# Ethical Issues in Research Ethics Governance and Their Application to the Malaysian Context

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# Abstract

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Evidence available shows that the ethics review process in Malaysia suffers from a range of problems (Kaur, 2011). These problems may be the result of a lack of training given for REC members and relatedly, it may stem from a lack of understanding of the role of RECs. Since Malaysia is striving to promote the country as a research hub for international collaboration, it is important that the ethics review system that is in place is well set up to ensure only ethical research are being approved. The aim of this thesis is to develop three important key elements of a framework that can be used to provide practical guidance for RECs and their governance in Malaysia. These three important elements of the ethics review process are: - the role of RECs, the criteria of REC membership and the acceptability of variation in decisions made between different RECs. These analysis is then applied to the Malaysian context. My initial recommendation is for RECs to adopt the Daniels and Sabin (1997) accountability for reasonableness model to assist with the decision-making process. The adoption of the model helps to clarify the role of RECs and can be used as a basis to develop the criteria for REC membership as well as to provide a better understanding of the acceptability of variation in decisions between different RECs.

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# CHAPTER 1: INTRODUCTION- BRIDGING THE GAP

In this thesis I aim to develop a basic foundation of a framework using three key elements that are central to this thesis to provide future practical guidance for the work of research ethics committees (RECs) and their governance in Malaysia. These key elements include the examination of the role of RECs, the criteria of REC membership and the acceptability of variation in decisions made by REC. They are chosen due to their relevance to the challenges that Malaysia is currently facing in this area.

This first chapter serves as an introduction to the issues and is divided into four sections. The primary focus is to sketch the development of RECs in Malaysia as well as to uncover the challenges they are having with the system. Section A is divided into two parts which outline the purpose of this study and provide a brief description of the overall thesis. The first part of Section B outlines the background to the development of RECs in developing countries of Southeast Asia (SEA) and the second part deals with the evidence available of complaints about RECs and the governance of research.

Section C will then shift to outline the contribution this thesis could bring to the development of research ethics in Malaysia. This is given by providing a detailed description of the challenges that Malaysia has with its research ethics governance and an introduction, in the light of the Malaysian context, to the main

ethical issues that will be discussed in chapters 2, 3 and 4. The last section will outline the research methodology used for this thesis.

## SECTION A

### *1. Purpose of this study*

RECs are central to the research ethics governance process. Their performance reflects the standards of the country where they operate. They are important because they act as gatekeepers in making sure that only ethical research is allowed to be conducted in that country. RECs have the authority to approve and reject studies based on their evaluation of what constitutes ethical research, and their decisions play an important role in the development of research in the region in which they operate.

What constitutes ethical research is contentious, especially when RECs often have to deal with uncertainties in terms of the potential harms and benefits of a particular research proposal. The attempt to balance these perceived harms and benefits can sometimes create a dilemma in the decision-making process. This is one of the reasons that the function of RECs is easily open to criticism by researchers and those involved in research. The uncertainty can mean that different decisions can be made by different RECs.

Since the work of RECs may also contribute to the advancement of research in their own country, it is crucial that RECs are clear about their role and what is

required of them, as well as the responsibility this entails. Being able to be clear about their role would help them justify their decisions whenever criticisms are raised. Therefore, there is a strong need to conduct studies on RECs to help improve and strengthen the system to ensure that all research conducted is ethically accepted.

In this thesis, the focus will be on the study of RECs in the SEA region and specifically Malaysia because of recent developments in that country. Malaysia's short history of having RECs may indirectly reflect a greater need to study the operation of its RECs and enhance their performance in order to make certain that they operate in accordance with what is expected of them. To the best of my knowledge, studies on RECs in Malaysia are still very limited. Existing studies appear to focus more on the importance of clinical research (Suleiman and Merican, 2000; Chandrasekharan, 1984; Merican, 2000; Zabidi-Hussin, 2007; Lim et al., 2010) rather than the RECs and their processes.

The importance of clinical research cannot be denied, but examining RECs is equally important to make sure that clinical research conducted in Malaysia is within ethical standards. The study of RECs is also crucial in making sure that their decisions do not jeopardise the integrity of researchers, research participants, the public or the research itself. Due to the lack of research in RECs in Malaysia, it is difficult to ascertain the specific problem it is facing with its RECs. However, since it has been found that members of RECs in Malaysia are still not clear about the system and the way they should make decisions (Kaur,

2011), it would be sensible to focus the study on the basic set-up of RECs and their decision-making process.

The central focus of this thesis consists in the development of an understanding of the role of RECs, the membership criteria for RECs and also reflection on the nature of judgements that RECs make in course of the decision making process. As these components are the essence of the work of RECs, progress on these questions may greatly benefit those involved in research ethics governance. This analysis may also promote the importance of being accountable to the decisions they make based on a strong understanding of the basic elements that lead to decisions that are valid and legitimate.

This study does not intend to criticise the way that current RECs are performing their responsibilities, but is more concerned with finding ways to improve the system and make certain that RECs in Malaysia particularly are comparable with those of developed countries. Malaysia can and should learn from developed countries' experiences in dealing with RECs. This learning process would also be beneficial for the development of clinical research in Malaysia, as it could give stakeholders in research the confidence they need to conduct ethical research there.

Since research ethics governance in Malaysia is relatively new, reflection on the way RECs function in developed countries can be useful. Through the developed countries' experiences in dealing with RECs and complaints raised about them, Malaysia could better understand the overall process of RECs and prevent

foreseeable problems. For example, since there have been debates about the role of RECs in developed countries and also since it has been shown that members of RECs in Malaysia are still not clear about the role of RECs (Kaur, 2011), Malaysia could find ways to be clearer about this when making decisions. This would enable RECs in Malaysia to justify their decisions based on clear account of their role whenever doubts about the validity of their decisions are raised.

In the context of this thesis, to prevent confusion, the term 'REC' is used throughout the thesis to mean any other similar body such as an institutional review board (IRB), a human research ethics committee (HREC), an independent ethics committee (IEC) and an ethical review board (ERB). All of these terms refer to the same type of committee that oversees research and has the responsibility to make a decision on whether a research proposal is accepted or rejected based on its ethical evaluation.

### *2. Study description*

This second part of section A will provide a brief description of the overall thesis. This study is divided into two parts: Part 1 will explore a number of ethical issues in research ethics governance and Part 2 will apply the analysis obtained to the Malaysian context. This study aims to provide some initial recommendations to improve research ethics governance in Malaysia. As mentioned, studies in Malaysia have been more focused on clinical research rather than RECs and their

governance. Thus, this study hopes to provide Malaysia with invaluable information on how to develop future RECs and ensure the validity of their decisions.

The first part of this study deals with three important issues and elements in the ethical governance of research and its legitimacy: (1) the role of RECs, (2) the membership and composition of RECs and (3) the variation in decision-making among RECs. Various complaints have been raised about the practice of RECs relating to these issues, which could compromise RECs' credibility and undermine their function. This justifies the need to examine them in great detail. Understanding the underlying problems that contribute to the emergence of these issues is also important to help to find ways to improve the system.

The second part deals with the SEA context, specifically focusing on Malaysia and the ways in which the issues from Part 1 might shape the governance system in that context. Complaints about RECs occur mostly in developed countries, but this does not necessarily mean that Malaysia and other SEA countries are facing fewer challenges with their RECs' review processes compared to developed countries. Examining questions concerning the role of RECs, the membership criteria of RECs and the acceptability of variation in decisions made by different RECs will help to justify their position in providing an ethical review of research proposals, and could certainly help Malaysia to enhance its own research ethics governance system.

These three elements are the basic elements in the operation of RECs. In order to make sure that RECs are performing within the ethical standards required of them, they need to be clear about these. Even though there is no clear evidence that Malaysia is experiencing problems with all the three elements, the available evidence that suggests that members of RECs and the supporting institution are still not clear about their role (Kaur, 2011) may indicate a bigger problem beyond the understanding of the role itself.

If those involved with research governance are not certain of the role of RECs, it is difficult to be certain about the membership criteria for them. As a result of the lack of understanding in their role and membership criteria, problematic variation in decision making among them is likely to occur. In such circumstances, the validity of the decisions made by them can obviously be questioned leading to complaints about the way they work. Therefore, a study of these three elements is crucial to ensure that RECs in Malaysia are performing to the standards required of them.

This study mainly focuses on how RECs should be established or modified to promote an efficient and effective ethical review system in the Malaysian context. However, this study will not cover all issues in the Malaysian or SEA context, as there will need to be more empirical work to investigate this. Interviews with researchers, participants and members of RECs from these countries, for example, may be needed to further investigate difficult ethical issues that become a burden on the research ethics governance system.

## SECTION B

### *1. Background*

In this section, I will describe the background that have led to the introduction of clinical trials in the SEA region. The impact of the increase in clinical trials being brought over to this region signifies a great need to have an established research ethics governance system that can successfully oversee research and its development. This is to ensure that research being conducted in this region is ethically sound and results produced by the research are valid internationally.

The globalisation of clinical trials has exposed SEA to the challenges that accompany it. Since industry and government sponsors in developed countries started shifting their projects overseas, particularly to less wealthy countries, clinical trials that were once focused on wealthy countries are now increasingly being established on a global scale (Glickman et al. 2009).

Outsourcing clinical trials in SEA has been shown to be less expensive. The overall process has also been shown to be faster due to the apparently less complicated regulatory regimes and the ability to accelerate the recruitment of participants from a large population in these countries (Gross and Hirose, 2007; Glickman et al. 2009). Garrafa et al. (2010) agree that one of the reasons clinical trials were introduced in developing countries was to avoid 'the more rigorous supervision mechanisms that exist in the countries from which the research originates' (p. 501).

Developed countries could view these factors as beneficial on their part, but the globalisation of clinical trials has now exposed SEA to the challenges of ensuring research are ethical. As a result, these countries need to improve their governance systems to ensure that they are comparable with those of developed countries, in order to avoid any exploitation taking place.

Ten of the eleven SEA countries (except East Timor) have united to develop the Association of Southeast Asian Nations (ASEAN), most of which (apart from Singapore) are still in the category of developing countries. These countries are Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar (Burma), the Philippines, Singapore, Thailand and Vietnam. Among these countries, Malaysia, the Philippines, Singapore and Thailand are the most involved with clinical trial activities (Virk, 2001; Rahman and Majumder, 2012), followed by Indonesia and Vietnam (Wong, 2009).

Singapore is more developed than the others, with the second-best health-care system in Asia (Gross and Hirose, 2007), and it therefore has a better infrastructure for conducting clinical trials. Besides Singapore, Malaysia appears to be the main focus for clinical trials in SEA (Virk, 2001; Gross and Hirose, 2007). On the contrary, other studies have shown that Malaysia is still behind in their clinical trial activities compared to the other SEA countries (Lang, 1998; Sahoo, 2012; Economic Transformation Program (ETP) Malaysia, 2013; Clinical Research Malaysia (CRM), 2014).

A recent study shows that Thailand has gained more recognition, with more clinical studies being carried out there since 2008 due to an increase in the availability of trained researchers and the low cost of their clinical trials (Korieth and Anderson, 2013). Recent developments also show that sponsors are choosing Singapore and Thailand to conduct their clinical trials because they have been shown to be strongly focused on quality, and do not have regulatory complications leading to a faster and efficient approval (Korieth and Anderson, 2013). Their favourable system indicates that their regulatory pathways are clear and at the same time compliant to the international standards making it more predictable (Korieth and Anderson, 2013).

The globalisation of clinical trials has opened up opportunities for SEA countries to create an additional source of income for their country (Glickman et al., 2009; Sahoo, 2012; Economic Transformation Program (ETP) Malaysia, 2013; Yathindranath et al., 2014). The clinical research industry for new drug development in 2009 ‘grew at an annual rate of 15 percent to exceed US$20 billion, with growth in Asia outpacing the market at an annual rate of 30 per cent’ (ETP, 2013 (pg. 255)). This evidently shows the opportunity for the SEA countries to develop through the development of the research industry.

As a result, enabling research in these countries could help to stabilise and strengthen their economies. Participating in global research may also help to increase the research capacity of the host countries, and can be viewed as an important platform for achieving higher standards of health care comparable to

developed countries. However, in their enthusiasm to provide an appealing setting to attract sponsors for clinical trials, these SEA countries may be compromising sufficient ethical reviews by RECs (Kaur, 2011; Douglas-Jones, 2012; Konrad, 2013; Coleman et. al., 2014).

One of the key methods being implemented by developed countries to ensure that their clinical trials are conducted ethically is ensuring that RECs are established in developing countries. By introducing the International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use, also known as the ICH Good Clinical Practice (GCP) guidelines as a set of standards, require them to adhere to the guidelines.

ICH-GCP came about as a consequence of previous studies that exploited research participants for the interest of researchers. It aims to protect research participants. It has been argued that compliance with the ICH-GCP is needed to ensure that research reviewed by RECs from developing countries is acceptable for the sponsors in developed countries (Torres, 2011). Compliance with the ICH-GCP guidelines helps to reassure the broader international community that the rights and safety of research participants are protected. At the same time, it also provides assurance that the results obtained are credible (Vijayananthan and Nawawi, 2008). Therefore, strict compliance to the guidelines can help convince sponsors in developed countries that research conducted in the developing countries has been conducted according to the acceptable standards outlined by the guidelines.

Although some developing countries are copying the ICH-GCP guidelines into their own GCP guidelines, without proper training and practice this may not in itself provide any beneficial impact to the overall system. Torres (2011) argues that training is important to help reduce violations of the guidelines. There is a strong need for training and compliance because of the perceived weaknesses in the protection of research participants in the developing countries especially in the past decade or so (Chokevivat, 2011). The reliance upon international guidelines like ICH-GCP provides reassurance that steps have been taken to strengthen the protection of research participants.

It has also been suggested that there may still be cases of research being done in developing countries by researchers from developed countries who do not seek ethical approval in the host country (Hyder et al., 2004; van Teijlingen and Simkhada, 2012). This may happen because the researchers from developed countries are ignorant or paternalistic (van Teijlingen and Simkhada, 2012) or perhaps because there is no enforcement in the developing country for needing such ethical approval prior to the start of the study.

Although the focus of their study is not directed specifically towards SEA, Hyder et al. (2004) found that there are still studies that are not being ethically reviewed in the host country or the country from which the trial is being sponsored. Their study surveyed the opinions and concerns regarding ethical review processes among researchers in developing countries mainly researchers from Asia,

followed by researchers from Africa and South America. However, details of the specific countries in the regions were not specified.

It was found that 25 per cent of the respondents reported that their research had not been ethically reviewed by an ethics committee or the Ministry of Health (MOH) in their country. They also found that 44 per cent of the respondents' research had not been through any form of technical, scientific or ethical review by their MOH.

This study clearly shows that developing countries depend heavily on developed countries to make decisions for them. It can be argued that decisions made in developed countries are prone to be accepted by developing countries without a need to review the study again themselves. This can imply that developing countries are not confident in their own ability to make decisions. It might also imply that they have inadequate knowledge and resources to make decisions. Perhaps they have just a lack of interest in making sure that studies are reviewed appropriately. However, suggesting that developing countries alone are to blame is not fair, because their lack of training and understanding of the role of RECs may have contributed to this environment.

These findings were not focused on the SEA countries but since most of the SEA countries are still categorised as developing countries, they should be taken seriously. The absence of studies examining this problem in SEA does not discount the fact of the possibility of such occurrences in the SEA countries. These findings should be taken as a caution that such practices exist and careful

considerations on how to prevent this should be given emphasis. Possibly, with such caution, the practice of research ethics in the SEA region can be further improved.

Without careful ethical consideration in reviewing research proposals, the establishment of RECs in the SEA region may falsely be interpreted only as a requirement of international sponsors for attracting international clinical trials. This is because of the prerequisite requirement that RECs are established in the host countries before sponsors in the developed countries can decide to collaborate with them. However, not having the adequate support, resources or interest to step up to the necessary standard required of them, the establishment of RECs may just be there to fulfil the criteria needed of them prior to them being involved in international collaborations.

With this in mind, the very purpose of RECs to review research studies to ensure they are ethical will be ignored possibly by members of RECs who are not trained to make ethical decisions and also by researchers who are keen to be involved in international collaborations. If RECs were only created to promote research being conducted in their countries, then this will clearly compromise the authority of RECs.

The presumed idea that the creation of RECs alone can attract international sponsors can obviously lead to the problematic function and confusion about the role of RECs especially with the absence of understanding about what they are actually for. It is not surprising if members of RECs are uncertain as to what the

role entails particularly when emphasis is given most to the promotion for international collaborations instead of the support to train and educate them on the importance of having RECs as bodies that oversee research to ensure that they are ethically sound.

The globalisation of clinical trials therefore brings an important problem to developing countries regarding the adequacy and efficiency of their ethical reviews. Concerns about the capacity and credibility of RECs in developing countries to evaluate proposals, oversee research studies and protect participants have been raised (Glickman et al., 2009; Louisa et al., 2012). These concerns are raised mainly due to the worry that RECs' have the lack of expertise and ability to properly conduct ethical review (Louisa et al. 2012) which may compromise the protection of potential research participants especially those in the developing countries with a poor background of education, economic and health status (Glickman et al. 2009).

Without adequate assistance and training, the performance of RECs in developing countries may still be poor. With an interest in monetary gain from international clinical trials, research involving human participants taking place in developing countries may raise doubts about the validity of their decisions.

### *2. Evidence of complaints about RECs and their governance*

It fits in the context of this chapter to lay down the evidence of complaints raised about the work of RECs to give a better picture of the problems. With the details about the complaints, focus can be given to the surrounding concerns with RECs to find ways to resolve them. Even though complaints presented are not specifically about the work of RECs in the SEA countries, the need to take precaution for preventative measures to avoid similar complaints necessitates the study of these complaints to uncover the problematic functions of RECs.

The processes surrounding research ethics have been around for longer in Western developed countries because of previous research ethics scandals. The exploitation of participants that came to light in these research scandals has resulted in a more protective research environment towards participants today. Several additional decades of experience in research ethics have also provided opportunities for researchers and members of ethics committees in developed countries to improve and enhance their governance system.

Even with a longer history and more established RECs, there are still complaints about the process and decisions that are being questioned and debated. In what follows I consider some of these complaints that are mainly centred on the claim that RECs are inefficient. RECs have been entrusted with the responsibility to ensure that risks to research participants are minimised, that the benefits of the research outweigh the harms and that society as a whole could gain from the beneficial impact that the research could offer (Keane, 2008).

However, RECs and the research ethics governance system have been widely criticised for being inefficient and ineffective, and therefore have not been successful in fulfilling their role (Emanuel et al., 2004b; Helfand et al., 2009; Saver, 2005; Straight, 2009). It has been argued that the review conducted by RECs are frequently viewed 'as a barrier to be overcome rather than a constructive process that will minimize risks and enhance safety' (Emanuel et al., 2004b: p. 286).

It is claimed that RECs have been behaving unethically by not disseminating results (Savulescu et al., 1996; Flicker et al., 2007); lacking in transparency (Sheehan, 2008; Ashcroft and Pfeffer, 2001; Kerrison and Pollock, 2005); being overly concerned with processes and grammatical errors (Ashcroft et al., 2005; Angell and Dixon-Woods, 2009); not monitoring and evaluating their decisions (Shaul, 2002); and encroaching into the researchers' domain by commenting on the scientific design (Kravitz, 2007; Dawson and Yentis, 2007).

Complaints about RECs in developed countries may also reflect the recent development of RECs in developing countries, as concerns about the quality of RECs in these countries have been raised (Crawley et al. 2002; Coleman et al., 2014). Coleman et. al. (2014) argue that RECs in developing countries 'face numerous barriers to conducting ethics review effectively and efficiently' (pg. 2). These barriers include the lack of training and networking and also the lack of essential resources.

It is not surprising for RECs in developing countries to receive such criticisms when long-established RECs in developed countries still receive them and are continuing to try to improve their research ethics governance through further research into their current system.

A discussion of an example of a research misconduct that occurred in Korea a few years ago will help to illustrate the need for developing countries with little experience in research ethics governance to pay more attention to improve and strengthen the existing system. Although Korea is categorised as a well-developed country, rather than a developing country, its establishment of RECs is still relatively recent and its experience may be easily comparable with those of developing countries.

Research misconduct by Woo Suk Hwang has been argued to be the result of patchy 'national regulation, ethical standards and cultural norms' (Saunders and Savulescu, 2008). Hwang and his team were found to have fabricated data in their research on cloning to get their paper published in 2004 and 2005 in *Science* magazine. It was later revealed that his stem cell research involved the unethical acquisition of human eggs (Kim and Park, 2013). Prior to the discovery of the misconduct, he had been a well-respected scientist who had received a lot of support from the government and the public, as they believed that conducting this research could have a positive impact on the development of the country.

Surprisingly, prior to his research, there was no ethics committees at the College of Veterinary Medicine at Seoul National University where Hwang worked

(Han, 2006). In order for him to proceed with his research, an ethics committee had to be established to review and approve his research. Increasingly such review is required by the larger international journals. As someone who was highly respected in his institution, Hwang was able to choose the members of the ethics committee himself. It appeared that the establishment of this committee was just a formality, however, since the committee members were not even aware of their appointments (Han, 2006). It is no surprise that his research was not reviewed properly, since the aim of the review procedure in this case was just to satisfy a formal requirement to allow his research to progress.

It is a concern in a country that is as well developed as South Korea that the knowledge of research ethics is still low. A survey carried out in 2005 on biotechnology researchers in Korea showed that 46 per cent of the participants were not aware of the Declaration of Helsinki and 39 per cent had only heard of it but did not know what it comprised (The Dong-a Ilbo Editorial, 2005). This low level of education in research ethics may have contributed to the lack of awareness of what is required to produce ethical research.

A good deal can be learnt from Hwang's research scandal in Korea, especially as it occurred in the last decade. This case shows that the establishment of RECs is still very recent and that the level of knowledge of research ethics is worrisome. If a proper solution in terms of adequate support and education is not found to improve the governance of research ethics, this kind of misconduct is likely to continue unchecked. This also shows the need for developing countries,

the majority of which have a short history of research ethics, to learn from this incident. This case provides a valuable insight into the need for valid and legitimate ethical oversight that is able to ensure the necessary requirements for ethical research.

As mentioned earlier, concern about RECs' quality has been raised globally (Kim et al., 2003; Akabayashi et al., 2007) and perhaps it is even more worrying in developing countries. Their qualities and capabilities are still being questioned, especially since the competency of RECs in developing countries remains unknown (Silverman et al., 2014). In their study using a self-assessment tool to assess the operations of RECs in low- and middle-income countries, Silverman et al. (2014) found that RECs need significant improvement regarding their criteria for membership and training for their members. Their study found that members of RECs still receive inadequate training, since most of the committees in their study did not require their members to undergo any sort of training (Silverman et al., 2014).

The reason that members of RECs require training in research ethics may be because of the need to familiarise themselves with the issues surrounding ethics in research. Presumably, one of the most important area for training is in the area of protection of human research participants since much emphasis has been given to it especially when referring to the ICH-GCP guidelines and the Declaration of Helsinki. It has been recommended that members should undergo training to assess risks of research and understand the vulnerability component

of research participants in order to strengthen the protection of research participants (Hamadian and Johansen, 2011).

A more important element for training however, should be in the understanding of the role of RECs in making sure that members are capable of making the right decision. Members need to be clear of the role and responsibilities of a REC in order for them to function optimally. A glimpse of knowledge on the ICH-GCP guidelines or the Declaration of Helsinki may not provide them with the adequate skills in making ethical decisions about a particular research study. What is more important is that they are trained to understand what RECs are actually for. Perhaps, it is crucial to inform them from the outset that the role of RECs should not be confined to only protect research participants but should go beyond that.

This is important because confusion about the role of RECs when reviewing research proposals may have contributed to the rise of concerns and complaints about RECs. It appears that some RECs may be more concerned with the informed consent process while others are more focused on the promotion of the research. With continued advances in medical technology, the roles and objectives of RECs have also become more complicated as they attempt to satisfy the needs of both the research participants and the researchers.

The need to review RECs' efficiency and effectiveness has become more urgent because of the need to realign their roles and objectives to meet those that have been entrusted to them, and also to justify the need for their establishment. It is important that RECs are clear about what is expected of them from the process

of the ethical review, because confusion about their roles may be the sign of a failed system of research ethics governance.

Research ethics governance oversees the ethical conduct of research and maintains the ethical standards that are required to ensure the delivery of high-quality ethical research. Ethical standards are needed to ensure that the decision-making process is justified and that RECs have credibility and genuine legitimacy in their delivery of valid decisions. Therefore, finding ways to improve the governance system is crucial to help maintain its authority in providing an environment for RECs to perform their role competently, and also to ensure that approval of research is made only after a strict evaluation of the ethical issues concerned.

In order to do this, it is important to rethink the role of RECs especially in light of the need to protect research participants and at the same time to attract sponsors. If it is to conclude that RECs' role is only to protect research participants, then it is unethical to promote research as the more research being done, the more participants will be exposed to the research risks. However, since the benefit of conducting research can be substantial for the promotion of health, it is impossible to reject the importance of promoting research studies especially in studies that have the potential to contribute to great benefits. The best way forward is to re-examine the role of RECs instead of focusing on only the protection element.

Besides being clear about the role of RECs, as knowledge and training are also important to assist with decision making, it is crucial that members are chosen based on the criteria that they could help in this process. Maintaining the authority by the appropriate members of RECs could help in making sure that decisions made are valid and legitimate. At the same time, to ensure that all decisions made by RECs are well-grounded, another step forward is to look at the nature of their judgement and the acceptability of the variation in decisions made by RECs when reviewing a same or similar research proposal.

All these elements are the basic steps in making sure that the outcome of the final decision is ethically valid. It is an imperative need to study and examine these elements in-depth to make certain that RECs are clear about what they are for and what it entails. Doubts and complaints raised by researchers over the work of RECs and their decisions can certainly be avoided once RECs are clear about these.

## SECTION C

### *1. The research gap*

In the context of this thesis, discovering the research gap will enable us to appreciate the contribution and importance of this thesis to those involved in the research ethics governance particularly those in Malaysia. The inadequacies in research in Malaysia on the central elements of this thesis has encouraged this

study with the aim to create an initial basic framework for the work of RECs and their governance.

The establishment of RECs in SEA is still ongoing, in contrast with developed countries, where many issues have already been discussed and some may have been resolved. Understanding the problems that occur in developed countries can assist developing countries in solving their own problems with research ethics governance. If RECs in developed countries have been continuously criticised in performing their role, we can be confident that there is more to learn about RECs in developing countries, and in the context of this thesis, in SEA, particularly Malaysia. Perhaps the reason that there are fewer published complaints about RECs in SEA is that they have been overlooked or that the importance of ethics review systems in these countries has been ignored.

Since there are still research studies that bypass review in their host countries, it is important to establish the essential value of the ethical review of future research studies in developing countries, particularly to avoid their exploitation. Therefore, RECs in developing countries and SEA should take the necessary steps to ensure that their research ethics governance system is not being exploited by researchers and sponsors from developed countries.

It is clear that developed countries are taking the opportunity to conduct their studies in developing countries for the reasons mentioned earlier. However, there is a danger that the developing countries may just be a platform for them to conduct clinical research without the necessary precautions that should

accompany such research. A major initiative taken to improve ethical review in developing countries was the establishment of the Forum for Ethical Review Committees in the Asian and Western Pacific Region (FERCAP) in 2000.

It was noted at the time that the protection of human research participants in developing countries was weak (Chokevivat, 2011). There were few established RECs, and most of these had no standard operating procedures (SOPs) (Chokevivat, 2011) and were not clear about their role and function (Torres, 2011). To improve the situation, FERCAP aims to support the establishment of RECs in the region by conducting conferences and training programs (Chokevivat, 2011). Apart from the training to enhance research participants' protection, FERCAP also provides training and assistance for RECs to develop their SOPs (Chokevivat, 2011).

The Strategic Initiative for Developing Capacity in Ethical Review (SIDCER) was formed with the help of FERCAP and is another organisation that was established to enhance human protection in research (Karbwang-Laothavorn, 2011). A recognition programme by SIDCER was created to assess and evaluate RECs' ethical review practices to ensure they meet the highest standards of protection based on the international standards and established guidelines (Hamadian and Johansen, 2011). It has been suggested that a recognised REC by this programme may offer sponsors the confidence that the research proposal has been reviewed according to the accepted standards required of them (Hamadian and Johansen, 2011).

However, since there are still concerns about the competency of the RECs in developing countries (Louisa et al., 2012), relying heavily only on programmes such as FERCAP and SIDCER to solve the problems with RECs may not be enough. The work of FERCAP and SIDCER without doubt have certainly contributed to major improvements in the development of RECs in the region but with the challenges globalisation has brought to the region, supplementing their work can further enhance the improvements. These challenges include the lack of skilled researchers, the proper functioning of RECs and inadequate regulatory framework (Lang, 1998; Sahoo, 2012).

Further studies on RECs examining in detail the basic set-up of RECs and their process of decision-making may help to supplement the work of FERCAP and SIDCER. As they seem to be more concerned with the element of protection of research participants, further examination into the role of RECs may help to enlighten the underlying problem RECs are facing when making decisions especially when faced with ethical dilemmas.

Concern over the amount or degree of protection of research participants in developing countries as compared to other ethical principles in research ethics has been raised (Kim et al., 2003). This may be due to the worry that the 'wide disparities in education, economic and social standing, and health-care systems may jeopardize the rights of research participants' (Glickman et al., 2009: p. 818). This worry may also be the reason why many have argued that the main

purpose of RECs should be to focus on the protection of human subjects (Chokevivat, 2011; Hamadian and Johansen, 2011; Panichkul et al., 2011).

Presumably, this worry may have also driven many guidelines to outline their first objective as to protect human research participants to prevent them from being exploited (Jesani, 2011). Unavoidably, this may lead to the assumption that RECs' primary focus should be on the protection of participants. However, in real-life settings, the protection of research participants may not necessarily be the primary focus. Some RECs may focus more on the research benefits to the participants and society than the protection of research participants, but this does not directly render them unethical. What is most important is to understand that only concentrating on protection ignores the reality of the decisions which also need to take into account the benefits to participants and the benefits of the research to the broader community.

The study of RECs should not be taken lightly, especially with the concern raised over their quality and function. It is important to examine in detail the underlying problem that affects their performance and their ability to conduct ethical review of research proposals. Inadequate ethical review is a worldwide concern because of the consequences it carries. In-depth analysis is needed to study the problem with RECs so that a framework can be developed to assist them in their function, especially since there is still a lack of research on the issues relating to RECs in SEA and particularly in Malaysia.

It is crucial that RECs understand their role, are clear about the criteria required to establish a properly constituted REC, and are able to clarify and justify their decisions in cases of variation between one REC and another. It is important that studies are being conducted to take the necessary steps to improve the quality of RECs so they can maintain their authority in making decisions about which research projects are considered ethical and which are not.

Many studies have been conducted examining RECs in Western countries, as discussed above, but there have been few on Asia (Akabayashi et al., 2007; Douglas-Jones, 2012). This is possibly due to the lack of awareness of the importance of RECs in a research setting. Perhaps, as it has been suggested earlier, the main focus of research has always been emphasised more on the development of clinical research rather than the processes prior to it. Therefore, the need to fill this gap to study RECs and their governance is imperative if the aim is to develop and enhance the system.

This lack of research also implies the need for researchers to realise the importance of RECs in a research setting. RECs are not just created to fulfil the requirement of ICH-GCP to review research proposals prior to the start of the research – their importance goes beyond that. RECs are the front line in making sure that all research being conducted in their country is evaluated with vigilance and great care so that only good-quality ethical research is allowed.

## 1.1. Malaysia

In this section, I will examine the challenges Malaysia is facing with its research ethics governance system. This is important in the overall context of the thesis because it will enable us to appreciate the importance of conducting this study to the Malaysian context. The research ethics governance system in Malaysia is relatively recent and arguably they may still lack the competency to conduct ethical review. The consequence of this may affect the validity of their decisions and may compromise the RECs' credibility as bodies that govern research.

Malaysia's health-care system is one of the most advanced among developing countries. This is partly because of the importance of health care as a component of the country's development (Suleiman and Merican, 2000). The future of the health care system of a particular country may be closely linked to the quality of the research being conducted in that country. Good-quality research is likely to enhance the system for the benefit of the public through the formulation of health policies that improve health care (Suleiman and Merican, 2000).

Since Malaysia has made health care research a priority, the National Committee for Clinical Research (NCCR) was established in 1997 to encourage clinical trials in Malaysia. Besides this, a major step taken to strengthen research was the establishment of the National Institute of Health (NIH) (Suleiman and Merican, 2000), which was officially launched in 2003, and the creation of the Malaysian medical research ethics committee, a national ethics committee established in 2002 that mainly reviews research conducted by the MOH and research that uses

the MOH facilities. Besides the medical research ethics committee, the other types of RECs that review research proposals in Malaysia are those in academic and private settings that review proposals that come only from their own institution (Kaur, 2011).

Malaysian Government believes clinical research is an important area that could contribute to the economic growth of the country. With this in mind, the government has developed a program called the Economic Transfer Program (ETP) in 2010 as part of the Malaysia's National Transformation Program to assist in the establishment of Malaysia as a developed nation in year 2020 (ETP Malaysia, 2014). The aim is to generate a gross national income (GNI) per capita of USD15,000.

To achieve this target, ETP has developed 12 National Key Economic Areas (NKEA) that could significantly contribute to the program. One of the areas is the healthcare NKEA which aims to contribute USD10.4b to GNI in 2020. Clinical research is one of the focus of the healthcare NKEA and therefore places the need to attract more local and international companies to do more research in the country (ETP, 2013). In year 2013, Clinical Research Malaysia (CRM) recorded new 195 clinical trials in the country. This has exceeded the government's target for the year.

CRM is a non-profit organisation established by the Government of Malaysia in 2012 'to promote Malaysia as a preferred global destination for industry sponsored clinical research' (CRM, 2014). The establishment of this

organisation provides evidence that the government is striving towards achieving its target of 2020. With the development of various organisations, Malaysians can be confident that they are progressing well towards achieving the target of 2020. The major sponsors for international clinical trials in Malaysia are Pfizer, Sanofi-Aventis, Novo Nordisk, Boehringer Ingelheim and GlaxoSmithKline (Sahoo, 2012).

In addition and in order to help ensure that research is good quality, all researchers in Malaysia who intend to do clinical research are required to undergo formal GCP training and certification (Merican, 2000), which arguably is intended to reassure the public that researchers are properly trained. Certification programmes for researchers have also been established in Japan, Korea and Singapore (Louisa et al., 2012).

However, GCP training is only required for researchers prior to their participation in clinical research trials, not as a standard part of their training. Attending a GCP training course once and being certified does not guarantee that the researchers' conduct will always be within the required ethical standards, especially since the efficacy of GCP certification remains unknown. It appears that the role of GCP training is to educate researchers and provide reassurance of good practice although it is also possible that the training may be ineffective in educating the researchers.

It would be more practical if the GCP training were an ongoing process that required researchers to renew their certificate every few years, for example, for

as long as they are involved in clinical research. This may enhance their knowledge and emphasise the importance of such training in making sure that their research is conducted in an ethically acceptable way.

Besides GCP training, the study of research ethics in Malaysia is also very important as clinical research has brought new challenges to the country. Reflection on the ethics of research should be an integral part of the system to enable international collaboration but at the same time not to compromise the need to protect the rights of participants. More importantly, the study of research ethics will enable researchers and members of RECs to work through specific new issues as they arise. With few studies on RECs and the governance of research ethics being carried in Malaysia, it is difficult to ascertain the specific problems with the system. Nevertheless, from the evidence gathered, it still imperative to find ways to improve the existing system.

The impact of the globalisation of clinical research on Malaysia is an issue that clearly needs to be dealt with by making sure that Malaysia is fully equipped to face this challenge. The main concern is the risk of Malaysia compromising the protection of research participants in its quest to become a research hub for international clinical research (Kaur, 2011). The increase in clinical research by international sponsors has been seen to strengthen the country's economy, and this obviously creates a strong drive to secure Malaysia's future economy. There is therefore a danger that the government 'might be less vigilant about providing

adequate systems of subject protection' (Kaur, 2011) in view of these perceived benefits to the country's economy (p. 232).

Kaur (2011) conducted a study to look at the adequacy of ethical review by RECs for the protection of vulnerable participants in Malaysia and had conducted interviews with eight members from Malaysian ethics committees. In an interview with one of the members of RECs who was also the Director of the Network of Clinical Research Centres at that time gave an insight that he was struggling between his role to promote clinical research as a lot of funding had been allocated for the research project and his role to protect research participants. From her study, Kaur (2011) concluded that there is 'an urgent need for reform of both the law relating to mentally incapacitated adults as well as the way in which ethics review is conducted in Malaysia' (p. 40).

As emphasis has been given on the development of clinical research, it is unfortunate that the same emphasis is not given to the research on RECs. Currently, there are no ethics regulations for RECs in Malaysia.There are no regulation that mandates ethical review prior to the start of research, except for its ICH-GCP guidelines, the Malaysian Guideline for GCP and the Guidelines for Applications to Conduct Drug-Related Clinical Trials in Malaysia, developed by the NCCR. They require research and ethical review prior to the start of all drug-related research involving human participants, and approval from the National Pharmaceutical Control Bureau (NPCB) (Kaur, 2011).

Since there are no regulations, adherence to guidelines remains voluntary and research that is not narrowly drug-related may be taken lightly, and not have to go through the ethical review by RECs or receive the same level of scrutiny. However, in Malaysia, it appears that all research conducted by public institutions and those receiving public funding are required to adhere strictly to the guidelines issued by the NCCR (Kaur, 2011). This requirement can be seen as an assurance that research conducted in Malaysia is at least being evaluated prior to its commencement, even though the process of evaluation by RECs remains unclear due to the lack of research on their work. Furthermore, the adherence to the ICH-GCP guidelines is important to ensure that the results obtained are valid world-wide.

It may appear sufficient that all these requirements have been put into place to ensure good ethical research. However, the efficiency and quality of the review process by RECs, as already mentioned, remains unclear. ICH-GCP guidelines rely heavily on the Declaration of Helsinki, and in doing so may not ensure the adequacy of the RECs' review process. This is because the Declaration of Helsinki has relatively little to say about the processes of review and oversight. Furthermore, the ICH-GCP guidelines do not focus only on the ethical aspects of clinical research, but also cover the technical and administration aspects. They therefore may not be the best source of adequate information for RECs in making sure that their reviews are satisfactory.

Interestingly, given the compulsory requirement to adhere to the Malaysian Guideline for GCP, which clearly states the need to conduct clinical research based on the ethical principles in the Declaration of Helsinki, most members of RECs are still unaware of the details outlined in the declaration, and, more worryingly, do not understand the role of RECs (Kaur, 2011). This can be due to the fact that members of RECs are not given any kind of formal training prior to their appointment as committee members (Kaur, 2011).

This highlights a serious concern with regard to the quality and validity of the decision-making process made by RECs. It is impossible to perform well when members have insufficient knowledge about what they are supposed to do to guarantee that their decisions are of good quality and legitimate. Besides the absence of formal training, this may also occur because members of RECs are not required to undergo any sort of training certification, unlike researchers, who are required to attend GCP training and be certified (Kaur, 2011).

Another possible underlying problem with the adequacy of RECs' reviews is the absence of requirement for an ethicist to be included among the members of RECs. Members are usually composed of clinicians, scientists and lay representatives of the community, the majority of which have a scientific background (Kaur, 2011). This shows that RECs in Malaysia rely heavily on the input from members with clinical and scientific backgrounds. Ethicists, in contrast, may actually play a more important role in being able to analyse the ethical issues more readily than other members.

Given the fact that members receive inadequate training and that the majority of the members that form a REC are from a scientific background, it is clear how these committees can struggle to evaluate the ethical component of a research proposal. There is a tendency that they may overlook important ethical issues that to them may not be a concern. This shows that there may be a possible problem with the adequacy of ethics reviews made by RECs in Malaysia due to the lack of training given to their members.

It has also been argued that the RECs' role is just to satisfy the public that ethical issues have been considered in the review of a research proposal (Kimura, 1989). This is a problem if the creation of ethics committees is solely viewed as an essential bureaucratic procedure for achieving certain standards, while putting aside the essence of team deliberation and decision-making (De Lecuona, 2011). This is even worse if they are being created only to satisfy the criteria of ICH-GCP with the sole intention to attract sponsors without the necessary training and resources to make sure that they are well equipped with the ability to conduct a proper ethical review of research proposals.

A study conducted by Dissanayake et al. (2006) in Sri Lanka reported that since ethical review became compulsory in order to present and publish research, the number of RECs has increased rapidly. It is a requirement set by the International Committee of Medical Journal Editors (ICMJE) that those who wish to publish their work need to demonstrate that their research has been approved by a REC (ICMJE, 2013). The rise of RECs due to this may also be

the case in Malaysia and the worry is when they are created solely for this purpose by neglecting their role to provide proper ethical review process. Not being aware of this situation the research oversight might be compromised.

Only one REC in Malaysia has so far been recognised by the SIDCER Recognition Programme, and this is the medical research ethics committee of the Malaysian MOH in 2013. In comparison, Indonesia has six recognised RECs, the Philippines has nine recognised RECs and Thailand has fifteen recognised RECs (SIDCER Recognition Programme, 2005-2013). This shows that compared to the other SEA countries, Malaysia is still behind in its awareness of the importance of RECs in the development of research in its country.

Although Malaysia appears to be actively involved in clinical trials, its clinical trial activity is still at a low level (Shulz, 2012; ETP Malaysia, 2013; Clinical Research Malaysia (CRM), 2014). This may be the reason that Malaysia has been promoting itself as a suitable place to conduct clinical research. This also may show that the importance of RECs in the development of clinical research is being neglected. Focusing only on ways to improve the conduct of clinical research in order to attract international sponsors to Malaysia is not sufficient and may only compromise the quality of RECs.

Finding ways to improve the ethical review process should not be neglected, as this can contribute to the improvement of research in the country as a whole. If Malaysia is able to show that it possesses a robust ethical review process, this may at the same time give sponsors the confidence to choose Malaysia to

conduct their clinical research. As discussed, one of the main problems with RECs in Malaysia is their lack of training. If the establishment of RECs is only focused on satisfying the requirements for ICH-GCP, then it is difficult to understand the role of RECs beyond this.

It is important that Malaysia is aware that many studies conducted in developing countries by sponsors in developed countries may not have been approved in those developed countries (Angell, 1997). This awareness would allow Malaysia to be more alert in making sure that only research that is ethical can be conducted in Malaysia. In order to be able to be vigilant in this way, it needs to strengthen its ethical review process by improving its RECs' skills and knowledge of research ethics.

The problem with inadequate training is also being faced by Thailand, since research conducted by Panichkul et al. (2011) found that 43.4 per cent of the RECs he reviewed in Thailand did not provide training to their members. The study also found, unsurprisingly, that this has led to an insufficient number of staff with adequate knowledge in research ethics. Providing an effective ethical review is the very essence of RECs, and without the necessary knowledge to carry out this function, RECs will inevitably be seen as incompetent.

A lack of data on how RECs work in Malaysia again may imply that research ethics may be taken lightly, and that there is a corresponding lack of awareness of the importance of RECs in Malaysia. It is clear now that the need to focus on Malaysia is justified to help provide a framework for RECs in Malaysia that can

improve the current system. It is important that Malaysia does not just focus on developing clinical research, but that it also enhances its research ethics governance, since RECs are the gatekeepers for deciding which research studies should be allowed to be conducted in their country and which should be rejected.

Adequate knowledge in research ethics is not just about knowing the Declaration of Helsinki but more about the ability to use the guideline efficiently. Besides that, those who are well equipped with sufficient knowledge in research ethics are also those who have the ability to apply their knowledge in relation to the activities involved in the process of ethical review by RECs. These include the understanding of the role of the RECs and what it entails, being aware of the criteria for the composition of a REC and the understanding of the acceptability of variation in decisions made by different RECs. These components that make knowledge in research ethics adequate are the essence to my thesis.

### *a. Bridging the Gap*

My study aims to provide the beginning of an efficient framework that allows RECs to reach decisions that are reliable, with indisputable quality. As mentioned, this thesis is not intended to criticise the current standards but focuses more on finding ways to improve the system. I am interested in the way RECs make decisions because improvements in this process could make a huge

difference to the research ethics governance system overall, and I believe that this is the essence of ethical research.

A study on research ethics governance is important, especially for a developing country like Malaysia, for ensuring that ethical standards are on a par with those in developed countries, particularly when there is a lack of available data on the current REC system. It is very important that RECs are able to detect ethical issues in a research proposal readily to ensure that approved research is being conducted ethically.

It is also important that RECs in developing countries learn from those in developed countries to improve the research review process. This is because without being able to show confidence that the review process is adequate in these countries, it is difficult for them to attract developed countries to conduct their research there (Simpson et al., 2009). The study of RECs would also promote responsibility over the governance of research ethics.

This study is the first step for improvement, through its examination of the issues mentioned earlier: the role of RECs, the membership criteria for RECs, and acceptability of variation in decisions made by different RECs. Therefore, my study aims to provide a sketch of framework based on Western input to reshape and educate the RECs in Malaysia and promote competence. This study does not hope to recommend rigid rules for the oversight of clinical research but rather intends to assist the system in facing the challenges that globalisation has brought into the country as mentioned earlier.

***b. The relevance of the central issues in this thesis to the Malaysian context***

In this part of the chapter, I will justify the relevance to link the central issues of this thesis to the Malaysian context. This will provide us with a better understanding of why it is important to reflect on the ways RECs function in developed countries to shape the framework for the research ethics governance in Malaysia.

From the previous discussions, it can be concluded that the main problem Malaysia is having is the lack of training that leads to the lack of understanding of the role of RECs. Understanding the role of RECs is the basic requirement in order to make an ethically sound decision when reviewing research proposals. Since this basic requirement is lacking, perhaps, the problem with RECs in Malaysia goes further beyond this.

It is very likely that with inadequate understanding of the role, there will also be a lack of understanding of who should be on the committee. The criteria for REC membership is closely linked to the reason why RECs are established in the first place. This shows that members play a significant role in ensuring that RECs are able to make an ethically acceptable decision based on what they are for.

It is obvious that with the lack of understanding of the role of RECs, different RECs may have different perceptions on what they are for. This may extend to their different perception on who should be on the committee possibly resulting in the variation of decisions made by the different RECs. The issue with variation

is not limited to differences in decisions made by different RECs in the same country but may stretch to include differences in decisions made by RECs from different countries collaborating on the same research project. This is relevant in the Malaysian context as Malaysia is keen to promote the country for international collaboration and may possibly encounter such variation.

As discussed earlier, the lack of understanding of the role of RECs is not just a problem in Malaysia but also a problem in developed countries. This is supported by the evidence shown earlier about the complaints on RECs and its function. In fact, debates about what they are actually for continues in the developed countries (Garrard and Dawson, 2005; Edwards et al., 2004a; Shaw, 2014). Therefore, it is useful to rethink about the role of RECs based on the analysis available in the developed countries since little has been done in Malaysia on this. The study on the role of RECs will be discussed in chapter 2 of this thesis.

The account on the role of RECs may also help establish a basis to examine who should be on the committee. This is important to ensure that only those who are qualified are selected to help with making the right decisions. Chapter 3 will be dedicated to the examination of the criteria for membership of RECs. Another essential element to the work of RECs is the examination of the review and reasoning processes that can determine the acceptability of variation in decisions made by different RECs which will be discussed in Chapter 4. Chapter 4 complements the discussion in Chapters 2 and 3 because it provides a detailed discussion on the effects the role of RECs and the membership criteria have on

the decisions. Chapter 4 also describes in detail the principles that should be involved in ethical review and this supplements the relevance condition of the accountability for reasonableness model in Chapter 2.

All three chapters are interrelated and should be used together to provide a complete understanding of how RECs work. The study of these chapters based on developed countries may provide beneficial insight to the future work of RECs in Malaysia. Analysis from these will be discussed in Chapter 5 to provide recommendations for the Malaysian context.

## SECTION D

### *1. Research Methodology*

This study focuses only on a desk research methodology. The approach used involves a conceptual and argumentative analysis, where the processes of constructing and analysing the arguments are an ongoing part of the study. The initial starting point of the analysis and therefore the initial data for the study, is provided by the academic literature in research ethics and by the international and Malaysian guidance on ethics and research governance, which were obtained from libraries and the internet.

The start of this thesis begins with a limited empirical claims about the state of the research ethics governance in Malaysia. Since the information is limited, it is only broadly understood and used as a way to highlight the key elements

central to this thesis. General consideration of the ethical problems in this thesis are not specific to Malaysia but generally applicable to all those involved in research ethics. Importantly, this thesis builds from a general impression of the challenges Malaysia is facing and starts to shape the more general theoretical considerations that remain problems globally and returns to the application of the analysis to the Malaysian context.

Books, academic journals and information from the internet are used for the analysis. In the discussion for Chapters 2, 3 and 4, sources are mainly from the books and academic journals. In these chapters, materials obtained with regard to the issues being examined are mostly from the Western countries, mainly the United Kingdom and the United States of America, where they have been discussed. Compared to the Malaysian context, published sources for these chapters can reasonably be obtained from the libraries including online journals.

The problem with Chapters 1 and 5 is the lack of published materials on the work of RECs in Malaysia. As a result, materials used are mainly from the internet including newsletters and websites. These information provides the basic understanding of the clinical trials activities in Malaysia but not on the work of RECs in Malaysia.

Information regarding the Malaysian medical research ethics committee is obtained from the committee's website. Since the SOP is not freely available online, I have contacted the committee in order to obtain a copy. However, as

the committee has just been recognised by the SIDCER program, the new SOP is still under construction at the time of the writing of this thesis.

Since there are no specific details available on the website about the background of each member, I identify members based on their institutions listed on the website. Members are mainly composed of those who represent the science and medical faculties, which I then classify them as members from the scientific and medical background. This will be discussed further in the discussion of Chapter 5.

There is only one substantial qualitatively robust study on RECs in Malaysia, which was conducted by Kaur (2011) and focused on the adequacy of RECs' reviews for vulnerable participants. Although Kaur (2011) focuses on the protection of vulnerable participants, her findings and discussion on the RECs' reviews are valuable to the understanding of the work of RECs in Malaysia.

Due to the lack of sources in Malaysia, Kaur (2011) also faces the challenge to conduct her research and relies heavily on materials obtained from the United Kingdom and the United States of America. Since she only interviewed eight members of RECs in Malaysia, the overall result of her study may be biased and not represent the whole community of RECs in Malaysia. However, as there are no further studies on this, her discussion can be taken as an initial step towards further understanding of the situation of RECs in Malaysia, particularly on her finding of the inadequacy of RECs review process for the protection of vulnerable participants.

Different from Kaur's (2011) work, my thesis aims to provide an initial framework for RECs' review process in Malaysia by introducing the model of accountability for reasonableness developed by Daniels and Sabin (1997). My interest lies in the decision-making process among RECs and believe that the basic requirement for a proper decision-making starts with the understanding of the role of RECs. Using the materials obtained for Chapters 2, 3 and 4, I start off to analyse the basic ethical principles that are relevant to the on-going debates surrounding the role of RECs. These principles are namely the principle of protecting research participants, the principle of informed consent and also the principle of benefits to the participants and broadly to the community.

I then developed three models based on these principles to study whether one of the principles can be used to describe the role of RECs. Materials mainly from the academic journals obtained discussing these principles are used to develop these models. However, after analysing the discussion of each model, I came to a conclusion that each model has its own strengths and weaknesses and is not suitable to be adopted to represent the role of RECs.

After the analysis, I believe that the model of accountability for reasonableness by Daniels and Sabin (1997) can help to achieve a fair and legitimate process in which it is impossible to choose one model over another. This model of accountability for reasonableness has been adopted to assist with the understanding of the role of RECs and at the same time, it is relevant to the

understanding of who should be part of the committee and assist with the decision making process which will be discussed further in Chapters 3 and 4.

As described, this thesis focuses mainly on the theoretical discussions to create an initial framework for the work of RECs. Empirical research was not done for the purpose of this thesis because my aim is to examine how the process ought to be done in relation to the understanding of the role of RECs that affect the other discussions in this thesis. Starting off with theoretical discussions, I believe findings from this thesis will create a basis for future empirical research to understand the specific problems Malaysia has. The discussion on future empirical work will be discussed in Chapter 5.

# CHAPTER 2: RETHINKING THE ROLE OF RECS

## INTRODUCTION

There have been debates going on about the functioning of RECs in which there are claims that they have failed to function properly (Ashcroft and Pfeffer, 2001; Saunders, 2002; Emanuel et al., 2004b; Saver, 2005; Garrard and Dawson, 2005; Taylor, 2007; McDonach et al., 2007; Helfand et al., 2009; Straight, 2009; Grady, 2010; Abbot and Grady, 2011; London, 2012; Joffe, 2012; Shaw, 2014). This mainly concerns with the way they review research proposals and how they make judgments. One of the concerns raised is the way how different RECs make different judgments based on the same research proposal. It is important to understand that the concerns about how RECs should function depends importantly on what they are supposed to do. It is crucial to be clear on why we have RECs and what they are for because how RECs should work depends highly on them.

In view of the fact that it is unclear what RECs are for, it is not a surprise that much of the discussions have been focused on the claims that they have failed to function properly. In order to understand the questions of why we have RECs and what they are for, it is important to be clear about their role because this represents the basic foundation to the answer to these questions. However, since the role of RECs is also unclear, this certainly warrants an in depth analysis into

the examination of the role of RECs to ensure that RECs are equipped with the basic requirement to function properly.

There is confusion about aspects of the role of RECs as the authorised body that oversees research and debates about their actual role are ongoing (Garrard and Dawson, 2005; Edwards et al., 2004a; Shaw, 2014). It might have been argued that the role of RECs should be to ensure that proper informed consent is obtained from participants. However, others have suggested that RECs should focus on the protection of research participants (McDonach et al., 2009). Considering there is no consensus on what RECs' main focus should be when making decisions, their own confusion with regard to their role is no surprise.

On the face of it, guidelines have been created to assist RECs in carrying out their responsibilities by providing a list of principles for them to adhere to. As an example, although the Declaration of Helsinki is available to guide RECs, it is not clear how to apply all the principles when these conflict. Principles for making judgments about the ethics of medical research are given but which principle should be prioritized in a conflict is not clear. RECs members may put their own values on which principle is most important, depending on their interpretation and understanding of a particular principle.

Most guidelines seem to suggest that the protection of research participants is the primary role of RECs because this is usually mentioned first. This may have led some RECs to assume that their primary focus should be on the principle of protection (Cave and Holm, 2002). However, in everyday practice when RECs

deliberate on their decisions, the protection of research participants may not necessarily be the primary focus. Furthermore, what counts as the protection of research participants may also be interpreted differently (Edwards et al., 2004a). In certain situations, other considerations may override the need for protection. As a result, these different interpretations of what the ethical priority should be may be causing confusion over the role of RECs.

More importantly, depending on guidelines alone may not be the best way to understand the role of RECs, since there are claims that available guidelines such as the Nuremberg Code, the Declaration of Helsinki, the Belmont Report and the Council for International Organizations on Medical Sciences (CIOMS) are lacking in different specific areas of ethical guidance from one to another (Emanuel et al., 2000).

Differences in the understanding of the RECs' role may also affect the decision-making process between different RECs, so that one REC may prioritize a certain principle, such as the protection of research participants, while another REC may prioritize a different principle in a similar research situation. This inconsistent application of principles in the decision-making process may provoke criticism from the public and researchers over the variation in decisions made as a result of this. I will discuss these issues and their consequences in depth in chapter 4.

It is reasonable to assume that RECs should have a uniform way of performing their responsibilities and in this context, to have the same focus of their role

because of the presumption that researchers tend to expect their proposals be treated and judged equally, especially in the case of the same or similar research proposals. Ensuring that researchers are treated fairly without favouring one over another is a way forward that would create and sustain their trust in the research governance system (Keith-Spiegel et al., 2006; Spellecy and May, 2012).

On the assumption that having a uniform process is the best way to conduct research oversight, the first step is to make certain that the role of RECs is justified and clarified. This step is significant because the role is an essential element in guiding the decision-making process, with the aim of guaranteeing a justified decision. Once the role of RECs is clear, it will be easier to make justified judgments, as they will have some guidance in making decisions, especially when faced with ethical conflicts. At the same time, RECs would be readily able to defend their decisions whenever necessary.

This chapter will discuss the following three principles: (1) protecting research participants, (2) beneficence (providing benefits to participants and the public) and (3) ensuring that proper informed consent is obtained from participants, as they are the most relevant to the conduct of research oversight by RECs and have been widely used in guidelines for RECs. This chapter will also examine whether RECs should ideally prioritize only one principle over the others, or whether they should consider all three principles without prioritising one over another.

This chapter will be divided into three sections. Section A will proceed by discussing three different models constructed using the three principles

mentioned above. Each model comprises the consideration of all three principles but with a different emphasis on each one in the decision-making process. This will allow a clear view of the different ways in which each model could shape how RECs work. In Section B, I will continue the discussion of Section A to focus whether it is plausible to adopt one of the models. I will then focus my discussion in Section C to the adoption of accountability for reasonableness model that I argue can help assist RECs to be clear about their role. This chapter does not intend to describe or criticise the current practice of RECs but aims to make progress on what ought to be the role of RECs.

## SECTION A

### *1. Principles and Models*

In this chapter, the term 'principle' is used to describe a foundation of research ethics that helps to guide RECs in deciding whether a research study is ethical. The principles discussed here are: protecting research participants, providing benefits to participants and the public, and ensuring that proper informed consent is obtained from participants. Furthermore, they are part of the seven requirements suggested by Emanuel et al. (2000) that help to determine whether clinical research is ethical. It does not mean that only these principles matter when making decisions, but they are the basic principles that have been at the heart of arguments with regard to the role of RECs (Garrard and Dawson, 2005; Edwards et al., 2004a; Shaw, 2014 Mastroianni and Kahn, 2001).

The models developed below are used to describe three sets of examples that use different principles as their primary consideration when making decisions. These models are intended to provide a detailed description of the consequences of using one principle over another in making decisions and to demonstrate whether decisions made on this basis are justified. The differences between one model and another may also reflect the practices of different RECs when valuing these principles differently. The three models will clarify if it is necessary to have only one primary consideration in making decisions or if there is a need to look beyond just focusing on one primary principle. This process will work towards achieving a more satisfactory framework that illustrates a role for RECs that is acceptable to all.

## *2. The three models*

### 2.1. The Consent Model

In the consent model, RECs focus primarily on ensuring that informed consent (or more generally, the enrolment process) is adequate and is obtained from all participants. As the informed consent process is the main consideration in making a decision, on this model RECs are less worried about the protection of research participants and the benefits of the research. This is because consent from participants indicates their willingness to be exposed to the potential harms that may come along with the research, as long as they have been given adequate information about the risks and benefits. On this model, RECs rely on the

participants' ability to decide for themselves about the risks of the research based on the information provided by the researchers.

It has been argued that participants who are competent should be allowed to decide for themselves about the degree of risk that they are prepared to face (Edwards et al., 2004a; Shaw, 2014). Shaw (2014) argues that the role of RECs should change from protecting participants from harm to being less paternalistic, by focusing on the design and relevance of a study and the informed consent process. He believes that the potential participants are the ones most suitable for assessing the level of acceptable risk, and this may also include extreme risks that may cause death as long as proper informed consent has been obtained. Edwards et al. (2004a) also believe that RECs should not be unnecessarily protective or paternalistic in deciding which risks are acceptable for participants, and that they should focus on ensuring that valid consent is given by participants. They argue that participants should be the primary decision-makers in balancing the benefits of research against the risks.

What is most important is making sure that potential participants are fully aware of the potential risks and benefits, instead of rejecting research studies they think may expose participants to very high risk (Shaw, 2014). In some cases, the likely benefits of the research may outweigh the risks to participants to an extent that refusing and rejecting a participant's willingness to participate would be unreasonable. For example, research studies to find a vaccine for Human Immunodeficiency Virus (HIV) should be allowed to proceed even though the

risk of harm is high, since the possibility of finding a vaccine amounts to a very significant need to conduct this research, and may reduce the cost of treatment substantially if it is successful.

Shaw (2014) compared the participation of adults in high-risk sports such as skydiving and bungee jumping and their participation in high-risk research, and found no reason that competent adults should be denied their participation in high-risk research when they are allowed to take part in these high-risk activities. He argues, therefore, that if adults can participate in high-risk sports, there should be no objection in them participating in high-risk research that could contribute to the benefit of the society, when this positive effect is not possible in their participation of sports. He further argues that even if there are no benefits to society, their participation in the research could still contribute to furthering knowledge in a particular research area.

Miller and Joffe (2009) further argue that the risk of participating in research is similar to the risk of live-organ donation by unrelated donors. There has been a campaign to increase the number of living organ donors for kidney transplantation to save the lives of patients in need (National Health Service (NHS), 2009), despite the possible substantial risks they face through the surgical procedure (Miller and Joffe, 2009). Since this is the case, it can be argued that participants who are willing to risk their lives for the benefits of others should be allowed to participate in high-risk research.

Importantly, when research is rejected based on a REC's view of the unacceptable risk that it poses, this indirectly denies the opportunity to make an autonomous choice by the potential participants who would like to participate in the research, and at the same time denies those who are in need access to potential new drugs that could have been brought into market if the research had been allowed to progress (Shaw, 2014).

Proponents for this model might argue that informed consent is more important when research involves greater harm. So if a research study brought with it a higher risk of death, RECs might think that informed consent mattered a good deal more than if the risk of harm was mere inconvenience. For example, in a research study to find a cure for cancer, if the risks involved taking medications that may cause severe adverse reactions that could possibly lead to the participants' death, then informed consent would be crucial.

It is important that on this model, the risks are assessed independently of the participant's view of what risks are acceptable to them. This would allow potential participants to decide for themselves which studies with which risks they would be willing to participate in, considering that they would be more inclined to participate in studies with risks they consider to be minimal for them or studies that have a favourable risk to potential benefit ratio. After all, it can be assumed that if a particular research proposal involves a very high risk then it may be unable to recruit participants due to their unwillingness to participate. As a result, in this model, research will be primarily controlled through the

recruitment of participants. The advantage of this is that novel research would be easier to be approved (Shaw, 2014) and could perhaps contribute more to the current knowledge in medicine.

### *a. Concerns surrounding this model*

There is a risk that this model might jeopardise the trust and confidence the public have in the research industry if there is no proper guidance and monitoring to ensure adequate information about risks is given to participants. As mentioned by Edwards et al. (2004a), 'public trust could be threatened by research using competent people who had given valid consent, if these participants were to die frequently or in particularly terrible circumstances' (p.90).

Although it has been argued that as long as potential participants have received an adequate explanation of the potential risks and benefits, including any uncertainties that may accompany the study (Shaw, 2014), there is still a chance that participants may not understand the explanation fully and may be misguided in their decision to participate. Getting RECs to focus on making sure that explanations are set out clearly (Shaw, 2014) is desirable, but in a real setting it may be difficult to observe the process of researchers providing information to each and every participant, especially when the study involves a large number of participants.

A second concern about having a heavy dependence on informed consent is the possible invalidity of the consent itself. The adoption of a consent model suggests that RECs are confident that all participants understand the information given by researchers during the consent process. However, it has been argued that receiving consent from participants does not necessarily mean that they understand the research completely (Corneli et al., 2012). It may just mean that information has been given to them but does not confirm they have understood the information. This is important because if RECs rely entirely or more heavily on informed consent, they need to understand the criteria that affect the process of obtaining consent:

(1) The informed consent information document or patient information sheet must be clear, with the language and content made easy for a layperson to understand. If it is poorly constructed, then information given to participants may be misleading and therefore any consent taken may not be valid.

(2) Obtaining consent may be a flawed process because the way the information is given is dependent on the researcher and does not confirm whether participants understand them or not. In his paper, Dawson (2009) argues that there is evidence showing that many 'competent adults cannot understand the information that is given to them to the degree necessary to hold that they have given a fully informed consent' (p.101).

(3) Participants tend to make mistakes and they may just simply be wrong about their understanding of the possible risks. Different participants may understand

and perceive a similar situation differently based on their level of education as well as experience, and as a result may be wrong in their evaluation of the risks involved.

***b. The importance of this model***

This is an autonomy-based model that upholds potential participants' right to decide whether or not they want to be involved in the research. According to Beauchamp and Childress (2009), 'an informed consent is an individual's autonomous authorization of a medical intervention or of participation in research' (p. 119). To respect the potential participants' autonomy would mean to acknowledge their rights to their own views on the risks involved in the research, and their ability to make choices and take actions based on their views (Beauchamp and Childress, 2009).

Their decision may be made on the basis of their assessment of the risks and benefits of the research to them personally and of the benefits of the research more broadly. The benefits of adopting this model may mean that more research is permitted and hence that there is a higher chance of broader public benefit from research. As a result, research would be primarily controlled through the recruitment of participants as long as the process of informed consent had been made to the satisfaction of the RECs.

On this view, a well-equipped participant with knowledge of the research is entitled to make a decision about participation based on his or her understanding of the risks that may be involved. In this situation, it may be difficult to argue that the participant has no right to make his or her own decision, and the consent model would seem the most suitable model to be adopted. Since informed consent itself is seen as protection against deception and coercion, RECs should not worry too much when participants have willingly consented to their participation in research studies, regardless of how high or minimal the risks are. The most important focus is that research studies are well reviewed by RECs in order to allow participants to decide for themselves (Shaw, 2014).

Edwards et al. (2004a) suggest that RECs should discuss cases with researchers if they are concerned with any unnecessary risks involved in a research proposal, but they should never decide for the participants whether or not they can participate in the research due to the risks involved. They further argue that RECs could insist that the informed consent sheet is made clearer with regard to presenting information about the possible risks of the research.

If proper informed consent is obtained, this can protect both participants and researchers. Participants are protected from coercion and being deceived, while researchers are protected because participants have willingly decided to take part in the research despite the risks they have been informed about. In this model, since the participants are the ones agreeing to take part in the research and exposing themselves to risks that they view as acceptable, it might also suggest

that participants are protected from harms that they care about as opposed to harms that others judge to be important which will be discussed in detail in the next model.

### 2.2. The Protection Model

It appears that many have assumed that the main focus in the role of RECs is to protect research participants from harm (Garrard and Dawson, 2005; McDonach et al., 2009; Angell, 1997). Garrard and Dawson (2005) believe that the primary role of RECs is to protect research participants, and they argue that RECs should be the ones to evaluate the balance of the risk and benefit of a particular research and to reject any research where the harm exposed to participants is too great even with benefits.

The protection model focuses on the protection of research participants over and above any other factors. This paternalistic approach is defined by Beauchamp and Childresss (2009) as focusing on decisions to prevent harm, even when these decisions go against the potential participants' preferences. This approach aims to ensure that participants' welfare and safety are the main focus. Compared to the other models being discussed in this chapter, it may appear that this is the most familiar, as it is thought that a concern for the protection of participants originated in the history of research ethics to ensure that research participants are not harmed (McGuinness, 2008).

It has been argued that it is a worry if the guidance available for RECs does not state a primary consideration for the principle of the protection of research participants, as this may show that there is a possible departure from focusing on protection towards a stronger desire to advance existing knowledge through research (Angell, 1997; Cave and Holm, 2002). Angell (1997) argues that this is the reason why the Declaration of Helsinki has stated that the primary obligation for researchers is to focus on the protection of research participants because there is a 'strong temptation to subordinate the subjects' welfare to the objectives of the study' (p. 847). The focus on the benefits of the research may potentially compromise the interests of research participants (Cave and Holm, 2002). If RECs want researchers and the public to trust them and if they also want to uphold the authority given to them, RECs would need to show that their main concern is the protection of research participants (Davies, 2008).

McGuinness (2008) argues that the protection of research participants should always be favoured when conflicts of interest occur between the research and the participants. This shows a strong inclination towards believing that the primary focus for RECs should be on the protection of research participants.

Contrary to Edwards et al. (2004a), Garrard and Dawson (2005) argue that even with informed consent, RECs should reject research that causes harm to participants. They believe that the primary consideration should always be to protect research participants because even though consent has been given by competent participants, their 'judgment might be clouded by such things as

irrational fears, or an over-optimistic view of research, or a misplaced sense of altruism' (p. 420).

Garrard and Dawson (2005) also suggest that not all patients would like to make their own decisions. Some patients may prefer RECs to make judgments on their behalf (Garrard and Dawson, 2005). This may be because participants are not confident with their evaluation of the risks and benefits or perhaps they have a lack of knowledge in the area of the research. Giving consent to participate in research by relying heavily on their own judgment may be a burden to them if they are not prepared to do so (Franck et al., 2007). Therefore, relying on RECs' decisions would give them the confidence to participate in research and at the same time release them from the worry of making a wrong decision.

For Garrard and Dawson (2005) the way RECs are set up should give them the authority to make decisions to protect research participants. Their ability to deliberate on ethical issues might be due to the assumption that they should be composed of experts from various backgrounds (I will discuss about this more in Chapter 3). With this in place, the public can have confidence in them and thus build their trust in RECs. RECs need to be trustworthy to maintain the public's trust by being compliant with the relevant ethical principles (O'Neill, 2002). Trust is an important element to attract future participants and the public. Once the public is confident that RECs are competent at making decisions based on their expertise in research, this may increase future participation and support for future research.

### *a. Concerns surrounding this model*

If this model is adopted, there may be a lot of research being rejected to avoid any potential harm. If RECs are being too restrictive by being unreasonably overprotective of research participants, they may actually inhibit scientific and economic development (Simpson et al., 2009).

One of the problems with this model is that it gives full and so arguably too much authority to RECs to decide which harms should be allowed and which should not. Variation in understanding harm may exist because of the different interpretations of harm between individuals. One REC may approve a research study because the harm is minimal but another REC may reject the same proposal because under their interpretation the harm is unacceptable. It is therefore important that the definition of harm is clear to avoid disputes between RECs and provide a more systematic approach for the protection of participants.

The difference between this model and the consent model is that in this model, it denies the participants' opportunity to make an autonomous choice whether to participate or not in a research. Thus, denies the idea that the participants' view of harms and benefits should be respected.

***b. The importance of this model***

If RECs decide not to focus on the protection of participants, it may threaten participation from future participants. Participants may fear that without adequate protection from an authoritative body such as a REC, their participation in the research may expose them to a danger of being harmed. If this happens, future research may not be able to take place with the support of participants, and without research, further improvements in health care may not be possible. In this view, RECs should have the full authority to reject proposals that contain a serious risk of harm to research participants, in order to prevent them.

## 2.3. The Benefit Model

Mastroianni and Kahn (2001) argue that the role of RECs in focusing on the protection of participants from harm in the 1970s has now changed to having a focus on ensuring access to the potential benefits of the research. A clear sign that this shift has occurred is 'the waiver of informed consent in research in emergency settings, written into federal regulations in 1996' in the United States (Mastroianni and Kahn, 2001: p. 26). Similar to the United States, there is also an informed consent waiver in emergency research in the UK as stated in the Medicines for Human Use (Clinical Trials) Amendment (No. 2) Regulations 2006 (Lecouturier et. al., 2008). Mastroianni and Kahn (2001) argue that 'the waiver is the ultimate endorsement of an emphasis on the benefits of research

since it suggests that research participation is so beneficial, to individuals and society, that we must guarantee access even for those unable to consent' (p. 26). This shows that a focus on the benefits of research now exists in which some research is so important that even when potential participants are not able to give their consent due to being unconscious in a medical emergency, for example, their participation in research for the benefits of the knowledge is crucial.

The benefit model gives priority to the benefits that may be gained from research. The adoption of this model is more likely to prevent unnecessary research and to focus on the advantages of conducting a research study. As benefits are the main focus compared to the other principles discussed earlier, the greater the benefit that would be expected to be gained from a research study, the higher the risk of harm that would be tolerated. In this model, harming participants is justified as long as the research provides a beneficial impact to the participants and society.

Miller and Joffe (2009) argue that one of the areas of research that may expose participants to a high risk of harm in view of the great benefits that can be gained is the research into public health emergencies. This is because the outcome of this research is critically important to providing benefits to the public when urgently needed. In the application of this model, it can be justified for a participant to die (and certainly to risk death) for the overall benefit to society gained from the research. Being able to discover a cure for a life-threatening condition would have a huge impact on the improvement of health care, and also

reduce the overall cost of treatment. Therefore, even if the research may expose participants to great harm, the expected benefit would offer a greater reward for the future.

Edwards et al. (2004a) argue that exposing participants to a risk higher than minimal is justified if the research is able to provide them with benefits. Patients who are desperately ill may be prepared to participate in very high-risk studies in view of the possibility that they might benefit from their own participation (Reynolds, 2002). They may think that since they are terminally ill, for example, they might participate in high-risk research in case it succeeds in finding a cure for them.

Westra et al. (2010) argue that rather than worrying about the acceptable level of risk when making decisions, RECs should provide a procedure for exceptions when dealing with research that is exceptionally promising and important. In this model, RECs rely more heavily on the responsibility of researchers to ensure that the risk of harm is tolerable. This also indicates that they are more confident that researchers are aware of the participants' safety and well-being, and therefore would not expose participants to unnecessary harm. Overall, on this model, RECs should first and foremost ensure that the research stands to bring benefits before considering any other features of it. This also means that the value of such research frames the further considerations.

### *a. Concerns surrounding this model*

The problem with the adoption of this model is that in research, there is no guaranteed benefit. RECs can only assume that there is a chance of a benefit in research and a certain probability of achieving it, but they cannot be certain that the expected benefit will be fully achieved. The only evidence that RECs can rely on may be given by the systematic review of previous studies that may help to determine the possible benefits of the proposed research. Therefore, they may need to rely heavily on the information given by researchers and the confidence they have in achieving it.

Miller and Joffe (2009) argue that due to the uncertainty of the potential benefits of research, justifying the need for high-risk research is challenging. Furthermore, there is a likelihood that the commitment to protecting participants may be weakened (Mastroianni and Kahn, 2001), especially if there is an excessive promotion of scientific and economic development that would allow an extreme permissiveness of research, which may lead to abuse, injustice and exploitation in research (Simpson et al., 2009).

Following the negative reaction from the public in response to two previous research studies that resulted in the deaths of Jesse Gelsinger and Ellen Roche in the United States of America, Miller and Joffe (2009) argue that this indicates that the public do not agree with research that involves a risk of very significant harm, even though the potential benefits may be great. If participants continue to die in research due to their participation in it, it can clearly compromise the

public's confidence in the whole research enterprise. Care should be taken with regard to the level of risk that is seen as acceptable, in order to maintain the public's support and trust in future research (Miller and Joffe, 2009).

***b. The importance of this model***

There is a broad range of benefits that research could bring into the life of participants, future patients, healthcare system, healthcare practitioners and the society. With the adoption of this model, more research, including novel research, is likely to be approved and may subsequently contribute to the advancement of health care. Researchers and RECs owe an obligation to patients to provide treatments that will benefit them or at least not harm them. The only way that they can come to know, really, what is harmful or beneficial is through research.

It has been argued that members of the public have a responsibility to participate in research that could provide benefits to society (Mastroianni and Kahn, 2001; Harris, 2005). Therefore, it is important to educate society about their role in research studies. It is sometimes the case that participants and society may not gain an immediate benefit from a research study, but findings associated with participants' involvement could benefit others in the future. This might be the case with the 'blue skies' research in which it is more speculative compared to the goal-driven research (Linden, 2008)

If a research study provides no benefits, then it can be argued that it would be useless to the improvement of health care (Emanuel et al., 2004a). This means that research with a high chance of producing a benefit to society should be allowed, while research with a low chance of producing a benefit or with no benefit at all should be rejected. This also relates closely to the harm that participants may be exposed to, since research with a greater potential benefit might allow a higher risk of harm, while research with less or no potential benefit should not allow research participants to be exposed to any harm. .

There should be at least a minimal beneficial value for a research study to be allowed to progress, through which it could contribute valuable information to the field of health care. There is a need to conduct research in many fields to cover gaps in medicine, and the most important research is that which is most useful. Therefore, allowing research without any real potential benefit to proceed, even though it harms no one, is unjustified. This is because there will always be risks involved even it is just the time that the researchers spend conducting it rather than something else.

## SECTION B

### *1. Can one of the models be chosen as a basis for the role of RECs?*

The principles in these three models are all interrelated. If one model is chosen over another, there would be a chance that RECs would still need to consider the

other principles every time when facing a conflict. Since every research study is different and may expose participants to different types of risks and benefits, it appears unsuitable to define the role of RECs as needing to focus on only one principle at a time. Edwards et al. (2004a) and Garrard and Dawson (2005) have argued about the primary role of RECs, and it is without doubt that debates over their role will still continue.

The tendency to choose just one model and so to prioritize one principle from the three described above should be resisted. This problem could be avoided by educating those involved in the decision-making. Because each different research proposal poses different problems and needs, it is difficult to predict in advance which model is most suitable. Instead, it seems more plausible that RECs should balance and weigh the different principles in each context.

It is important to establish that there is a very close relationship between benefit, harm and consent. It would be difficult and inappropriate to separate them when making decisions. All principles are equally important and it is difficult to prioritize generally which principle should be the most important. A general inclination to prioritize a principle will only create dilemmas when making decisions because each research proposal should ideally be treated individually, and the general application of a rigid prioritized procedure may not be the best option to adopt.

### *2. How do we decide the best role for RECs?*

This section intends to make it clear that worrying about the relative priority of the principles will not solve the problem. Since there is no clear consensus or guidelines on their primary role and so in this context, the principle that should be prioritized, debates surrounding this will surely remain (Emanuel et al., 2004a). What is most important is to understand what RECs are for, and that their function should not necessarily be focused on only one principle.

Understanding what RECs are for is very important because if we stick to the conception that they are only created to focus on one principle such as, for example, to protect research participants, then when they are faced with research that has the ability to produce great benefits but with great risks attached, it is difficult for RECs to decide what to do. Some may reject the proposal in view of the risks but some may approve it in view of the benefits. If RECs firmly believe that they are there to protect participants, then those who approve this type of research may be seen as making an unethical decision.

Therefore, finding a way to resolve this kind of dilemma is more important than arguing about which principle should be the primary one. Furthermore, since focusing only on just one model may not be sufficient and may still invite disagreements about which principle should be RECs' priority when making decisions, finding a way to unlock this problem is important to ensure that decisions made by RECs are legitimate and valid. Most importantly, RECs need to be able to justify their decisions so that these do not cast any doubt upon them.

## SECTION C

### *1. Accountability for reasonableness*

As recommended by Daniels and Sabin (1997), accountability for reasonableness is a way to develop a fair and publicly acceptable process for making legitimate decisions. Researchers have been argued to have a lack of confidence in RECs due to their lack of accountability and their inability to justify their decisions (Cave and Holm, 2002). Failure to provide adequate justification over the decisions made may cause researchers to feel marginalised and to have subsequent hostile feelings towards RECs (Keith-Spiegel et al., 2006). Therefore, having transparency in decision-making by adopting a fair process may provide assurance to the public that RECs are competent at making decisions.

### 1.1. A fair process adopted by Daniels and Sabin (1997)

Since it is difficult to agree on the primary role of RECs, finding a way to resolve the disagreements among RECs is the best way forward. It is important to note that disagreements in this context are reasonable disagreements and therefore warrants a system that could take all these principles into consideration. Daniels (2004) suggests that a fair process is likely to help in making decisions in contexts where we cannot consistently settle disagreements especially when they are reasonable.

Reasonable disagreements exist because RECs can reasonably disagree by choosing one principle as their primary role over another based on the earlier discussions of the three models. Each model as described is important and has its own strengths. However, each model also has its own weaknesses and therefore, choosing one model as the role of RECs is not the answer. There should be a legitimate process that helps to clarify the role of RECs to avoid confusion during the decision-making process.

There are guidelines available to assist RECs in making decisions for example the Australian National Statement on Ethical Conduct in Human Research (2007) and the Government Arrangements for Research Ethics Committees (GAfREC) (2011) prepared by the Department of Health, United Kingdom. However, these guidelines do not specifically guide RECs on the process of decision-making especially when in conflict.

Referring to Section 5 of the Australian National Statement on Ethical Conduct in Human Research guideline (2007), it does provide general information for the work of RECs. However, it does not cover specific details on the issue with the role of RECs as discussed in this thesis. The fact that there have been debates about the role of RECs, it is paramount that we understand the role and what it entails. It is important to adopt a system that could allow for a better undertstanding of this to assist in the process of decision-making.

The adoption of an appropriate system needs to be able to clarify the role of RECs and minimise disagreements. It is also important to ensure that decisions

made are legitimate and are acceptable to the RECs, researchers and participants. As mentioned, the model of accountability for reasonableness developed by Daniels and Sabin (1997) is capable of providing a fair and just system to the process of decision-making.

This process allows for the consideration of all the principles discussed in a fair process that maintains the legitimacy of the decisions. The main reason for the adoption of this model is because it allows transparent decision-making that provides the ability for researchers and participants to be involved in the process. This system allows them to better understand the decisions made by RECs and if necessary provides them with the ability to challenge the decisions. Transparent decision-making has also been argued to represent good governance (Daniels, 2004).

With this in place, rather than arguing about the role of RECs and what it should be, this model of accountability for reasonableness moves forward by taking into account the principles involved and the importance to provide justifications and rationales for the decisions made. By adopting the model of accountability for reasonableness, even if universal agreement cannot be achieved, the decisions made can at least be reasonable and legitimate to those who disagree. Furthermore, this process will allow for transparent decision-making and has been argued to represent good governance (Daniels, 2004). There are four conditions that lead to this process and guarantee accountability for

reasonableness, which may act as a framework to determine how RECs should make decisions.

### 1.2. The conditions (Daniels and Sabin, 1997; Daniels, 2004; Sheehan, 2008)

***a. Publicity condition:***

Decisions and their rationales should be made publicly accessible. This is because the public have a right to know about decisions that may affect their lives. This transparent process should allow a rationale of the decision to be presented to the public in a way that they are able to clearly understand (Daniels, 2004).

***b. Relevance condition:***

Rationales for the decisions must be relevant, appropriate and agreed upon by those affected by the decisions (Daniels, 2004; Hasman and Holm, 2005). It is important that to be able to provide these rationales, RECs need to have relevant knowledge with regard to the issues being discussed. Any disagreements during the decision-making should also be made known to the public so they can understand the nature of the deliberation (Daniels, 2004). This condition is the most important in providing a justification for the decisions (Sheehan, 2008).

***c. Revisability and appeals condition:***

Those affected by the decisions should be allowed to challenge the decisions made.

***d. Enforcement or regulation condition:***

Regulation of the process to ensure that Conditions 1 to 3 are met.

### 1.3. The importance of a fair process

The reason that this process may help to solve the problem over the issue of the role of RECs is because it allows the decisions to be publicly criticised and lets those who are affected by the decisions to challenge them if needed. The public in this context refers to researchers, potential participants, sponsors and others such as family members of potential participants who feel affected by the decisions made by RECs.

The adoption of this process is also important to ensure that researchers are being treated fairly. Keith-Spiegel et al. (2006) argue that a fair and just environment provided by RECs may actually prevent unethical behaviour. The feeling of being treated unfairly by RECs may result in researchers' loss of trust in the ethical review system, which in turn reduces their confidence in that system (Keith-Spiegel and Koocher, 2005). Perhaps the debate about the role of RECs

was initiated by researchers' frustration over the work of RECs and their lack of justification.

Burris and Moss (2006) argue that if there were a system for researchers to voice their criticisms over the decisions made by RECs, RECs would be more responsive to those criticisms, especially if they were able to give adequate justifications for their decisions (Keith-Spiegel et al., 2006). Burris and Moss (2006) further suggest that this practice would reduce the potential cynicism among researchers towards the practice of RECs.

One way to increase transparency in the decision-making process would be to increase public scrutiny of the decisions made by RECs (Candilis et al., 2006). Increasing transparency would also allow a better understanding of how RECs assess the risk–benefit ratio in making their decisions (Reynolds, 2002). Being accountable by providing a procedure for participants to complain and by being transparent has been argued to actually facilitate and improve the ethical conduct of research (Silverman et al., 2014).

As a result, the model of accountability for reasonableness, as adopted by Daniels and Sabin (1997), may be the best way to decide how RECs should be making decisions, especially since it is difficult to agree on the primary role of RECs. The overall outcome may not only be that RECs are assisted in making decisions but also that a good relationship is maintained between RECs and researchers.

### 1.4. The problem

Making decisions and rationales public may mean that RECs need the public to participate in the deliberation of decisions. However, it has been argued that making these public does not necessarily mean that the meetings of RECs need to be made public (Sheehan, 2008). What is most important is that decisions are made accessible to the public. Having meetings in public may expose RECs to confidentiality issues and at the same time may restrict RECs' freedom in making ethical decisions (Ashcroft and Pfeffer, 2001; Sheehan, 2008).

All conditions except Condition 3 above (the revisability and appeals condition) appear to be possible to comply with. It is a problem to adopt Condition 3 because most approved studies will already have started by the time they are made known to the public. Therefore, the public would not be able to challenge the decisions made by RECs. Without this possibility, the adoption of the accountability of reasonableness approach will not be able to solve the overall problem of the issues discussed in this chapter.

#### *a. A case example (Netto, 2007)*

This case example will be used to illuminate the problem with Condition 3. A research using Viagra to treat childhood pulmonary hypertension was conducted despite recent findings showing that children taking a higher dose of this medication are at a higher risk of death. Since Viagra is also associated

commonly with the treatment of male erectile dysfunction, it is no surprise that this has raised concerns among the public. However, it is difficult for them to challenge the decision made by the responsible REC, as these complaints were only made after the studies had started and were made known to the public.

This case study is used to provide an example of a case that might invite concerns from parents and public over the safety of research on children. The use of this case is to highlight the importance of being able to challenge the RECs' decisions whenever they feel necessary especially when it concerns the safety of their children. In specific, there are no available public debates or newspaper coverage on this matter. However, since parents have been found to be concern about the consequences and impact of clinical trials on their children in particular the unknown or unexpected harm (Caldwell et al, 2004), it is reasonable to believe that parents can be anxious about the use of Viagra in their children since the drug is only approved for adults and not children even at the time of the study.

The United States Food and Drug Administration (FDA) has now released its recommendation against the use of Viagra in children except in cases where the doctors believe that the benefits of treatment outweigh the risks to children ( The United States FDA, 2014). This recommendation against the use of Viagra in children was made based on the observation in a long-term clinical trial of children who suffered from pulomoray hypertension. It has been observed that the mortality rate has increased with the increased use of the drug.

It can be easily understood that it is normal for parents to fear the safety of their children. Their fear of their children's safety could even extend to the fact that some parents refuse to vaccinate their children due to their concern over the safety of vaccination (Smith et al, 2011). Although this appears to be caused by the lack of education on the importance of vaccination, this shows that their decision-making is primarily affected by their perception of safe. It can be argued that with the adequate knowledge and information, parents may be willing to take greater risks that may have the potential to treat and cure their children's condition (Caldwell et al, 2004). As discussed, not knowing the transparent impact of the study on their children may increase their fear of the possible consequences of harm.

***2. Is adopting the Daniels and Sabin (1997) approach acceptable?***

Without an appropriate process for the public to be able to voice their concern, it would still be difficult to justify the decision-making process and the ultimate decisions made from the deliberation. Since there is a problem in applying the Daniels and Sabin (accountability for reasonableness) approach, it is important to decide whether to use the approach, modify it or abandon it completely. Examining the approach carefully, I suggest that it should be modified to align with Condition 3 mentioned above.

Decisions should be made publicly accessible to guarantee the participation of the public because they play an important role as participants in research studies. These decisions could be made accessible on RECs' websites to enable those who are concerned with the decisions to challenge them. However, it is important that the public be given time to challenge the decision prior to the start of the research. Time frame is also an important issue, as a reasonable amount of time should be allowed for the public to challenge the decision, but this process should not delay the start of the research, especially research into emergency medical treatments.

Another solution to this problem is the creation of a registry for decisions made by RECs, which can only be accessed by registered users, such as researchers, potential participants who are interested in participating in clinical trials and those who are concerned about the rights of participants. Once the decisions have been made, the public have every right to argue against and challenge those decisions in view of any concerns they may have about them.

It is also important to clarify that making RECs' decisions public would not mean that the public would be able to join the RECs' meetings. Their participation may interfere with the decision-making process. Therefore, public participation in meetings should be confined to just the involvement of lay members as representatives of the whole community. However, with regards to challenging decisions made by RECs, the public as a whole community could

challenge those decisions if they were concerned about the appropriateness of a particular research study.

It can be argued that with the implementation of the model for accountability for reasonableness, the workload for RECs will also be increased. The need to prepare documents with their justifications and rationales and publish them publicly may add to the burden of their current work. There will need to be more administrative work because of these requirements. Therefore, this might deter their voluntary participation as a member of RECs. In addition, with such bureaucracy this might also obstruct research.

On the other hand, documentation of their decisions can be seen as a positive requirement that could assist them in future decision-making (Coleman, 2004a). Proper documentation is required in a medical setting and it is no surprise that this should also be required among RECs that review clinically related research proposals. In fact, documentation allows RECs to be more careful in their deision-making process (Coleman, 2004a). The recommendation for RECs to adopt the model of accountability for reasonableness follows from the general trend that now favours openness and accountability (Ashcroft and Pfeffer, (2001); Sheehan (2008). It is reasonable to believe that with appropriate openness, doubts about the work of RECs and how they make decisions can be significantly reduced. Instead of obstructing research, this model appears to encourage good practice among RECs because of the need to be transparent in their decision-making.

Considering the demand required from members of RECs with the adoption of this model, it can be argued that they should be paid. However, payment to members can create conflict of interest that may jeopardise the process of decision-making. Cain (1992) on the other hand, argues that even without payment to members, conflicts of interest among members cannot be avoided because some members may receive their basic salary from the institution where the RECs originate. Therefore, Cain (1992) further argues that members should be paid. Payment to members may not be problematic after all since recently, the Health Research Authority (HRA) of the National Health Service (NHS) has produced a guidance for allowance payment for the Chair of the National Research Ethics Service (NRES) RECs (Corrigan and Kirkbride, 2011). This is due to the recognition of additional responsibilities required from the Chair. The Chair is entitled to £3500 per year.

It is true that with the implementation of this model, more work is required for the documentation of the RECs' decision-making process. Additional responsibilities will also be required to ensure that decisions made for similar cases be treated similarly using a system called a case law model which will be discussed in great detail in Chapter 4. It is important to acknowledge that these additional requirements are for the benefit of all those involved in research and for research itself. Recognising this additional burden, it is reasonable to suggest that members of RECs be paid. Perhaps, the policy written for the NRES Chair's

allowance could be used as an example for future guidance on payment for members.

## CONCLUSION

The role of RECs is to make research ethical. It is important not to argue about what should be their main role but to find ways to apply their main principles to produce a justifiable decision-making process. If one principle is given priority over another, there is a high probability that disagreements will occur due to the nature of the differences between individuals and committees. Therefore, adopting the approach of accountability for reasonableness seems to be a sensible option for allowing justified decisions to be made.

Since research are different from one another, it is important that RECs deal with each of them separately. In some cases, there is a need to be more concerned with the informed consent process while in other cases, we should focus on the protection of research participants. This will depend on the relevance condition of the accountability for reasonableness model when reviewing research proposals. All the three principles discussed are reasonable and should be taken into consideration in ethical review but what is more important is that these principles should not be generally prioritized.

When using the accountability for reasonableness model for reviewing research proposals, members of RECs should be readily able to detect the relevant ethical

principles at issue which should not be limited to only the three principles discussed. Besides these principles, others may include the consideration of scientific value and validity, fair subject selection and respect for potential participants as described by Emanuel et al., (2000). This process will be discussed in detail in chapter 4. RECs should make decisions based on what concerns them the most and are able to provide the rationales for their decisions. These processes should be made public so that those affected by the decisions are given the opportunity to challenge the decisions made.

With such process, not only that the confusion about the role of RECs can be resolved but this process could certainly help RECs in their decision-making process and thus, allow them to be more efficient and effective in their role to make research ethical.

# CHAPTER 3: WHO SHOULD BE ON THE COMMITTEE?

The conclusion from the previous chapter provides a basis to the overall discussion of this chapter. The previous chapter has introduced the importance of being clear about the role of RECs to make sure that research are ethical without being overly concerned about one principle over another. Since debates about what should be the role of RECs are still on-going and to the lack of agreement on any one of them, the adoption of the accountability for reasonableness model developed by Daniels and Sabin (1997) helps to provide a fair and publicly acceptable process in making legitimate decisions. Their model of the accountability for reasonableness has been used as my reference to develop a clear understanding of the role of RECs.

The criteria for the REC membership is closely linked to the understanding of what RECs are actually for. Since there is no formal consensus on the role as discussed in Chapter 2, criteria for membership given by most guidelines remains open to disagreement, especially as they do not provide justification for the criteria of members.

McNeill et al. (1994) argue that it is important to be clear about the 'criteria for selection of suitable members, the proportion of institutional and noninstitutional members, and the need and justification for the various categories of required membership' (pg. 530). This is because the selection of members can significantly influence the RECs' decision-making process. In order to be able

to justify the reasons for their selection, it is important to understand the role of RECs before deciding who should be on the committee board to make the decisions.

In this chapter, I will examine the criteria for REC membership based on my discussion in Chapter 2. I do not aim to advocate a drastic change in the current composition of REC membership. Perhaps indeed, the current composition may not require any changes. Instead, my aim is to understand the criteria for membership that properly constitutes a REC that could assist in the decision-making process and understand the rationale behind their selection as members.

This chapter will be divided into three sections. Section A will provide a justification of the need to examine in further detail the criteria for the membership of RECs. Section B will use the three models used in Chapter 2 to illustrate the importance for the selection of members in shaping the decision-making process. Finally, Section C aims to provide a basic structure for the selection of members based on the conclusion I made in Chapter 2 regarding the account of the role of RECs.

## SECTION A

RECs, as the name suggests, implies that ethics play an important part in the work of the committees, especially during the decision-making process. Given this, it may be of some concern if members of an ethics committee do not possess

any special training in ethics or at least are incompetent to deliberate on ethical matters. Hoffman et al. (2000) in their survey of hospital ethics committees in Maryland, United States, found that the majority of them do not have members with any qualification or training in ethics. They argue that their findings show that during the setting-up of committees, importance is not placed on the ability of members to deliberate on ethical issues. Even though the study was focused on hospital ethics committees instead of RECs, it can be assumed that both types of committees face a great deal of ethical issues relating to health care making them similar.

Without appropriate training or qualifications, the ability of members to deliberate on ethical issues and their authority to make decisions could be questioned by those who are negatively affected by those decisions (De Vries and Forsberg; 2002a). It can be argued that having ethical training would enable members to conduct the process of decision-making more effectively and allow others to have more confidence in them performing their responsibilities.

Many studies have shown that there is as yet inadequate training in ethics among members of RECs in developing countries (Silverman et al., 2014; Kaur, 2011; Panickul et al., 2011). This may also be a problem in the developed countries. Saunders (2002) argues that the reason for this may be that members often 'lead professional lives in which educational time is thought best devoted to further medical, pharmaceutical or nursing education- not to REC matters' (p. 536). He

further argues that it is difficult in practice ‘to insist on such training in a voluntary system’ (p. 536).

Training in ethics for members of RECs should aim to allow members to be familiar with the ethical arguments and reasoning which are the basic components to the deliberation of ethical issues in research. Training for members should also aim to provide them with the ability to understand the ethical review processes. This includes the understanding of the principles involved in the process mainly the understanding of the protection of research participants, the benefits to the participants and also to the broader community and the understanding of the informed consent process.

It might be that the initial expectation of the public on ethics committees is that they are composed of members who know something about ethics. It would then come as a surprise to learn that members are actually not familiar with ethics. In fact, findings have shown that the majority of the committees being studied do not have members who are trained in ethics (De Vries and Forsberg, 2002a; Hoffman et al., 2000). The lack of training might cause them to be unfamiliar with the ethical issues in question and may compromise the ethical review.

Ethical training should aim to facilitate ethical research. Importantly, training given to members of RECs should not be aimed to train them to be ethicists but provide the necessary understanding of the function of RECs and how to operate the system. Ethical training should constitute the basic understanding of the role of RECs (as discussed in Chapter 2), the understanding of the ethical principles

and relevant conditions pertaining to a particular research proposal under review (also discussed in Chapter 2 and will be discussed in Chapter 4), and the understanding of the process of decision making (will be discussed in Chapter 4). These create a basic approach for the ethical component of training for members of RECs.

Besides this ethical component, training should also include the understanding of research methodology, 'its application to patients and populations and the broader regulatory, legal and moral environment' (Davies et al., 2008). Although the other components are equally important, since the focus of this thesis is on the ethical aspect, other aspects will not be discussed in detail.

Besides the lack of training for members that could lead to the problem with incompetency, another problem with the set-up of RECs is the lack of justification regarding the criteria given for the composition of the committee. The training for members and the criteria for composition are two different elements that are interrelated to provide the basis for a properly constituted REC. Without clearly defined criteria, inappropriate members may be selected and without training, members will not be well equipped with the knowledge to conduct an ethical review. These can negatively affect the decision-making process and the resulting final decision.

As mentioned, guidelines merely list the criteria for membership, but lack any sustained explanation of why the types of membership listed should be part of a committee. (Department of Health (DOH) in United Kingdom (UK) , 2011;

National Health and Medical Research Council (NHMRC) in Australia, 2007; Department of Health and Human Services (DHHS) in United States (US), 2009). They do suggest that a committee should be composed of a broad range of members from various background and expertise, but not in specific detail.

Broadly, the reason given for such is to ensure a diversity of members from various backgrounds to build a dynamic team to reach the best decisions possible. The selection of members have been suggested to include scientists, lawyers, ethicists (McGuinness, 2008), lay members (McNeill et al., 1994) and independent members (Macklin, 2008) with a balance of men and women (Moermen et al., 2007).

The diversity of the composition of a REC aims to ensure that when making decisions, the committee might achieve a balance between protecting research participants and at the same time consider the benefits of the research (McNeill et al., 1994). It is possible that with members from various backgrounds, their contribution to the arguments can help achieve a more holistic discussion. The need to incorporate members from various backgrounds can also be assumed to inform the public that the committees are adequately formed by members who are qualified to discuss a variety of sensitive ethical issues (Lane, 2005).

However, it is unclear that diversity in composition leads to the most effective process in making decisions, possibly due to the lack of research in this area (Lane, 2005). It can be argued that diversity does not actually influence the effectiveness of the decision outcomes made by RECs. Instead, what can

possibly provide a positive impact to the deliberation of the decisions made by RECs is the influence brought by the selection of suitable members.

The lack of a clear justification of why certain types of members should be on the committee might also invite criticism over the way decisions are made, especially when members deliberate about and decide on issues that are outside their area of expertise. It has even been argued that the reason for the selection of some of the members of RECs is unclear and that their participation in the committee is unessential (McNeill et al., 1994). As a result, the quality of decisions made can be legitimately questioned and committees rightly face scrutiny from researchers and other stakeholders involved in medical research concerning their credibility in performing their responsibilities.

Many have criticised the work of RECs but there appears to be significantly less work done regarding the way RECs should be set-up (DeVries and Forsberg; 2002a). Since there is no clear consensus on the way RECs should be set-up, this may have contributed to the variation in the composition between one REC and another. Different composition undoubtedly has an effect on the standards and procedures adopted by the different RECs and thus can contribute to unwarranted variation in their decisions. Understanding the possibilities of having a more uniform set of criteria could in a way help to reduce unwanted or unjustified variation between them.

As Schuppli and Fraser (2007) suggest, being clear about the role of RECs 'could help to clarify the most appropriate membership structure' (p 297). Even though

it has been made clear that the best way to justify the role of RECs is to go through the process discussed at the end of Chapter 2, it is important in this chapter to discuss the various ways criteria of membership could be set up according to the three models described earlier. This will increase clarity regarding the ways in which the membership criteria for RECs are connected to the question of what RECs are for. The result of this would allow a better understanding of the membership criteria when deciding RECs' membership composition based on the role of RECs at the end of this chapter. This will also eventually help in suggesting a more uniform set of criteria for membership that can be applied universally.

The work of this chapter is important to secure trust from the public in the decisions made. It is reasonable to assume that the public would want members of RECs to have the necessary qualifications to ensure that the decisions they make are the best possible. Determining the appropriate people to be members of an ethics committee is a key element of guaranteeing legitimacy. This will provide a platform for further improvement in the research review process.

It is important that RECs and the authorities responsible for their operation can show that their composition provides them with the ability to efficiently and appropriately carry out their responsibilities and also be able to assist researchers in their proposals so that RECs can secure and maintain their relationships with the researchers (Lane, 2005).

## SECTION B

### *1. The relationship between the models and the criteria for their membership*

The reason why this chapter relies on the models described earlier in Chapter 2 is because it can illustrate the impact each model has on shaping the set of criteria for the membership of RECs. Each of the different models will imply different types of membership criteria to ensure that relevant expertise is on the committee board to deliberate on the issues in the way that the model requires. Using these models will help to make clear the relationship between the role of RECs and who should be on the committee. The understanding of this relationship will be useful in discovering the set of criteria based on what they are actually for at the end of this chapter. This section will start with the discussion based on the consent model and will then focus on the benefit model and the protection model.

### 1.1. Composition criteria for membership of the consent model

As described in Chapter 2, the consent model is one in which informed consent is the RECs' primary consideration when making decisions. With informed consent as the focus, RECs should be built up by members who have the expertise to deliberate on issues surrounding the process to ensure that the potential participants are given adequate information regarding the risks and benefits of a research proposal to allow an informed decision to be made.

To be able to evaluate the issues surrounding the informed consent process, members must be able to relate well to the potential participants' expectations and needs. The ability of the members to empathise with potential participants will help shape the informed consent according to the potential participants' capability of comprehending the information given. This is important so that potential research participants can decide whether or not to participate in research based on the information given.

Making sure that the informed consent process is adequate and appropriate for participants is crucial to avoid them being exploited. Exploitation of research participants has occurred in the past by experimenting on them during the research without obtaining their fully informed and freely given consent. Since then, informed consent has been the centre of debate in research ethics to make sure that the current practice has shifted from exploiting participants to respecting them in this way.

Since informed consent is centred on respect of potential research participants, it is important on this model that members are recruited from those who understand the community from which they would be recruited. Lay members are one of the types of membership that may help improve the informed consent process. They are selected from a community not affiliated with the institution it serves and are able to empathise with the potential research participants (Lane, 2005).

Lane (2005) conducted a study of members of RECs in the United States to examine the relationship between their role on the committee and their perceptions of the process and found that lay members from her study were unsure of their purpose on the committee except of making sure 'that the consent form is understandable' (p138). This shows that it is clear that even to them, their main responsibility lies within the informed consent process.

In addition, Saunders (2002) also argues that lay members' participation in the committee specifically concerns the provision of opinions in terms of the relevant information that should be passed to the potential participants. The reason for this may be that they feel that they represent the people who will be receiving the consent forms and that they have the responsibility of making sure that the forms are within the acceptable standards. Their insight is important to inform how the research might affect the potential participants (Saunders, 2002).

As a result, their participation during the ethical review of research proposals is beneficial because of the way they aim to make the consent forms clear and also because they are able to make sure that researchers provide adequate explanation to potential participants regarding the risks and benefits of the proposed research (DeVries and Forsberg; 2002a).

Most importantly, the role of lay members is paramount on this model because of their ability to provide their perspectives on what the potential receiver of the consent forms might understand and what they might want to know. This is

perhaps the key role in the decision-making process that influences the final outcome of their decisions regarding the research.

Besides the lay members, ethicists trained in research ethics may also contribute to the deliberation on decisions surrounding the issues of informed consent. Ethicists are those who are professionally trained and qualified in ethics. They are those who are familiar with the processes of ethics review mainly the literature, arguments and reasoning involved in making decisions.

Members who have a background in ethics may have a good understanding of the history of informed consent and will be likely to be more appropriate judges of the proposal than those from the medical field. Their ability to examine ethical issues will also help them to criticize the consent documents in making sure that potential participants receive all the ethically required information with regard to the proposed research.

Since there is a tendency for people to be biased in their decision-making in certain ways, relying on lay members alone may not be the best solution. Therefore, incorporating other members who could relate well with the process of informed consent could certainly ensure that the process can be well examined.

Social scientists and psychologists are also important in the composition of membership based on this model because of their ability to understand the society and their behaviour more effectively. They are the ones who might be

able to understand how people make decisions and why they do so. This would allow them to anticipate the needs of the potential research participants with regard to the information of the potential risks and benefits.

In conclusion, because the central focus of this model is on the ethical context of the consent process, the decision is best made by those who are well placed to judge from the perspective of those who will be going through that process. As discussed above, it appears clear that this model should only be composed primarily of lay members, followed by ethicists, sociologists and psychologists.

### 1.2. Composition criteria for membership of the benefit model

On this model, the main consideration for the REC is the benefit of the research. As opposed to the consent model, if the REC's primary focus is to promote research to gain the benefits it could offer to medicine and the broader community, members should be composed of those who are well placed to encourage the promotion and approval of research that has the potential to produce these benefits. With this model, there is a tendency for more research to be approved and so to provide a greater contribution to the current state of knowledge in medicine.

In order to focus on the potential benefits of a particular research proposal, membership of the REC should include those with a primary interest in promoting research that has the potential to benefit the participants and public.

Members should not be unnecessarily protective of the potential participants especially when the expected overall benefits outweigh the risks of the research.

Members from the medical and scientific fields such as doctors and scientists appear to be the most suitable types of members to be on the committee. This is because they have the relevant expertise similar to the researchers proposing the research and thus are likely to understand the research better. This also provides an advantage for the members when dealing with issues surrounding this model during the discussion as they are able to relate well with the process on how to promote useful or valuable research. Most importantly, they are in the position to judge how the research might contribute to medicine and science.

To be specific, those who are suitable may include public health specialists, epidemiologists and population health scientists who are in touch with the practice of medicine on the ground and therefore, have the knowledge of the needs and priorities of doctors and nurses within the healthcare system. They are also the ones involved in public health and healthcare commissioning and are knowledgeable about the prioritisation of research according to the needs of the global and local population.

Lay members are not suitable to participate in the committee due to their inability to comprehend technical matters and in particular to see the broader clinical picture into which the research fits. McNeill (1993) argues that lay members' participation in the committee is relatively unimportant due to the fact that they do not have the relevant expertise of the other committee members. The lack of

expertise may also lead to poor deliberation on decisions when ethical, medical and scientific issues were brought into discussions.

In conclusion, on this model, the primary focus of membership in the composition of RECs are those who have the relevant professional training in the medical and scientific fields to enable a broad appreciation of the population level effects of the research on medicine and its practice.

### 1.3. Composition criteria for membership of the protection model

As discussed above, the composition criteria for RECs will look different depending on the model of the role of RECs that we adopt. On the final model, the primary focus is the protection of research participants. Here, members of the committee should be alert to any issues in the proposed research that may compromise the welfare and safety of potential research participants.

With this role in mind, there may be a tendency to reject proposals and limit research when members think the risk is too high for the participants, even if the potential benefit of the research is great. This model is based on the idea that RECs should take a generally paternalistic stance to their decision-making and be prepared to make decisions on behalf of participants. Therefore, to make unbiased decisions, members should not have any vested interest in promoting research which might compromise the safety of future participants.

Scientists may have competing interests in the research proposed and decisions might be biased towards the promotion of research without the evaluation of harm that may be imposed on the research participants. Therefore, their involvement would be risky in which protection of participants could be compromised.

Clinicians on the other hand are the ones that should be on the committee board as they might evaluate the risks better and make decisions to proceed with research only when they are satisfied that the level of risk is acceptable. In addition, they will be more familiar with what the participants or patients will go through because of their clinical experience and expertise. It is important that they are independent clinicians who are knowledgeable about a range of conditions and treatments and are capable of judging the impact of the study on the participants.

Lay members may not play any role if the issues concerned are to be directed towards the protection of participants as they do not have the expertise to deliberate on these issues. Furthermore, lay members may not directly represent the patients as they are not the patient themselves. Perhaps, a more suitable member might be the patients themselves. They will better understand what they want to be protected from.

In conclusion regarding this model, members should be selected from those with clinical experience, especially those who are independent and not related to the research in any way. Their expertise will help ensure that participants are well

protected from foreseeable harm. The difference between this model and the benefit model is in the importance of selecting members who are independent and not related to the research being reviewed. This is to avoid any conflict of interest that may compromise their judgement.

## SECTION C

In Chapter 2, I argued that each of these models was inadequate as complete accounts of the role of RECs. However, using the models has been helpful to illustrate the role that members might play in shaping the decision-making process. Before I focus my discussion on the final criteria of membership based on my conclusion of the role of RECs, I will first explore the necessary number of members that could help create a good committee. This is important to make sure that only the necessary and suitable members are selected to ensure the effectiveness and efficiency of a particular REC.

### *1. The necessary members*

McNeill et al. (1994) performed a study of members of RECs with the aim of examining the different influences different members had during discussions and found that a strong influence exists over the discussion from medical professionals with little from the lay members. This may be due to the fact that

in most committees the majority of members come from the medical field and therefore it is likely that discussions are centred on the technical issues leaving lay members unfamiliar with the discussion (Schuppli and Fraser, 2007).

Another possible problem with having the majority of members from the medical field on a committee is the possibility of them overlooking the protection of participants and instead focusing on the benefits of research (De Vries and Forsberg, 2002a). This can be prevented by reducing the number of members from the medical field and striving to achieve a balance with members from the community. It is also important to include independent members from the medical field who are not related to the research to prevent biased decisions.

Even though doubts have been raised about whether the participation of lay members 'can effectively balance any bias that medical, scientific, and other institutional members may bring to the committee' (McNeill et al., 1994: p. 526), it is difficult to deny the fact that their participation is actually important to represent the community in view of the need to make judgments involving the interests of the community (Weijer and Miller, 2004). Their participation is also important to help to 'ensure the integrity of the process by making research institutions more open and accountable to the public' (Schuppli and Fraser, 2007: p. 298). Therefore, Schuppli and Fraser (2007) suggest that the number of lay members on a committee should be raised to make sure that their views are taken into greater consideration during the decision making process.

The Governance Arrangements for Research Ethics Committee (GAfREC) in the UK (2011) states that the REC should be composed of experts and lay members. The maximum number of members allowed is 18 and the minimum number of members for a REC is seven, as this is the amount of members needed for a quorum. The Code of Federal Regulations (title 45 part 46) in the United States (DHHS, 2009) states that the minimum number of members is five but does not state the maximum number. The National Statement of Ethical Conduct in Human Research in Australia (NHMRC, 2007) states that the minimum number of members is eight but as in the United States, it does not specify the maximum number.

The number of members of a committee may affect the efficiency of the committee in making decisions. It is important to find just the right amount of members in a committee to assist the decision making. Although they did not specify in detail the ideal number of members for RECs, Candilis et al. (2012), found that a larger group of REC members with 15 or more members may prevent the majority from participating in the discussion. This is even more obvious if the REC chooses to adopt a primary reviewing system in which with each proposal, a member will be assigned to review and discuss it with the other members during the committee meeting. Based on this system, most of the discussion within the RECs will be dominated by the chairs and designated reviewers (Candilis et al., 2012).

This reflects the importance of the selection of members because if the committee is to rely heavily on the chair and designated reviewers, each and every member of the committee should be competent in examining details of the ethical issues presented in the research proposals to ensure that they are able to contribute to the discussion and detect issues that have not been tackled by the chair or designated reviewers. Otherwise, it can be argued that the downside of this practice is the reliance on the primary reviewer's view without representing the whole committee (McNeill et al., 1994).

For example, when scientists (particularly when they are affiliated with the institution where the REC originates) are given the task of primary reviewer of research proposals more frequently, there is a chance that the discussion may lead to the promotion of research instead of protection, especially when most rely on the primary reviewer's comments without the opportunity for other members to express their views (McNeill et al., 1994). Therefore, as McNeill et al. (1994) suggest, if RECs decide to opt for 'primary review', composition of membership for the committee should be equally composed of members from the institution and those not from the institution to ensure that they are independent in their views.

Candilis et al. (2012) argue that instead of having a larger group of members in RECs, committees could invite external specialists to review research proposals related to their expertise. Since medicine now consists of various specialised fields, it is impossible that members who are doctors or scientists in a committee

know in detail each and every research area in medicine. To have all types of specialists from the medical field as members will only make the committee larger and may not necessarily contribute to the overall decision making.

Therefore, the suggestion to invite external specialists whenever needed during the meetings will be beneficial for the committee. This is a good idea in which the number of members could be kept to a minimum, avoiding those who are not essentially needed in a committee from being part of it. Whenever RECs review a research proposal, when there are no committee members who are specialists in the field, inviting external specialists would make the review more comprehensive and valid.

Besides inviting external specialised experts for their expert opinions,RECs can also where appropriate, invite patients themselves as their views and opinions may be more relevant to the actual participants' views and needs (Staley, 2013). Even though lay members represent the community, they may not represent the whole of the community. Due to the extensive range and scope of research being proposed, their participation as representatives of the community 'cannot adequately provide the perspectives of the full range of research participants' (Anderson and Dubois, 2012: p. 953). Invitation of patients may even extend to the invitation of children, whenever research on them is going to take place (Coyne, 2010).

Another option for the involvement of patients in the committee is by creating a patient focus group. This group would allow for a better understanding of their

perspectives. It has been argued that their participation has improved research (Staley, 2013). Patients do not necessarily have to be physically present for discussion but rather can provide their opinions in writing to comment on the research.

This could allow RECs to be more sensitive with the issues that the potential participants' perceive as needing more attention. At the same time, this could also provide an opportunity for the patients to raise their concern regarding issues they find might affect their protection. Hurst (2001) suggests that patients who have concerns about the research should be given the opportunity to discuss those concerns with an independent expert member who is not affiliated with the institution.

***2. Finally, who should be on the committee?***

In this section, I will bring together the arguments of the previous chapter and the discussion above to examine in detail the criteria for membership to ensure that RECs are properly composed of suitable members based on what the REC's are actually for. As discussed in the previous chapter, the role of RECs should not be focused only on one model. Consideration of the principles discussed in all the three models is equally important when members make decisions. Therefore, an adoption of a fair and publicly acceptable process is the best way to guide RECs in making legitimate and valid decisions. This process, adopted

from Daniels and Sabin (1997), is called the accountability for reasonableness model.

This process is designed to ensure that all decisions made by RECs are seen as acceptable by those involved in research. This is important because disagreements over the role of RECs may remain unsettled and may only invite criticism over the way they work. With the adoption of this process, determining the role of RECs is not the most important issue; what is most important is that the decisions they make can be justified and accepted by the public and researchers, hence making the decisions legitimate and valid, and at the same time, making the committee accountable for their decisions.

The role is to make certain that the research is ethical. According to the accountability for reasonableness model, all research will be decided on a case-by-case basis instead of relying on finding a universal agreement of the role of RECs. This has been discussed in great detail in Chapter 2. In this chapter, understanding what they are for enables the selection of only the necessary types and backgrounds of members to participate in the committee to perform the role to ensure research are ethical.

Since it is now clear what RECs are for, in this section my discussion will focus on finding the criteria for the composition of a REC that suits the role of RECs that I have discussed. It is important when deciding who should be on the committee that the reason and justification for why they should be part of the

RECs is readily available especially to overcome doubts raised relating to their authority in making the decisions.

It will be unreasonable to list specifically who should be on the committee because in some RECs in certain countries for example, finding the specific people with the specific qualifications may not be possible. Therefore, in this section, I will suggest six categories of people with different backgrounds who appear most suitable to be part of a properly constituted REC that can ensure that research is ethical based on the earlier discussion on the criteria of members for the models (consent model, benefit model and protection model).

### *2.1. Clinical experience*

Having professionals from this category as members of RECs is invaluable due to the fact that they can relate well with the clinical situation of the patients and participants. As professionals with clinical qualifications, they are also the ones familiar with the nature of the research proposed and the possible impact the research has on the patients and participants. They may include doctors, nurses and pharmacists.

The difference between these members and the scientists, as has been illustrated in the models, is that scientists may have the tendency to promote research and focus on the benefits while they may be more concerned about the protection of participants from potential harm, especially if they are independent of the

research and institution. Their hands-on clinical experience enables them to better understand the risks and benefits of research to the patients and participants.

### *2.2. Health system experience*

In addition, RECs can also include epidemiologists or public health consultants who are more familiar with the research methodology and the prioritisation of research in health care. Their inclusion as members is important to make sure that the method of research is in place. This indirectly protects participants from unnecessary risks and at the same time may be able to enhance the research by making sure the methodology is correct with a possible higher likelihood of gaining benefits.

### *2.3. Research experience*

Professionals from this category may include researchers and scientists who are more familiar with the research and its context. They may also be the ones most enthusiastic about promoting research, compared to professionals from the clinical category. Instead of hands on clinical practice, they are usually involved in the science behind the research and may be working in the laboratories, for example.

### *2.4. Ethical and legal experience*

As described in the informed consent model, an ethicist is someone who is professionally trained in ethics who is familiar with the range of relevant arguments and processes of ethical review. Their role in RECs is to ensure that the whole process and the discussion in particular are conducted in the correct way. This is done by making sure that the discussion is not biased, all issues are considered fairly and equally and most importantly it is not dominated by one group only. With their knowledge and expertise, they are expected to be able to evaluate and analyse the argument given by the other members.

An ethicist would definitely be helpful in examining ethical issues. Their participation in a committee would possibly make the identification of ethical problems easier. McGuinness (2008) suggests that an ethicist should be part of a REC. Although she did not clearly specify in detail the reason for the inclusion of ethicists, it can be argued that their participation in a committee might help to reduce biased conclusions significantly (McGuinness, 2008).

It seems clear at this stage that they have a specific role that is directly related to the accountability for reasonableness model adapted from Daniels and Sabin (1997). As this model suggests a case-by-case basis without the focus on only one principle, it is important that ethicists are included to ensure the balance of committee's discussion as well as the ability to provide the rationale and reasoning for the discussions made. However, finding a professional with the right qualification as ethicists may not be easy. Therefore, it is important to not

make it compulsory to have them as members but it would be valuable if RECs are able to find the right person for the role.

Besides ethicists, lawyers might also be able to fit into this role. They are also the ones likely to be familiar with arguments and reasoning but may not necessarily be familiar with ethical review. One possible argument for them to be included as members of RECs is the fact that they are familiar with the law and their ability to provide expert opinions regarding the legality of research. However, they may not be able to contribute to the ethical judgement. Perhaps, rather than including them as members, they might be referred to whenever their advice is needed.

### *2.5. Citizen experience*

Lay members should be members who are not experts in medicine, science or the law and should not be affiliated with the institution (McNeill et al., 1994). They need to be independent from the institution to avoid any conflicts of interests as they are the ones who represent the community in making sure that potential participants receive the necessary information with regard to the risks and benefits of a research proposal. As described in the earlier model of informed consent, they are involved with the interpretation of information sheets and making sure that consent is appropriate.

Their contribution might be very helpful in understanding the perspective of potential participants. It is important that members have insights into what the potential participants want and expect from research. At the same time, their participation can also balance the discussion of the committee from focusing on the technical aspects of research to the consideration of the interests of potential participants and broader community. This helps to ensure that the process is accountable to the public (Schuppli and Fraser, 2007; Staley, 2013), thus making their role more specific in relation to the accountability for reasonableness model.

Religious scholars may also be part of this category. Their involvement is particularly important whenever conflicts about certain religious issue arise in research. However, it can be argued that not all research studies would involve contentious religious matters and therefore, their inclusion as members may not be essential. They may however be important in some cases and that is when RECs can invite them for their opinions.

In Malaysia for example, Islam is the official religion and if there are doubts about religious matters pertaining to research, this can be brought to the attention of the National Fatwa Council Malaysia (National Fatwa Council Malaysia, 2014). Fatwa refers to the Islamic ruling achieved through meetings and consultations with relevant experts for the purpose of making decision. Once decision has been made, RECs can then make decisions based on the Islamic ruling provided by the National Fatwa Council. In fact, their Islamic ruling can

even be absorbed into research guidelines for example the Malaysian guidelines for stem cell research and therapy (MOH, 2009).

### *2.6. Patients experience*

Lay members represent potential participants but they are not patients themselves. Therefore, their views may be limited to their own values and opinions. Therefore, having patients to represent themselves would help RECs understand better their concerns. However, including them as members may not be reasonable because each research would involve different types of patients. The best option would be to invite them whenever necessary for their opinions.

### *3. Amount of members*

In all the categories described above it is important to ensure that RECs have a balanced discussion. For example, inclusion of those from the clinical experience category may balance the discussion to ensure that it is not primarily focused on the benefits of research. Another key to ensure that the discussion is not biased towards the research is the need to have members who are independent of the institution where the research will be conducted. Even though clinicians can be more protective for the safety of their patients, RECs cannot put aside the possibility that they may have some vested interest in the proposed

research. Therefore, a balance of independent members with members from the institution where the REC originates is imperative.

With the combination of the groups from the clinical experience category and research experience category, as well as independent members, we can be assured that at least the discussion will not be biased. This is crucial because the deliberation of decisions provides great impact on the final decision. It is important to ensure that the decision does not compromise the protection of participants and at the same time does not compromise participants' potential of enjoying the benefits research could offer.

As discussed earlier, if the number of professionals from the clinical and research experience categories is greater than the number of lay members, there is a tendency that they will dominate the discussions. Therefore, it is important to ensure that the number of lay members is equal or almost equal to the number of members from the other categories.

It is difficult to put a figure on the number of members for the final makeup of a REC. But it appears clear at this stage that perhaps 12 members, with 6 being from the clinical, health system and research experience categories, 2 from the ethical and legal experience category and 4 from the citizen experience category should be sufficient. It is important that out of the 6 members who are from the clinical, health system and research experience categories, 3 are independent members.

As a quorum, at least 6 members should be present with at least 3 members from the clinical, health system and research experience category with one of them being independent of the institution, one ethicist and 2 lay members. The compulsory presence of an independent expert and lay members is important to ensure that decisions made are not biased. Hence, I suggest that the essential makeup of an REC should be 12 members to serve as permanent members and when necessary specialists and patients can be invited to participate in the deliberation of decisions.

In terms of gender representation, both the National Statement on Ethical Conduct in Human Research in Australia (NHMRC, 2007) and CFR Title 45 Part 46 in the United States (DHHS, 2009) state that members should be equally represented by both men and women. However, GAfREC in the UK (DOH, 2011) does not clearly state a requirement for a balance of gender. Gender equality may be important to avoid discrimination against women.

Furthermore, since lay members have been decided to be an important representation of the community, it is reasonable to suggest that representation of women in the committee is important for the potential women participants. It has also been suggested that with 'adequate representation of women on committees that evaluate research proposals may encourage equitable representation of men and women in research' (Silverman et al. 2014: p. 4). Therefore, it is reasonable in this context to have a balance of men and women from the 12 members suggested.

The inclusion of a balance of gender, race and age may represent the community and may influence the decisions, but following from the accountability for reasonableness model, intrinsically their inclusion does not affect the process of decision-making involved in the model. Therefore, this does not affect the criteria of membership in the context of this chapter but they may be included for political reason depending on the policy of certain countries. Most importantly, the categories I have suggested earlier appears to satisfy the conditions of the accountability for reasonableness model and therefore, sufficient to ensure that RECs are able to make research ethical.

## CONCLUSION

It is unclear whther the different composition of membership among different RECs has contributed to problems in the outcome of their decisions due to the lack of research in this area. However, it can be argued that their different composition of membership may have led to the different emphasis given in their discussion between one REC and another based on the amount of types and background of members (Stark, 2011; Stark 2012). This can be clearly seen in the above discussion of the different composition of membership based on the three models. Due to the different types of members participating in the different models, their primary consideration will also differ.

In order to avoid obvious variation in the procedures and decisions made by RECs, there is a strong justification to have a standardised membership composition among the RECs. With the composition being similar from one committee to another, the decision-making process could also be assumed to be similar due to the composition of members with the same background and expertise. Even though this may be difficult to achieve, working towards this will help in reducing unnecessary variation between RECs.

The suggested 12 members in the conclusion is not very different from most of the composition of RECs and they also include members from various backgrounds. Other studies have shown that the average member in an ethics committee is from around 13 (De Vries and Forsberg, 2002; Kim et al, 2003; Helfand et al., 2009) to about 16 members (Candilis et al., 2012). As mentioned earlier in this chapter, my aim is not to advocate a change in the current membership but rather to understand the composition criteria in relation to the role of RECs and what they are actually for. With the understanding of the rationale for their membership, it is easier to appreciate the members' roles in their contribution to the process of decision-making.

# CHAPTER 4: IS VARIATION IN RESEARCH ETHICS COMMITTEES' DECISIONS ACCEPTABLE?

## INTRODUCTION

In the previous two chapters, I have discussed about the role of RECs and the influence it has on the criteria of REC membership and their training. These are the basic two elements that can assist RECs to function properly. This chapter will shift the discussion into a more specific problem on the acceptability of variation in decisions made by different RECs that can occur even with a clear understanding of the basic two elements. In this chapter, I will discuss in detail the processes of decision-making that can influence the final decision that RECs make to be able to examine when variation can be seen as acceptable.

Most importantly, before deciding whether variation is problematic or not, first we need to understand the meaning of variation in the context of this chapter. Then, we need to be clear about the kind of variation is at issue. This will finally help to understand whether the occurrence of variation is something that RECs need to avoid.

Differences in the decisions made by two or more different RECs reviewing the same proposal or proposals that are relatively similar are, in what follows, referred to as 'variation'. Besides variation in decisions that occur between

different RECs, variation could also occur in decisions made by the same committee at different times. This refers to the different decisions made over time by one particular REC. An example of this could be that a relatively similar research project reviewed by one REC was previously approved but then later rejected.The issue of variation is important because it has invited criticism over the work of RECs (Goldman and Katz, 1982; Veatch, 1987; Davies, 2008; McDonach et al., 2009; Abbott and Grady, 2011).

This kind of variation in decision-making has been an issue for many decades (Goldman and Katz, 1982) and is still one of the major concerns surrounding RECs today. It is important to understand the significance of variation, as it is still unclear whether it is problematic. Since RECs do not conform to one uniform standard or set of guidelines, it is not surprising that decisions may vary from one committee to another.

On the face of it, variation looks to be a problem when the differences in decisions involve 'judgement over what research is considered ethical' (Edwards et al., 2004b). In this case, it becomes very important that the issue with variation is dealt with, as RECs ought to strive to promote ethical research; if different decisions are made that could create unethical research, then developing a solution to the problem of variation is crucial.

The issue with variation would have been a straightforward problem before the establishment of Multicentre RECs (MRECs) in the UK in 1997, when each proposal had to be submitted to a number of different RECs in different

locations. The issue of variation would have been the result of different requirements in the application procedures of different RECs (Al-Shahi, 2005), different concerns about the ethics and methodology of research (Penn and Steer, 1995) or different concerns with regard to the patient information leaflet (Sheehan and Yusof, unpublished manuscript). This is still a problem in the United States (Klitzman, 2011) and possibly other parts of the world. In SEA for example, variation in decisions might occur between two countries collaborating on an international research project due to the possible variation in standards and values.

The Report of the Ad Hoc Advisory Group on the Operation of National Health Service (NHS) Research Ethics Committees (DOH, 2005) was created following criticism from researchers about variation, in order to improve the procedures for ethical review (Mayor, 2005). Now in the UK, the 'NHS ethics review system has been explicitly designed to ensure that research conducted on patients in the NHS is only reviewed by one REC' (Sheehan and Yusof, unpublished manuscript).

Although this is the case in the UK, but since complaints have been raised earlier about the problem with variation, the National Research Ethics Service (NRES) has decided to focus on the issue of the consistency of decisions between different RECs by establishing a programme of Shared Ethical Debate (ShED) (Lamberty, 2008). The aim of this programme is to improve the quality of ethical review and promote consistency (Davies, 2008; Heasman et al., 2011). In this

programme, ‘a single research application, previously reviewed and ultimately given favourable opinion, is reviewed again by a number of RECs to explore consistency in decision-making’ (Heasman et al. 2011: p. 13). This shows that variation is still an important concern and as McDonach et al. (2009) claim, the issue with variation remains unresolved.

An absence of variation does not necessarily mean that RECs have made the right decision. It is important to note from the outset that different individuals think differently and have different values; therefore, a certain amount of variation is unavoidable. The most important and plausible step seems to be to justify the existence of variation among different RECs. This would help in determining when variation can be seen as acceptable during the process of decision-making.

This chapter aims to address the question of the acceptability of variation in decisions made by different RECs, by first examining the evidence that shows a problem with variation and then understanding the significance of variation in decision-making by RECs to determine whether and what kind of variation is acceptable. Most importantly, in deciding whether variation is problematic or not, I need to be certain about how and when variation occurs during the decision-making process. The information gained could then help in identifying which type of variation is acceptable.

My argument is that certain kinds of variation in RECs’ decisions are acceptable and justified. Variation can occur at the procedural stage and at the content stage,

and understanding the nature of variation will help to determine which types of variation are acceptable. A strong reason for finding an answer to the question posed is to avoid unnecessary criticism about the conduct of RECs that could jeopardise their authority in making decisions. Finding an answer would definitely contribute to improving the review process and providing a better understanding of the way RECs work.

I will divide my discussion into five sections. In Section A, I will discuss the evidence that claims that variation causes a problem to researchers and their work. In Section B, I will discuss the possibility that the occurrence of variation is not overall problematic. Then, in Sections C and D, I will discuss in detail the nature of variation and examine the kinds of variation that are acceptable. Finally, in Section E, I will propose a solution to improve the decision-making process conducted by RECs.

## SECTION A

### *1. Problems with Variation – Evidence of Complaints*

As variation often occurs without clear justification, researchers have argued for a reduction in variation among RECs (Abbott and Grady, 2011). In this section, I will examine the possible problems that may have been caused by variation in decision-making by RECs, by analysing the complaints raised by researchers on this issue. If variation is found to be problematic, then finding ways to solve the

problem with variation is the best way to improve the review process for RECs and to secure the confidence that stakeholders should have in RECs.

The reasons for thinking that variation might be a problem can be divided into two categories:

1) Different decisions made by RECs cause a hindrance to research

2) Different decisions made by RECs reduces researchers' confidence in the review system

This section will set clear that variation occurs in different kinds. Examples of cases in the first category below will demonstrate that variation can occur in the final decision as well as the reasons given for the decisions. These 'reason variation' and 'decision variation' will be discussed in section C.

### 1.1. Different decisions made by RECs cause a hindrance to research

Variation has been shown to cause delays in research (McDonach et al., 2009) and can lead to a fear of it being a hindrance to research (Saunders, 2002; Mansbach et al., 2007). Researchers may expect that the same or similar research proposals would be treated using the same or similar criteria, which would then lead to the same judgment being made about them by different RECs. However, many studies have shown that these expectations have not been met, due to the variation in judgments among RECs that occurs even when the same or similar

proposals are reviewed by them (Goldman and Katz, 1982; Tan, 2004; Woollard, 2000; Abbott and Grady, 2011; Angell et al., 2006).

In their study in the UK, Angell et al. (2006) showed evidence that variation in decision-making exists by comparing the decisions made by three different RECs on the same proposals, which were reviewed independently by each committee. Out of the 18 application proposals reviewed by the three RECs, seven proposals received variation in the decisions made. It is interesting to note that in one case where the three RECs reviewed the same proposal, the first made a provisional decision, the second made an unfavourable decision, while the third decided that the application was outside the remit of governance arrangements for RECs.

Even though these three different decisions only occurred for one application, while there was a similar decision between two RECs against one REC in the other six applications, Angell et al. (2006) argue that this amount is significant and may pose a problem for researchers, as the process may show problems in performance. The different decisions made may cause frustration to researchers and be a hindrance to their work. However, whether the variation has caused problems remains unclear, because there are no details about the consequences of the varied decisions on the outcome of the research (Davies, 2008). Evidence of variation in decisions between different RECs does not automatically prove it to be a problem.

In a review published in the British Medical Journal, a medical student wrote about her disappointment in dealing with RECs and argued that different RECs tended to focus on different concerns (Tan, 2004). She had submitted her research proposal to three different RECs and was disappointed when it was rejected each time; she felt that the RECs were only a hindrance to the development of her research project. Her research was about patients' desire for active medical intervention, and she wanted to use a vignette of a stroke scenario to study the factors that would affect people's wishes when they became unable to provide consent themselves.

Tan submitted her proposal to the first REC, but her proposal was rejected because of the concerns raised about the use of terminally ill patients as participants, the proposed large sample size of 200 participants, and the exclusion of participants whose first language was not English. She was told to modify her proposal and resubmit her application.

After modification, she decided to submit two new applications to two different RECs, neither of which was the one she had previously applied to. One new application to one REC was to recruit 50 day-care hospital patients who were over 60 years old and not terminally ill, while another new application was submitted to another REC to recruit 50 hospital visitors (rather than hospital patients) who were over 60 years old. Both her proposals were rejected.

Both RECs rejected her proposal in view of her choice of participants and claimed that participants over 60 years old were too frail. However, she was also

denied approval when she enquired whether the recruitment of healthy 20-year-old participants would be possible. She was disappointed that their decisions were not transparent and was denied involvement in their meetings.

In this example, it is clear that all three decisions were the same: that is, all three RECs rejected the research. However, the variation in the reasons given for rejection is the key point of this example. The first REC and the two later RECs appeared to have different reasons for rejecting the proposal. Tan (2004) argues that this variation in reasons and concerns caused the obstruction of new research that has a potential to improve patient care in medicine. Perhaps, if the RECs' concern is about the harm that may be caused to participants regardless of their age and condition, the first REC should have raised this earlier. When the issue was only raised about acutely ill patients and the large sample size, it can be concluded from the first REC that they were not concerned if participants were recruited from a non-acute condition, regardless of their age. However, it was clear from the other two RECs that even with modifications, the study was still not given a favourable opinion.

Thus, problems raised with variation do not just affect the different actual decisions made by RECs but also the different reasons given by RECs and which may or may not eventually affect the final decisions. This shows that in examining the issue of variation, we should not just focus on the variation of decisions but should also look carefully into the variation of reasons given by RECs, because both types of variation may be problematic.

Another example of a case that provides a clear explanation of the problems with variation that may be a hindrance to research, was given by Woollard (2000). He claims to have experienced 'worrying inconsistencies in the decisions of ethics committees' when he submitted his research proposal to three different RECs and received three different judgments. Since his study was on pre-hospital emergency care using a randomised controlled trial to compare the effectiveness of two dosing regimens of intravenous analgesic nalbuphine for patients, he had difficulties in obtaining informed consent.

The first REC decided that without informed consent from participants, he could not proceed with his research. The second REC, however, supported his view that informed consent was not appropriate in this trial, but wanted a legal opinion before providing a final decision. Finally, the third REC agreed that informed consent was not needed for the trial and approved his project. In this example, it is clear that all three different RECs made different decisions, and these three different judgments can obviously cause confusion for researchers regarding the criteria taken into consideration by different RECs for approval. The resultant confusion may also lead to researchers not having confidence in RECs' review process and hence perhaps doubting the validity of their decisions.

The problem with variation that appears in this second case is the inconsistent consideration of the value of informed consent. Three different decisions would mean that RECs are still not clear about the value of certain key ethical principles in relation to certain situations – and in this case, an emergency scenario. There

is a possibility in this case that the different RECs went through different reasoning processes, which resulted in different decisions being made by all three of them. The dosing regimens for intravenous analgesic nalbuphine were still controversial at the time of the study, since there were other studies claiming that a low dose of nalbuphine was just as effective as a higher dose, and had fewer adverse effects (Woollard et al., 2002).

In an emergency scenario, informed consent does not seem appropriate as it could delay the administration of treatment (Emanuel et al., 2000). Furthermore, in this case, clinical equipoise existed in relation to the effective dosing of intravenous nalbuphine. Therefore, an absence of informed consent would be justified to ensure the overall benefit for future participants, and most importantly, research participants were not exposed to unnecessary harm.

It appears that in this second case, it was permitted by law and generally accepted to be ethical. The first two RECs that rejected the study might have made a mistake. However, I am not particularly interested that this might be a clear mistake made by RECs. What is not clear is the extent to which it is unethical to make a different judgment in this case.

In addition to the issue with variation, Barraclough (2004) suggests that different RECs tended to respond differently to the same question. He argues that RECs have become a huge burden to researchers and as such, a hindrance to research in medicine. It is unethical if RECs' unpredictable variation in decision-making has caused a hindrance to research (Nicholl, 2000) and if RECs reject proposals

they ought not to. RECs should be careful not to accept research that they ought to reject or reject research that they ought to accept.

On the face of it, for example the clear cut cases, it might be suggested that RECs should be educated about what should and should not be rejected. Clinical research is growing fast to help to improve patient care in medicine. If a research project is delayed or rejected for unjustified reasons, this could create an obstacle to the development of clinical research and health care. So on this view, finding ways to uncover the problem with variation and providing a solution would help to reduce problematic variation and restore researchers' confidence in RECs.

### 1.2. Different decisions made by RECs reduces researchers' confidence in the review system

The occurrence of variation in decision-making by different RECs has showed that RECs are a part of different review processes (McWilliams et al., 2003). This might lead to the possibility that the level of scrutiny in their reviews may also be different from one another (Silverman et al., 2001). Therefore, participants may be exposed to inconsistent protection (McWilliams et al., 2003) and as a result, legitimate doubt can be cast on the adequacy of participants' protection.

Inconsistent protection of participants can also be caused by the possibility of different views being adopted by RECs about the level of risk participants are

exposed to (Abbott and Grady, 2011), and RECs' variable understanding of other research risks and benefits (Candilis et al., 2006). One REC may view a particular risk as unacceptable while another may view the same risk as acceptable. These different views seem irrational and may compromise the safety of participants (Abbott and Grady, 2011).

The evidence that shows inconsistent protection for participants and future participants may cause the public to be fearful. This may then have further negative consequences not only for participants but also for researchers, the integrity of RECs and the integrity of clinical research (Abbott and Grady, 2011). Research productivity may reduce and the adequacy of RECs' decision-making may be questioned (Abbott and Grady, 2011).

RECs are expected to protect the welfare and rights of participants by providing an adequate and legitimate review process. However, their inability to provide the necessary protection for participants may render RECs incompetent. In addition, variation in decisions has also raised concerns among researchers about the lack of transparency in the RECs' review process and about the justifications for their decisions (Anderson and Dubois, 2012). The confidence that researchers have in the ethical review system may be diminished if RECs do not adequately justify their decisions (Cave and Holm, 2002).

Variation in decision-making among RECs may also lead to game playing whereby researchers may choose to submit their proposals to the REC that they think will be more lenient (Edwards et al., 2007). It is obvious that game playing

seems to create a solution in terms of avoiding RECs that will most certainly reject their proposals. However, game playing is not a sign of having confidence in RECs, and may instead be evidence of a failed system. If RECs have an adequate and a more uniform review process, there should be no question about problematic variation that leads to researchers' dissatisfaction of the final decisions made by RECs.

In this second category, examples given show that variation raises the question of RECs' efficiency in making decisions (Hirshon et al., 2002). Variation in terms of the inconsistent protection shows a problem of the understanding of the basic key ethical principles and may lead to unethical research. This category demonstrates the need for RECs to be familiar with the stages of the reasoning process that include the procedural and content stage which will be discussed in section D. This will prevent discrepancy in any of the basic key ethical principles and allow RECs to understand when variation is permitted. Referring back to Chapter 2, this is also the reason why going through the process of accountability for reasonableness is important to ensure that decisions made can be justified.

Therefore, as Prentice and Antonson (1987) argue, it is imperative to recognise variation and take all the required steps to avoid it. This is especially when complaints raised due to variation can be justified in which the consequences might lead to unethical research.

## SECTION B

### *1. Is Variation Really a Problem?*

From the discussion above, it is clear that variation can be a problem in some situations. However, it can be argued that in other situations, variation in decision-making is legitimate and may not be problematic (Edwards et al., 2004b; Abbott and Grady, 2011) because it is unavoidable and just a part of the review process. Ethical deliberation requires making judgments about values and may plausibly and justifiably invite disagreements not only between two RECs but also between two members of the same REC.

If a consistent approach is favourable, there may be a loss of independence in the opinions given by the committee members (Sayers, 2007). If this happens, the decision-making process may be affected and the quality of the decisions made could be jeopardised. It can be argued that one of the most important reasons that RECs need to review research proposals is so they can deliberate on the ethical issues presented in the proposals as a team.

It seems crucial for the process that REC members are free to make judgments and express their views, which may differ among them, and this process does not always result in a unanimous decision. This process of deliberation that includes different opinions from different members is the reason the review process is comprehensive. If RECs deny this process and favour only a consistent approach in the review process, they may lose the very essence of ethical deliberation in the review process of decision-making.

### *2. Variation is Just Unavoidable*

Kerrison and Pollock (2005) argue that variation in RECs' decision-making is unavoidable, especially when there is no centralised body that is responsible for coordinating and determining the review system. Variation in decision-making among ethics committees is also not inherently inappropriate due to the fact that committees are given the freedom to interpret and apply the regulations (Silverman et al., 2001).

There are no guidelines on how to weigh the benefits against the risks that participants are exposed to (Miller and Joffe, 2009), and therefore the uncertainty of the potential benefits may be a negative factor in the reasoning that leads to their decisions. Even if there was a fixed way to calculate these benefits and risks it would remain unclear how to value the resulting number. As a result of this, there is a high chance of discrepancies in decisions based on the individual or committee's values and in their weighing up of ethical principles. Here, it is important to note that different people value things differently. Therefore, each REC member has his or her own values concerning which risks are acceptable when weighing them against the potential benefits.

If we want to eradicate variation completely, RECs should be given a formula to guide them in balancing risks against benefits (Sayers, 2007). However, if a formula is to be introduced, it should not interfere with the ethical process in decision-making so that the essence of ethical deliberation can remain. With a formula, decisions could be guided towards a more consistent approach if all

RECs complied with it. However, consistency of process would still not be guaranteed, as going through the decision-making process entails that disagreements are inevitable.

If consistency is favoured before an in-depth analysis of the problem with variation, there may be a risk that the consistent process may overshadow the deliberation of ethical principles (McDonach et al., 2009). Ethics is about deliberation, and an unnecessary checklist to ensure consistency may interfere with the overall process of decision-making.

As discussed above, variation in decision-making can occur in the review process as well as in the final decision that is made. Therefore, in section C I will discuss in detail the nature of variation to better understand the underlying cause of its occurrence. I will then move to section D with a discussion on the reasoning process, with the aim of investigating in-depth the acceptability of variation in decision-making.

## SECTION C

### *1. The Nature of Variation*

As shown in sections A and B, variation occurs for various reasons and may be influenced by different decision-making processes adopted by different RECs. Variation may raise concerns about the validity of RECs' review and decisions (Silberman and Kahn, 2011). In order to understand whether variation is really a

problem, it is important to understand the nature of variation in the process of making decisions. This understanding will better equip us with the ability to analyse the forms of variation that are acceptable in the RECs' process of decision-making.

This section will focus on a description of the nature of variation that will allow an understanding of the different types of variation that can occur during the decision-making process. There are two types of variation that may occur during the process. The first type is the variation in the final decisions and the second type is the variation in the reasoning process.

A clear understanding of when variation is acceptable and when it is not is crucial for ensuring the progress of good ethical research. Without an understanding of variation, good ethical research may be rejected if decisions are affected by variation.

### 1.1. 'Decision Variation' and 'Reason Variation'

In what follows, 'decision variation' is when different decisions are made for the same proposal by different RECs while 'reason variation' occurs when the reasons for decisions are different among RECs. It is important to understand the difference between these two to determine the acceptability of each one, because they relate closely to how RECs make decisions.

In ‘decision variation’, it refers to what RECs say about their final decision and in ‘reason variation’, it is about the reasoning on why they make the decision. Most importantly, we should not just focus on the decision but what matters is the reason or the justification of the decision as well. Examples of decision variation and reason variation are given earlier in section A of this chapter.

## SECTION D

### *1. Variation at the Procedural and Content Stages*

In this section, I will explain the ways in which variation between committees can arise through the reasoning process. This process consists of two stages: the procedural stage and the content stage. The procedural stage includes the processes and structures of reasoning, while the content stage includes the value and analysis of reasoning (Sheehan and Yusof, unpublished manuscript).

At the procedural stage, if different RECs are set up differently, variation may occur within the procedural requirements of a committee. These procedural requirements include some of the issues that have been discussed in chapters two and three: the different composition of committee members or different standard operating procedures. That is, the same composition of qualified members from various backgrounds for different RECs may contribute to a higher chance of reaching the same decisions. When RECs are composed of members with similar

backgrounds and expertise from one REC to another, the issues raised and discussed may also be similar.

The same is true of standard operating procedures. It is clear that if RECs use different standard operating procedures then their review processes will also be very different from one another. However, even with the same composition of REC members operating with the same standard operating procedures, it is difficult to guarantee that the review would be consistent. There is still the possibility that members would think differently, even if they were from the same background and had the same expertise, and they may interpret and apply the same standard operating procedure differently. Nonetheless, having the same composition and using the same standard operating procedures appears justified to ensure that decisions are fairly made based on a similar approach and process.

A more important component of the procedural stage that would determine whether variation at this stage is acceptable or not, is the range of ethical principles that should be considered in the review process as essential for making decisions as discussed in Chapter 2. If the range of ethical principles is limited then RECs can be reasonably sure that they have the correct range of principles. This is because the analysis of ethical principles is the initial step towards the content stage. The procedural stage can be further divided into two stages, which will be described below.

At the content stage, variation among RECs can occur as a result of differences in understanding and application of the principles of a particular research

proposal. This stage involves the process of providing a rationale for the decisions made (Sheehan and Yusof, unpublished manuscript) and is based upon the deliberation of the specific ethical principles involved in a particular research proposal, as previously decided at the procedural stage.

### *2. The Two Procedural Stages*

When members of an ethics committee meet to review a proposal, the discussion of ethical issues and principles will be raised based on the different opinions members have on the various issues relevant to the proposal. For example, one member may be most concerned with the informed consent process while other members in the team may be more concerned with the justice principle being applied to the study. Both issues are important but the differences in weighing these principles may provide difficulties for members to make a justified and unanimous decision.

Reaching a unanimous decision can be assumed to be an ideal conclusion made by RECs (MacPherson, 1999); National Research Ethics Service (NRES) United Kingdom (UK), 2012) because this indicates that all members agree to the discussion and final decision. However, as mentioned earlier that different members may have different thinking styles, it is important to appreciate that decisions can reasonably vary from one member to another. Further discussion in this chapter will help RECs to recognise the acceptability of differences in

their views. It is possible to reduce disagreements within a committee but it is important to accept that unanimity may not always be possible. More importantly, in the process of arriving to a decision, members of RECs are able to justify their opinions.

These stages are intended to categorise ethical principles, from the basic general ethical principles of research ethics to the analysis and application of the principles to a particular proposal. An explanation of each stage will help to identify the ways in which variation can occur in the decision-making process.

### 2.1. The Basic General Ethical Principles

General ethical principles in research ethics represent an organised system that could clarify the relevant principles that need to be considered in the assessment of a research proposal. If different RECs adhere to a different set of ethical principles, this could mean that if the same proposal is given to different RECs, there is a high likelihood that these RECs would approach the ethical issues involved in the proposal differently.

Here, the discussion will focus on the general ethical principles that could be taken into account as basic considerations when reviewing research proposals. At this stage, it would seem most appropriate if RECs adopted and applied the same ethical principles. This would enable RECs to consider and decide on the same relevant ethical issues pertaining to the same proposals. If variation occurs

at this stage, then this type of variation may be problematic because basic ethical principles should be considered to be the essence of the process of reviewing research proposals.

Even though there is still no universal framework for RECs on basic ethical principles, it can be argued that the basic principles are those that are common to members of RECs who are familiar with and have been trained in research ethics. Therefore, if different RECs have different basic ethical principles, this could also imply that RECs are not trained to the required level before reviewing research proposals. The lack of training and education of members of RECs would severely impair their understanding of what is needed to approve research that is ethical.

Furthermore, it also appears reasonable for researchers to expect RECs to review their proposals in an organised way and that RECs would deliberate over the same ethical principles and issues. These basic ethical principles may not be applied by all RECs, but encouragement to develop a consistent approach at this stage would be valuable for reducing the existence of unnecessary variation.

Principlism is a system of basic moral principles that is commonly used as a general rule in the reflection on ethical issues in a proposal. Principlism includes the principles of autonomy, beneficence, non-maleficence and justice. These principles form just a basic outline for the deliberation of more specific issues, which are then discussed in detail at the content stage. For example, the principle of autonomy is a general principle that serves as a basis for a deeper analysis of

the issue of informed consent in relation to a particular research project (Beauchamp and Childress, 2009).

At this very first procedural stage, what is most important is the consideration of all these principles in relation to research proposals, rather than the weight that is given to each principle. The weighing of each principle is more relevant to the evaluation and analysis of the content, which is considered at the content stage and will be discussed later.

Besides having principlism as a system of basic principles that should be taken into consideration by RECs when reviewing proposals, Emanuel et al. (2000) have also provided a list of relevant ethical principles that are required to make research ethical. It is important that RECs be given a list of ethical principles that are systematic and able to provide a framework for their review process. This would help them to be aware of all the ethical principles that should be considered during the decision-making process.

Emanuel et al. (2000) have suggested seven ethical requirements to help determine whether a research project is ethical by incorporating 'traditional codes, declarations and relevant literature on the ethics of research with human subjects' (p. 2701). They suggest that members should consider a proposal's scientific value and validity. Furthermore, RECs should ensure that subject selection is fair, the risk–benefit ratio is favourable, research proposals are independently reviewed by individuals who are not affiliated with the research being reviewed, informed consent is given by participants, and there is

continuous respect shown to participants and potential participants in the research.

Since there is still an absence of universal agreement regarding what constitutes basic ethical principles, the suggestion by Emanuel et al. (2000) appears to be suitable for use as a benchmark in guiding members of RECs to make ethical judgments when reviewing research proposals. However, as mentioned earlier, although there is no universal framework for basic ethical principles, it can be argued that the principles presented at this stage should be common knowledge among members of RECs, and that variation in these basic principles should not be acceptable.

### 2.2. Choosing the Relevant Principles

At the first procedural stage, all basic ethical principles are laid out to ensure that all RECs are aware that these are required for the discussion and review of research proposals. This second procedural stage requires that the ethical principles derived from the previous stage become more specific to the research proposals discussed. Important relevant principles that require further analysis and discussion are chosen. This process of choosing which of the general principles are relevant and important may differ from one individual to another, and therefore may also differ from one committee to another.

However, even though variation may occur at this stage, it does not seem appropriate because choosing which principles are relevant and important to the research proposals may be a straightforward process, especially to well-trained members of RECs. Taking the example given by Woollard (2000) earlier, all three RECs gave priority to the discussion of informed consent. Even though their decisions were different from one another, their chosen principle was the same. The discussions that resulted in their decisions are considerations of content rather than procedure.

Once RECs have decided on the relevant important principles that need further discussion and analysis, they will then enter the content stage, which concerns the consideration of these specifically chosen ethical principles. Therefore, it is clear at this point that variation is not acceptable at the two procedural stages. If variation occurs here, this would reflect a lack of training and education given to members of RECs, as the procedural stage is the basic step in identifying important problems in relation to the proposal.

### *3. The Content Stage*

At the content stage, proposals are reviewed by examining the specific principles listed at the procedural stage in detail and also by determining which principles are more important than others. What is most important at this next stage is the focus that RECs have on the reasons and rationales for their decisions and their

ability to justify what has been decided. Since RECs are expected to be procedurally consistent, it can be thought that RECs will also be consistent at the content stage.

However, even with a consistent approach at the procedural stage, the process at the content stage is still exposed to variation due to the nature of the thinking process between different individuals. As has been stated earlier, different members may think differently. Even when specific ethical principles relevant to the research being discussed have been agreed, different individuals or committees may weigh up these principles differently (Beauchamp and Childress, 2009). For example, one member may see informed consent as the most important issue of the proposal, while another may want to focus on the benefits of the research. The differences in weighing and balancing the principles against each other could obviously create the occurrence of variation among RECs and also among members in a committee.

In order to balance the principles concerned, the aim would be to find reasons that support the decision about which of the principles should prevail (Beauchamp and Childress, 2009). This process would require deliberation by members of RECs, and the opinions of members can obviously differ from one another. It would be challenging to judge one member to be right and another to be wrong, especially if their disagreement was reasonable. Both decisions may be sufficiently justifiable. However, it is important that the process prior to their decision be consistent so as to ensure that all relevant ethical principles have

been considered. This is to make certain that RECs do not overlook the principles that need in-depth analysis and consideration. Without this process, important principles may be left ignored.

For all these reasons, it is difficult to expect consistency at the content stage. It is possible that variation in weighing the principles could be reduced within a committee, but this may not be possible from one committee to another. As long as RECs are aware of the relevant ethical principles at issue, variation in their decisions at this stage may be acceptable due to reasonable disagreement. To accept variation and to claim that a disagreement is reasonable, it is also important to ensure that the members of RECs involved are well trained and educated in the field of research and research ethics, so as to make certain that decisions made are within the realm of adequate knowledge.

Making sure that members of RECs have the necessary knowledge and training to make decisions is crucial for ensuring that any decisions made are acceptable. For example, a 'committee that systematically rated a high risk substantial harm to participants as a relatively minor consideration in the face of largely speculative research' is unacceptable (Sheehan and Yusof, unpublished manuscript). In this case, it is not the risk of variation but rather the flaw in the final decision itself that renders the judgment unacceptable.

It is also important that members of RECs are able to justify their decisions. Especially in cases with variation, when researchers decide to challenge the RECs, the committees should be able to justify and defend their decisions. This

can only be done if members have gone through every detail of the ethical principles and are able to analyse the important issues presented in the research proposals. It is important that researchers are able to understand the rationale behind every decision made by RECs. This links back to the process of accountability for reasonableness in chapter 2.

As has been discussed in this section, the reasoning process consists of two stages: the procedural stage and the content stage. The procedural stage mainly involves the structures and processes that lead to a more substantial argument and the analysis of the research proposal at the content stage. As the procedural stage is the basis for further analysis, a consistent approach at this point is favourable because any variation may reflect poorly on RECs' system for making decisions. However, as the content stage involves more discussion and deliberation of specific principles in relation to the proposal, this stage may allow variation as long as decisions can be justified to be ethically acceptable.

## SECTION E

### *1. The Solution*

The Report of the Ad Hoc Advisory Group on the Operation of NHS Research Ethics Committees (DOH, 2005) admits that variation in decision-making by RECs can irritate researchers and that variation is inevitable due to the independent interpretation of ethical principles by the different committees. The

Report suggests that variation could be reduced by assisting RECs in their decision-making. It recommends that case studies of 'good practice' be provided to members to guide them in handling difficult ethical issues.

Case examples are beneficial for making things clearer. However, as discussed in the previous sections, variation at certain stages is just unavoidable and not inherently bad. Therefore, the solution to the issue with variation should go beyond case examples.

### 1.1. A proposal for a case law model

Variation is likely to occur despite a uniform process and approach, due to human nature. Therefore, I would like to propose a 'case law model' as suggested by Daniels and Sabin (1997) to provide a way of achieving justified consistency. In their paper 'Limits to Health Care: Fair Procedures, Democratic Deliberation, and the Legitimacy Problem for Insurers', Daniels and Sabin (1997) propose that a case law model be used to reconcile the problems faced by Managed Care Organisations (MCOs). Even though their suggestion is not directed towards the decisions of RECs, I believe that the use of a case law model would help to solve problems with unacceptable variation in decision-making among RECs.

In line with this idea, Coleman (2004a; 2004b) also suggests a similar approach to avoid variation in decisions made by different RECs. Noah (2004) on the other

hand, argues against the implementation of this model because he belives that with the adoption of this process, RECs will face overwhelming workload. As argued by Coleman (2004a), it is more likely that Noah (2004) misunderstood the basic justification for this suggestion and therefore, misses the essence of the importantance of having a proper documentation of the RECs' decision-making process that could benefit future research.

The proposal for this model does not mean putting aside the reasoning process that should be the fundamental element in deliberations. I am proposing that this model be used to document the rationale and justification for decisions already made by RECs to allow fairer and more consistent decisions to be made in future when similar proposals are being reviewed. Fairer and more consistent decisions when reviewing the same or similar proposals would 'contribute to the perceived legitimacy of the decision-makers' (Daniels and Sabin, 1997: p. 327) and secure the trust and confidence of stakeholders in RECs' review system.

Case law is a compilation of reports that provides novel decisions made by the courts and acts as a precedent for future similar cases. A model like this would allow similar cases to be treated the same. Therefore, if used in the RECs' review process, this would provide the basis for a fair approach in deliberating about judgments of similar cases and could guarantee stakeholders that any decisions made would be justified based on previously documented decisions.

As a result, researchers could be assured that they would be treated equally, and they would be clearer about what considerations to anticipate in the RECs'

review process. Previous decisions would act as a reference for future decisions (Sheehan and Yusof, unpublished manuscript). This is especially important in analysing the risk–benefit ratio. Without clear guidelines, previous decisions would help in establishing an appropriate judgment. With the model, disputes on the acceptable risks could be dealt with by referring to previous decisions. This would ease the burden placed on members of the committees during their debates. If flaws are noticed from previous decisions, errors could be corrected, thus providing a better decision-making model for future studies.

The question now is whether it would be possible to implement a case law model in the review process. It would provide fairness, as similar cases would be dealt with using the same approach. However, questions of confidentiality may arise due to the fact that reports would be shared among RECs. If the decision-making process for RECs should be made with privacy and confidentiality, then a case law model may not suit the system.

Some might argue that a possible problem with the implementation of this model is the exposure of risk of having the researchers' ideas and proposals duplicated. This is also relevant to the issue with pharmaceutical companies intellectual property if details of their work is made public. Therefore, it is important to be clear on how the system works to ensure that these are not problems that could deter the implementation of this case law model.

Ideally, the case law model should be implemented internationally so that a uniform process could be achieved between countries especially in research that

involves international collaboration. However, due to the expected differences in cultures and religions between different countries, I suggest that this model be implemented nationally. With this model, RECs will be able to refer to their own previous decisions and also to the previous decisions made by the other RECs within the country. Similar cases is expected to be treated similarly by the RECs in the country.

The issue of confidentiality and intellectual property is not worrisome in this model because details made known in this model are details that are already available to the public in clinical trials database such as *clinicaltrial.gov,* managed by the National Institute of Health (NIH) in the United States of America. This database is available to anyone with internet access who are interested with information regarding clinical trials around the world.

In addition, details about the study will also be made known to the participants in the informed consent forms (Ashcroft and Pfeffer, 2001). Therefore, what is most important to be made known to the public is not the confidential details of the discovery and mechanism of the proposed drug but the rationale and justification for the decisions made to allow or reject the proposals. The public here means those who might be affected by the decisions such as researchers, sponsors, participants and their family.

Ashcroft and Pfeffer (2001) argue that researchers should not worry about the possibility of having their ideas stolen because ‘data and methods are nothing without skill, experience, and ingenuity to exploit them; research on the

replication of scientific experiments has shown just how difficult this is if the replicators lack the skills and resources possessed by the originating group'.

In addition, by adopting this model, decision-making can be more transparent and this has been proposed to hold decision-makers more accountable for the reasonableness of their decisions (Daniels and Sabin, 2008). RECs have been criticised for their lack of transparency (Tan, 2004), and the application of a case law model seems plausible for allowing transparent decision-making. Researchers could be assured of the consistency of decisions and, most importantly, of the clarity of the process and decisions. This would allow for the system to be easily evaluated and would thus enhance the effective oversight of medical research. Researchers may also have more confidence with the system, as they would be able to understand the requirements expected of them.

Even though Silberman and Kahn (2011) do not specify their arguments with a case law model in mind, their arguments seem to agree with a case law approach. They argue that having a system of collected data on decisions and deliberations made by RECs is beneficial. They further argue that it would be helpful to have a system that observes the decisions made by RECs to enable RECs to learn from one another and to help researchers understand RECs better. Data collected on RECs' decisions would enable an open discourse between RECs and the public, ensuring that all decisions that are made meet the requirements (in the context of this paper, 'the public' means the researchers, sponsors and participants).

Silberman and Kahn (2011) also claim that uncertainties faced by RECs when making decisions could be improved with this system.

It is important that RECs document their rationales and justifications for decisions made for future reference. They may identify similar problems but their solutions may be different. This is when the application of a case model would be beneficial in guiding RECs when making decisions, by referring to the previous decisions of a similar research proposal. In addition, there would also be a strong reason for RECs to be more careful when making decisions and when providing their rationales for any decisions made, as their judgment would be available to researchers and other RECs.

## CONCLUSION

Ethical principles are open to argument because they are not absolute. If they were absolute, RECs would not be needed to deliberate on ethical issues because decisions could be made by just referring to a specific principle or code. Variation is criticised because of a misconception of what it entails; it is necessary to understand the causes and the underlying problem of variation before rejecting it.

This chapter has given evidence of complaints raised about variation and has discussed in great detail the nature of variation. It is now clear that the occurrence of variation at the different stages of the review process may determine their

acceptability. I have argued that variation at the procedural stage is unacceptable because elements in the procedural stage are the basic elements that need to be considered in an ethical deliberation. At this stage, it is important that RECs strive to achieve consistency not just by ensuring they understand the basic ethical principles that should be considered in a review process, but also by ensuring that the composition of RECs in terms of their qualified members is the same from one REC to another, and that these members use the same standard operating procedures in their application. The discussion of the composition of RECs has been discussed in Chapter 3.

Variation at the content stage is acceptable because it deals with more specific ethical principles that need further deliberation. At this stage, it is difficult to achieve consistency due to the nature of thinking styles among individuals. Different people think differently, and therefore as long as the basic principles have been identified relating to the research proposal being discussed, further arguments about the content are bound to be as varied as the opinions given by the members. What is most important is that the disagreements are reasonable.

As a solution, I have proposed a case law model that documents the rationales and decisions made by RECs for future reference when dealing with a similar research proposal. The previous decision would allow RECs to refer to the principles being considered and would guide them through the deliberation of the current proposal being reviewed. Furthermore, this model would also permit

transparency in their decision-making and create a better understanding of what is required in terms of their considerations during the review process.

The process discussed in section D and E of this chapter is closely linked to the process discussed in Chapter 2. Both discussions complement one another in making sure that RECs are capable of reviewing research proposal to ensure research are ethical. Finally, the answer to the question of this chapter, as has been discussed, is that variation in RECs' decisions is acceptable as long as RECs have a consistent approach in the procedures that guide them through their analysis of ethical arguments.

# CHAPTER 5: PRACTICALITIES AND CONCLUSION

This chapter aims to link the findings from the previous three chapters to create three basic key elements of a framework for the Malaysian context. In Section A of this chapter, I will clarify the current situation in Malaysia in relation to its ethics review system. Section B will then proceed with a review of the overall arguments of this thesis in relation to the Malaysian context, and will aim to provide a practical framework for the work of RECs and its governance in Malaysia. Finally, conclusions will be drawn.

## SECTION A

### *1. Overview of the current situation in Malaysia*

Malaysia has a multi-religion and a multi-racial society. It has a population of about 30 million people (Department of Statistics Malaysia, 2014) with a majority of Muslim population. Islam, as stated in the Constitution of Malaysia is the official religion but other religions for example, Christian, Buddha and Hindu are welcomed to practice in Malaysia alongside Islam (Constitution of Malaysia, 1957). As a multi-racial society, Malaysia has a population composed of mainly Malays, followed by Chinese and Indians.

Since religion in Malaysia plays an important role in the society, this affects the decisions made in regards to the practice of science, medicine and technology. An example would be the prohibition of use of medicinal products containing porcine material for Muslims and bovine material for Hindus. However, in Islam for example, there are flexibilities in regards to the Islamic ruling especially when there are no alternatives to the medication that contains porcine.

This can be seen in the ruling made by the National Fatwa Committee on the use of low molecular weight heparin from porcine for patients to treat blood clots. The committee has decided that the use of low molecular weight heparin is permissible (National Fatwa Committee Malaysia, 2009). This such ruling is important especially to inform and reassure patients of the acceptability of using the medication. Since Islam is the official religion, such Islamic ruling has been incorporated into the practice guidelines for health professionals.

This shows that the committee plays an important role in making decisions whenever doubts arise. This role also extends to their involvement in clinical research where their expertise is needed to deliberate on contentious matters. An example is their involvement in deliberation about the acceptability of using tissue bank as treatment for patients. The committee's decisions not only assist medical practitioners but also provide patients or research participants the confidence to receive treatment or be part of the research.

Clinical research in Malaysia began more than 30 years ago but only became a focus for the country about two decades ago (Clinical Research Malaysia

(CRM), 2012). It all started in the late 1990s with the increase in the globalisation of clinical research, during which Malaysia became aware of the importance of clinical research for its own development. Since then it has striven to promote the country as a research hub in SEA. This can be seen from the establishment of various centres and research committees, namely the Clinical Research Centre (CRC), the CRM and the NCCR to support the work of researchers.

The number of clinical trials conducted in Malaysia between 2005 and 2009 ranges from around 50 to 69 per year (Seerangam, 2014), mainly Phase III trials (Seerangam, 2014;Zakaria, 2014). Malaysia strongly believes that research can benefit its economy, and therefore aims to have conducted a total of one thousand clinical trials by 2020 (Goh and Michael, 2013). With this aim, it is no surprise that Malaysia is actively promoting and marketing itself as a trial hub (Goh, 2013) by placing policies and 'programmes aimed at enticing sponsors to its shores' (Kaur, 2011: p. 38). In addition to this promotion, CRC has also organised a project to 'increase the number of clinician investigators in MoH, increase the numbers of better quality research projects and groom the next generation of clinician scientists' (Goh and Michael, 2013).

Even though the CRC's aim is to 'improve patients' outcomes through quality and ethical clinical research' (CRM, 2012: p. 13), there has been very little discussion on the aspects of ethical reviews compared to the promotion of clinical research in Malaysia. By putting an emphasis on GCP training for researchers, Malaysia believes that this is sufficient to prevent unethical research

(Edis, 2014). It is, however, surprising that unlike researchers, members of RECs do not need to go through such training in Malaysia.

Kaur (2011) argues that there is a concern that the review process does not engage in meaningful ethical deliberation due to the lack of training of the members of RECs. Ethical reviews in Malaysia are relatively new and are 'carried out because it is mandated by the ICH-GCP' guidelines (Kaur, 2011). Perhaps with a focus on the promotion of research, the importance of examining the process of ethical review has been overlooked. This should be a concern because as Kaur (2011) argues, this focus on the promotion of research could compromise the ethical review system in Malaysia and expose research participants to a risk of being exploited by developed countries.

If Malaysia aims to promote itself as a research hub for international collaboration, it is important that it strengthens its research ethics governance because this could provide sponsors with the confidence that the Malaysian system is comparable with those of developed countries. This is also important so that any ethical decisions that are made can be relied upon and are internationally valid.

Conducting a study in a country with a poor research ethics governance system may pose difficulties in ensuring that the research taking place is ethically sound. Problems may arise not only during the research itself but also when the results are published because their validity may be questioned. Therefore, it is understandable that sponsors from developed countries who are looking to

benefit from the research being conducted will only choose countries that can provide them with an assurance that the research taking place is ethically sound and will produce valid results.

In the UK, there is a law (the Medicines for Human Use (Clinical Trials) Regulations 2004) that requires ethical approval from RECs prior to starting a clinical trial ;- failure to obtain ethical approval from a REC counts as a criminal offense (McGuinness, 2008). This provide an assurance that all British research has been reviewed by RECs. Unlike the UK, however, Malaysia does not have any law requiring ethical approval prior to the start of clinical research. Guidelines have been made available, but without being upheld by law, ensuring strict adherence to these guidelines may still pose a problem.

Kaur (2011) argues that the Malaysian system strictly adheres to the ICH-GCP guidelines 'because almost all drug trials carried out in the country, including the current drive by the government towards the expansion of the clinical trial enterprise, revolve around trials sponsored by multinational pharmaceutical companies' (p. 45). This shows that Malaysians can be confident that research conducted in Malaysia will have been reviewed by its RECs.

Nonetheless, as most of the content of the ICH-GCP guidelines is concerned with technical and administrative aspects and is not specific to RECs, these guidelines have been argued to be unsuitable for providing a complete framework to assist RECs in making their decisions (Kaur and Choong, 2014). In addition, as discussed in Chapter 1, the ICH-GCP guidelines rely heavily on

the Declaration of Helsinki, which does not provide adequate guidance for RECs' processes of review and oversight. Therefore, there is definitely a need to replace these guideline with something more specific to RECs to assist them in their decision-making process.

Kaur and Choong (2014) argue that to have a meaningful ethical deliberation, RECs should be given a framework that 'provides a discourse that is accessible to all the different parties who engage in ethics decision-making' (p. 27). This is in line with my suggestion of adopting Daniels and Sabin's (1997) model of accountability for reasonableness, as it provides just what Kaur and Choong (2014) might have in mind because any decisions made can certainly satisfy those who are involved and affected by the research.

The concern raised by Kaur and Choong (2014) with regards to the inadequacy of the ICH-GCP guidelines to provide a framework for the work of RECs is alarming because this has been the main reference for RECs in Malaysia. In her study on RECs in Malaysia, Kaur (2011) concluded that the RECs 'do not engage in meaningful ethical discourse' due to their lack of understanding of the role of RECs and also the lack of training of their members (pp. 235-236). With an emphasis on the promotion of research and little attention given to the ethical review aspects of this research, there is an urgent need to conduct further studies on RECs and their work to ensure that a proper system of ethical review is in place.

The discussion above has made it clear that despite Malaysia's claim that it has efficient ethical processes (CRM, 2012), it is actually facing challenges with its RECs and its governance, possibly due to a perceived lack of importance of the ethical review process compared to the promotion of clinical trials. Therefore, it is imperative that further studies be conducted to help create a framework to assist RECs in their ethical review process, as suggested by Kaur and Choong (2014).

## SECTION B

### *1. Revisiting my earlier arguments*

Details from the discussions in Chapter 2, 3 and 4 would give RECs in Malaysia an invaluable learning experience that will help to enhance the current research ethics governance system in the country. As previously mentioned, RECs and their governance are still relatively new compared with those of developed countries, and the fact that there are still very few studies being conducted in this area especially on the function of RECs and how they make their decisions justifies a strong need to examine the basic framework for the development of a good ethics committee.

Although concerns about the quality of RECs have been raised, mainly in developed countries, Malaysia should not ignore the importance of examining the quality of its RECs to ensure that they reflect those of developed countries.

This is important to ensure that they make the right decisions and more importantly, so they are able to justify these decisions. The aim should not only be to develop clinical research 'in tandem with the development in developed nations' (NCCR, 2014) but should also be to strive to develop a proper ethical review system comparable with those of developed countries.

The discussion on the central issues of this thesis in Chapters 2, 3 and 4 creates a basic framework for the work of RECs and may help RECs to function in the way they are expected to. Since there is a lack of understanding of the role of RECs as well as a lack of training of its members, it is possible that there is also a lack of understanding of the suitable types of members that RECs should be composed of. These have been discussed in Chapters 2 and 3.

The reason that it is imperative that RECs understand and be confident about the their role is to ensure that their deliberation process is focused towards producing ethical research. This understanding also helps to lay down the criteria for REC membership. It is important to be able to justify the reasons for the selection of members to ensure that they are selected based on their ability to contribute to the productive deliberation of decisions.

Chapter 4 not only addresses the issue of the acceptability of variation in decisions made by different RECs but also complements Chapter 2, which provides a detailed description of the process of decision-making. This is crucial for helping to ensure that RECs are equipped with the necessary skills and knowledge to be able to make ethical decisions based on the model of

accountability for reasonableness. The process of decision-making outlined in Chapter 4 then proceeds to provide an understanding of what kinds of variation are acceptable for different RECs to make.

Although there is no specific evidence pointing towards the problem of variation in decisions among different RECs in Malaysia, the fact that Malaysia has been focusing on the enrichment of clinical research collaboration with international sponsors means that being familiar with this issue would benefit future collaborations. Malaysia may eventually face challenges with variation of decisions made between itself and the international sponsor but what is important at this stage is to understand the processes of decision-making and when in the process variation is acceptable. With this understanding in place, if the issue of variation occurs in the future, Malaysia will be able to deal with it.

In the rest of this section, I will revisit my arguments from Chapters 2, 3 and 4 to relate them to the Malaysian context.

### 1.1. The role of RECs

In Chapter 2, I have argued that the role of RECs is unclear and that there is a strong need to be certain of what they are actually for. Being clear about the role of RECs would help to harmonise research collaboration between countries worldwide and this could bring more confidence and trust from researchers. As mentioned in Chapter 1, according to a study conducted by Kaur (2011),

members of RECs in Malaysia are still not certain of the role of RECs. They appear to be confused between the role to protect research participants and the role to promote research to ensure that they can attract international sponsors to conduct research in the country for the benefit of local participants and the broader community.

Both of these principles (protection of research participants and promotion of research for wider benefits) are interrelated and equally important. It would be difficult to advocate that RECs should focus only on one of the principles, because doing so would mean that they would be wrong if they decided to focus on another chosen principle.

It is not surprising that RECs are confused about their role because this also occurs in the other parts of the world. Debates have been on-going about what the role of RECs should be, especially in developed countries where they have been established longer and have faced open criticism from the public, and particularly from researchers. However, there is still no clear answer to resolve this confusion.

Going back to Chapter 2 using the three models developed, I conclude that it is impossible to claim that RECs should primarily focus on one principle over the others because of the equal importance of all the principles discussed. If RECs cannot decide on either one of the models, there should be a way to resolve this confusion to assist them in making the right decision and also to help them produce a more uniform process of decision-making.

Therefore, I believe that adopting the accountability for reasonableness model developed by Daniels and Sabin (1997) is the best way forward to produce decisions that are acceptable and legitimate. Daniels and Sabin's accountability for reasonableness is not a straight forward application for RECs but might act as a framework that helps to clarify the role of RECs.

The reason this might solve the confusion is because the model provides a process that allows decisions to be made based on a case-by-case basis to achieve a fair and publicly acceptable decision. It does not emphasise the need to adhere to a specific principle that determines the role of RECs but focuses on producing ethical research. This is important because ethical issues in research proposals may be different from one research proposal to another. What is most important is that the adoption of the model allows for a systematic and thorough process of ethical review without abandoning any of the related ethical principles discussed.

This model has four conditions: - the publicity condition, the relevance condition, the revisability and appeals condition and the enforcement or regulation condition. These conditions have been discussed in detail in Chapter 2, and provide the practical steps toward an ethical process of decision-making. In the application of this model to the Malaysian context, one important question would be: how can RECs in Malaysia satisfy these conditions?

In order to answer this question, I will again use the case example given in Chapter 2 on the use of Viagra on children. One of the clinical trials conducted in Malaysia is a study into the possibility of using Viagra (which was initially

created to treat angina pectoris but has since been prescribed widely for the treatment of male erectile dysfunction) on children aged 1 to 16 who suffer from pulmonary arterial hypertension (Netto, 2007). The study is a randomised and double-blind placebo controlled trial involving about 12 children within the age group described. Because Viagra has been associated with male erectile dysfunction, its use in children has been contentious in the view of the public. There have been attempts to request clarification with regard to the justification of the research but those involved decline to provide any information (Netto, 2007). This has raised doubts about whether the decision made by the REC responsible is ethical, especially when guidelines are not binding and there is no law enforcement on the conduct of RECs (Netto, 2007).

This example clearly illustrates the problem with research that is carried out in secrecy. Secrecy may provide the public with the impression that there may be a hidden agenda when reviewing research proposals especially when the research involves the lives of children. If this case was to follow the process of the accountability for reasonableness model, the public might not be suspicious about the research study's objectives.

To satisfy the conditions for this model, RECs need to ensure that the public will have access to their decisions and rationales. It is important that RECs make clear the relevant principles related to the case to satisfy the relevant condition of the process. For example in this case, it appears that the relevant principles include all three principles discussed in Chapter 2 (informed consent process,

protection of research participants and benefits of the research to the children). The RECs members would need to decide whether the risk-benefit ratio is acceptable. It would also be important for the consent process to be in place to avoid the exploitation of those in need of treatment.

Pulmonary arterial hypertension in children can limit their activities and may lead to death if untreated. The possibility that Viagra could treat such a condition in children provides a promising future for them. The benefit, if successful, could impact not only the children involved in the trial but also children in the broader community. If RECs could be satisfied that the conduct of the study would not harm the children in any way that could make their condition worse, and that the informed consent process undertaken by the children's caregivers is adequate and carried out in the proper way, there should be no need for them to be anxious about having to justify their decision in such way that the public could understand it.

Their decisions and rationales should be publicly advertised especially to those whom they think might be affected by their decision. They could advertise their decision on the RECs' website or the website of the institution where the study will take place. This would allow those who might still not be in agreement with the decision, despite the rationales, to challenge the decision. Any concerns raised are important for addressing any issues that may have been overlooked during the decision-making process. It is also important to allow for a reasonable delay before the research begins to allow for the decision to be challenged. It is

always important to provide a way for those who are affected to challenge the decisions to avoid any discrimination or exploitation. With such a process in place, the public could be more confident in the system especially when they can be assured that their voice will be heard whenever they deem necessary. Once a decision can satisfy the public and those involved in the decision, the research would be able to proceed. To ensure that the process is systematic, it needs to have some sort of regulation to ensure that all the conditions are met.

If decisions are made in such a way, RECs can be confident that they can secure the public's trust in research. This is contrary to what has been happening in the Viagra case, as concerns have been raised in view of the REC's decision to keep important information about the research confidential. One of the key advantages of using this model is that it allows RECs to have a transparent process of decision-making that makes them accountable for the decisions they make. By having a transparent process, RECs could assure the public that they are competent at making their decisions and are fully responsible for them. This is crucial to avoid and prevent doubts about RECs' authority to perform ethical reviews on research proposals.

The case above provides a valuable example for Malaysia to understand the benefit of making the process of decision-making transparent and for RECs to be held accountable. It is important to inform those involved in the research that RECs are prepared to accept responsibility for the decisions they make. This will

positively impact the governance system, which the public may be more inclined to trust if it is not conducted in secrecy (Fazel and McMillan, 2001).

Besides adopting the model of accountability for reasonableness, another way of ensuring that the ethical review is transparent is by making the RECs' standard operating procedures (SOP) publicly available on their website. At the moment, SOPs for RECs are not freely available. RECs should strive as far as possible to ensure they maintain the public trust. If they handle their ethical review in secrecy this may eventually lead to a loss of the public trust. Making SOPs freely available also provides the researchers with the information they might need to understand the review process so that they can prepare their proposals to meet the RECs' expectation.

Researchers may be confused over what issues are being debated in RECs' reviews due to their lack of clarity on the process (Spellecy and May, 2012). They may want to become familiar with the review process to anticipate problems with their research proposal and to take any necessary steps to avoid them. They may not be able to conform to the requirements asked of them if they do not know what these are (Spellecy and May, 2012). It is difficult to respect the system that RECs adopt if the process is not made clear to researchers, and a lack of respect may compromise RECs' authority in reviewing research proposals.

It appears plausible for Malaysia to adopt the accountability of reasonableness process especially when RECs are unclear of their role. The process clearly

shows that it can assist RECs in performing their role to ensure that research studies are ethical. Not only will the public have more confidence in the system but RECs will also have more confidence in the decisions they make.

It is important to note that, in applying the accountability for reasonableness model, members of RECs should be trained to be familiar with this process and the decision-making process that has been described in detail in Chapter 4. The reason for this is that when members decide on the relevant principles to satisfy the relevant condition, they need to be knowledgeable to detect any issues with the relevant ethical principles. The description of the reasoning process in Chapter 4 may also inform RECs of when it is acceptable to provide different opinions in relation to the relevant principles.

Therefore, in the Malaysian context, the adoption of the accountability for reasonableness model can provide practical benefits to the research ethics governance system. With an adequate understanding of what the model entails, I believe that Malaysia will benefit greatly from its implementation.

### 1.2. The membership composition of RECs

Besides not being clear about the role of RECs, another aspect of concern regarding RECs in Malaysia is the lack of training given to their members (Kaur, 2011). Similar to the role issue, this problem is not specific to Malaysia, as noted by Silverman et al.'s (2014) study on RECs in other developing countries, which

found that members also received inadequate training. They further conclude that one of the key areas requiring further improvement in RECs in developing countries is the composition of their membership and their training.

As mentioned above, even though the application of the accountability for reasonableness model helps to clarify the role of RECs, without the necessary training, members may still not be able to perform efficiently and effectively. The training of members is important to equip them with the knowledge they need to undertake an ethical review and to help them become more familiar with ethical arguments. This is important for them to readily detect relevant ethical issues.

The model of accountability for reasonableness relies heavily on the decision-maker to make decisions they find most appropriate and suitable. Only with training, will they be able to make ethical decisions based on the model. The purpose of this model is to assist RECs in the process of decision-making but it does not act independently without the necessary skills to conduct an ethical review.

Besides training, the selection of members for RECs is crucial because they are the ones contributing to the productive deliberations of decisions. The influence of the types of members on shaping the decision-making process has been discussed in Chapter 3. In order to appreciate the reason for the selection of REC members, it is imperative that we understand the rationale for their membership criteria.

The medical research ethics committee in Malaysia reviews all research conducted by the MOH. The guidelines for this ethics committee broadly suggests that 'members shall have various backgrounds to promote complete and adequate review of research activities commonly conducted by the MoH' (MOH Malaysia, 2012). It stipulates that 'members shall include at least one member whose primary area of interest is in medical science, at least one member whose primary area of interest is in non-medical / non-scientific areas, and at least one member independent of the MOH' (MOH Malaysia, 2012). It further gives a list of example of who should be part of the committee but does not provide specific reasons for this.

In addition, similar to the guidelines for RECs provided by the UK's DOH (2011) and the Australian NHMRC (2007), it does not provide any specific requirement for an ethicist to be part of the committee. There is no specific definition for an ethicist but based on the context of this thesis, an ethicist is someone who holds a qualification in ethics education and is familiar with a range of ethical arguments and processes of ethical review. Churchill (1978) argues that ethicists should refer to philosophers. He further suggests that an ethicist should be someone who is 'qualified to examine, explore, and illumine the complex facets of moral questions, and to clarify their logic: but he stops short of telling people what is right or wrong' (Churchill, 1978: pg. 14).

I believe that due to the current rise on the need for ethicists in RECs and clinical ethis committees, the training of ethics education may just be adequate to obtain

the necessary skills just as Churchill (1978) suggests. However, the inclusion of ethicists in RECs should not be made compulsory as the availability of ethicists with good qualification may not be as many as experts in science and medicine. In Malaysia, there may not be enough properly qualified ethicists to be part of the RECs in the country and if the inclusion of an ethicist is made compulsory, this may affect the overall legitimacy of the RECs' decisions.

As discussed in Chapter 3, the inclusion of an ethicist as part of the members of RECs is beneficial in view of his or her capability to ensure that the process of decision-making is conducted in the right way with the fair and equal consideration of all issues and the avoidance of any biased conclusions. In Malaysia, due to the importance of Islamic religion in the daily practice of Muslims, having ethicists with adequate knowledge of Islamic ethics is beneficial to the work of RECs. Islamic ethics is not significantly different from the Western ethics originated in the United States of America. The difference between Islamic ethics and the Western ethics is the reliance on the Quran and Sunnah (guidance from the Prophet Muhammad).

Islamic ethics also considers autonomy, beneficence, maleficence and justice. In addition, before reaching a conclusion mainly in areas that raise doubts, guidance is sought from the Quran and Sunnah. Unless there has been an established Islamic ruling, the process of making new decisions in relation to new technologies for example, is best conducted by the National Fatwa Committee. Therefore, requiring ethicicsts to have the knowledge on Islamic ethics should

not be considered compulsory. What is important and required for the role of ethicists should be similar between Malaysia and the Western countries. Broadly, they should be familiar with the process of ethics review and the relevant arguments.

In regards to the participation of Islamic scholars in ethics review, it is important to understand that not all research proposals contain elements of doubts in relation to Islam. Areas that may need more attention in regards to the relationship between Islam and medicine are possibly the reproductive and stem cell research. This is when the participation of Islamic scholars are needed. Once an issue raised about the acceptability of a certain technology to the Islamic practice, the Islamic scholar will need to deliberate on this matter by seeking guidance from the Quran and Sunnah.

In certain difficult cases, the problem will be brought to the attention of the National Fatwa Committee for further deliberation. The meeting of the National Fatwa Committee as mentioned earlier in Chapter 3 not only consists of Islamic scholars but also experts in the field of medicine and technology. Once decision has been made, RECs could apply the decision to their review process.

The guidelines for the Malaysian medical research ethics committee further states that it should not be composed of entirely men or women and should not be represented only by one ethnic group. The current committee is composed of 32 members but there are no specific details of their roles in the guideline (MOH Malaysia, 2012). Although the list of members does not specify their specialties,

it can be argued that the majority of them are from a medical and science background. As discussed in Chapter 3, with a majority of members from a science background, there is great tendency for any discussion to be focused towards the interest of science and medicine and may compromise the interest of the broader community. There may also be a tendency to influence decisions based on their own values and personal research interests (Kaur, 2011).

To avoid biased decisions, Kaur (2011) suggests that the composition of members should be balanced by the inclusion of more lay members 'drawn from a larger and more diverse pool of society' and independent members who are not affiliated with the institution and also not related in any way to the research (Kaur, 2011: p. 234).

It is difficult to be certain that a majority of members with a clinical and science background is problematic in Malaysia because of the absence of research on RECs and their composition in Malaysia. However, research available from developed countries, as discussed in Chapter 3, have shown that this is a possible problem for RECs with similar compositions. It is important that Malaysia brings this issue forward for future research that will look into the influence that individual REC members have on the outcome of the decision-making process.

A total of 32 members make a large committee for REC, and this has been argued by Candilis et al. (2012) to be larger than necessary. They argued that 'larger groups hinder individual participation and lead a small number of speakers to dominate' (Candilis et al., 2012: p. 18). Not only would this appear to create an

inefficient meeting, they have also argued that with a larger group, the cost needed for the maintenance of the REC is higher than necessary.

A lack of training for members and an unbalanced composition of committee members gives a strong reason for Malaysia to focus on ways to improve its RECs. Even though there are not many studies being conducted on this, the evidence gathered by Kaur (2011) should be an eye opener for the need for further research on RECs in Malaysia.

Based on the discussion in Chapter 3, one way of improving the composition in the Malaysian system is to reduce the number of members to only those who are really necessary. An increase in the number of lay members with the possible inclusion of an ethicist will help to balance the discussion better. It is important to consider the suggestion given earlier to invite external experts and patients whenever there is a need to get their opinions. It should be a basic understanding that the committee does not need to include all types of specialists as its members because it is impossible to include everyone due to the extensive range and scope of the field. It seems more appropriate to include only those who could contribute in each meeting, and then to seek the opinions from particular external specialists or patients whenever necessary on a case-by-case basis.

Many have criticised the work of RECs but there appears to be significantly less work done regarding the way that RECs should be set-up (DeVries and Forsberg, 2002a). Since there is no clear consensus on this should be done, this may have contributed to the variation in the composition between one REC and another.

Different membership composition undoubtedly has an effect on the standards and procedures adopted by different RECs and so can contribute to unwarranted variation in their decisions. Therefore, being clear about the rationale for the criteria of membership could perhaps allow a more uniform composition of RECs.

As a conclusion, I suggest that Malaysia take the necessary steps to ensure that selected members of RECs are trained to be clear about the role of RECs. This is crucial especially since Malaysia is striving to make the country a research hub for international collaborations. With this in mind, getting things right is the key to making international sponsors have confidence in the system and thus decide to conduct their research studies there.

The criteria of membership listed for the Malaysian medical research ethics committee may not be significantly different from what I have suggested, but what is most important is that Chapter 3 has provided an invaluable insight into the need to understand the reason for the selection of members to ensure that only those who are suitable to be are made part of the team. This will also help to keep the REC at an appropriate size so that each member can contribute in the productive deliberation of the decision-making process.

### 1.3. Variation in decision making among RECs

Chapter 4 deals with the issue of variation in decisions among different RECs based on the review of a similar research proposal. This chapter on variation helps to illustrate the stages of the reasoning process involved in decision-making. There are two stages in the reasoning process:- the procedural stage and the content stage. The procedural stage mainly involves structures and processes that lead to a more substantial argument in the content stage.

Knowledge on an ethical review process would not be complete without an understanding of these processes. Being clear about the role of RECs is just the first step in making sure that the focus is right. I have concluded that variation in decisions made is acceptable at the content stage because it deals more specific ethical principles that need further deliberation but not at the procedural stage.

In Malaysia, it appears that researchers who plan to conduct multi-site trials only need to submit a single application to the Malaysian medical research ethics committee (Kaur, 2011). Therefore, the issue of variation in decisions between different RECs may not be a problem in Malaysia.

Since Malaysia is keen to invite international sponsors to collaborate in research, it could encounter variation between its own decisions and those made by the sponsor REC in international collaboration. It can be argued that variation that is caused by local values is justified. However, Goldman and Katz (1982) argue that RECs should still strive for consistency in decisions. This may be because

whatever research is bound to be unethical in developed countries should also be unethical if conducted in developing countries (Macklin, 1999).

With the globalisation of clinical trials, Malaysia should be aware that there may be a tendency for exploitation especially when the recruitment of research participants has been known to be easier and faster in Asia due to its large population. Another reason may also be due to research participants' possible lack of awareness of their rights to be fully informed of the process of the research study.

Macklin (1999) gave an example of ethical issues that have arisen with the collaboration between the United States and China on a study to investigate the effectiveness of a certain drug that could reduce the incidence of birth defects. At the time of the study, due to cultural differences between the two countries, individual informed consent was rarely applied in China and could deter the participation of research participants especially as it involved the use of a placebo for some participants. Since obtaining informed consent was not possible for the researchers in China, the United States' REC concluded that it was unethical to conduct the study.

The Chinese researchers, however, proceeded with the study but modified the informed consent process to the China context with the development of 'community consent', where they had to obtain consent from government leaders, health authorities and the family of the research participants. Once they received consent from the community, they then explained the study to the

potential participants. However, Macklin (1999) argues that the way China conducted the study was still unacceptable in the United States because they informed the female participants that the pill that they would receive would be beneficial to their health. This statement was false and deceptive to those who participated. However, the researchers in China claimed that the study would not have been able to progress without such statement.

Macklin (1999) further argues that 'the reason why informed consent is an ethical requirement even when the proposed research carries a very low or virtually nonexistent risk of harm, as in some social or behavioural investigations, is that people can be wronged even when they are not harmed' (p. 193). This is because 'their right to self-determination is violated' (p. 193).

In Malaysia, it can be argued that individual informed consent is not a problem even though some might prefer spousal approval prior to individual consent. However, what is important for Malaysia to understand from the case study above is that cultural differences do not discount the need to carefully conduct an ethical review in order to detect any possible ethical issues that may cause a problem to the conduct of the study. I agree that if a study is found to be unethical in the sponsor country, there is a strong need to be very careful in the evaluation of the ethical review in the host country. Any variation in this sort of decisions should be carefully examined to avoid exploitation.

Furthermore, if RECs are able to satisfy the conditions laid down by the model of accountability of reasonableness, there should not be significant variation in

decisions even between different RECs from different countries. Therefore, the understanding of the chapters in this thesis should not be regarded in isolation because each chapter complements each other to provide part of the key elements of a framework for the work of RECs.

## CONCLUSION

In conclusion, all three chapters (Chapters 2, 3 and 4) provide the basic foundation for the work of RECs. More importantly, they provide part of a framework for RECs to work independently with the skills they need to ensure research studies are ethical. The aim is to help Malaysia achieve a standard comparable with those of developed countries and to help it to be ready to face any challenging ethical issues in research proposals presented to them. It is also important that Malaysia is equipped with the necessary knowledge to avoid being exploited.

The work that I have done in Chapters 2, 3 and 4 fits nicely in the Malaysian context. They appear reasonable to be implemented in the system especially with the benefit of having a fair process that is transparent and that RECs would be accountable for. Therefore, my initial recommendation would be for Malaysia to adopt the accountability for reasonableness model because it may positively enhance the current system. This is important as the aim is to produce research

studies that are ethical. Adopting the model in the Malaysian system indirectly applies my arguments of Chapters 3 and 4.

The Malaysian MOH has developed the National Medical Research Register (NMRR) for the purpose of registration of all research conducted in the MOH. The aim is to allow clinical research to be registered in a publicly accessible research register to 'ensure transparency and to increase public trust in the conduct of medical research' (NMRR, 2014). This is in line with my recommendation of having a process that is publicly accessible. Similar to the NMMR, besides just having the details of the clinical research aspect of a project, information pertaining to the justification of the RECs' decisions should also be publicly accessible. I believe the addition of the decisions will enhance the aim of making the clinical research transparent as well as increasing the public' trust in clinical research conducted in Malaysia.

Based on my recommendation to adopt the accountability for reasonableness model, I believe that the MOH could promote this model and implement it possibly in the way that they have established the NMMR. However, this may not be without challenges especially to the existing RECs in Malaysia. Due to the lack of research on the work of RECs, they may not perceive their current practice to be problematic. RECs may possibly be defensive on the way they make decisions and the idea of accepting this model may portray that they are not functioning properly. It is important that RECs understand that the application and implementation of this model is not to criticise and replace their

current practice completely. This model, on the other hand, hopes to assist in their decision-making process to ensure research conducted in Malaysia are ethical and decisions made are internationally acceptable.

The limitation of this study is that it relies only on argumentative analysis. Future empirical research on interviews with members of RECs, researchers and research participants in Malaysia and SEA are needed to further investigate difficult ethical issues that become a burden on the research ethics governance system.

As mentioned earlier in the research methodology section on page 45 that this thesis focuses mainly on theoretical discussions, further empirical research is warranted to examine the acceptability of the recommendations of this thesis to the Malaysian context based on the perspectives of those involved in clinical research. Since this thesis discovers the importance of adopting the model of accountability for reasonableness to assist with the decision-making process, further empirical research is needed to evaluate the understanding of the Malaysian society on the meaning of transparency and accountability to them. Participants should include members of RECs, researchers and past and future research participants. Their understanding and expectation in regards to these terms may impact the implementation of adopting this model to the Malaysian RECs. Perhaps their understanding of these terms (transparency and accountability) is different from the discussions in the developed countries

particularly in the United States of America where the model of accountability for reasonableness originates.

# APPENDIX

A paper has been written together with my supervisor Dr Mark Sheehan based on Chapter 4 of this thesis on the acceptability of variation in decisions made by different RECs. The paper entitled 'should the decisions of RECs be consistent?' has been submitted to the American Journal of Bioethics and is currently under review. This paper has also been used as a guidance by the National Research Ethics Advisors' Panel (NREAP) of the National Health Service (NHS) United Kingdom to promote consistency in decision-making across the United Kingdom. This guidance entitled 'consistency in REC review' can be accessed via internet at http://www.hra.nhs.uk/documents/2014/10/consistency-rec-review-2-may-2014.pdf. Attached in this appendix is the guidance produced by the NREAP.

NHS
Health Research Authority

National Research Ethics Advisors' Panel

# Consistency in REC Review

## Summary


1. **Consistency** is taken to mean that, for any specific application or other, similar, applications, Research Ethics Committees (RECs) give the **same decision** for at least roughly the **same reason**.

2. Consistency refers to both ***consistency of procedure*** (SOPs/Membership etc.) and ***consistency of content*** (decisions and their associated reasons).

3. **RECs should be procedurally consistent**. That is, they should

    - **be similarly constituted**;
    - have **access to the same information and expertise**; and
    - **consistently apply standard operating procedures**;
    - **consider the same range of ethical 'categories'** in the process of their review.

4. **Whilst consistency in terms of content** (i.e. REC opinions and their associated justifying reasons) **is desirable**, **different committees may legitimately come to different decisions about the same research proposal**.

5. However, **there are limits to the range of decisions that are acceptable**.

6. These limits (and so the values of RECs) should be **contextualised by taking into account relevant "real world" clinical and research practice**.

7. **Recommendations:**

    - **Contextualisation** requires **broader engagement with researchers**, **patients and the public** regarding the values, standards and practicalities of current clinical practice in specific parts of medicine.

    - **Past decisions/decisions of other committees** regarding similar research should be more formally taken into account as part of the review of new applications.

    - **Appropriate Opinion Type.** The decision regarding the appropriate opinion type (favourable, provisional, unfavourable etc.), consistent with the reasons and requirements underlying that opinion, is a matter of *procedure* amenable to SOPs and thus should be formally taken in consultation with the REC Manager and/or other HRA staff.

## Introduction

8. The overall objective of the National Research Ethics Advisors' Panel is to help Research Ethics Committees deliver robust, consistent and fair decisions. This paper aims to clarify what is meant by 'consistent decisions' and how we might better promote consistency amongst RECs.

9. RECs have occasionally been criticised for exhibiting an unjustifiable level of variation or inconsistency in their decisions. This is supported by academic papers that discuss variation in decision-making by RECs[1] as well as evidence provided by the National Research Ethics Service's own Shared Ethical Debate[2] exercises. Recent ShED reports have shown that presenting RECs with the same application results in a range of opinions being given, both in terms of opinion type (provisional, unfavourable, favourable (+/- additional conditions) etc.) and the reasons cited for their opinion.

10. This document sets out what is meant by "consistency", whether it can and should be achieved and finally, practical suggestions are made to improve the consistency of REC decision-making.

## What is "Consistency"?

11. For the purposes of this document consistency is taken to mean that **RECs give the same decision for at least roughly the same reason.**

12. It is important that REC decisions are not 'one-off' and consistency requires that two RECs would give the **same decision** (or the same decision for roughly the same reason) **in a series of similar cases**.

13. Consistency can refer to either **consistency of *procedure*** or **consistency of *content***.

### Procedural Consistency

14. Procedural consistency means consistency of the **structure and process involved in the making of decisions** rather than the decisions themselves.

15. **RECs should be procedurally consistent.**

16. The argument for this assertion rests upon the **principle of justice** or fairness, i.e. all applicants for ethical review should be treated equally and subject to a fair process. A system in which REC decisions are inconsistent (one researcher's application is approved whilst another, similar, application is not) due to difference in procedures is unfair. Research participants should be able to expect that any research they have been involved in has been subjected to the same process as other, similar, research studies.

17. In practice, this means that RECs should be:

    - **similarly constituted** (number and type of members relevant to the type of applications reviewed);

[1] Edwards et.al.(2004), report 19 empirical studies on this or related issues whilst Abbot and Grady (2011), in their systematic review of empirical research evaluating ethics committees find 16 looking at variation in process and outcome.
[2] The Shared Ethical Debate (ShED) is a process of ethical review of a single application (previously reviewed by an NRES Research Ethics Committee (REC)) undertaken by a number of RECs with the purpose of reviewing consistency in decision making and issues raised at meetings.

- have **access to the same information and expertise**; and
- **follow consistent operating procedures**[3].

18. In addition, RECs should consider the **same range of ethical 'categories'** in the process of reviewing each proposal[4]. For NHS RECs these will be the categories used in the latest HRA 'Ethical Review Form' as published (and Ethical Review Form for MCA Studies') i.e.:

- **Social or scientific value; scientific design and conduct of the study** (including involvement of patients, service users and the public, in the design, management, and undertaking of the research)
- **Recruitment arrangements and access to health information, and fair research participant selection**
- **Favourable risk benefit ratio; anticipated benefits/risks for research participants (present and future)**
- **Care and protection of research participants; respect for potential and enrolled research participants' welfare & dignity**
- **Informed consent process and the adequacy and completeness of research participant information**
- **Suitability of the applicant and supporting staff**
- **Independent review**
- **Suitability of supporting information**

19. It is reasonable for all stakeholders, including researchers and potential participants, to expect that RECs will consider the same set of issues for each research proposal. Given this, RECs should have a common understanding of what each category involves and explicitly consider each of them. The minutes should be produced in a consistent format using the above categories in order to clearly demonstrate the REC has taken into account each of these issues as part of the review process.

## Content Consistency

20. Content consistency means consistency of **opinions** given by the REC as well as the **reasons** that justify those opinions.

21. Such consistency would require that **RECs should reach the same decision about a particular research study, for broadly the same reasons. However, unlike procedural consistency it is less obvious that we should expect consistency in terms of content from RECs.**

[3] The current NRES Standard Operating Procedures for Research Ethics Committees (Version 5.1, March 2012) are available at: http://www.hra.nhs.uk/resources/after-you-apply/knowledgebase-nhs-rec-review-outcomes/nres_sops_v5-1_2012-03-14-2

[4] Similarly, Emanuel et al. have proposed 7 requirements that they argue systematically elucidate a coherent framework for evaluating the ethics of clinical research studies: (1) value (2) scientific validity (3) fair subject selection (4) favourable risk-benefit ratio (5) independent review (6) informed consent (7) respect for enrolled subjects. What Makes Clinical Research Ethical? Emanuel et al. JAMA. 2000;283(20):2701-2711. doi:10.1001/jama.283.20.2701.

22. Individuals, and by extension, individual committees, will value (weigh or judge) different ethical elements differently and can do so in a way that would be considered reasonable[5]. **Reasonable disagreement between the members of the committees will translate into reasonable disagreement between committees**.

23. The direct consequence of this is that two RECs (that are procedurally consistent) **may legitimately reach different opinions about the same research proposal**.

24. **However, there are limits to the range of valuings or weightings, and thus decisions, that may be considered acceptable**. We would not accept *all possible* combinations of weightings of the ethical considerations in research[6]. Whilst the decisions that RECs make can vary (so long as they are procedurally consistent) they **should do so only *within certain limits***.

25. **These limits (and so the values of RECs) should be calibrated against the limits of accepted, relevant "real world" clinical and research practice.**

26. It is reasonable for all stakeholders to expect that once all of the ethical categories have been considered and taken into account by the REC that the REC will apply the **same opinion type**[7] for broadly the **same reasons**. The choosing of the applicable opinion type, as opposed to the exposition of the complex reasons behind that opinion, is essentially a question of appropriate *procedure* and thus may be determined by reference to standard operating procedures.

27. **It is important that RECs always provide clear *reasons* for their decisions** (explicitly linked to the ethical categories) within the minutes and subsequent opinion letters. RECs should reference any published guidance used to inform their decision.

## Limiting the Range of Acceptable REC Decisions

28. Limits on the range of acceptable REC decisions can arise in two ways by:

    i. **Considerations of fair process;** and
    ii. **Appropriate contextualisation of the research as it would apply in the clinical setting.**

### Considerations of Fair Process

29. **The limits imposed by considerations of fair process** may be addressed by the following **general rule** which is derived from the argument that people can reasonably disagree about the relative priority of the ethical categories in particular cases:

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[5] Edwards et al. point out that *"If we were to reject the legitimacy of some differences in substantive decisions from person to person, from culture to culture, we should also have to reject the very need for independent review by RECs."* Edwards, S. J. L., R. Ashcroft, R., and S. Kirchin, S. 2004. Research Ethics Committees: Differences and moral judgement. Bioethics 18(5): 408 - 427.

[6] For example, a committee that systematically rated a high risk of substantial harm as a relatively minor consideration in the face of largely speculative research would be considered to be acting inappropriately. Similarly, a committee that treated any risk of harm or inconvenience to participants as of over-riding importance, no matter what the potential gains from the research would also be deemed to be equally inappropriate.

[7] I.e. 'favourable opinion with standard conditions', 'favourable opinion with standard and additional conditions', 'unfavourable opinion', 'provisional opinion' with request for further information, clarification or revision, 'provisional opinion' pending consultation with a referee, 'no opinion' refer to full meeting for further review of significant ethical issues (proportionate review only).

**Committees should consider each of the ethical categories as though it was the overriding ethical category for the given piece of research.**

## Appropriate contextualisation of the research as it would apply in the clinical setting

30. **The limits imposed as a result of the need for appropriate contextualisation of the research as it would apply in the clinical setting,** taking into account the values of participants and wider society, are related to how similar the research is to actual clinical or other practice and can be expressed as a concern that:

**Without appropriate contextualisation RECs can become isolated and removed from the practical context in which research is conducted, medicine is practiced and patients are treated.**

31. Contextualisation is designed to guard against weightings and biases that are the product of a lack of familiarity, knowledge or understanding of the way in which values are weighted by both patients and healthcare professionals in the actual context of clinical practice.

32. The relative weights given to the ethical considerations need to be adjusted so that they apply to the different clinical (or other) contexts in which the results of the research will be applied. For example, in the emergency care setting drastic measures must often be taken in the face of great risks, great uncertainties and with an incapacitated patient. In considering the ethical acceptability of research in this context the more usual trade-offs between compromised consent and risk of harm must be seriously revisited if the value of novel or existing interventions in acute, life threatening contexts are to be appropriately investigated.

## Previous REC Decisions

33. A researcher who was conducting a similar piece of research to one approved earlier by either the same REC or another one in the same system would be justified in questioning an unfavourable or provisional opinion. In such a case the **researcher would be entitled to an explanation for why the decision on their project differed from the earlier one**.

34. **Previous REC decisions (by the same or other RECs) should be considered as an indication (where appropriate) of what might count as a reasonable decision regarding the application currently under consideration**. Past judgements should not necessarily determine the current one, but it is important that the REC engage with them and, where the current decision diverges, an account given of the ways in which the current application is relevantly distinct from the previous one.

## Practicalities and Recommendations

35. There are a number of practical consequences for both procedural and content consistency that follow from the arguments provided above. Some of these have already been addressed or are being addressed by the HRA, whilst others are novel.

36. There is a need to assess the effectiveness of current and future initiatives with regards their ability to promote greater consistency. It is suggested that the HRA should identify appropriate 'key performance indicators' (KPIs) and/or other methods to measure and monitor consistency of REC decision making. The current Shared Ethical Debate (ShED) exercises, involving the review of the same application by several RECs, may provide a useful means to assess levels of REC consistency over time.

### Initiatives Already In Place / In Progress:

37. **Standard Operating Procedures (SOPs)** have been in use since 2004 and detail the review process and the mechanisms by which decisions are made by RECs.

38. **Health care professionals and active researchers are members of RECs**[8] and thus provide a level of **contextualisation** where the application concerns research within their clinical and/or research experience.

39. **Attendance of researchers at REC meetings** is strongly encouraged by NRES and helps to ensure that the REC is made aware of the context in which the research is taking place.

40. The **Shared Ethical Debate (ShED)** exercise was first introduced in 2007 and enables greater dialogue and reflection about both the process and the substantive judgements made across the NHS REC system. The ShED process now includes individual feedback to each REC regarding their performance, comparing this to the results from all RECs taking part, which promotes self-reflection and greater consistency.

41. New **Ethical Review Forms** have recently been made mandatory for use by RECs in order to standardise the review process. The minute templates will reflect the headings in the review template so that the minutes of the meeting are produced in a consistent format and will document that all ethical categories have been addressed.

42. **Transparency.** The publication of the decisions made by RECs and the reasons for those decisions alongside summaries of the research will present a resource available to researchers and RECs to explore previous REC decisions. This will also serve to promote public understanding of research as well as helping to ensure transparency and accountability.

43. **Pre-application Advice Service.** The HRA recently piloted the use of "HRA Ethics Officers" to investigate whether experienced representative of the NRES, will increase the proportionate of favourable opinions at first review, improve the timelines of review and reduce the administrative burden on RECs, through the provision of advice and support to the researcher and committee. Following completion of this pilot the possibility of rolling out this function throughout NRES as a 'pre-application advice service' is currently being explored.

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[8] The Governance Arrangements for NHS Research Ethics Committees (GAfREC) Harmonised edition (September 2011) states that "4.2.6 *Each REC should have expert members to ensure methodological and ethical expertise about research in care settings and in relevant fields of care, as well as professional expertise as care practitioners. This expertise should be appropriate to the types of research proposal the REC reviews*."

44. **Engagement with Researchers.** The HRA are currently setting up a workshop with REC members so that a group of researchers can present their proposed research along with guidance, evidence and results of previous discussion groups with other bodies to RECs in order to discuss the ethical issues involved and collate their views and opinions.

**Novel Recommendations:**

45. **Contextualisation** requires **broader engagement with researchers**, **patients and the public** regarding the values, standards and practicalities of current clinical practice in specific parts of medicine. Such contextualisation might be achieved through:

    - Extended discussions about broad programmes of research and the ethical issues that might arise in particular contexts between groups of researchers, patients and committee members including workshops on specific topics[9]; and
    - Greater involvement of REC members in the provision of early advice to researchers (from RECs who would not subsequently review any submitted application).

46. **Past decisions/decisions of other committees** regarding similar research should be taken into account as part of the ethical review of new applications. The 'institutional memory' of committee held within its members and associated HRA staff can serve this role to a certain extent as do initiatives such as the shared ethical debate and the NREAP/Chairs Regional Network Meetings. However, a more formal method for capturing and searching past decisions would facilitate the explicit consideration of previous decisions. The HRA have published research summaries since 2008, and will soon expand these to include the ethical opinion of the REC and details on how the opinion was reached. RECs should engage with these previous decisions and, where the current decision differs from these, an account given of the ways in which the current case is relevantly distinct from the previous one.

47. **Appropriate Opinion Type.** The decisions made by RECs and any associated issues identified that should be addressed by the applicant are primarily within the realm of *content* consistency (and thus the responsibility of the REC members). However, the application of the appropriate *opinion type*, consistent with the reasons and requirements underlying that opinion, is a matter of *procedure* amenable to SOPs and thus should be formally taken in consultation with the REC Manager and/or other HRA staff in order to improve consistency in the application of the opinions available to RECs. The current SOPs should be amended to clarify the involvement of HRA staff in this decision along with more detailed guidance on the specific criteria for each opinion type and the circumstances in which a REC's final opinion (but not the substantive *reasons* for that opinion) might be revised where an incorrect opinion type has been applied[10].

[9] For example, the HRA organised an "Emergency Research Workshop" on the 21 June 2012 in order to bring together researchers, members of RECs and other stakeholders together to discuss the ethical issues involved in this type of research.

[10] Currently, in line with para.3.60 of NRES SOPs v5.1, a REC may only vary its opinion where information is subsequently received suggesting that the opinion was based on a "factual error or misunderstanding". However, it is suggested here that the final opinion might be also varied where it is deemed that the incorrect *opinion type* has been applied (and this is not related to a factual error or misunderstanding) and that a change would not alter or otherwise interfere with the substantive underlying reasons for that opinion. E.g. a 'provisional opinion' might be inappropriately applied in a case where the changes required are limited and can be easily specified and thus a 'favourable opinion with standard and additional conditions' would be the appropriate decision category in line with SOPs.

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