the registry	IRB secretariat in Dar es Salaam (IHI, NIMR & MUHAS) Kilimanjaro (KCMC), Mwanza (Bugando), Mbeya (Mbeya Medical Research and Ethical Committee) and Zanzibar (ZAMREC)	Appendix 6	Review of databases from 7 IRBs
3	To assess the challenges and experience of submitting and reviewing protocols after introducing tablet PCs, from the perspectives of investigators and IRB members	In-depth interviews with investigators and IRB members	Investigators (who are project leaders and submitted protocols in the past one year) and IHI-IRB members were chosen to participate in this study	Appendix 1/2: In-depth interview guide	10 investigators 9 IRB members

2.4 Data analysis

Quantitative data were analysed using Stata software, version 10 (StataCorp, 2007). Descriptive statistics were conducted to determine the extent of variability in turnaround time for ethics review of protocols among different IRBs within Tanzania. This study also assessed the time taken from submitting protocols to receiving feedback or ethics approval. The analysis used median time instead of mean, as there were few protocols in some IRBs. The data shared was summarised and anonymised in order to ensure that individual respondents cannot be identified.

Qualitative data were analysed using thematic analysis. Braun and Clarke (2006, p. 79) define thematic analysis as “a method for identifying, analysing, and reporting patterns (themes) within data”.

Furthermore, these authors noted that the approach helps to shape and define the data set. Through its theoretical freedom, thematic analysis offers a flexible and suitable research tool which can provide a rich and comprehensive, yet complex, account of data (Braun & Clarke, 2006). The advantage of this approach is that the researcher can discover themes and concepts throughout the interviews and during the analysis (Rubin & Rubin, 2011; Taylor & Ussher, 2001). This approach does not need the detailed theoretical and technical knowledge required for quantitative data analysis and hence can offer a more accessible form of analysis (Braun & Clarke, 2006). The PI of this study coded and categorised the transcripts according to the themes informed by the study objectives, using Excel software. The Excel spreadsheet was used to distil the qualitative information from the respondents.

2.5 Validity, reliability and rigour

Measuring the reliability of study findings needs investigators to make judgements about the ‘soundness’ of the research in relation to the application and appropriateness of the methods used, and the integrity of the final conclusions (Noble & Smith, 2015). To enhance the reliability, validity and rigour of this study, the following strategies were applied: adoption of a mixed-methods approach; triangulation using more than one method during data collection approaches; and explaining to the participants about the purpose of the study, why it was conducted and with whom. The application of several research methods enables validation of data through cross-corroboration from two or more sources. Likewise, all interviews were audio-recorded and transcribed verbatim to allow for repeated revisiting of the data to check emerging themes and remain true to participants’ accounts (Noble & Smith, 2015).

Thematic analysis was utilised to detect and identify all issues that were generated by the study participants (Braun & Clarke, 2006); hence, these issues formed themes which the study analysed. However, thematic analysis is only appropriate when the study aims to understand the current practices of any individual (Braun & Clarke, 2006). Likewise, the study acknowledges limitations related to sample size, data collection, analysis and issues related to generalisation of the findings (Sandelowski, 1993). The reasons for this was the little funding received for data collection and limited time available to accomplish the dissertation.

2.6 Ethical considerations

2.6.1 Ethics review

This study was reviewed and approved by the Ethics Review Boards of Ifakara Health Institute (IHI), located in Dar es Salaam (IHI/IRB/No: 002 – 2017), University of KwaZulu-Natal in South Africa (BREC Ref. No. BE089/17), and the National Institute of Medical Research in Tanzania (NIMR) (NIMR/HQ/R.8a/Vol. IX/2534). Anonymity of all study participants was ensured by removing all

identifying information from analysis and reports. This study was undertaken by an experienced researcher who ensured adequate information about the study was available to research participants. Individual written informed consent was obtained prior to the interview from all participants who participated in this study; it was drawn up in the Swahili language. The informed consent form (Appendix 3) explained the aim and reasons for the study, any potential risks and benefits, and the anticipated time taken to complete the interview. Participants were given a chance to ask questions during the informed consent process, and they were also informed that they could withdraw from the study at any time without penalty. The study complied with the CIOMS/WHO *International ethical guidelines for health-related research involving humans* (Ryan et al., 1979; Steinke, 2004).

The results obtained from this study provide evidence that may usefully improve ethics review processes in the country. It is noteworthy to mention that the methodology applied realised the scientific objectives while guaranteeing research participants' confidentiality (Emanuel et al., 2004).

2.6.2 Participants' rights

The rights of participants were assured in terms of confidentiality and weighing the relative risks and benefits.

Confidentiality

Measures were taken to ensure the privacy, respect and dignity of all participants. Identities of participants were protected by ensuring that all data were anonymised. Confidentiality was also emphasised at the beginning of the interview, and a statement agreeing to maintain confidentiality was included as part of the participant consent forms. The researcher was also requested by the IRB to sign a non-disclosure agreement to maintain the confidentiality of participants' information.

Risks and benefits

We expected no risks to participants as a result of participation. The qualitative study took place at a convenient place for participants. The PI minimised intrusiveness by assuring participants that they did not have to take part in any aspect of the research that made them feel uncomfortable (or they were informed that they could refuse to answer questions).

The PI informed the participants that there were no direct benefits to participants from taking part in this research study. However, participants were informed that participation in interviews could provide benefits in terms of increased self-awareness, knowledge, understanding and decision-making capacity. Participants were not compensated nor did they incur any costs for participating in this study.

CHAPTER 3

RESULTS

This chapter describes the results from data collected in the cross-sectional survey of Tanzanian IRBs between March and May 2018. The first objective was to determine the extent of variability in turnaround time of reviewing protocols among the different IRBs. In addition, the chapter will also present results on the key factors that enable or constrain turnaround time of reviewing protocols at different IRBs. Lastly, the chapter will present the results on challenges and experiences of submitting and reviewing protocols at IHI after introducing tablet PCs. The data presented for this objective was from analysis of qualitative data from the perspectives of IRB members and investigators. Data were collected from the databases of Bugando, IHI, KCMC, MUHAS, ZAMREC, NIMR, and Mbeya IRBs. The timeframe for data collection was between April 2017 and April 2018.

3.1 Turnaround time

Data were reviewed from seven IRBs (as shown in Table 3). The study reviewed minutes and records for the protocols submitted between April 2017 and April 2018. Since data obtained from the records were limited for most of the IRBs, the results are reported using median time instead of mean days. The average turnaround time for each institution was as follows: IRB 1- 42 median days, IRB 2 - 27 median days, IRB 3 - 63 median days, IRB 4 - 90 median days, IRB 5 - 15 median days, IRB 6 - 21 median days and IRB 7 - 28 median days. IRB 5 and IRB 6 were the best performers in terms of the turnaround time. The median time for review across all IRBs was 32 days, with a range of 1 to 396 days (Table 3). The minimum number of days taken across all IRBs was 1 (that means protocols were reviewed on the day submitted), and the maximum was 396 days. In the researcher's observation, turnaround time tended to be shorter in IRBs with good records (such as date of submission, date comments sent or received and date when approval was received), as compared to the IRBs where records were poor.

Table 3: Turnaround time for reviewing protocols in the past year in Tanzania (April 2017 to April 2018)

IRB name	Number of protocols	Mean (days)	Minimum (days)	Maximum (days)	Median (days)	Standard deviation
IRB 1	48	48	1	147	42	33
IRB 2	80	27.6	12	152	26.5	18
IRB 3	10	63	17	101	63	29
IRB 4	44	114	10	396	90	84
IRB 5	11	55	6	235	15	70
IRB 6	30	26	1	97	21	22
IRB 7	20	44	1	153	28	40
Total	243	51	1	396	32	54

3.2 Key factors that enable or constrain turnaround time of reviewing protocols

Qualitative results suggested that seven thematic issues emerged after the interviews with IRB members and the secretariat in the visited study areas. The themes included the following: 1) procedures for receiving and distribution of protocols; 2) number of reviewers assigned to protocols; 3) duration of reviewing protocols; 4) decision-making process; 5) reasons for delayed feedback; 6) policies and guidelines; and 7) training of REC members. These will be presented in the following sections.

3.2.1 Procedures for receiving and distributing protocols

This study explored the procedures for receiving, distributing and reviewing protocols. With regard to the procedures, most IRB secretaries acknowledged that protocols are received and checked based on the checklist and the guidelines. Protocols are received in hard copies as well as soft copies. Protocols led by local PIs are reviewed and approved if they meet requirements, but proposals with external collaborators are reviewed and then channelled to NIMR for national approval (Appendices 4 and 5). Generally, the processes for submitting protocols to IRBs are similar, as described in the quotes below:

“Based on the checklist, we receive, we check as per checklist; we compile and send protocols to the reviewers.” (Secretariat, Participant 1 [P1])

“Four hard copies are submitted. They are registered at registry. In the unit, department of health ethics, protocols are checked based on the checklist. They are given number at the registry. They are stamped at the finance department as confirmation that the fee has been paid.” (Secretariat, P3)

“Protocols are received from the PI, checked against the checklist and see if fee has been paid. If the protocol is incomplete, it is returned to the PI for completion.” (Secretariat, P6)

“The secretariat receives the protocols and distributes to members; we receive both soft and hard copies. One IRB members is in Pemba Island. There is a requirement of receiving hard and soft copies. The meeting is held on the last Tuesday of the month but there is expedited review as well.” (Secretariat, P4)

“Students’ proposals are received from Director of Postgraduate Studies, while research proposals from investigators are received direct in this office of research and publication. Proposals from Director of Postgraduate Studies (DPS) are expedited review and proposals from investigators are categorised into two: local PI and external PI.” (Secretariat, P5)

3.2.2 Number of reviewers assigned to protocols

If protocol submission met checklist requirements, they were assigned to specific reviewers. Protocols were submitted to at least two or three reviewers. However, at IHI, ZAMREC and Mbeya IRBs, protocols were always submitted to all members of the committee. The circulation of the submitted protocols to the reviewers differed from one institution to the other. At NIMR, MUHAS and KCMC, a respondent reported: “It takes one to three days before the proposal is assigned to the reviewer” (Secretariat, KCMC (P6)), while IHI, Bugando, ZAMREC and Mbeya IRBs take a week. Thereafter, reviewers were invited to attend a monthly meeting to finalise the review process. At IHI and ZAMREC, for example, protocols are reviewed every Friday and Tuesday of the end of the month, respectively. In the visited IRBs, the number of members ranged from 8 to 16.

3.2.3 Duration of reviewing protocols

As it was explained earlier, protocols are submitted to the secretariat of the institutions under study. After the protocols are circulated to the reviewers, reviewers take an average of one to two weeks. Protocols are sent to reviewers to consider ethical and technical aspects of the research. However, some review boards reportedly took up to two months to review protocols.

“Usually protocols are circulated at least a week before the meeting, and all reviewers are asked prior to receiving of protocols if they will be available for the meeting or if they can submit their comments through the internet. So, there are no delays encountered, because all comments are given at the meeting with all members present.” (Secretariat, P8)

“Usually it takes three weeks to return feedback. However, if the feedback is delayed, the protocols are returned and assigned to another reviewer. Proposals are sent to three reviewers to look at ethical issue and technical aspects.” (Secretariat, P3)

“Usually the feedback from reviewers is between two weeks to two months.” (Secretariat, P1)

“It doesn’t take long time. On average, it takes a week to receive feedback.” (Secretariat, P7)

3.2.4 Decision-making processes

According to the IHI-IRB standard operating procedures, only members who participated in the review process and deliberations take part in the decision-making process. Members can only make decisions if the quorum requirements as stipulated in the relevant (SOPs) are satisfied. Any member with a conflict of interest regarding a particular proposal must not take part in the review of the proposal and subsequent decision-making process. Members with conflicts of interest must declare these and wait outside the conference or meeting room. Non-members such as project PIs and independent experts may be consulted as part of the review process. A decision should only be taken after there has been sufficient time to allow for review and discussion of an application in the absence of non-members from the meeting.

Almost all IRB secretariats reported that the decisions are taken by consensus or, when there is voting, then the position voted for by the majority becomes the IRB decision. In case there is a tie, other members who were absent are consulted or independent expert opinion is sought.

During the meetings, decisions regarding applications are categorised into the following:

- Approval
- Provisional approval in case of expedited review
- Conditional approval for proposals with minor changes required which can be verified by secretariat without submitting to full IRB meeting
- Major changes necessitating resubmission of the application to full IRB meeting or to appointed members of the IRB
- Deferment, pending a decision at a later date
- Disapproval.

For any decision made by the IRB, clear reasons and justifications are provided and documented in the minutes and in the communication to the applicant. This was similar across all IRB because during their formation, they adapted national guidelines to fit into their setting. If a proposal requires

expertise that the IRB does not have, the IRB secretary, in consultation with the chairperson, may engage independent experts to review and give their views.

“We set meetings and we sit to discuss the protocols and make decision: approved; approved with conditions or resubmission, whereas reviewers provide comments.” (Secretariat, P1)

3.2.5 Reasons for delayed feedback

There were some cases where feedback was delayed, especially when protocols were assigned to three reviewers and some of them did not share their feedback with the secretariat timeously. In addition, some members might not turn up for the meetings, and this may lead to an insufficient quorum and hence may lead to the postponement of the meetings. Most of the members are people with other responsibilities and full-time work; hence, they do have other conflicting responsibilities. Likewise, investigators may sometimes fail to adhere to the submission guidelines which may result in failure of reviewing their protocols in a timely manner. It was also reported that lack of experts to review complicated studies may also delay the review process of protocols. In addition, lack of compensation for IRB members' time during review of protocols was also highlighted as one of the challenges.

“Reviewers are busy with multiple obligations such as teaching, working in the hospital. So when you send a proposal to the reviewers, comments are not coming on timely manner until you make several follow-ups; until you notify members, maybe close to the meeting day, so that they can read the proposal.” (Secretariat, P6)

“It depends: maximum of two to three weeks. If the reviewer didn't turn up or provide timely comments, we request another reviewer who attended the meeting to check the proposal. If there is a major issue in the proposal, it will wait for another meeting. If it is not reviewed on time, we give a week and remind the reviewer. However, if it is not reviewed on time then the protocol is assigned to someone else.” (Secretariat, P5)

The following commonly raised queries were mentioned by participants. Firstly, requirements at institutional IRB level and the central IRB (NatREC), contributed to delays and duplication of efforts, and made the purpose of parallel submission redundant. The participants reported that for time sensitive proposals, an investigator may not submit to the central level (NatREC) until the approval from a local IRB has been obtained. Likewise, other common problems associated with the review process were aligned to data management and dissemination plan which were either not written properly or sometimes not included in proposals. In addition, the issues of sample size determination and assumptions, data ownership, storage and data transfer, and hosting of data were among the issues associated with the delays. For example, an investigator noted:

“MTA, and DTA should not be the reasons for delaying the project approval at institutional-IRB level whilst it is a legal document that is only recognized when completed and signed by NatREC.” (Investigator, P6)

In addition, other issues raised by the participants related investigators’ failure to submit a Data Safety and Monitoring Broad (DSMB) charter; specify local representation of DSMB members for clinical trials; mention the amount of blood samples to be drawn; , specify the list of specific tests to be performed on the collected blood samples; and specify how the samples would be stored or destroyed after the study. Likewise, some other important things mentioned by respondents related to the informed consent form (ICF). Participants said that most of the protocols did not specify or justify on how participant’s time would be compensated, the roles of each partner and/or contact information for the IRB. In addition, ICF are sometimes not comprehensive enough to include issues such as risks, benefits or purposes of the study:

“Issues about compensation is sometimes nowhere to be seen in the protocol or in the ICF. It may sometimes appear in the ICF but not in the protocol. In addition, the roles of each partners are not well specified and also lack of approvals from other review boards. Most protocols lack contact of the independent person from the IRBs and other ICF are not comprehensive enough to include issues such as risk, benefit and the purposes of the study.” (Member, P2)

Some of the members also faced challenges regarding making decisions on electronic data capture. There were no proper guidelines at institutional-levels and some delays were associated with finding a guidance on reviewing such proposals:

“Investigators may propose the use of electronic data capture which make it difficult to make decisions about such proposals and hence may lead to the delays.” (Member, P2)

It is evident from the study that investigators could somehow propel the delay by not adhering to the guidelines or checklist as reported below:

“The issues raised some were in the guidelines but the Investigators do not refer; but due to these, common issues raised now and then it is good to include in the revised guidelines.” (Member, P8)

“...investigators do not conform with the guidelines eg the application form; submission of Material Transfer Agreement; following the protocol submission format; references; objectives are not SMART.” (Member, P4)

In summary, majority of the participants reported that the most commonly raised queries when reviewing protocols were found in the methodology, dissemination and ICF sections. Issues in research questions and objectives not being Specific, Measurable, Attainable, Realistic, Time bound (SMART) were also reported by few participants.

3.2.6 Policies and guidelines

With regard to the policies and guidelines, respondents acknowledged that their institutions had guidelines. However, the most important challenge was that the guidelines are not updated in a timely manner. There was no plan for updating the guidelines in almost all visited IRBs. With the exception of Bugando and KCMC, it was reported that guidelines were outdated.

“We have standard operating procedures and the last update was in 2012.” (Secretariat, P1)

“There is a guideline which is applied to review protocols. However, it has not been updated since 2001. The second version was in 2009. It is the national guideline for health research ethics in Tanzania. It is in the NIMR website.” (Secretariat, P3)

“Yes, we have SOP and guideline adapted from NIMR and it was updated in 2016. There was a budget for updating the guideline.” (Secretariat, P6)

“We have a guideline but not updated since 2012.” (Secretariat, P4)

“Yes, we have a guideline but don’t remember the last update was when.” (Secretariat, P5)

“Yes, we have standard operating procedures. We usually update but there is no fixed time. Two years have passed since then but we have planned to set the time.” (Secretariat, P7)

3.2.7 Training of REC members

Most of the IRBs reported having trained their members using different approaches. However, for those whose new members had not been trained, it was reported that plans were underway to train them. Most of the members had completed online and short-term training organised by the NIMR NatREC, MUHAS and IHI. In addition, other avenues for training of IRB members involved participation in GCP training, whenever there was a clinical trial project training its team.

“Mainly online training such as www.TREE.org. We are invited by other colleagues e.g. MUHAS and NIMR. Last training was 2017.” (Secretariat, P1)

“Last time members’ training was 2008 (GCP training). However, different members have participated in different training, such as MUHAS and IHI, at different times.” (Secretariat, P4)

“Yes, we had training to review qualitative research, but I don’t remember exactly the date. But in 2017, we did refresher training for the members recruited in 2016.” (Secretariat, P5)

“Most of the time, we use projects to train members whenever they train GCP to their project personnel. Likewise, there is online training such as Collaborative Institutional Training Initiatives (CITI) which provide certificates.” (Secretariat, P6)

3.3 Challenges and experiences of submitting and reviewing protocols after the introduction of tablet PCs: The perspectives of IRB members and investigators

Four issues emerged regarding challenges and experiences of submitting and reviewing protocols after the introduction of tablet PCs, namely: 1) preference for electronic submission; 2) the challenges of using tablet PCs; 3) overcoming the barriers of using tablet PCs; and 4) suggestion for improvement of the review process.

3.3.1 Preferences for electronic submission

The secretariat of IHI-IRB introduced tablet PCs for the electronic review of protocols in 2015. Members received a one-day training on how to use the tablet PCs, including turning them on and off, and downloading and reviewing protocols. At the same time, investigators started to submit their protocols electronically in PDF format instead of hard copy. The protocols were received by the secretariat and were checked against the checklist (as shown in Appendices 4 and 5), prior to the electronic submission to the IRB members. Since the introduction of tablet PCs, there has not been any follow-up about the experience of electronic submission by the IHI secretariat with IRB members or investigators. This is the first attempt to share experiences from the perspective of IRB members and investigators.

A majority of the IRB members and investigators reported that electronic submission was easy and reduced the burdens associated with paper-based submissions. In addition, with electronic submission, there were no courier costs involved in distributing hard copies of ethics applications and supporting documents. Furthermore, members could access and review the protocols from anywhere using their mobile tablet PCs, as long as they had access to the Internet. Investigators acknowledged that electronic submission was easy, quick, and relatively inexpensive compared to hard copy submission. It was also mentioned that electronic submission could reduce the chance of misplacing protocols, and the

submission of incorrect protocols. Investigators proposed designing a way to keep submission records post submission of protocols.

The following typical statements from the in-depth interviews were recorded:

“Very easy, it simplifies the review as one can work from anywhere and it is relatively cheap. IRBs should have a system whereby the received protocols have evidence of stamping; it simplifies documentation. We submit electronically and we document in paper. Investigators should have an electronic file. As we move ahead, all data will be electronic; to file big documents is real hectic.” (Investigator, P3)

“Of course yes, I don’t carry protocols anymore. Electronic submission is more user friendly and the reviewer can quickly go through the documents to check anything; one can open a number of protocols at a time and can as well send protocols and receive on time; if you are on safari you can also access protocols (as compared to hard copy), but it is only when you come back you can read protocols. Likewise, there are some pages which might get lost during printing or binding, but for now we get full proposal without missed pages.” (Member, P4)

“In the old days it was time-consuming; costly - as one had to print and photocopy 15 protocols; cost of binding; investigators can now submit electronically to the secretariat. With hard copy, the secretariat could use a car to submit protocols to the members, and if protocols are affected by water - this was another issue ... and with electronic submission, reviewers can access protocols from anywhere.” (Investigator, P2)

“Yes, so many improvements have occurred. Reading a lot of hard copy is difficult but reading through the soft copy is much easier. It is also easy to comment and reduces the burden of carrying protocols to the meeting room and the reviewer can read protocols from anywhere. It is easy to review, to comment and easy to refer back for clarification.” (Member, P5)

“Yes, there has been very big improvement after introducing tablet PC. Firstly, it is easy to carry (portable), as compared to the time when we were carrying big files of hard copy. It is easy to share the comments straight to the PC; protocols can be accessed from anywhere.” (Member, P10)

IRB members reported that, with electronic submission, documents can be accessed faster compared to hard copy. In addition, one can write and respond immediately or after reading the protocols. Members also reported that reading on screen was easy as one can increase the font size to read according to their

preference. Electronic submissions also ensure that protocols reach reviewers without any errors, and reduce the chance of losses. For example, the following typical excerpts from participants were reported:

“The protocol is accessible; one can do the review at his/her convenient time. The documents are accessed faster than waiting for the hard copies to be delivered. And the inconveniences of having the hard copies handed to the member, while the member is not in the office to receive them; there could be a potential for losses. The tablet PC increases the chance of getting the protocol to the reviewer, conveniently, without any error. Reading through the screen is easy; one can increase the font size and read according to their convenient sight. Writing and sharing the comments is easy; one can respond immediately after or while reading the protocol documents.” (Member, P8)

“In short, electronic submission is quick, not time-consuming, reduces chance of misplacing of protocols, and submission of wrong protocols. For example, there was a protocol which was wrongly submitted to one of the regulating authority and received wrong comments. With electronic submission, it is not possible to mix documents. With regards to cost implication, it is obvious that paper based is expensive.” (Investigator, P4)

3.3.2 The challenges of using tablet PCs

IRB members reported actual experienced and potential challenges in relation to using tablet PCs. Among the challenges experienced was the need to have sufficient data to receive or download large files. The costs of downloading the files were covered by IRB members themselves and hence an expense compared to hard copy reviews. Some members also complained about the small screen of the tablet PC and poor connectivity to the Internet. In addition, insufficient training on tablet use and the associated review process was reported by most of the members. For example, most members did not know how to submit comments to the secretariat using the tablet PCs. Potential challenges related to the Internet were also reported. Members raised concerns that hackers could have access to the files submitted electronically and proposed that platforms be secured with restricted member access. The following examples were given:

“Biggest challenge is internet security, especially from hackers or access of private information to others. It requires support platform where members can log in into a secured platform. It also requires support software like adobe where you can overwrite and incorporate comments. There is a need for review friendly hardware, for example, the PCs where members can scribble.” (Member, P9)

“First of all, not all members are comfortable in using a tablet PC. When you read protocols and have got something to note down, you should write somewhere, but during the hard copy submission, you were just writing on the same paper. If you have nowhere to write, you might not get anywhere to write and can come to the meeting without comments. In downloading the files there is no problem; however, the challenge is to note down the comments.” (Member, P7)

“The challenge of uploading is when you have insufficient bandwidth. If it was submission during the deadline, this could be hard. But it is simple to use electronic submission as compared to paper based. It [paper-based submission] cost a lot and easy to make a mistake when inserting page numbers. It is expensive and printing cost is too much; it is time-consuming and requires someone to print and arrange papers. More than hectic, it requires more time.” (Investigator, P7)

Both the IRB members and the secretariat experienced similar challenges. At times when the secretariat wanted to share big files with members, they were forced to use Google drive (a tool to transfer large files). However, most members are not familiar with these technologies. IRB members and investigators explained:

“Challenges are there in receiving big files. If I want to send big files, I usually use Google drive but some members cannot access these drives. The PC screen is very small; I want one like A4. Members usually come with their comments written on a piece of paper or diaries. We have members of different specialties; for example, there are lay members who cannot access these devices.” (Secretariat & Member, P1)

“Access is fine. All IRB members had access but the problem was on downloading files from the Internet. However, sometimes the connection or downloading speed is slow. Also, PC should be fully charged because there is unreliable electricity. We had been given a tablet PC but we could not fully utilise the gadget. There was not enough time for training. It was user friendly - read and comment on the screen, but can share comments and write on a separate paper, [and] highlight and project.” (Member, P5)

“When outside the wifi network, sometimes we use our own mobile network for tethering. However, big files cannot be downloaded and typing speed on the tablet is also challenging. In addition, I need time to type. Initially typing speed was very low. There is no problem after the download.” (Member, P3)

“Generally, tablet PC is good as compared to paper based. The main challenge is to access the documents. For example, downloading big files is a challenge. It takes time to download as there is no good connectivity to the Internet. If the Internet was fast enough, there could be no problem. There is no problem in reviewing protocols using tablet PC, but the problem is in downloading the files. I have not used tablet PC to send my comments to the secretariat, but I usually share my comments during the meeting.” (Investigator & Member, P2)

It was evident from the above that there were differences in competency among members in using technology. For example, some members mentioned that it was possible to read and make comments on the screen, while others said it could not be done.

3.3.3 Addressing barriers to review using tablet PCs

Participants discussed developing an automated reminder to reviewers so as to avoid delays. It was also reported that electronic submission helps to reduce the turnaround time and hence improve the review process. Refresher training on how to complete the electronic application and upload the necessary documents was proposed as an important strategy to overcome the barriers. Furthermore, IHI-IRB members emphasised the importance of training and clear protocols on how to use technology, how to maintain confidentiality and how keep records.

3.3.4 Suggestions for improvement of the review process

During the in-depth interviews, IRB members and investigators from IHI were asked their opinion on how to improve the review process. Most of the respondents recommended the use of selected technology hardware and software that allows direct editing. Likewise, members suggested the use of a backup system with strong internet security features. It was suggested that this system should allow members to work on a portal that permits intersystem edits rather than download the protocols onto devices. In addition, members proposed that the IHI-IRB should be open for linkage with other user-friendly facilities such as calendars, meeting minutes, agendas, discussion boards, and should permit questions and answers among members.

Members also proposed the integration of indicators into the system to be linked with reporting and measuring the performance. Appropriate use of the gadget and timely provision of feedback to investigators was also highlighted. Although most of the challenges mentioned are not related to data access, most of the IRB members proposed to be given Internet bundles, as it takes considerable data to download the files. Looking into the discussion, it was obvious that the IRB secretariat should invest in technology and system strengthening as described in the following quotes:

“There are number of initiatives that have been established at IHI. Among these initiatives are quick email responses when submitting protocols, provision of tablet PCs to members and establishment of IRB portal. By centralising IRB and creating a portal, members can now receive the submitted protocols instantly. At IHI, investigators can receive feedback within two weeks. There is a need to congratulate members for the good job. From my own experience, there are institutions which delay the review process.” (Investigator, P2)

“Perhaps some more guidance is required at the beginning for members to familiarise with downloading documents, saving the review notes and sending emails on the tablet. Some members prefer to send comments using laptops instead of tablet PCs.” (Member, P8)

“What to improve is Internet stability, as most of them are not in the office, or give them ‘bundles’ to improve internet access.” (Member, P2)

CHAPTER 4

DISCUSSION

4.1 Variability in turnaround time

The aim of this study was to determine the extent of variability in turnaround times for ethics review of protocols among different IRBs in Tanzania. This was an important goal for this study because knowing the turnaround time will not only help the investigators to plan for their studies but also help the regulators to evaluate and improve their services. The median time for ethics review across the visited sites was 32 days, which is consistent with other studies (Adam, Kramer, Guillory, & Hancock, 2014; Caligiuri et al., 2017; Fontanesi, Magit, Ford, Nguyen, & Firestein, 2018; Silverman, Hull, and Sugarman, 2001). However, the maximum number of days for review ranged from 97-396 days.

Explanations for this discrepancy were attributed to delays in receiving comments from the reviewers, delays in receiving comments from the IRB and delays in PI responses to the comments. However, it was difficult to get exact dates of when the feedback was sent back to the investigators after the review of the protocols submitted, indicating inadequate record-keeping. Most of the visited IRBs had no records on the date when the feedback was received from the reviewers or sent to the PI. With the availability of better records, it could help to provide a clearer picture as to whether delay was on the part of the secretariat or investigator. In another study it was argued that the variation related to the turnaround time may be associated with the workload of reviewing protocols among the IRBs (Maskell, Jones, Davies, & BTS/MRC MIST steering committee, 2003; Page & Nyeboer, 2017). This study suggests that the observed variability might have been attributable to differences in receiving feedback from the secretariat and responding to these. Tensions between investigators and IRBs have been reported elsewhere (Adams et al., 2014), due to the time taken to review protocols and its implication in initiation of research projects. Delay in receiving approval was mentioned as the main concern by most investigators (Adams et al., 2014; Page & Nyeboer, 2017)).

Turnaround time has been proposed as among the parameters to measure the quality of an IRB's work (Adams et al., 2014). However, the findings of this study do not provide conclusive reasons for the delays and whether they originate from the investigators or IRB. It is therefore recommended to record the turnaround time as a parameter of quality in measuring IRB performance as proposed elsewhere (Caligiuri et al., 2017; Fontanesi et al., 2018)

4.2 Factors enabling or constraining turnaround time for protocol review

The study also explored the key factors that enabled or constrained turnaround time of reviewing protocols in different IRBs. This study looked at the procedures for submission of protocols, assigning of protocols to the reviewers, duration it took to assign and review protocols, policies and guidelines, as well as training of IRB members across the visited IRBs. With regard to the procedures, most respondents who were the IRB secretaries acknowledged that protocols are received and checked based on the institution's checklist and the guidelines adapted from the NatREC (Ikingura et al., 2007). If protocols were in line with the checklist, they were assigned to specific reviewers. Thereafter, reviewers were invited to attend the monthly meetings to finalise the review process. In this study, it is obvious that there were reported delay associated with the failure of investigators to adhere to the checklist or guidelines which is inline as with what has been reported elsewhere (Getz et al. 2011; Page & Nyeboer, 2017).

In these meetings, decisions were made by consensus. However, it was not always the case that members would attend the meetings. This may lead to an insufficient quorum, as documented elsewhere (Kass et al., 2007) and hence postponement of the meetings. Generally, looking into the procedures for submission of protocols to the secretariat of the IRBs showed that these were more or less the same across IRB institutions in Tanzania and beyond (Ikingura, 2007; Kass et al., 2007). Delays and obstacles to the commencement of research projects associated with IRB procedures and their lack of consistency and efficiency have also been reported elsewhere (Caligiuri et al., 2017; Hyman, 2012; Lidz et al., 2012; Lidz & Garverich, 2013; Kano et al., 2015; Klitzman, 2012; Page & Nyeboer, 2017; Silberman & Kahn, 2011).

With regard to the policies and guidelines, respondents acknowledged that their institutions had guidelines. In resonance with previous research findings (Kruger et al., 2014), a key challenge was that the guidelines are not updated timeously. There was no plan for updating the guidelines in almost all visited IRBs. SOPs should be updated regularly, at least every five years, as there are new developments in science and technology, which need to be accommodated (Fontanesi et al., 2018).

With regard to training of the IRB members, most of the IRBs reported that plans were underway to train new members. However, this was not guaranteed, as most of the IRBs had limited resources and training opportunities (Caligiuri et al., 2017; Kass et al., 2007; Klitzman, 2008; Ndebele et al., 2014; Milford, Wassenaar & Slack, 2006; Mokgatla et al., 2018). Most of the members had attended online and short-term training organised by the NIMR-NatREC, MUHAS and IHI. In addition, other avenues for training of the IRB members included GCP and online training in their institutions. In this regard, it is of paramount importance for the IRB members to be properly trained, and they must be supported to accomplish the important responsibilities of protecting potential research participants (Caligiuri et al.,

2017; Ikingura et al., 2007; Ndebele et al., 2014; Mokgatla et al., 2018). The secretariat in each of the visited IRBs should therefore ensure that IRB members benefit from regular training in order to protect the research participants. There are a number of online training opportunities for IRB members available, including Training and Resources in Research Ethics Evaluation (TRREE, n.d.), Collaborative Institutional Training Initiative (CITI program) and Protecting Human Research Online Training (PHRP).

4.3 Challenges and experiences of submitting and reviewing protocols at IHI after introducing tablet PCs

With regard to understanding the challenges and experiences of submitting and reviewing protocols at IHI after introducing tablet PCs, most of the IHI-IRB members and investigators acknowledged that electronic submission was easy to use and could reduce the workload of paper-based submission.

These findings are consistent with other studies (Hunt et al., 2016; Maskell et al., 2003) that electronic submission reduced the amount of paper used, and associated costs, and helped to address some of the problems with delays facing IRBs (Hunt et al., 2016; Maskell et al., 2003; Oder and Pittman, 2015).

Furthermore, this study underscores recommendations by other authors that shortening the turnaround time for protocol review would enhance the implementation of important clinical trials (Maskell et al., 2003) and time-sensitive research, thus supporting the use of electronic submissions.

Challenges related to technology (insufficient Internet bundles, poor connectivity, inadequate training on how to use electronic tablets) were among the most frequently reported challenges. In addition, concerns about the security of confidential files were also reported. Internet security challenges have been reported elsewhere (Frankel & Siang, 1999; Lu et al., 2005; Kotz, 2016; Sriram et al., 2009; Win, Susilo, & Mu, 2006). The information stored on the server can be accessed by different individuals, hence negatively impacting on preventing possible breaches of confidentiality. In this case, the main goal of protecting research participants cannot be enhanced. Win et al. (2006) mentioned that, with the development of wireless and handheld devices and connectivity to Internet through mobile phones, accessibility of information has improved, and it is important to safeguard the security of these devices so as to protect potential research participants. In addition, proper encryption schemes to ensure confidentiality were recommended (Frankel & Siang, 1999; Lu et al., 2005; Kotz, 2016; Sriram et al., 2009; Win et al., 2006).

4.4 Limitations of the study

Precautions should be taken when generalising the results of the study as it was carried out in only seven IRBs in Tanzania. Likewise, during the initial plan, the researcher intended to conduct in-depth interviews with COSTECH staff. However, the study could not find someone from COSTECH to be

interviewed, as there were no responses to the invitation made by the PI of this study. Likewise, data on the date when the feedback was provided to the PI was only available from a few IRBs; hence, it was not taken into consideration during the analysis. This could provide information on whether the delay was aggravated by members or investigators. Further studies will need to look at delays caused by both investigators and IRB members, and the implications for the review process.

Although this study was carried out in only a few IRBs, the findings may nevertheless be generally applicable to other settings of Tanzania and beyond the borders. This study identified important factors that enabled or constrained turnaround time of reviewing protocols in different IRBs in Tanzania. Our efforts to triangulate results from various data sources were intended to maximise reliability of the results and lessen possible bias (Krefting, 1991). Despite these potential concerns, the information provided will assist in planning a basis for monitoring the efficiency of IRBs in Tanzania.

CHAPTER 5

CONCLUSIONS AND RECOMMENDATIONS

The evidence from this study has shown that there is an urgent need to address the issues related to the delays in approval process in order to improve the turnaround time in Tanzanian IRBs. There are four broad recommendations, presented below.

5.1 Recommendations for investigators

Investigators should adhere to the submission checklist and guidelines to avoid delays in the ethical approval process. Failure to adhere to the submission guidelines may result in delays in reviewing protocols in a timely manner. Adams et al. (2014) reported that the main factors causing delays were from the investigator's side in responding to the comments in a timely manner. It is therefore important for the investigators to respond to comments from the IRB in a timely manner to avoid unnecessary delays which may impede the review process. Likewise, Caligiuri et al. (2017) have suggested an analytical framework for IRB quality improvement that considers adequacy of infrastructure, benchmarking and supportive technology.

5.2 Recommendations for IRB secretariat

As described in this thesis, it was noted that there were gaps related to security, and these may need to be resolved to augment the security of personal health information of participants (Win et al., 2006). It is therefore recommended to have a strong backup with a good security system that allows intersystem edits, and comments while keeping track. Furthermore, there should be training and clear protocols on how to use technology, how to maintain confidentiality and how keep an audit trail/records.

It is also recommended that IRBs keep complete and accurate records and develop a clear template that may yield important information. This information may include the following: the submission date of the protocol, date reviewed, date when the comments were sent to investigators, date responses from investigators were received and date when approval was granted.

In addition, it is recommended to have a backup system which should be open for linkage with other user-friendly facilities such as calendars, meeting minutes, agendas, discussion boards, and questions and answers among members. It is recommended to develop indicators linked to the system/portal for easy reporting and measuring the performance. It is further recommended that IRB members should be provided with data (airtime) so that they can download protocols conveniently.

5.3 Recommendations for capacity-building

Appropriate training on the use of tablet PCs and timely provision of feedback to investigators was also noted as an important issue. Plans for updating the SOPs and guidelines should be in place for all visited and other IRBs, which were not visited. It is also recommended for IRBs to develop their own electronic submission system as this can reduce the workload of using a paper-based system, and can guarantee internet security. With electronic submission there are no transport costs involved to distribute the bulky documents, and members can access and review the protocols from anywhere in the world. Proper training on SOP updates and use of tablet PCs, as well as on the online system submission, will help to reduce the turnaround time.

5.4 Recommendations for regulators or policy-makers

In Tanzania, the task to promote research integrity falls within the mandate of the Commission of Science and Technology (COSTECH) (Diyamett et al., 2010); however, currently there is an ongoing effort to develop the National Framework for Research Integrity. In the absence of a national framework to guide the conduct of research in Tanzania, IRBs (where they exist) have been serving that purpose (Tanzania Commission for Science and Technology, 2015). It is therefore recommended that the Commission direct some funding that will assist in capacity-building and monitoring of the already approved protocols.

5.5 Recommendations for future research

In this study we could not conclude which of the two sides, IRBs or investigators, caused delays. It is therefore recommended to investigate the time from protocol submission to approval, taking into account when responses are provided. A further potential study area is to find out whether the complexity of protocols contributes to the delays. In addition, it may also be good to enquire about the reasons for failing to use the existing IRB software from the developed settings. Lastly, there is a need to assess ethical issues using Emanuel et al. framework in relation to the biomedical research ethics committee in other settings (Tsoka-Gwegweni & Wassenaar, 2014)

5.6 Conclusion

This study highlighted important issues which need to be addressed in order to improve the turnaround time of protocol review in Tanzania and beyond. Adhering to the submission checklists and guidelines is highly recommended to ensure that applications are reviewed timeously. Additionally, it is recommended that IRBs invest in technology and systems strengthening to facilitate timeous processing of ethics applications. It is also important for the IRBs to develop their own electronic submission system as this can reduce the workload of using a paper-based system, and can guarantee internet security issues. In this regard, IRBs should keep complete and accurate records and develop

a clear template that may yield important information. Appropriate training on the use technology and timely provision of feedback to investigators may also contribute to the increasing performance of IRBs. Timely review is critical in ensuring that socially valuable research is implemented for the improvement of Tanzanian health systems and services.

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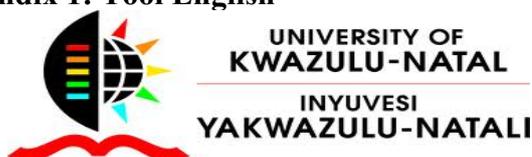
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APPENDICES

Appendix 1: Tool English



Understanding constraints and enablers of turnaround time for ethics review: The case of institutional review boards in Tanzania

Field guide: Targeted audiences are: IRB secretariat, members, investigators and key stakeholders

Section A: Objective 1 – To identify key factors that enable or constrain turnaround time of reviewing protocols in Tanzania

1. Tell me about your role in the review process. What has worked well and what has not worked well?
2. What are the main challenges in the approval process? (Probing issues related to follow-up protocol to the reviewers, what happens when one goes on leave (Who will follow?); is there any auto reminder for protocols delay to simplify follow-up?)
3. Are there plans in place to address the above-mentioned challenges? If yes, can you mention them? How are the mentioned plans implemented?
4. What is your overall opinion in improving the approval process?

Section B: Objective 2 – To determine the extent of variability of turnaround time of reviewing protocols among different IRBs within Tanzania

1. Can you please let me know the procedures for receiving protocols from the investigators?
2. What happens from when the protocol arrives until it is assigned to reviewers? How long does it take from the reception until it is assigned to reviewers?
3. How long does it take for the reviewer to review the protocol? What happens in those instances where reviews are delayed? How are decisions made to assign the protocol to another reviewer?
4. Does the committee have policies/guidelines that guide the review of protocols? How frequently are these guidelines updated? When was the last time they were updated?
5. What training has been provided to REC members on the review of protocols? When was the last time of training?
6. Now I would like to review some of your records from the time the protocol was received to when the certificate was issued (for the past five years).

Section C: Objective 3 – To assess the challenges and experience of submitting and reviewing Protocols after introducing tablet PC from perspectives of investigators and IRB members, respectively (IHI-IRB only).

1. What are the challenges of using a tablet PC in the review process? (Probe about accessing/downloading the files, reading through the screen, writing and sharing the comments.)
2. Have you noticed any improvement after the introduction of tablet PCs (What, if any)?
3. In your opinion, what should be done to improve the use of tablet PCs?
4. Would you recommend this tool to other reviewing boards?
5. (For investigators): What is your experience in submitting proposals electronically?
6. What were the challenges prior to the use of electronic submission? (Probe cost, time, convenience)?
7. What is your overall opinion for the IRB secretariat to improve the process (submission to certification)?

Section for D: To describe the commonly raised queries when reviewing protocols at IHI-IRB

1. What are the main issues raised when reviewing protocols? (Check the minutes, ask the secretariat.)
2. Are those issues addressed in the improvement of the guidelines?

Section E: What platforms/tools exist for reviewing of protocols in Tanzania?

1. Do you have any tool/platform to simplify IRB activities? If yes, which one, electronic? Paper-based tool? (Probe: tablet PC, Rhinno software or IRB developed web based?)
2. What are the challenges for the mentioned tools/platforms?
3. If not, do you have plans in place to use any of the tools/platforms in the future? Do you have a budget line for your plans?

Section F: Other stakeholders from the COSTECH, NIMR and MUHAS to air their opinion on how to improve ethics review process in the country.

1. What is your opinion with regard to the current regulatory framework related to ethics review of research involving human participants? (Probe who oversees research ethics, accreditation of IRB, monitoring approved research, capacity building and challenges, and opportunity that exist within research regulatory bodies.)
2. What are the main challenges in the approval process of research with human participants?
3. What should be done to improve ethics review processes in the country?

Socio-demographic characteristics of the respondents (*circle the appropriate answer*)

1. Sex 1) Male 2) Female
2. Age _____
3. Marital status
Never married = 1
Married = 2
Divorced = 3
Separated = 4
Widowed = 5
Living together = 6
Don't know = 99
4. What is the highest level of education completed?
5. Main economic activity
Employed
Government = 05
Parastatal (govt.) = 06
Parastatal (religious) = 07
Parastatal (others) = 08
Not employed = 09
6. Number of years on the REC?

THANK YOU

Appendix 2: Tool Swahili



Understanding constraints and enablers of turnaround time for ethics review: The case of institutional review boards in Tanzania

Field guide: Targeted audiences are: IRB secretariat, members, investigators and key stakeholders

Section A: Objective 2 – To identify key factors that enable or constrain turnaround time of reviewing protocols in Tanzania

1. Nieleze majukumu katika kupokea, kusambaza na kupitia maandiko? Katika utekelezaji wa majukumu yako, ni kitu gani ungependelea kiendelezwe na ni kipi unaona hakipaswi kuendelezwa?
2. *Je ni changamoto gani mnazipata wakati wa upokeaji, kupitiwa, kupokea mrejesho kutoka kwa reviewers na upatikanaji wa cheti (approval process). (Dadisi kuhusiana na ufuatiliaji wa andiko lililopelekwa kwa reviwera kwa mfano nini kinatokea mtu akienda likizo (nani atafuatilia?) Je kuna auto-reminder kurahisisha ufuatiliaji?*
3. *Je mnayo mipango ya kutatua matatizo yaliyotajwa hapo juu? Kama ipo nitajie. Je ni kwa namna gani mnatekeleza mipango hiyo?*
4. *Je una maoni gani kwa ujumla kuhusu kuboresha mfumo mzima wa kupokea, kupeleka kwa reviewers, kupata mrejesho kutoka kwa reviewers na kupatikana kwa cheti (Approval process?)*

Section B: Objective 2 – To determine the extent of variability in turnaround time of reviewing protocols among different IRBs within Tanzania

1. *Je unaweza kunielezea utaratibu wa kupokea andiko kutoka kwa watafiti?*
2. *Je nini kinatokea wakati andiko linafika mpaka anapopatiwa mtu wa kui-pitia? Muda gani unapita mpaka ipangiwe mtu wa kuipitia?*
3. *Je inachukua muda gani kupitia andiko? Je iwapo muda uliowekwa kupitia andiko umepita na hakuna majibu nini kinafanyika? Je ni muda gani umewekwa (maximum time) ili andiko liweze kupatiwa mtu mwingine?*
4. *Je kamati ina sera/mwongozo gani wa kupitia andiko? Kwa mara ya mwisho miongozo hiyo imefanyiwa marekebisho lini? (Mwezi/Mwaka)*
5. *Je ni mafunzo ya namna gani wamepatiwa wanakamati wanaongalia maandiko? Kwa mara ya mwisho wamepatiwa mafunzo hayo lini?*
6. *Kwa sasa ningependa kuangalia rekodi zako kutoka pale unaporikodi kupokea maandiko, na kutoa cheti cha kuruhusu utafiti.*

Section C: Objective 3 – To assess the challenges and experience of submitting and reviewing protocols after introducing Tablet PC, from the perspectives of investigators and IRB members, respectively (IHI-IRB only)

1. *Je ni changamoto gani mnazozipata kwa kutumia tablet PC kwa ajili ya kureview protocol? (Dadisi: kudownload, kusoma kupitia screen, kuandika maoni, na ku share mapendekezo)*
2. *Je kuna maboresho yoyote uliyoyaona baada ya kuanza kutumia tablet PC? Kama ndiyo, kivipi?*
3. *Una maoni gani ya kuboresha matumizi ya tablet PC?*
4. *Je unaweza kupendekeza TP zitumike katika IRB nyingine?*
5. *(Kwa watafiti) Je unaweza kutupa uzoefu wako kwa kutuma protocol kwa njia ya ki-electronic?*
6. *Je unaweza kunielezea changamoto zilizokuwepo kabla ya kuanza kutumia mfumo huo?*
7. *Je nini maoni yako ya ujumla wa kuboresha mfumo huu? (wa ki-electronic)*

Section for D: To describe the commonly raised queries when reviewing protocols at IHI-IRB

1. *Je ni mambo (comments) gani zinazopatikana kutoka kwa reviewers mara kwa mara? (Angalia minutes, uliza sekretariat)*
2. *Je hizo issues zinatumiwa/zinajibiwa katika kuimarisha miongozo?*

Section E: What platforms/tools exist in reviewing of protocols in Tanzania?

1. *Je mnayo tool/platform la kurahisisha shughuli za IRB (Dadisi kuhusu tablet PC, Rhinno software, Web-based, etc.)*
2. *Je kuna changamoto gani kwa hizo tool/platform*
3. *Kama hakuna, mna mipango yoyote kuhusu upatikanaji wa tool/platform siku zijazo? Unayo budget kwa ajili ya utekelezaji wa mipango hiyo?*

Section F: Other stakeholders from the COSTECH, NIMR and MUHAS to air their opinion on how to improve ethics review process in the country.

1. *Je ni nini mawazo yako kuhusu mfumo wa sasa unaohusiana na maadili wa kinchi kuhusu tafiti zinazohusiana na binadamu?*
2. *Je kuna changamoto gani katika kupitia/kuruhusu tafiti zinazohusiana na binadamu?*
3. *Nini kifanyike kuboresha kupitia maandiko ya kitafiti nchini?*

Socio-demographic characteristics of the respondents (*circle the appropriate answer*)

1. Sex 1) Male 2) Female
2. Age _____
3. Marital status
4. Never married = 1
Married = 2
Divorced = 3
Separated = 4
Widowed = 5
Living together = 6
Don't know = 99
5. What is the highest level of education completed?
6. Main economic activity
Employed
Government = 05
Parastatal (govt.) = 06
Parastatal (religious) = 07
Parastatal (others) = 08
Not employed = 09

THANK YOU

Appendix 3: Consent form



Understanding constraints and enablers of turnaround time for ethics review:

The case of institutional review boards in Tanzania

CONSENT FORM

Information sheet and consent to participate in research

Date: _____

Greetings

My name is Mwifadhi Mrisho, an MSc student from Department of Psychology, University of KwaZulu-Natal, in South Africa. My mobile phone number is +255 655 766675 (while in Tanzania) and +277 41 985 975 (while in South Africa). My email address is mwifadhi.mrisho@gmail.com.

You are being invited to consider participating in a study that seeks to **understand the factors that enable or constrain turnaround time of reviewing protocols in Tanzania: The case of IRBs in Dar es Salaam, Mbeya, Mwanza, Kilimanjaro regions and Zanzibar**. This study is aimed at determining the extent of variability in turnaround time of reviewing protocols among different IRBs within Tanzania, as well as identifying key factors that enable or constrain turnaround time of reviewing protocols, so as to find an appropriate intervention. Based on your knowledge/expertise related to the objective of this study, purposive sampling has been applied to select you/your IRB for inclusion in the study. The PI of this study will make sure that all IRB types (universities; research institutions and hospital-based) are represented. All consented members of the IHI-IRB will be involved in this study. Likewise, all secretaries of the visited IRB will also be involved as key informants in this study. The selected key investigators from IHI, as well as key informants from NIMR, TFDA and COSTECH or elsewhere, will be asked to participate in this study. This study is funded by the University of KwaZulu-Natal in collaboration with Ifakara Health Institute.

The study may inconvenience the participants in terms of time as they would be required to spend about an hour responding to the research questions. This study will provide no direct benefits to participants. However, the study is intended to improve the review process and also contribute to the process being environmentally friendly by using electronic devices to review protocols and hence reducing the use of paper.

Participation in this research is voluntary and participants may withdraw participation at any point; in the event of refusal/withdrawal of participation, participants will not incur any penalty or loss of treatment or other benefit to which they are normally entitled.

No costs may be incurred by prospective participants as a result of participation in the study. The researcher will bear all costs by meeting the prospective participants at a place of their convenience. There are no incentives or reimbursements for participation in the study.

Information that you provide will remain confidential and will only be used in this study. The PI will have access to the data and, during analysis, results will be coded so that your answers and results are not linked to your name. Information will be kept secured by the PI.

CONSENT

I _____ have been informed about the study entitled
**Understanding constraints and enablers of turnaround time for ethics review:
The case of institutional review boards in Tanzania** by the researcher Dr Mwifadhi Mrisho.

I understand the purpose and procedures of the study **Understanding of factors that enable or constrain turnaround time of reviewing protocols in Tanzania: The case of IRBs in Dar es Salaam, Mbeya, Mwanza, Kilimanjaro regions and Zanzibar** and I have been given an opportunity to ask questions about the study and have had them answered to my satisfaction.

I declare that my participation in this study is entirely voluntary and that I may withdraw at any time without affecting any treatment or care that I would usually be entitled to.

I have been informed that there will be no compensation or medical treatment and cost associated with the study. The researcher will bear all the costs.

If I have any further questions/concerns or queries related to the study, I understand that I may contact the researcher at (contact provided below) or the secretariat (contact provided below).

If you have any questions or need clarification at any time before signing the consent form or during the study period, do not hesitate to ask me. I may be contacted through +255 655 7666 75 or mwifadhi.mrisho@gmail.com. This study has been ethically reviewed and approved by the Ifakara Health Institute Review Board (approval number _____ and University of KwaZulu-Natal _____).

In the event of any problems or concerns/questions, you may further contact the secretariat, Institutional Review Board Mr Bakari Fakh through +255 713 545 802 or you may also write to:

**The secretariat,
Institutional Review Board
Ifakara Health Institute
P.O. BOX 78373
Dar es Salaam
Tanzania**

Signature of participant

Date

**Signature of witness
(where applicable)**

Date

Appendix 4: IHI-IRB application checklist

S/N	
1	Signed cover letter from investigator (should also include physical address, fax number telephone numbers preferred personal number and email address)
2	Protocol contents to include summary of the study, background, objectives, rationale, methodology, personnel, budget, justification, if applicable a statement of compensation for study participation (including expenses and access to medical care) to be given to research participants, and agreement statement to comply with ethical principles set out in relevant guidelines
3	An electronic version of research protocol
4	Informed consent (English and Swahili)
5	Instruments for data collection (English and Swahili, when applicable)
6	Up to date CVs of PI and co-Investigator (if applicable)
7	Investigator's brochure, if it is clinical trial
8	Importation approval by the Tanzania Food and Drug Authority (may be submitted at a later stage)
9	An adequate summary of all safety, pharmacological, pharmaceutical, and toxicological data available on the study product, together with a summary of clinical experience with the study product to date (e.g., recent investigator's brochure, published data, summary of the product's characteristics).
10	All materials to be used (including advertisements) for the recruitment of potential research participants must be attached to the protocol.
11	Budget
12	The study must be approved by IHI Thematic Group Leader
13	A signed copy of an invoice with cost centre or receipt of payment should be attached

Source: IHI-IRB application form

Appendix 5: NIMR application checklist: (a) New proposal/amendment

S/N	
1	National Health Research Ethics Committee (NatHREC) Application Form
2	Cover letter with institution logo signed by PI or CO-PI
3	Commitment letter from affiliated institution and/or local government officials
4	Full study proposal(s) or amendment (s) with all relevant sections: Summary, background and rationale, objectives, methodology, ethical considerations, budget and budget justification, references and appendices, etc.
5	Informed consent forms/assent forms in English and Kiswahili with institution logo and local PI and NatHREC contacts
6	IRB approval certificate from affiliating institution(s) where applicable
7	Data collection tools in English and Kiswahili
8	Elaborated recruitment procedure
9	Written information to be provided to participants in English and Kiswahili
10	Curriculum vitae (CVs) and composition of the research team
11	Evidence of application and registration fees payment (bank slip)
12	Filled-in Data Transfer Agreement (DTA) and/or Material Transfer Agreement (MTA) (where applicable)
	For clinical trials: Additional documents must be submitted with application
13	Investigator's brochure and case report forms
14	Proof of insurance coverage arrangement
15	List of DSMB members (with at least one Tanzanian)
2. Renewal or extension	
1	Cover letter with institution logo signed by PI or CO-PI
2	Progress report of study indicating what is to be covered in the renewal period
3	Copy of previous ethical clearance certificate
4	Evidence of payment (bank slip)
Progress report	
1	Cover letter with institution logo signed by PI or CO-PI
2	Progress report of study including status of: <ul style="list-style-type: none"> - Activities that have been conducted - Activities that remain to be conducted
3	Copy of previous ethical clearance certificate

Source: NIMR checklist form

