

IN FAIRNESS TO FUTURE GENERATIONS: ETHICAL DECISION MAKING IN HUMAN EXPERIMENTATION

by Ceciel Kempers
s1244698

Master of Science thesis
Philosophy of Science, Technology and Society
Track: Philosophy of Technology
University of Twente, Enschede
Faculty of Behavioral Sciences

June 2014

Supervisors

Primary supervisor: Prof. Dr. Mark Coeckelbergh
Second reader: Dr. Marianne Boenink

Summary

This thesis reflects on the ethics of human experimentation in the practice of clinical biomedical research. It is widely acknowledged that in order to improve medicine and public wellbeing, it is eventually required to experiment on human beings. While this step is necessary it is not without moral controversy. In fact, a fundamental ethical concern is that research exposes human beings to risks while the benefits are enjoyed by others. This is morally controversial, and it is key for decision makers to critically assess research protocols whether the risks can be justified compared to the benefits. In therapeutic settings, the aim of research is to provide an immediate benefit to the research participant, and therefore the risks involved are more easy to justify compared to non-therapeutic settings in which the benefits are not enjoyed by the participants themselves, but by future generations. Therefore the main purpose of this thesis is to investigate *when* it is justified to experiment on people if the benefits are enjoyed by future generations.

The approach taken begins from the perspective of justice, because questions of fair distribution of benefits and burdens in research are inherently questions about distribution. But reasons of participation in research and the allocation of research benefits and burdens grounded in justice give rise to a number of questions when it comes the what should be done on behalf of future patients. To understand what acting on behalf of future generations entails, the discussion is analyzed against the background of intergenerational justice.

Furthermore, this thesis investigates whether considerations regarding future are included in ethical review in practice, and in what way. It is argued that reviewing process implicitly assumes that properly designed research protocols will amount to benefits for future patients, but that this is actually not evident. I argue that in order to justify research burdens to current participants in non-therapeutic research, the interests of future generations should be taken more upfront.

Acknowledgements

With the completion of this thesis my time as a student has finally come to an end. I have enjoyed all these years of learning, especially these last three years studying Philosophy of Technology. I would lie if I would say that writing this thesis was easy, in the sense that it's just another essay, but then with five times as many words as what you are used to in this master's programme. It has been an absolute challenge, the working in solitude, coming up with something original, reading the superior work of pioneers in the field, trying to understand the complexity of the problem, writing something comprehensive, throwing out numerous written sections, building again to amount to something better, doubting my capacities whether I was getting at something at all, anxiety whether I would make it in time, and creating something decent enough to pass. Life has felt like a rollercoaster at times. In the end I can say I have learned a lot, and while many additional questions remain to be answered, I feel like I have done some ground work for looking at the issue from a point of view that has not yet been considered by others. I will leave it up to the reader to decide whether I succeeded in shedding some new light on the issue.

My first and foremost expression of gratitude is to my supervisor Mark Coeckelbergh, who's encouragement, enthusiasm and guidance have been invaluable in contribution to this thesis. I cannot thank him enough for his time while working at two different universities at the same time. It must have been a challenge. I have always enjoyed the fruitful discussions we had that have resulted in the final product.

Second I would like to thank Marianne Boenink for her critical assessment of my work and numerous sharp suggestions for improvement regarding both the theoretical part of this thesis and in particular the empirical part, as well as the organization of the thesis as a whole. Her guidance regarding the formulation of interview questions and the analysis of the results has been of crucial importance in developing my skills as a researcher and structuring my own thoughts.

Third I would like to thank those members of the METC's in the Netherlands who responded positively to my request for interviews regarding the ethical reviewing process in practice. I have learned many things about the dynamics of ethical reviewing that sometimes took me by surprise.

Many thanks to the PSTS students and professors that have made my time studying at the University of Twente an unforgettable experience. Although it was often challenging to combine studying with a position in the Ideefiks board and working a part time job, I wouldn't have done it any other way.

To my friends and family, who have never stopped believing in me when times got rough: thank you for all of your love and support and offering distractions at the necessary moments. Especially Nadya, Faustin, Melis, Selina, my parents, my dear sister Maria and my tower of strength Raoul. I wouldn't have made it without you.

Ceciel Kempers
Enschede, June 2014

Table of contents

Summary.....	2
Acknowledgements.....	3
Chapter 1 – Introduction.....	7
1.1 The value of biomedical research.....	8
1.2 Research on human beings, the moral controversy.....	9
1.3 The distinction between therapeutic and non-therapeutic research.....	10
1.4 Non-therapeutic research: an intergenerational issue?.....	13
1.5 Research question.....	14
1.5 Methodology and thesis outline.....	15
1.5.1 Thesis outline.....	16
Chapter 2 – Considerations of justice in biomedical research.....	18
2.1 The concept and conceptions of justice.....	19
2.1.1 Accounts of justice.....	19
2.1.1.1 Justice as a virtue.....	19
2.1.1.2 Property, utility and rights.....	21
2.1.1.3 Equality, fair procedures and mutual advantage.....	22
2.2 Distributive accounts of justice.....	23
2.3 The concepts of justice in biomedical research.....	26
2.3.1 From burdens to benefits.....	28
2.3.2 The right to be protected from exploitation.....	29
2.3.3 Distributing fairly.....	31
2.4 Conclusion.....	34
Chapter 3 – Intergenerational justice and caring for future generations: motivations to promote biomedical research.....	36
3.1 Bringing the future to the present.....	36
3.2 The problem of posterity.....	37
3.3 Future generations and the ability to care.....	39
3.4 Obligation, duty and responsibility.....	40
3.4.1 Obligations and duties.....	40

3.4.2 Rights of future generations.....	42
3.4.3 Objections and limitations to a language of rights of future people.....	43
3.4.4 Supererogatory duties.....	45
3.5 A duty to conduct research?.....	47
3.5.1 The nature of rights and duties in research.....	47
3.5.2 Improving the future of health care, a demand by justice?.....	47
3.6 Other motivations.....	50
3.6.1 A transgenerational polity.....	50
3.7 Conclusion.....	51
Chapter 4 – The dynamics of ethical review.....	54
4.1 Independent ethical review.....	55
4.1.1 Ethical review boards.....	55
4.2 Principles of research ethics.....	56
4.3 Criteria of ethical review.....	59
4.3.1 Research design in terms of scientific validity.....	59
4.3.2 Scientific value.....	60
4.3.3 Clinical value.....	61
4.3.4 Risk-benefit ratio.....	62
4.3.5 Informed consent.....	64
4.4 Time related aspects.....	66
4.5 The interests of future patients in ethical review.....	68
4.6 Conclusion.....	70
Chapter 5 – Conclusion.....	73
5.1 Reflection and recommendation.....	76
Bibliography.....	78
Appendix.....	81
Appendix I – Interview questions.....	79

Chapter 1

Introduction

The purpose of this thesis is to reflect on current ethical discourse in contemporary biomedical research which involves experimentation on human beings. Achievements within this field of research in the previous century have resulted in a tremendous improvement of health care and the battling of disease. Experiments on human beings are conducted on a daily basis, ranging from testing new surgical instruments and prosthetics to the effectiveness of new medical drugs. However, the history of human experimenting has shown that not all experiments are without moral controversy. From a philosophical point of view, this raises the question of under what circumstances we can consider an experiment morally permissible. This deliberation does not happen in a vacuum, but is informed by social, political and juridical aspects, addressing the limits of the moral obligation to act in the interest of others beside reasons of self-interest. In order to understand biomedical research on human beings it is important to investigate the values that underlie these research practices, and which responsibilities and obligations are required from the involved parties. What has been less explicitly stated by scholars in bioethics are the interests of future generations, and how these interests inform research goals in the short and long-term. My aim in this thesis is to make this aspect more explicit by investigating how the concerns regarding the interests of future generations of patients inform ethical decision making in practice.

In order to gain insight in the values that are involved in the practice of research, the philosophical concept of (social) justice will provide a fruitful starting point of the investigation. After all, in the modern age the concept of justice is often understood as what can be considered fair, equitable treatment to what is due to persons (Beauchamp and Childress, 2001; Swift, 2006). To address the component of intergenerational conflict which arises in some kinds of research, the philosophical discussion of intergenerational justice might prove itself also useful to this thesis, since it specifies a way of thinking of what our duties regarding future generations are (Meyer, 2010; Thompson, 2009; Partridge, 1976), but also their limitations.

1.1 The value of biomedical research

In a medical utopia, whenever a person would become ill, he could be cured adequately and immediately, be it through therapeutic drugs, interventions, or a curing machine such as Medi-Bed, as depicted in the 2013 Hollywood movie *Elysium*. Such machines provide the ultimate dream of medicine; an ultimate non-invasive diagnosis and treatment, in less than a couple of minutes, provided in one's home without visits to hospitals, clinics or pharmacies. In respect to some illnesses we have come close to this ideal world with the widespread access to vaccines and antibiotics, but reality learns us that absolute cures without side effects are rarely discovered.

The non-acceptance of researchers and medical professionals of the statement that some diseases are 'just incurable' has led to a vibrant research community and numerous medical achievements (Foster, 2001). Medicine is in need of research in order to advance, and while there is still a lot of work to be done, the history of medicine has shown that remarkable progress has been made the past century. To improve medical care, it needs to be accepted that medical research is required, it is indispensable to say the least. While some argue that the ultimate aim of medicine is to prevent diseases from happening in the first place, we need to recognize that in order to establish what can be considered a healthy living research is required. In addition, if a person falls victim to a disease due to unhealthy living, treatments are required. One way or another, research is required for both determining causes and the development of treatment.

The value of medical research lies also in the possibility to adequately monitor and assess disease and treatment. The endorsed scientific method provides insights that are far more unlikely to be noticed in uncontrolled distribution and unmonitored treatment. This is helpful for the physician in order to make adequate choices regarding which treatments to provide, but even more so for the benefit of the patient, both current and future ones. A striking case is the childhood leukemia, which had 100 percent mortality rates less than one century ago. Carefully organized research involving the random allocation of children to either latest treatment or experimental trials has brought the mortality rate back to 50 percent, speaking in favor of what medical research has to offer, especially on the long run (*ibid.*, 4).

The need for research requires sacrifices of both participants and investigators; participants carry the burdens of undergoing an experiment, while investigators (or physicians) need to maintain an open mind towards 'new knowledge' and methods,

since past achieved theories and practices might not suffice anymore in the wake of advancing medical knowledge. In order to advance medicine, both eligible participants and researchers (or doctors) need to be encouraged to make an effort, while safeguarding the personal interests of the participants. This has been disputed, some authors suggest that the virtues of a good doctor are in conflict with those of a good researcher; the researcher having his obligations to advance (medical) knowledge, while the doctor should be concerned with the best interests of his patients. I contend that both are not at odds with each other, although the allegiance might seem at odds, the virtuous doctor needs to know of the knowledge medical research establishes in order to underpin his decisions of what lies in the best interests of his patient. Furthermore, the patient's wellbeing and his interests inform the goals of research on their turn, creating a dynamic enterprise.

Some say that medical research does not need justification, that it is a public good that benefits society at large (Schaefer et al, 2009). It is in everyone's interest that medical practices keep on improving, to alleviate the suffering of current and future people who fall victim to harmful diseases. Stated as such, the practice of medical experimentation implies there is nothing controversial about medical research, and that patients have an obligation to their future fellow patients to undergo experiments. Others claim that research experiments should be designed in such a way that participants will enjoy therapeutic benefit, as is currently required for research on children (Bos and Tromp, 2013). These views are reasonable, few would deny that they rather receive treatments instead of undergoing experiments only for the sake of benefitting others. But research is also required for determining long term effects of treatments. Allowing treatments to be put on the market early without monitoring their long term effects, involves risks that might not be anticipated upon yet, as was the case with diethylstilbestrol in the 1970's (Foster, 2001).

1.2 Research on human beings, a moral controversy

It is recognized that experimentation on human beings is absolutely necessary in order to gain understanding about the working of its body and subsequent physiology (Beecher, 1959; de Beaufort, 1986). Not only is this practice suitable to gain understanding for the advancing of basic science, but also the possibilities this knowledge provides for the development of medication and undertaking measures to protect health. In that sense, human experimentation can be considered a "social necessity" (Beecher, 1959, 4), yet only to be undertaken when more simple ways of obtaining the necessary information fail to be of assistance. The misuse of human

experimentation has resulted in disgrace and infamy, as disclosed by Beecher in 1966 in his revolutionary essay “Ethics and clinical research” published in the New England Journal of Medicine, in which he described twenty-two historical cases of misuse of patients in clinical research studies. In the wake of these revelations, the practice of human experimentation became of major political concern, and led to subsequent mandates to regulate the enterprise of clinical research in the United States (Rothman, 1987) and Europe.

What is controversial about experimenting on human beings? Don’t we all enjoy the benefits of medical advancements of past generations? Isn’t it obvious to continue the quest of investigating new therapies, to improve overall societal wellbeing? In my opinion, utilitarian statements such as “for the good of society” should be treated with care, since these do not justify to exploit or mistreat one person for the benefit of others. Every individual person needs to be treated respectfully and with dignity. This entails that every person needs to be treated as an individual, with his own history, values and specific interests. To properly care for each person, these characteristics have to be taken into account in order to make an ethically sound decision of what a patient requires. Therefore the generalizing practice of allocating patients blindly into clinical trials might not be the most appropriate response when a patient comes in to the care of a caretaker (Foster, 2001). Especially blind studies are morally problematic, since the patient will not know whether he or she is actually receiving treatment or a placebo. In fact, contemporary allocation processes are handled by a computer to get rid of a doctor’s biased views, in order to achieve reliable results. This implies that while the doctor depends on the *knowledge* achieved through randomized clinical trials to provide the best care for his patients, the means of obtaining that very knowledge are morally questionable, by removing the personal approach of doctor-patient relationship, that is deemed so valuable in medicine.

1.3 The distinction between therapeutic and non-therapeutic clinical research

The design and aim of a clinical trial is of interest in discussing moral aspects of biomedical research. Some clinical trials, especially advanced ones, aim to provide treatment to the patient, while others are designed only to advance medical knowledge, having no therapeutic aim to benefit the research participant. This distinction is very important in order to evaluate moral dilemmas, but is often difficult to make. For example, to provide a therapeutic benefit one needs to administrate a specific dose of a drug or other substance to invoke a response. So, if a low dose of a drug is administrated, the likelihood of such a response would be very low, rendering

the experiment 'not having a therapeutic benefit', while the *aim* of the clinical trial is to provide therapeutic benefit. Conversely, a clinical trial aimed not to provide benefit could evoke a response that can be considered to provide a therapeutic benefit for the research participant. It seems that that *in practice*, there can be no clear distinction of what can be considered a therapeutic and a non-therapeutic experiment. To resolve this I will define a non-therapeutic experiment as those experiments that *do not have the aim* to provide any benefits to the research participant. These experiments include so called phase-1 or 'first in man' experiments, in which a small number of healthy research participants are undergoing a procedure to gain insights in so called pharmacodynamic and pharmacokinetic effects of a substance; phase-2 experiments, in which the substance is administered to a group of patients suffering from a specific disease in which the substance is aimed to be of use, to explore the mechanism or efficacy and safety. The line becomes blurred during phase-3 experiments, in which a substance is administered to a larger group of patients suffering from a disease at which the substance is aimed to be of use, to determine which concentration of the substance could have a therapeutic benefit, or in which the substance is to be compared with already existing treatment, to determine safety and efficacy for longer term use. Important here is that the drug has already proven to be effective, making it harder to distinguish between therapeutic or non-therapeutic use. So called phase-4 experiments, which are conducted to optimize dosage for therapeutic use, I will not consider to be non-therapeutic research, since it focuses on fine-tuning of a substance that has proven to be effective in phase 2 and 3, and is *aimed to provide benefit* to the participant. Other biomedical experiments I consider to be non-therapeutic are those which are aimed to gain knowledge regarding a particular disease (for example the withdrawal of human tissue for scientific experiments), and diagnostic experiments to determine how a particular disease can be detected. To emphasize, all of the aforementioned experiments are not aimed to provide any immediate benefit the research participant, but are designed to gain new knowledge. This means that whether an experiment qualifies as therapeutic or non-therapeutic is determined by its *ex ante research design* and *aim* (de Beaufort, 1986, 21). The categorization of therapeutic and non-therapeutic is of moral relevance, because these procedures are not by definition harmless. Issues of what can be considered fair with respect to the interest of participants who do not enjoy benefits of the research they participate in are very relevant to ask in the justification of human experimentation. After all, people evaluate risks and harm differently when they might have an immediate benefit compared to when they do not.

A begging question following this contention is of course, if these experiments are not aimed to benefit the research participant, then who is to benefit from non-therapeutic research? A possible answer is the researcher, by reaping the fruits of the labor in the form of generated data, and new knowledge, contributing to scientific understanding. Another answer is the physician, because by improving the knowledge within a certain field he or she can provide better health care. But eventually the generated results are aimed to translate into new therapies to benefit the wellbeing of future generations of patients.

An important component informing ethical conduct regarding human subjects research is the concept of justice. Historically speaking, the focus on protection of test subjects has been of main interest after WWII, after the atrocious exploitative experiments of physicians employed by Nazi's came to light. But more recent scandals such as the infamous Tuskegee Syphilis Experiment that ran from the early 1930s until the 1970s and was funded by the public health service in the United States of America have enacted the necessity of human subject protection against exploitation. Considerations of justice have informed many protectionist policies that have been established since, primarily focusing on risks of biomedical research. However, since the early 1990s, attention has shifted to fair access to the benefits of research, for example to provide experimental therapies to individuals suffering from HIV/AIDS in clinical trials. It seems then, that norms are shifting from protection to access. However, putting too much emphasis on access to research undermines the possibility that research might also involve risks and harm, that might not result in any benefit for research subjects at all, or at least overshadow the benefits. To tackle part of this dilemma, measures have been taken regarding ethical guidance and legal arrangements. In order to provide protection for so called 'vulnerable' populations – children and mentally impaired adults – access to participate in research is granted only when the research to be undertaken has a minimal risk or provides immediate benefit to the research subject; it has to have the potential of a therapeutic benefit. This shift from protection to access to research applies only to a particular type of research subject, namely patients suffering from illnesses. However, research that does not hold therapeutic benefit is still carried out on a large scale as well, involving healthy volunteers as research subjects as well as certain groups of patients. This latter type of research will be the focus of this thesis. Especially concern regarding the ethical treatment of research subjects and the requirements of justice in research are in need of special attention, in order to determine what is ethically acceptable research.

1.4 Non-therapeutic research, an intergenerational issue?

As mentioned in the preceding section, investing in clinical biomedical research is aimed at improving medicine in order to provide better treatments for future generations of patients. This is particularly evident in non-therapeutic research, which does not have the aim to benefit the research participant. In practice it might be possible that a research participant enjoys certain benefits himself, but if that happens it should be regarded as luck, since the research design is aimed at achieving generalizable knowledge, not benefiting the individual participant. If successful, the eventual research results will benefit future generations. Improving medical care implies that we value the fate of current patients, but also future ones. Making a commitment to improve the wellbeing of suffering people is one of the biggest reasons to undertake action to do research in the first place. But this effort is not limited to the wellbeing of those who are currently alive and in need of help. It is also about the fate of the patients that will be walking into waiting rooms in the future. Therefore, the effort of clinical research and care has an intergenerational character. Research is carried out in the present, in order to benefit those who will live in the future. Just as patients currently alive enjoy the fruits of the labor of the ones that came before them. But how much can we ask to do on the behalf of future generations? Current research participants in non-therapeutic research carry burdens and risk their health, while future patients get to enjoy the benefits. Is this fair? And if so, why is this the case? Is there a morally relevant distinction between what we should do for the future and for the present living? One can imagine that people in the future might deal with different issues, and our efforts to finding cures to their benefit might not be necessary in the first place. This is especially relevant as efforts are made for the people living in the distant future. Not many researchers have devoted attention to the role of the interests of future generations in their analysis of clinical biomedical research. Most of the debate regarding the future centers around environmental issues, in which it is estimated that future generations will be worse off than currently living, under the influence of climate change, pollution and resource depletion. Researchers in that field conclude that we should not harm them, and therefore take action on their behalf. But in the case of clinical research and care, the issue is different if not inverse. We take on burdens for future generations so they will be better off than we are in the present. Instead of not harming future people, we seek to benefit them.

1.5 Research question

As mentioned earlier, the conviction to do good and the quest to eliminate invasive diseases that cause suffering and pain might lead one to think that moral justification of experimenting on human beings might withdraw into the background (de Beaufort, 1986, 5), and yes, some of these experiments might be considered harmless. Scientific based medical research and their technological off springs have the ability to expand the capacity to do good, but also to do harm, as any person undergoing chemotherapy might testify.

In biomedical research seems to be a tension between the protection of human research subjects and the value of societal well-being informed by medical scientific advancement. The health and well-being of human beings is brought into danger for the benefit of gaining insights into biological processes of the human body, that might assist in the translation into better health care or other applications in the future. While this sounds reasonable, the actual translation is not given. This is why a lot of effort nowadays is devoted to translational research, in which the outcomes of research in basic biomedical sciences has to be made useful for practical application to contribute to human wellbeing. My interest within this dilemma is to what extent can we speak of a fair treatment of research subjects, and at what point we are speaking of exploitation for the sake of science or the future, and whether we can draw such a clear line. At one side of the line are physicians and researchers, who strive to unravel more phenomena and gain insights in the workings of the world, and at the other side there are patients suffering from diseases that are awaiting cures (or improvements in treatment) for themselves, and for future generations.

In the Netherlands, as in many other European countries and the United States, mediating between the interests of science, society and individuals involved as research subjects are Medical Ethical Review Boards (METC's) and in some cases the Central Committee for Research on Human Beings (CCMO), who evaluate research protocols that involve human experimentation. Their task is deciding whether the research can be pursued or not. My interest is which particular criteria are evaluated by these committees, and how the question regarding benefits of research for future generations informs their decision making regarding risky experiments. This thesis focuses on these matters, bringing me to the formulation of the main question:

In light of non-therapeutic biomedical research: under what conditions is it fair to experiment on human research subjects for the benefit of future generations?

In order to answer this main question, several sub-questions need to be answered:

- What is non-therapeutic research and who is to benefit from current biomedical research which has no therapeutic aspect for the participants?
- Which concepts and principles of justice are endorsed in biomedical research, and by whom?
 - What is fair, equitable or appropriate in light of what is owed or due to persons, current and future generations?
 - What is owed to future generations in terms of medical advancements, wellbeing and/ or welfare?
- How do ethical review boards evaluate research protocols in non-therapeutic settings with respect to the interests of future generations?
 - Which factors or criteria are considered when one speaks about the interests of future generations?
- What are the normative implications of intergenerational considerations of ethical review boards for a just treatment of human research subjects?

1.6 Methodology and thesis outline

To answer the main research question and subquestions a literature review will be conducted in chapter 2 and 3, reflecting on current discourse in biomedical ethics. A conceptual analysis of the aforementioned ethical principles will be conducted. Especially an analysis regarding the concept of justice and how principles of justice function in informing policies adopted in the biomedical sciences governing human experimentation are in order, to provide an answer to the main question above. The question implies that non-therapeutic clinical research primarily serves the interests future generations, therefore an analysis of the philosophical discussion regarding the responsibilities towards future generations will be included as well.

To supplement the theoretical part of the research, a qualitative research was included to make explore the attitude of board members of ethical review boards regarding interests of future generations in ethical review more explicit. Since it was not possible to access reviewed research proposals to investigate to what extent intergenerational aspects were involved in ethical deliberation (in retrospect), this qualitative research involved interviews with members of Medical Ethical Review Boards (METC's) in the Netherlands and the CCMO. The focus in these interviews was on the criteria ethical review board consider in their decision making process, which specific criteria are considered when a research protocol is evaluated that requests to

conduct experiments on humans that have no therapeutic benefit for the participant, whether there was a difference in criteria between evaluating high risk research and low risk, how the tradeoff between burdens and benefits is made, and whether the interest of future generations are considered at all, and if so, in what way.

1.6.1 Thesis outline

The first chapter will serve as introduction, and provide the background of the topic of this thesis. In this chapter the value of biomedical research is introduced, the practice and necessity of research involving experimentation on human beings and the issues connected to this practice, leading up to the main question of this thesis and narrowing down to the question what non-therapeutic research is, who is to benefit from it and how it is related to intergenerational justice.

The second chapter first discusses the concepts of justice that are part of discussion in political philosophy, using Ryan (1993), Estlund (2012), Swift (2006), Kymlicka (2001) and Rawls (1971). Thereafter, the conceptions of justice that are endorsed in biomedical research involving human research subjects will be discussed, to provide an account of which concepts and principles of justice are endorsed when in (bio)medical research, and by whom. Especially distributive and intergenerational justice are considered to discuss what are considered to be fair, equitable or appropriate acts in light of what is owed or due to persons, from the perspective of macro- and microlevel politics. Especially in non-therapeutic research, where no benefits to current participants are aimed at, what is and should be considered fair burdens by Dutch law for medical experiments involving human beings (WMO, 1998), policy makers and Ethical Review Boards to those who are directly affected by the research.

The third chapter focuses on what is owed to future generations in terms of medical advancements, or overall well-being. Using Foster (2001), de Beaufort (1986), Beauchamp and Childress (2001), Buchanan and Miller (2007), Emanuel, Wendler and Grady (2012), a notion of distributive justice that is largely endorsed in evaluating human experimenting regarding non-therapeutic research and the benefits for future generations shall be discussed. To provide a context of the discourse on responsibilities towards future generations, the philosophical debate on intergenerational justice will be provided, in order to investigate the relation between distributive and intergenerational aspects of biomedical research more extensively, using literature of Feinberg (1970), Partridge (1976), Barry (1989), Thompson

(2009) and Gosseries and Meyer (2010). A conceptual analysis of the nature of obligations, duties and rights shall be discussed, to provide a normative account of which obligations are required to serve the interests of patients, and by whom.

The fourth chapter focuses on the horizons of ethical evaluation of Ethical Review Boards, and is be largely informed by empirical research based on interviews with committee members of medical ethical review boards and the work of research ethics by Emanuel, Wendler and Grady (2012). The questions central in the qualitative research focused on in this chapter are how ethical review boards evaluate research proposals in non-therapeutic settings with respect to the interests of future generations. Which factors are considered when one speaks about the interests of future generations? Furthermore, the attitude of ethical review boards towards a timeline in non-therapeutic (experimental) research is investigated, to determine whether the expected benefits for future generations is connected to specific promises and expectations of researchers, and whether this is considered in the ethical decision making. Which criteria are evaluated, which are related to the future, and in what way? In the second part of this chapter I will focus on linking back the outcomes of the conducted interviews regarding the actual ethical evaluation of non-therapeutic research to the considerations of justice developed in chapter 2 and 3 to make a normative analysis of the criteria that are taken into account in the ethical review of research protocols.

In the concluding chapter I will provide a summary of my argument. The chapter will cover an overview of the conclusions of each of the chapters to give an answer to the main question. Furthermore, this chapter will the discuss the limitations of this thesis and recommend issues worth investigating in the future.

Chapter 2

Considerations of justice in biomedical research

As stated in the introductory chapter, this thesis will focus on the practice of human experimentation in non-therapeutic biomedical research. In non-therapeutic research, questions of justice are very evident, ranging from the allocation of scarce resources to the distribution of benefits and burdens of research. Especially the question regarding the benefit of the outcomes of research for future generations will be emphasized throughout this thesis, to what extent it is fair that current generations of human test subjects are experimented upon without enjoying any benefits themselves. This chapter shall focus on the conceptions of justice as a discipline in political philosophy, followed by the use of justice in biomedical ethics, especially regarding human experimentation.

The first part of this chapter will highlight the scholarship on the concept and conceptions of justice, starting with a very short history of thought in the Western tradition, starting with the ancient philosophy of the Greeks. It starts with the notion of justice and the aspects scholars associate when speaking about justice: merit, entitlement, desert, fairness, and rights. The second part of this chapter will focus on the use of principles of justice in bioethics, which largely informs policies regarding moral deliberation and decision-making with respect to biomedical research and the use of human research subjects, in order to provide an answer to the main question of this thesis.

Due to the rich and exhaustive available literature within the field of political philosophy that centers on justice, this chapter cannot cover in detail all that has been written. It is also not aimed to be as such. Rather, it provides an impression of the most relevant theories about justice for the aims of this thesis by scholars in the field of philosophy. The method endorsed here will be conceptual analysis, because in order to talk about a rich notion like justice I feel it is important to unravel what the concept implies and which interpretations inform theories of justice.

2.1 The concept and conceptions of justice

In order to make a relevant analysis of what is required or demanded by justice, it is fruitful to first introduce the concept and the different interpretations of justice related to specific problems, such as distribution and social aspects of justice.

The concept of justice is a rich, diverse notion that is explicated in various ways. In a concise understanding, justice is about moral rightness, about giving people what is due to them. In the most narrow sense, justice tells us what is morally required from us to do, other than doing what is morally praiseworthy. Stated as such, justice implies *moral duty* (Swift, 2006, 11-12). Up until today, there is no simple monistic theory of justice available, rather, justice is informed by many so called “ultimate values”, like equity, liberty, the common good, rights, and so on (Kymlicka, 2001, 3).

2.1.1 Accounts of justice

2.1.1.1 Justice as a virtue

Historically speaking, discussions on the topic of justice in political philosophy date back to antiquity, perhaps found first in the writings of Plato around 400 BC. In his work *Republic*, Plato understands justice as a virtue, relating to an internal property a person’s soul might possess, required to lead a virtuous life. A just individual acts in accord with a harmonious soul, guided by the good. In that sense, a just person would not be capable of being unjust, since his soul is permeated by all that is good, incapable of being seduced by self-interest and evil.

Likewise, for Aristotle justice is grounded in virtues which are necessary for leading a good life. However, Aristotle treats virtues as means between two extremes, in which justice falls between giving or receiving either too little or too much (*Nicomachean Ethics*). Furthermore, justice is a distinct virtue in addition to being the sum of all virtues, because a just man acts informed by everything he ought to do, but acting just is distinct from acting merciful, prudent, courageous and other related virtues (Ryan, 1993, 8-9). Aristotle, like many other modern writers, distinguishes between two types of justice, one focusing on rectification (or correction), the other on distributive justice. For my purposes here I will only go into the latter one, because while it might be interesting to think about experimentation on criminals as an act of retribution for their crimes, my emphasis will focus on experimentation on volunteers. Distributive justice, according to Aristotle, is heavily informed by a notion of *merit*. The amount of resources and goods a person is to receive is directly

proportionate to his/her merit. In practice, this means that people that do well ought to receive more than people that do less well. It is based on a ranking system in terms of goodness, although it is not quite clear whether the goodness of a person lies within his own control, or is primarily due to external factors (ibid, 9). The same goes for merit, Aristotle does not specifically address the question of what counts as merit, nor who is to judge.

Medieval thinkers like Cicero, Saint Augustine and Thomas of Aquinas have developed their theories based on ancient ideas about justice as put forward by Plato and Aristotle, especially the latter two tried to interweave theological ideas into their philosophies. Cicero, like Plato and Aristotle, understands justice as one of the cardinal virtues, which combined comprise moral goodness. Justice, forming the fundament of society, serves the common good by striving after *what is good for all*. Rather than perceiving justice as an-eye-for-an-eye, Cicero believed we ought to act justly without relying on vengeance for the injustices that might have been done to us. It is about restoring imbalances in damaged social relations by persuading others to endorse your way of thinking.

Saint Augustine's philosophy is considered to be Neo-Platonic, supplemented with Judeo-Christian ideas. Augustine endorses a platonic notion of justice as one of the cardinal virtues, which for him entails that justice is giving each person what is due to them. But contrary to Plato, Augustine connects justice to a divine law, to which human laws and rules are subordinate. A just rule or law is one that is in accordance with the divine law of God, for it to be a law at all. As already mentioned above, the understanding of justice as giving people what is due to them is a rather obscure notion, for it is not quite clear who is to decide. However, the Christian influence provides a starting point, because each person is equal for being a child of God. Alas, the drawback of his approach is that it entails that the only just society is one informed by Christianity.

Aquinas's ideas originate from Aristotelian ideas about justice, combined with Christian thought. As Augustine and Cicero, Aquinas understands justice as one of the cardinal virtues required for moral goodness, in which justice calls for proportional equity, informed by natural right, which in turn are founded on the will of God. It is with Aquinas that justice is first associated with rights, namely respecting the rights of others (Ryan, 1993).

2.1.1.2 Property, utility and rights

David Hume was highly skeptical of the notion of justice as a virtue. Contrary to Plato, Aristotle and Augustine and Aquinas, he grounded justice not in reason but as derived from our passions. Hume endorses a specific account of what criteria a quality needs to fulfill in order to qualify as a virtue; it needs to be useful to a person or to others, meaning that it has to give a pleasant feeling of approval. Still, justice can be considered a virtue, but only in the sense that it is useful and beneficiary (pleasing) for others, not for individual purposes. Hume's theory of justice entails that justice is unnatural, for it exists only in social conventions. To him, justice exists only within the context of property and rejects the claim that justice is about giving each person their due. He believed that justice is about respecting property, with the motivation that human beings possess a sentiment for humanity: a willingness to do good in service of the well-being of society (ibid., 10).

According to Mill, justice can be distinguished from other moral notions because of its stringency. He understands justice in terms of rights, more specifically what people have a right to on utilitarian grounds, namely that which promotes general happiness. Other dimensions of justice according to Mill are to give people what they deserve, and to keep promises to one another. What is excluded from his analysis is the feature of equality. Mill's argument for a utilitarian account of justice is rather complex and boils down to equating justice with social utility, meaning that the just way to act is to promote the greatest happiness for all, rendering actions just only in terms of their subsequent consequences. This is a problematic view, because it does not provide any guidance to which acts can be categorically forbidden, any means to achieve a desirable end can be justified.

Robert Nozick's understanding of justice entails that a just society is one that endorses a minimal state regimen, because that is the only social organization that is consistent in respecting individual liberties (or rights). For distributive justice, this entails that the state has no right to claim resources of its members in order to redistribute them. Rather, Nozick understands justice as entitlement. The only way exchange of goods can be just is when they are the result of bargaining between two (or perhaps more) parties in which both consent to the exchange or transfer. The role of the state here is to ensure that this process is the only way of transfer or exchange, to ensure that no one violates another's ownership (ibid., 14). If the wealthy want to aid the poor, they must do so out of their own motivation, as a charitable act. Justice does not require from them to give up some resources they are entitled to.

2.1.1.3 Equality, fair procedures and mutual advantage

In a modern western understanding, justice is associated with fairness and individual rights, the former beings most strongly put forward by John Rawls in *A Theory of Justice* (1971). While Rawls takes Hume and Mill as his starting point, the conclusions he arrives at are very distinct from those of his predecessors. Justice, according to Rawls, regulates social co-operations on an institutional and political level. As such, Rawls concerns himself with the mechanisms through which particular outcomes are achieved (Ryan, 1993, 13). Ideas that lie at heart of Rawls's theory of justice are "the original position" and "the veil of ignorance" (Swift, 2005, 21). Rawls understands justice as fairness, and starts from the viewpoint of a society emptied of content, meaning that deciding upon what can be considered most fair can best be achieved by people who are ignorant of how they will be affected by it. This is what Rawls calls the veil of ignorance (Rawls, 1971, 12), which ensures that no one is advantaged over the other in deciding which principles are fair, since there can be no bias based on natural chance or social class. The principles are the outcome of a bargain based on radical equality, a status quo. Extremely important to note is that Rawls does not equate justice with fairness, the notion of justice as fairness refers only to the situation in which the principles of justice are decided: under fair circumstances. The logic that goes into this is that people will choose more fairly once they are deprived of background knowledge. For Rawls, this is the ultimate sense of equality between persons. Rawls endorses two principles that form the fundament of justice: first that each person is given a maximum liberty in accordance with a liberty for all, and secondly that distribution of social goods are allocated in such a way that the least advantaged members of society are benefited and each member of society deserves a fair equality of opportunity. Inequalities are justified as long as the least advantaged members are benefited from those inequalities.

In summary, throughout history philosophical thinkers have had many ideas about what justice might entail. These ideas can be grouped into several different conceptions; virtue as remarked by the ancient Greeks, fairness in procedure as emphasized by Rawls, entitlement as advocated by Nozick, equality (Dworkin) and desert (Aristotle). In their turn, these conceptions inform institutions and policies that organize a society. For example, distributive justice concerns the appropriate distribution of benefits and burdens, based on norms of what can be considered fair, which, in common modern understanding, is what is owed to people. This entails the distribution of responsibilities, resources, wealth, property, and opportunities. Each

of the ideas put forward by the aforementioned authors will provide different answers to what can be considered fair in distribution. Because experimentation on human beings invokes questions of exactly distribution of benefits and burdens, it is relevant to include different accounts of distributive justice before proceeding to how principles of justice are endorsed in ethical guidance and legal arrangements. In the next section such an overview of theories of distributive justice is presented.

2.2 Distributive accounts of justice

Egalitarianism

Different accounts of distributive justice account for how distribution is to be carried out. Egalitarian accounts are premised upon equality between persons as citizens, meaning that there should be no difference in treating people with respect to social status, wealth and moral worth. Sometimes egalitarianism is about the elimination of social inequalities, promoting more equality in the distribution of income and wealth, referred to as Strict Egalitarianism (Lamont and Favor, 2013). But this latter is a contested view, someone who endorses egalitarianism primarily focuses on the former notion, the equal treatment of persons, based upon the belief that people have an equal share of moral worth and dignity (Arneson, 1990).

The Rawlsian tradition endorses the Difference Principle when it comes to distributive justice: first, “(1) Each person has an equal claim to a fully adequate scheme of basic rights and liberties, which scheme is compatible with the same scheme for all; and in this scheme the equal political liberties, on only those liberties, are to be guaranteed their fair value” followed by the second principle “(2) Social and economic inequalities are to satisfy two conditions: first, (a) they are to be attached to positions and offices open to all under conditions of fair equality of opportunity; and second, (b) they are to be to the greatest benefit of the least advantaged members of society” (Rawls, 1993, 5-6). These principles are revised compared to the formulation of the principles of justice in *A Theory of Justice*, in which the latter condition of the second principle (2b), that focuses on the benefitting of the least advantaged members in society, was not involved. When conflict occurs, the first principle has priority over the second principle, in which 2a has priority over 2b, meaning that basic rights and liberties should never be sacrificed for attaining benefit for the worst of members of a society.

Entitlement

The entitlement approach to justice often advocated by libertarians such as Nozick, holds that we ought to respect one's self-ownership and their right to own property, favoring fair procedures over outcomes. Nozick's theory proposes an entitlement theory that has three components: (1) "A person who acquires a holding in accordance with the principle of justice in acquisitions is entitled to that holding", (2) "A Person who acquires a holding in accordance with the principle of justice in transfer, from someone else entitled to the holding, is entitled to the holding" and (3) "No one is entitled to a holding except by repeated application of (1) and (2)" (Nozick, 1974,). For distributive justice this entails that no institutional redistribution is in order, someone acquires only by means of transfer, or voluntary donation. For Nozick, institutionalized redistribution by means of taxation can be perceived as an intrusion of one's private holdings. The only role for the state is to oversee the transfer of private holdings, and protect people from unjust transfer, such as theft or fraud. Principles of fair distribution have no place in entitlement theories of justice, and can therefore be seen as a direct objection to Egalitarianism and Rawlsian approaches to justice. Goods are made by people, and therefore owned by that very people, or the ones who exchanged something for the acquisition of those goods. The same goes for talents, one's talents belong to his or herself, and cannot be used by some party to benefit others, unless one consents to this.

Utilitarianism

Utilitarian approach to distributive justice holds that the choices to be made in allocation of goods and resources should be consistent with benefit for the greatest amount of people. It has to be in accordance with the principle of utility; meaning that institutions have to be arranged in such a way that the greatest net balance of benefit for all individuals that make up a society is achieved. Stated at such, utilitarians endorse a teleological account of justice that focuses on outcomes instead of procedures. What makes an action just or right is if it maximizes the good, which is interpreted as the principle of utility. A famous objection to utilitarianism is articulated by Rawls for the fact that utilitarians do not account for the distinctiveness of people. Utilitarianism might work for individuals, meaning that people can sacrifice a period of time of their lives to attain greater happiness (in the sense of utility) afterward, but it fails to be applicable for a society as a whole. To make people suffer for the net benefit of others can be considered immoral (Lamont and Favor, 2013). Similarly, the interests of minority groups are always disfavored in utilitarianism.

Welfare theory

Welfare theories of justice focus on the level of welfare of people, and distribution is valuable insofar as it affects the welfare of people. Welfare theorists endorse the view that there is an interpersonal measure which describes the good quality of an individual's life. These components might involve friendship, love, personal achievement, acquisition of knowledge, experiences. Welfarists assign scores to each of these components, and based on some formula the wellbeing of a person can be calculated. Similarly, there is an index for bad components that impair wellbeing, and the overall welfare of a person is calculated by simple arithmetic by subtraction of bad from good components (Estlund, 2012,). This measure determines what is owed to one another and institutions can be arranged as such, in order for everyone to have a decent quality of life, based on a threshold level of overall welfare, or poverty line. Often these arrangements endorse a maximin index, meaning that the level of welfare of members in a society that are the worst off should be maximized, and that this should be assigned priority. However, problematic in this point of view is that people differ from each other in what they think is valuable and comprises a decent quality of life, so it does not matter, in a moral sense, that everyone has the same or should be treated the same. This objection then implies that justice requires that we maximize overall moral value, running in danger of collapsing in utilitarianism and facing the same objections. Other objections hold that choices of measure in welfare comparison are arbitrary and elitist in assigning what fundamentally makes a life good or bad. It fails to take into account the differences between people, their goals and conception of the good. Therefore, the objection holds that enforcing a system based on an arbitrary objective measure of the good might be unjust because it might be in conflict with what people value and their own view the good.

Desert

Desert-based approaches to justice hold that people should be given what they deserve, based on their individual achievement and actions. The roots of this theory can be traced back to Aristotle, who thought that virtuosity of moral character could be used as a measure of distributive justice. Modern thinkers follow John Locke in the basis of what is deserving, grounding their account in merit. What people deserve is determined by the value of what they produce, to enjoy the fruits of their labor. Desert-based approaches follow three principles: (1) Contribution, (2) Effort, and (3) Compensation (Lamont and Favor, 2013). For desert-theorists, distributive justice should focus on that people earn what they deserve, based on the three principles

stated above. Importantly, the social relevance of the product of labor is important in determining what is to be deserved. People contribute in varying degrees to what is desired by other people, and should be compensated accordingly. An objection to desert payment entails that the benefits one can enjoy over his labor lie to a great extent outside of one's control, which makes the claim by desert-theorists that people should choose responsibly in the allocation of their efforts problematic.

The different approaches discussed above are primarily of liberal nature, with the exception of egalitarianism, meaning that they were emphasized and developed in modern liberal democratic societies. Many approaches (some more than others) have informed policies regarding just distribution and social institutions, while many theories disagree with each other. In the next section I will discuss how principles of justice are conceived and endorsed in the context of medicine and biomedical research in particular.

2.3 The concepts of justice in biomedical research

Principles of justice conceived and endorsed in the context of biomedical research are rich and diverse, centering on obligations to protect individuals from exploitation, equality in access to participate in research and healthcare, the fair distribution of scarce resources and the requirements of the state to provide an adequate health care system and invest in the curing of diseases. Furthermore, justice is also involved when speaking about social values that underlie biomedical research (Buchanan and Miller, 2007, 373).

In this section I explore which theories of justice are endorsed in biomedical research, and in particular the considerations grounded in justice regarding a fair distribution of benefits and burdens. After all, in biomedical research a benefit regarding medical practices is strived after, in the form of enhanced and improved medical care. But in order to achieve a benefit, participants are required to carry the burden of serving as a subject of experimentation. Questions about who is to be recruited, who shall carry the burdens and who will enjoy the benefits of the outcome of the research are questions of distributive justice. In this case, *injustice* would mean to put burdens on someone that are too high, or denying someone a benefit to which he or she has a rights claim. But when are burdens too high? What justifies them? The same holds for the allocation of benefits. Who deserves them, and why? Theories of distributive justice aim to answer these questions by trying to explain what a fair distribution requires. As becomes clear from the section above, what counts as a fair distribution

that might justify burdens has different origins. For example, desert-based approaches will hold that anyone who contributes to a desirable cause have to be compensated by enjoying the benefits achieved by that cause, while utilitarian theories will specify that burdens are justified if they contribute to the overall net wellbeing of a society. None of the approaches can provide an answer that will satisfy everyone, each has their own flaws. Furthermore, conflicts emerge when certain distributed goods become scarce, and trade-offs have to be made. In such cases, what is required is a proper *balancing* of different considerations. Theories of distributive justice provide tools for thinking in order to clarify certain assumptions and considerations of what needs to be done to reach a fair decision.

One of the principles governing distribution of social resources is the principle of need. This is specified as that justice requires that we help those in need, whom without our help will be fundamentally harmed or severely affected (Beauchamp and Childress, 2001, 228). This covers a range of different needs, such as severe physical injuries, basic nutrition and nonmaterial aspects such as information, which can be perceived as fundamental needs. Other principles that can be identified are those premised upon the conceptions of justice as specified in the previous section, according to effort, contribution, merit, free-market exchange or equality. These above mentioned principles have informed public policies, some more than others, with respect to different spheres and contexts. Some of the principles are in conflict with each other, which pose challenges for developing a coherent moral system, implicating that a proper balance is in order.

Buchanan and Miller (2007) believe that justice is involved at three levels in the practice of medical research. First, they relate justice to duties of the state, meaning to what extent the government has moral duties to invest and support biomedical research with the aim of securing public health and well-being. Second, justice lies at the heart of the fair distribution or allocation of resources to biomedical research. Third, the principles of justice that are involved within research itself, such as the just treatment of individuals that participate in research programs and the ethical criteria that have to be met in order to conduct research with human beings. These principles are of course not completely distinct from formal principles of justice, nor are they independent from them. The first principle relates to the interpretation of justice as a virtue in an Aristotelian sense, while the second principle Buchanan and Miller endorse is related to issues of distributive justice, and the third can be perceived as a part of non-maleficence and fair opportunity to participate.

I will not make a full analysis of the social institutions that could be required by state. This is because it is too lengthy to discuss here, and although it is relevant regarding the underlying values of providing health care which in turn inform what needs to be done to secure public wellbeing, it is a distinct question which could cover an entire thesis of itself. I will only discuss the obligations of the state in a minimal way as they relate to the issues connected to human experimentation. An analysis of duties, obligations and rights are included in the next chapter. In the remainder of this chapter I will look at the issues of distribution of benefits and burdens involved in human experimentation.

2.3.1 From burdens to benefits

Until recently, the main focus in bioethics was on the risks and burdens of research, especially regarding non-therapeutic research. Justice requires that potential and actual research subjects need to be protected from harm, abuse and exploitation (Beauchamp and Childress, 2001, 226). So called “protectionist policies” focus on the allocation of benefits and burdens, the primary concern being unfair distribution of burdens. However, in light of the AIDS epidemic, a focus shift has directed attention to the benefits of research and fair access to experimental treatments, in- and outside the setting of clinical trials. As such, less emphasis has been placed on the risks involved.

This tension between protection of research subjects and access to the benefits of research has recently sparked debate again in the Netherlands, in which the government proposed a new law, which specified that vulnerable populations, in this case children suffering from cancer, were denied access to experimental drugs that were only tested on animals, unless the risks involved were limited to a minimum and therapeutic benefit was guaranteed. Pediatric physicians, patient organizations, parents, and the children involved objected against this decision, emphasizing that if the participant involved would not benefit from it, then they still wanted to participate for the sake of future patients. The politician endorsed the view that children are vulnerable and need to be protected from possible harm involved in research. Critics objected that the interests of the children were not looked after and the new law involved overprotection, denying the possible participants from making their own decisions and basically sentence them to death (de Volkskrant, 2014).

The need for protection of research subjects has gained a lot of attention after WW II, when the horrendous experiments conducted on (primarily Jewish) prisoners in

concentration camps came to light. These experiments involved injection of ink into eyes (in attempt to change the color of the iris), transplantation of limbs and organs between individuals, cross-species breeding, sterilization, freezing, malaria injection and head trauma, often resulting in death, or permanent disability. In all cases the research subjects were forced to cooperate, voluntary consent was never obtained. In the aftermath of the Nuremberg Trial's, the Nuremberg Code (1949) was set up to govern the experimentation involving human research subjects. The Code primarily served to protect research participant from exploitation, stating ten rules for conducting experiments, the most paramount one obtaining voluntary, informed consent of the research participant. Fifteen years later, the Declaration of Helsinki (1964) was instated that focused specifically on biomedical experiments on human beings, adding clauses that research proposals had to be reviewed by independent boards, and that human research has to be preceded by animal experiments. Since its introduction, the Declaration has been revised multiple times, covering 37 statements as of 2013, compared to 11 in 1964. The Declaration of Helsinki is not an institutionalized document by law, but was developed by efforts of the medical community itself, providing international guidelines to govern research.

2.3.2 The right to be protected from exploitation

Explicated in the document are that the interests of the research participant should have priority over any contribution of the research to science and society. This is also the attitude in research ethics. In practice it means that this way participants are protected from strictly utilitarian consideration of justice which holds the view that the right thing to do is that which maximizes the wellbeing of the greatest number of members of a society. It recognizes that each participant should be treated as an individual, and the right not to be exploited for the sake of 'the majority'.

The right not to be exploited has its origins in respect for persons and the right of physical inviolability (de Beaufort, 1985, 127). But when exactly are we speaking of exploitation? Of course, someone is exploited whenever he or she is deceived or tricked into joining an experiment, for example by being lied to about possible known risks or the aim of the experiment. So much for the obvious. But one could also be exploited when burdens are too high, for example by being exposed to very invasive techniques or methods that require a lot of one's time.

Some have related exploitation in research to contract theories of justice (Emanuel et al., 2004). They hold that in essence, justice applies when two parties agree to pursue

a common goal, rendering what is just is a procedure. When both parties consent to their respective duties required to achieve a goal, no matter what the balance of revenues are, justice is achieved. The problem with this view is that it neglects power imbalances that might be involved in research transactions. For example, the pharmaceutical industry outsources its research facilities to third world countries, where it is easier to recruit research participants. The people who participate in their research programs do not have another option, because the company promises them a form of access to medication that they cannot obtain by other means, simply because there are far less facilities compared to developed nations. However, the results of the research such as the actual developed medication is brought to the market in these developed countries, because they are able to pay. This indicates that the benefits of the research are primarily enjoyed by the pharmaceutical company, and not the research participants or the country they originate from, striking a huge power imbalance. On account of 'fair benefits' one could say that these research participants are in fact being exploited for the benefit of the developed countries, even if they do consent to participate in the research program. Consent does not protect people from exploitation. Especially in situations where people are in a disadvantaged position and have no other options because they are poor, their needs might be so high that they are willing to consent to anything that slightly improves their situation shortly (during the trial), because the alternative is even more dreadful. Often these countries do not provide basic health care and joining a research study provides their only way out. Similarly, consent also does not protect people from exploitation who participate in clinical trials in developed countries. Many patients who cannot be provided with an existing treatment anymore are willing to try anything experimental that has the slightest chance of helping them. If there are no alternatives available, people will often agree to anything that will improve their situation, even when the distributions of benefits and burdens might be out of proportion, rendering the proposal 'fair' on contract theory, that grounds justice in negation. I think this is mistaken. Locating justice in consent and mutual agreement is not enough to protect people from exploitation.

How can these issues be resolved? Ballantyne (2008) proposes that a normative notion of fair benefits is required to improve the situation of the weaker party, in this case the research participant. To overcome exploitation what is truly required here, Ballantyne suggests, is a normative notion of fairness in distribution of benefits and burdens to which one can measure the actual proposed distribution of benefits (ibid, 243), in order to truly judge what is fair and unfair. She does not provide a substantive

account as to what such a notion might include, but refers to the following principles: “benefits, risks and burdens [...] should be tested against the best current prophylactic, diagnostic and therapeutic methods,” and “every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study”. Both these requirements are stated as such in the revision of the Declaration of Helsinki, made in the year 2000. The important message is that one needs a normative notion in order to distinguish between fair and unfair distributions, supporting the protection of vulnerable parties, but also what can reasonably be asked to do. A normative notion would aid by describing in a more sophisticated way the significance of burdens, serving as a reference point.

2.3.3 Distributing fairly

However, it is not easy to determine what the absolute minimum threshold or even the maximum threshold of permissible research burdens are. Everything depends on context. Consider for example the research regarding cancer medication. Is it fair to ask people who are already suffering from an invasive disease to join a clinical trial, meaning they should carry even more burdens? At first glance this seems very unfair. But the alternative, asking healthy volunteers to test cancer medications is perhaps even worse, because they do not have the target disease and the medication is very aggressive. This would imply that the medication could do far more harm for healthy volunteers in proportion, compared to cancer patients who are already less healthy, and in some cases could benefit from the new drug under study.

The right not to be physically violated should be interpreted as the right not to be subjected to unnecessary actions that could result in harm during the experiment, or afterwards. Exploitation or abuse should be understood as those situations in which someone is harmed on purpose, in which either dependency and defenselessness of the subject are being utilized to such an extreme that the interests of the research subject are not taken to heart at all. This applies to both adults and children. This means that certain non-therapeutic experiments are not allowed, but those that do not put the wellbeing of the research subject at risk at all can't be objected against that easily. Especially when the results that can be obtained could be important for significantly improving wellbeing, be it for a specific group of people or on a larger scale, now or in the near future. However, in the case of children it is crucial to recognize that they should not be included in research programs if the same results could be obtained by experimentation on adults. Children should only be included in

research if there is no other way. But caution is required. Treating children as ‘tiny adults’ is an unjustified claim, because children’s bodies react differently than adult ones. Their organs function in a different way, so prescribing them with medications that are successfully tested in adults does not automatically mean they are suitable for children. In order to advance children’s medicine, children are required to participate in research programs.

But how can benefits and burdens be distributed fairly? In non-therapeutic research (and even in therapeutic experiments) research participants do not share in the benefits of the research, but they do carry the burdens. A fair distribution entails that burdens and benefits should be fairly, equally distributed, but it is not easy to assign to whom. One position is that every potential user of health care that shares in the benefits established by research, should also share in the burdens (de Beaufort, 1985, 86). Simply because they can benefit from the results of conducted experiments. Does this imply that in that case *everyone* has a duty to sign up as a research participant, as a civic duty? Some claim this is the case. Schaefer et al (2009) mention an obligation view of participation: if the burdens are not excessive, than it is morally required to participate in research. This is a very demanding argument, it would transform many acts that are considered charitable and noble into morally required acts. Moreover, acting beneficent by doing something good for society does not provide any guidance regarding risky acts. One would be under the obligation to act to benefit society, even if the very act itself involves risk and harm. In my opinion this is unreasonably demanding, but adopting a weaker version in which people have to perform a limited amount of beneficent acts would not help, because it lacks substance as to which acts are superior over others.

Another argument claims that we should view biomedical research is a public good. Public good means “one person’s use of that good does not diminish another’s use of that good; and, it is impractical to prevent people from using the good” (ibid., 3). This is contrary to private goods, which are diminished upon use by others, and it is feasible to withhold others from using it. Examples of public goods are national security, a fireworks display, street cleaning, and clean air. Enjoyment of national security or fireworks does not diminish if it is enjoyed by other people too. Important to note is that who provides this public good is irrelevant (Scheafer et al, 2009). Biomedical research is in service of generating public good, namely generalizable knowledge (ibid., 3). I would like to add that this knowledge itself is not the only thing to value, but also the possibility to contribute to better health care. Moreover, using

the generalized knowledge does not deprive others. By making the knowledge publically available, innovation can be stimulated, leading to improvements in surgical techniques and medical treatments. The achievements of the past centuries testify to this, but more importantly the efforts of clinical investigators and research participants were indispensable for the developments we enjoy today. Therefore, the accumulation of medical knowledge that benefits society at large, made possible through experimentation on human beings is an enterprise we should support and promote, also for future generations. It seems that these arguments provide ground for an obligation for each person to participate in biomedical research, to contribute to the public good of medical knowledge by “splitting the bill”. However, rather than to state that every individual citizen has a personal obligation to participate, I would suggest that instead it is important to support the system that makes these advantages possible.

According to Schaefer et al, everyone has a *prima facie* duty to participate, meaning that these duties can be overruled by more compelling duties. For example, the protection against excessively burdensome research overrules the obligation to participate. The limitation of obligation theory is the lack of specificity. Which duties are more compelling than others? There is no formula to determine how much one has to do in order to do “his fair share”. Imagine someone who has been unfortunate in the natural lottery and is in need of many public goods such as health care to make a decent living. Is it than fair to say that such a person is obliged to do more than someone who is less dependent on these facilities? I would argue that this is not the case, but there is nevertheless an obligation to do *something* back. Following Ballantyne (2008), in order to make a judgment regarding what is required, a normative notion is required against which we can assess these duties.

According to de Beaufort (1985, 86) it is important to distinguish between therapeutic and non-therapeutic biomedical experiments. In case of therapeutic experiments it would not be unjust to ask sick patients to carry more burdens than healthy participants, simply because they have a chance to immediately enjoy the benefits. To fairly distribute the burdens would then mean that the burdens are shared fairly by the ‘members’ that specific group of patients. I agree with this. For example, it would be required that patients suffering from rheumatoid arthritis would all share some burden in order to improve the wellbeing of the entire group, instead of asking relatively small populations of patients time and time again to participate in experimental programs (even if they yield benefits).

In the case of non-therapeutic experiments it is far more difficult to determine what a fair distribution entails. In those cases people are asked to carry burdens that do not have an immediate compensation in the sense of health benefits, as is the case with therapeutic research. What can be considered fair in these cases? It seems impossible to strike a balance without invoking the obligation account as presented by Schaefer et al. But it seems unfair to say that people who are ill should carry all of the burdens, because those are in and of itself not distributed equally. It is hard to say something about that on grounds of justice, because there is no equal starting position. And invoking an argument grounded upon the claim that anyone could get ill and therefore should be required to participate in research seems very (if not too) demanding.

Still there is reason to think that it is fair to experiment on people without offering them direct compensation in the sense of health benefits. I think the legitimacy of non-therapeutic research is grounded in the fact that we need to help to improve the position of disadvantaged members of society, to offer them or their fellow companions in the future a better position so can have a more equal standard of living that comes close to the people that are healthy. As said earlier, sickness and health are not distributed equally, but lie often outside of one's own control. To compensate for these inequalities it is important that we make an effort as a society. But who in society should make an effort, and what is morally required to do for strangers?

There is also a gap between improving the situation of individuals that are currently suffering from diseases, and improving the situation of that group of people as whole, which implies a far larger group that stretches from patients currently alive to the ones that will live in the future. As mentioned in the introductory chapter, non-therapeutic research is inherently an intergenerational affair. Witnessing the pain and suffering of members of society currently alive, should stimulate us to do something to improve the situation of those specific, but also those who will walk into the waiting rooms in the future. Justice requires from us that we take action, because people do not choose to become ill on their own accord. It is often a matter of fate and being unlucky, and especially on grounds of egalitarian considerations we should strive to close the gap between the fortunate and the unfortunate.

2.4 Conclusion

Questions about human experimentation invoke considerations about distribution, therefore I focused in this chapter on distribute justice, and how it plays a role in the research involving human beings. As we saw, there is no single comprehensive theory

of justice that can be applied to everything. Rather, it is a combination of different sets of values that underlie research practices. Utilitarian statements that the overall wellbeing of a society should be promoted is reflected in public health programs, the effort to develop vaccines, while egalitarian considerations reflect that we should help people who are in a disadvantaged position by promoting their wellbeing.

Promoting health and happiness in the form of adequate health care requires that we keep on improving on treatments and diagnostic methods that are now regarded as a standard practice, but are far from ideal themselves. This means that we have to gain insight in human biology through clinical experimentation, and making sacrifices by carrying burdens. Distributing these burdens fairly over society is a difficult issue. Putting additional burdens on those who are already ill because they enjoy the benefits of efforts of past research participants seems quite unfair. At first glance it would be more fair to include everyone who enjoys in the benefits of health care in ongoing research, simply as a symbolic reciprocal service for the efforts of people from the past who have made medical advantages possible that can be enjoyed by current living people. But this seems unreasonably demanding. No one has asked past participants to join medical experiments, therefore current living people should not be obligated to continue their legacy by definition. But I think this position could be more nuanced. Yes, past generations have done us a service, and we should be grateful for that, but what reasons are there to think we have an obligation to carry on their legacy?

In the next chapter I will take a closer look at what is morally required to do for future generations in terms of medical improvements, and which considerations regarding the future are morally required to inform our actions.

Chapter 3

Intergenerational justice and caring for future generations: motivations to promote biomedical research

In the previous chapter I discussed how aspects of distributive justice inform the bioethical debate and subsequently the debate surrounding experimentation on human subjects in biomedical research. To be specific, I have discussed how justice considerations inform protectionist policies, in terms of acceptable research risks. I have argued that biomedical research is an enterprise focused on helping people by trying to gain more knowledge regarding human physiology and in particular pathology, in order to find cures or treatments that can help to eliminate or battle disease. While the goals of the research are primarily informed by current problems and diseases, and some forms of research are therapeutic in nature, the non-therapeutic research practice is inherently *future oriented* in terms of its aims and benefits. Research is conducted in the present with the aim of ultimately *benefiting people in the future* in terms of prevention and treatment. In the introduction and previous chapter I have discussed the value of biomedical research and how the benefits and burdens are distributed. But so far, the question regarding benefits for future patients has been neglected. Moreover, the question regarding future generations and what is owed to them in terms of medical advances is neglected in the entire field of bioethics. In this chapter I want to investigate whether future considerations can play a role in motivating current generations to undertake research and advance medical care, and if so, how.

3.1 Bringing the future to the present

One of the requirements for ethical permissible research is that research must have social value for research risks to be acceptable (Rid, 2012, p. 205). Yet, clear concepts to determine this are absent from the current (academic) literature. Within this chapter, I would like to focus my attention on how concerns regarding future patients and future medical treatments could inform the goals and aims of biomedical

research. Besides, I want to investigate whether considerations regarding future generations can serve in determining social value of the research. In order to investigate this, I will turn to the available literature on intergenerational justice to help clarify some of the concepts when one talks about the interest of future generations and how these are connected (or, in conflict with) with interests of present generations.

Intergenerational justice has so far been neglected in bioethics. However, there are clear indications that future benefits are taken into account within the current experimentation on human beings. Therefore, I think it is legitimate to ask what these considerations regarding future generations are, and whether thinking about what is owed to future generations in terms of health care which can help informing the clinical research practice.

Before proceeding to inquire how intergenerational considerations can inform ethical decision making regarding experimentation on human beings, it is important to first analyze the current discourse on intergenerational justice. This will help indicate some of the issues that have intergenerational concerns, by looking at the different aspects involved when thinking about the interests of future generations, and how current generations are involved in the way future human beings will experience life, health and happiness.

I will also touch upon the difficulties that arise within this debate, such as the moral status of future generations, which demand different courses of action from present generations. In the second part of this chapter I will focus on how these insights in duties, obligations and rights inform clinical research, in particular the experimentation on human beings. I will argue that the obligations of the state to provide and promote health and happiness are sometimes in conflict with the interest of the research participants, and that an adequate balancing of the value of research and just treatment of the research subject are in order. I will argue that the conduct of research is noble and necessary, and reflects caring for both present and future patients, but that these interests should never outweigh the interests of research participants, reflected in the research design.

3.2 The problem of posterity

The domain of intergenerational justice has a very short history. While intergenerational fairness and sovereignty can be traced back to political thinkers at the end of the eighteenth century, philosophers picked up on intergenerational issues

as late as the second half of the twentieth century (Gosseries and Meyer, 2009). Under the accumulation of concerns regarding long-term consequences of climate change and the survival of social institutions, philosophers started to consider intergenerational issues. Most notably, John Rawls was the first contemporary political philosopher to pick up on this in his monumental work *A Theory of Justice* (1971), where he explicitly considers “justice between generations” (p. 259). For Rawls, justice between generations entails that there are certain moral duties that current living people owe to their descendants (Thompson, p. 10). As mentioned in the previous chapter, Rawls argues that there are ‘circumstances of justice’ (1971, p.), in which justice can either be conceived as ‘mutual advantage’- requiring that principles of justice equally advantaging all parties, or ‘impartiality’- which “looks only to the advantage of parties in an original position constructed so as to deny them knowledge of their actual prospective advantages and disadvantages under alternative principles” (Barry, 1989, 189). Both circumstances of justice which Rawls describes, cannot hold for parties that are alive at different places in time. Time operates unidirectional, which entails that only people currently alive can influence the living circumstances of their successors, making them either better or worse off. Future generations can’t return any favors. So, if justice is equated with mutual advantage then there can be no such thing as justice between generations (ibid., p 189). However, if justice is conceived as impartiality as illustrated by choosing fair principles, justice can be stretched to hold between generations, if people are ignorant of which position in time they will be. Rawls proposes a “motivational assumption”, in terms of stretching our concerns for immediate descendants in terms of wellbeing.

Until very recently, the discourse on justice (and ethics in general) focused on moral obligations between contemporaries, and agreed that moral significant acts can only happen between two identifiable parties. This was primarily so because the consequences of decisions and actions undertaken by human beings were affecting only those close to us, in both time and space. But, under the influence of globalization, the current boundaries of justice and obligation do not hold anymore, which demand new social institutions. Consider for example the debate on nuclear technology, which can be perceived as one of the most evident cases in which the interests of current and future generations are interrelated. Apart from the destructive possibilities of usage that accompany nuclear power, we are facing an equally important problem concerning radiotoxic waste.

These issues imply that for the first time in history, current generations wield a power to influence lives of prospective future generations - both human beings and nonhuman beings - and with this power comes a responsibility to make the right decisions. Much of these responsibilities can be related to what we think would be just. The question whether we have a duty towards future generations is not easily answered by a simple yes or no, many aspects are involved. One could for example argue that no, we do not have a moral duty to posterity, for the simple reason that posterity does not exist, and therefore cannot be said to have a claim to anything presently existing. The moral status of future generations is therefore different from currently existing humans. To structure the current discourse of intergenerational justice, which is spoken of in the moral language of rights, obligations and responsibilities, I will first look at objections to duties to posterity, followed by affirmations that yes, there is a compelling reason to think we owe something to our successors.

3.3 Future generations and the ability to care

One of the objections to duties to future generations holds that current generations are not able to care for their successors. The idea behind this is that if they would have an obligation, it would follow that they actually can, reflected by Kant's maxim *ought implies can*. So, if they are not capable to care, there is no such duty. The validity of this argument is informed by the lack of ability in predicting the future (foreseeing), which makes it all the more troublesome to make proper arrangements to safeguard interests of future generations. So, it follows that if it is not possible to predict the needs and interests of future generations, the necessity to preserve anything for them is weak. This contention however, can be questioned, which I will come to in the next section.

Another question one might ask is if future generations will miss what they have never known, such as wildlife, certain social goods or benefits. If not, present generations would not have to bother to preserve these things.

Another important objection holds that bringing about desired results through science and technology are counter-productive, an evident example being in infrastructure and logistics; the development of freeways has increased traffic jams. The intentions were good, but hasn't resulted in the desired goal. Likewise, the success of being increasingly able to sustain human life has resulted that people reach

a higher age, but a higher age is accompanied by more extensive medical needs, which has spiked medical costs.

These objections leads me to ask the question, can we care for future generations at all? Can we afford to spend time and effort in bringing about results which are accompanied by a new set of problems we can't anticipate? Is it beyond our capabilities to be expected to improve the prospects for generations to come? And perhaps most importantly, do future generations actually *need* our concerns? I contend that to a certain extent, yes we can. Yes, they do need our care and concern, and we should take posterity into account in deciding which science and technology to develop. To speak about health concerns, there will always be people suffering from diseases due to be unlucky in the natural lottery, not by *choice*. And those people deserve attention and care in order to have a decent quality of life.

The discourse on intergenerational justice can be divided into two parts: one focusing on instantiating policies with the aim not to harm future generations, the other on the promotion benefits (Partridge, 1976, 4). The first is what Partridge calls "the negative approach to posterity", informed by the view that it is far more difficult to provide benefits (as highlighted in the objections above), than it is to avoid identified causes of future suffering. Moreover, future generations should decide for themselves what their happiness constitutes, and make adequate arrangements in its pursuit, instead of being told what is important by present generations, and being denied freedom to choose. Rather, present generations are obliged not to limit their options of choice, having a *duty* to *refrain* from action. Considering nuclear technology again and the problem of radiotoxic waste, we have a duty not to put burdens on future generations for millennia to come to deal with radiotoxic waste that we've created. However, this implies a tension between the obligations we have to our contemporaries and to our successors, for the simple reason that we are in need of energy to fuel many aspects of our lives during our own lifetime, but not at the expense of the liberties of future generations. So a legitimate question might be, how far into the future should our obligations stretch? And what is the nature of these obligations, what do they ask of us?

3.4 Obligation, duty and responsibility

3.4.1 Obligations and duties

In the literature on intergenerational justice, the terms obligation and duty are used interchangeably by authors within the field. According to Partridge, there is however

a slight difference between both terms and their use in common language. He follows Brandt (1964) in characterizing the features involved in both terms. First, the use of obligation can be used in different contexts, being either social, legal and moral. These contexts may overlap, but can also be at odds with each other. For example, Partridge mentions that we could think of something as an “immoral law”, which is valid in legal terms, but not on moral grounds. Moral duties, Partridge contends, exist within a certain (linguistic) context, which reflect certain associations of the use of the words. Furthermore, there can also be an “extended” use of the term, which is on a higher level of abstraction, involving less connotation due to the fact that the situations in which the term is used have less in common (ibid, 12). For Partridge, following Brandt (1964), an obligation is a requirement of a service between two parties, in which one is to provide the service, and the other the recipient. The nature of the obligation is necessary, yet voluntary, because if not it would be rather coercion than obligation. Furthermore, an obligation is always in service of reaching a goal, and importantly, it is a *compelling* act to perform, rather than specifying what “ideally ought to be done”. It reflects a certain dignity, for failing to perform what according to the obligation is required, will reflect badly on one’s personal character, in the form of shame and guilt. Duties, on the other hand, arise in different (linguistic) context. A duty is more formal, which arises in performing acts connected to a certain professional station, like police official, or a lawyer. The duties that come with these professions are considered to be vital to the continued or to be reached welfare of the institution, and the person performing a duty is expected to act accordingly. On the more abstract level, Partridge contends that a duty need not be correlated to a specific profession or office, or to a specific organization. In that sense, on the abstract level the words “duty” and “obligation” are similar: to perform an act in such a way as a goal to be reached. And, similar to obligation, failing to perform one’s duty reflects badly on a person’s character. Interestingly, Brandt perceives of obligations and duties in the positive sense, and holds that negative duties, in the sense of a duty or obligation *not* to act such and such, is rarely observed in ordinary linguistic use. Partridge argues that although one might not phrase duties and obligations in the negative form, that does not rule out their existence. Rather, they are just not *phrased* as such, but in a positive way. It is here that the relation between duties and obligations and rights intersect. For if I could have said to have a duty not to interfere during a speech, according to Brandt it would be positively phrased in the sense that I have a duty to “let the other party speak” (ibid, 14).

Still, the analysis of linguistic uses of the terms obligation and duty might not be very fruitful, the contextual usage is far too narrow and arbitrary, while at higher levels of abstraction, the terms obligation and duty are almost identical. In that sense, the term 'duty' and 'obligation' can be said to belong from the same family of concepts, to which *responsibility* can be added. Partridge, following Feinberg (1966), argues that a responsibility is similar to a duty in the sense that they both hold a person accountable (or liable) for performing a certain act, placing a burden on that very actor. However, according to Feinberg, a responsibility is a goal, and leaves it open to the actor how to achieve this particular goal, it does not specify a means of obtaining it (Feinberg, 1966, 141). From the analysis Partridge offers, a responsibility can be perceived as more flexible, but also more stringent. It refers to a particular task, of which the one having the responsibility is liable should he or she fail to perform it.

3.4.2 Rights of future generations

Another way of thinking about intergenerational justice has a different starting point. Instead of asking which duties current generations have to future people, they start by questioning the nature of rights future generations have, which in turn pose duties on current generations. Again, these can be categorized in social, legal and moral terms. For the purposes of this thesis, I will focus on moral rights. Moral rights differ from legal rights in the sense that violating a moral right is not punishable by law. For example, breaking a promise to a friend does not imply prosecution, other than possible consequences for the friendship itself. To have a right, means to have a legitimate claim to restrict another party's liberties and have a say in how this party should act (Hart, 1955, 183). These rights-claims can be either general or specific, the distinction lying in the difference between dealing with specific persons and contexts (a right of a child to be protected from harm by its parents) and more general ones (the right to freedom of speech). Joel Feinberg (1973) continues by emphasizing that a further distinction can be made between positive and negative rights; a positive right referring to a positive duty on another party, a negative right referring to a negative duty on another party, in which positive and negative refer to doing something (act) or refraining from action. Rights can be in conflict with one another; a specific right might in some circumstances overrule a general right. John Rawls refers to general rights-claims as holding under conditions which can be considered "all-things-equal", whereas sometimes specific rights might overrule, the situation being characterized as "all-things-considered" (Rawls, 1971, 340-341). But general

rights can be in conflict with each other as well. The most compelling right then overrules.

Rights only apply in circumstances that are inherently social and controllable. If one lives in solitude on a uninhabited island, a language of rights cannot be applicable. Similarly, in situations that do not lie within human control, one cannot speak of rights. One cannot have a right to not having their house destroyed in a tornado. Insofar as situations being controlled by human beings, one can speak of rights. As Partridge writes: “[...] to have a moral right means that one is morally justified in restricting the freedom of others who are, correlatively, morally required to accept [restrictions upon their liberty], either by performing required activities or by refraining from other activities” (Partridge, 1976, p. 26).

In summary, the terms “duty”, “obligation” and “right” are considered to be interrelated in modern philosophical understanding, and can be phrased in the following manner:

- (i) If X has a duty to Y, Y has a valid rights-claim on X.
- (ii) If X has a valid rights-claim on Y, Y has a corresponding duty to X.

The opposite holds as well, concerning (i) if there is no person Y to have a rights-claim, person X does not have a duty, and (ii) if Y has no duty to X, it means that X has no valid rights-claim (ibid., p. 21).

Yet, there are circumstances in which rights and duties to not entail each other necessarily. Feinberg (1966) holds that we can speak of duty in the sense that we feel a *need* to perform an action, regardless of its reason. It could be anything. Furthermore, some moral duties are not owed in light of specific rights-claims of identifiable parties, but are required by general moral principles. I will say more about that later. Before I turn to moral duties that do not entail rights, I will first discuss the difficulties in applying a vocabulary of duties and rights to intergenerational relations.

3.4.3 Objections and limitations to a language of rights of future people

One of the objections against a theory of intergenerational justice is that considerations of justice can only hold between contemporaries (Meyer, 2008). This argument is based on the claim that future people, because they do not yet exist as persons, they cannot be ascribed any rights that could place duties on current living people. This implies that if they cannot be ascribed rights in the present, present

generations cannot violate them. Yet, this would mean that only rights that can exist in the present can be the only morally significant ones, and that the rights of people that will live in the near or distant future would not matter to present moral conduct. They can only be ascribed rights when they come into existence, and be entitled to anything that is available *then*.

A second argument against attributing rights to future generations holds that future people cannot have any claims on present goods or services, purely based on their non-existence in the present. Future generations are “merely potential” (Partridge, 1990), and a lack of claims entails that there can neither be rights.

A third objection holds that it possible and appropriate to ascribe rights to specific groups or classes of people, but only insofar as they consist of *identifiable* members. Future generations, by definition, do not have any of such identifiable members. Thus, it is concluded that no existing person can claim a specific right on behalf of future generations.

Another argument against an intergenerational justice holds that the “circumstances of justice” cannot hold between current and future generations. Barry (1989), following Hume and Rawls, observes that two theories of justice can be identified: (i) justice as mutual advantage, and (ii) justice as impartiality. Mutual advantage is specified as a contract between two identifiable parties: an agreement to move from some status quo to some new arrangement that is prospectively beneficial to both parties. Justice underwrites mutually advantageous cooperative arrangements, whether they arise from explicit agreement or not. Furthermore, these agreements arise out of self-interest, be it long- or short-term. Just terms of cooperation are those that would have been agreed upon by people trying to do the best for themselves (ibid., p. 367). Moreover, *reciprocity* is a core element in many in theories of justice (ibid., p 361). As discussed earlier, there can be no such thing as reciprocity between current and future generations. Only the present generation can affect the living circumstances of future generations, like past generations have affected theirs. So, if justice is equated with mutual advantageous cooperation, it follows that there can be no considerations of justice between generations. However, if justice is to be understood as impartiality, there can be room for an intergenerational theory of justice. I will come to this later.

In this section I have specified some issues regarding the ascription of rights to future people. Most of them are related to them being non-existent yet. However, these

objections do not inhibit present generations to include future generations within their moral community. In the next section I will discuss that there can be duties to future generations that do not necessarily require rights in order to be morally significant.

3.3.4 Supererogatory duties

In the preceding sections, I have discussed the relation between obligations, duties and rights and argued that certain rights entail duties, and vice versa. This raises issues for a theory of intergenerational justice, for if duties are *always* correlated with rights, it is to some extent problematic to speak about duties to future generations, since conceptually speaking, they cannot be ascribed rights insofar as they do not yet exist. However, there are duties that do not necessarily entail rights, which open up possibilities to include concerns for future generations within current morality.

According to Partridge, a category of duties that do not entail rights are duties of 'perfection', 'self-sacrifice', 'love' or 'gratitude' (Partridge, 1976, p. 29). These duties can be categorized as "duties of supererogation", which appears a self-contradictory term by meaning "duties beyond the call of duty". Perhaps these duties are best described as duties an agent places on him or herself, out of a compassionate sentiment of feeling the requirement to ascribe moral duties to oneself that do not hold for 'the average Joe'. As such, these duties include moral heroic acts, beyond the scope of duties and rights.

Other duties that do not entail rights are duties of self-fulfillment, which find their origin in the Aristotelian tradition that holds that a moral agent ought to seek knowledge and wisdom, develop his natural traits, purely from the perspective that these duties are required in order to attain the good life (ibid., p 31). This duty of self-fulfillment is not owed to anyone other than the agent himself.

Similarly, charitable duties do not entail rights. These acts stem from benevolence, and are motivated by a sentiment of sympathy, or a concern for humanity. One feels that it is his duty to perform certain acts in order to promote the good. In turn, beneficiaries should not feel that their rights are satisfied, but should be grateful for receiving something. They are not in any sense entitled to it by rights. An objection could be made by asking on whose behalf these duties are undertaken in the first place. If it can be answered by 'attaining to the *rights* of the needy', then a these duties do entail rights. Yet, the grounds for acting charitable can be informed by abstract moral principles. Furthermore, uncorrelated duties (e.g. duties that do not entail

rights) do not arise from voluntary agreement with others, they are not reciprocal in the sense that the beneficiary has to do anything in return for receiving a benefit, and beneficiaries are not identifiable as persons or specific groups.

How do these uncorrelated duties relate to future generations? First, from the above analysis it is clear they are not tied to posterity by rights-claims. But they are nevertheless duties to benefit future generations, or not to harm them, to the extent that agents possess the knowledge and capacity to bring about these results.

Furthermore, although we cannot ascribe rights to future generations for reasons mentioned above, which makes it difficult to place duties upon the present living (insofar as duties are connected with rights), there are certain features that allow them to be part of our moral concern. For one, present living can be certain that the human species will continue to exist. Second, it has become clear that the present living can influence the living circumstances of people in the future, and therefore they should be taken into consideration within current practices. Insofar as current living are able to prevent harm to them. It would be very bold to say that we have a reasonable belief that we can affect the lives of future people and the possibility to harm them, and conclude that they are excluded from our moral responsibility. Foresight and capability are important factors in determining moral responsibility. If we have the capacity to avoid foreseeable harm, then time in itself is not a relevant aspect to exclude other human beings from moral consideration, even if they live in the future.

It is also suggested that the continuation of human life at a level of high well-being places a duty upon current generations to secure the interests of the future. Meyer (2005) describes this duty as that current living people owe it to past generations who have benefited them to continue their legacy, out of respect, and should preserve these inherited goods and circumstances. Furthermore, they should refrain from inhibiting these future-oriented projects to continue, or influencing the circumstances in such a way that future-oriented projects cannot continue. This is not an obligation owed to the future, but to the past, yet the benefits are for the future.

Thompson (2009) discusses lifetime-transcending interests. Lifetime-transcending interests are interests that are not bound by a specific allocation in one's lifetime, but are "those interests that have as their subject matter events, objects or states of affairs that either existed before the lifetime of the person who has that interest or that will exist after her lifetime" (Gosseries and Meyer, 2010, p. 7). The idea is that through

consideration of concerns that succeeding generations will have, or the unfinished projects left behind after one has been deceased, or the legacy of ancestors, we can accept obligations to pursue specific projects. Thompson makes a communitarian argument that entails that members of a specific community have a moral interest to continue certain habits and institutions, which “enable legitimate lifetime-transcending demands to be made and fulfilled” (ibid., p. 8). This argument implies that through carrying on the legacy of predecessors, *trans*generational obligations are put upon the present living, to secure the conditions required for these lifetime-transcending interests to flourish.

3.5 A duty to conduct research?

In the preceding sections I have discussed the nature of duties, obligations and rights and how they can inform intergenerational moral concerns. In this part of the chapter I will focus on the implications of the analysis for the biomedical research enterprise. What is the nature of the enterprise of biomedical research? And how are these features connected to rights and duties of current and future generations? These questions will be the topic of the remaining part of the chapter.

3.5.1 The nature of rights and duties in research

In the context of research involving human experimentation, moral rights and legal rights are highly intermixed. The research subject that volunteers for participating in a study has a right not to be put in high danger on purpose and without their knowledge, and has a right to withdraw from participation if he experiences discomfort. He also has his rights protected by law, which governs the research involving human test subjects, by providing strict rules and guidelines to the researcher. In that sense, the right of the research subject not to be harmed on purpose places a negative duty on the researcher not to harm.

3.5.2 Improving the future of health care, a demand by justice?

Do future generations have a *right* to better health care? Under circumstances of scarcity this might not be possible, because following the principle ‘ought implies can’, if we cannot provide better care, than we are certainly not required to do so. In that sense, no one is required to provide people better health care. However, it does mandate a transformation of the duty, namely to do as much as possible to establish better health care, so people need to do whatever is possible to create circumstances that can possibly promote better health care (Partridge, 1976). A few objections are

in place. First, this presupposes that we are morally required to act benevolent while there is reason to think that beneficent acts from non-obligatory, moral ideals that are not obligatory for anyone to undertake. I think this is the case for medical research, while there are theories of justice that specify that there is a right to a basic minimal health care. Moreover, it is difficult to draw the line between which acts of beneficence are obligated, and which are supererogatory (Beauchamp, 2013). If we to say that the actions of researchers to expand medical knowledge with the ultimate aim of improving medical care are supererogatory, it would mean that they have the status of moral heroes or saints. Yet, medicine tends to the healing of the wounded and ill, and while the acts of tending to those who are in need are beneficent and stem from a motive of benevolence, they are not saint-like. Rather, they are morally required. In that case, it can be argued that we are required to provide the best care as possible. However, for many diseases we are unable to provide proper care. In order to improve on this research is conducted. In that sense, research is necessary and morally required, in service of attaining to the needs of people who are ill or wounded. Does this exclude future generations? I don't think so. While the benefits of research are aimed at those who will become ill in the future, it lies also in our best interest to do something about it *now*. We are not bound only to tend to the people who are ill now, but also the people who will become ill in the future. And this provides all the more reason to conduct research and improve medical care in the present, especially when current practices are not ideal and can be considered bothersome for patients. Yet, does justice then demand that we improve on health care for the sake of future generations? Or are there limitations?

An argument in favor of grounding research in demands of can be provided by looking at John Rawls' thought experiment of the original position. In the original position, people are choosing principles of justice behind a "veil of ignorance", meaning that they choose the principles and institutions that will govern their society without knowing where they will end up as citizens. This way, because the people in the original position are ignorant of their social status or personal circumstances, it is ensured that people will choose the fairest principles of justice. Moreover, according to Rawls, the criteria that will govern justice between generations have to be chosen in the original position (Rawls, 1971, p. 292). This is significant with respect that people in the original position are equally ignorant where they will end up *in time*, meaning they don't know to which generation they will belong. So, virtually, the interests of all generations will have to be considered in the original position, in order to come to the principles of justice and the rules they will live by. Curious to note here

is that people behind the veil of ignorance will choose principles and rules that will govern the institutions for their successors, are at the same time making provision for themselves (Partridge, 1976, p. 147). However, Rawls complicates his case by stating that the people in the original position belong to the *same* generation, but it is not clear *when* they will live. Therefore, a clause of what needs to be “saved” for future generations cannot apply, in the sense that saving for other will not be of advantage to them. Therefore, a *motivational condition* has to be added. Rawls offers this by a “heads of families” position, to the extent that heads of families are indeed concerned about their immediate successors in terms of advancing their welfare. This means that the provisions for the future are accomplished by a *caring motivation* of people in the original position. This caring motivation is shared by all generations, establishing a “chain-link obligation” in which justice holds among all generations.

From the preceding section it can be concluded that the interests of future generations are secured by the motivation of the present generation to care for them. The span of these motivational responsibilities then only stretches to immediate succeeding generations. For the purposes of this thesis I will not go into detail about the limitations of such motivations, because in the case where our present decisions can evoke harm to future generations (recall the example of nuclear waste), this motivational responsibility is inadequate. However, I think for the context of health care and biomedical research, this is a reasonable timespan to endorse.

So, according to Rawls, one of the demands of justice is that we save for successors. One might wonder what Rawls means by “just savings”. At lengths, Rawls seems more concerned with saving economic goods, rendering his theory of justice an economic one. However, by “capitol”, Rawls does not only mean the saving of economic goods, but also the preservation of knowledge, education, social institutions and culture, so as that future generations can enjoy these. While Rawls does not explicitly mentions health care, I think health care can be grouped under the social institutions Rawls discusses. It follows that *preserving* medical care is required by justice.

But what about *advancing* medical care? Early in *A Theory of Justice*, Rawls discusses “genetic endowments”, and hints that present generations need to “[...] take steps at least to preserve the general level of natural abilities and *to prevent the diffusion of serious defects*” (p. 108) (Italics added). I take this to mean that the prevention of diffusion of serious defects means that present generations are obligated to undertake measures to carry out research into these “serious defects” in order to

establish treatments to prevent them from occurring, or at least to treat them when they occur. In that sense, advancing medical care is a requirement of justice.

3.6 Other motivations

So far, I have not discussed the legitimacy of Rawls original position. If the reader would like to refute my argument that justice demands that we undertake research in order to advance medical care, I will here specify other moral grounds for engaging in research, that are not grounded in justice *per se*.

Throughout this chapter I have discussed the nature of moral duties, rights and obligations. I have discussed that some duties entail rights and vice versa, while there are also duties that do not entail rights. The latter group of duties are the ones premised upon abstract moral principles or can be understood as duties of self-fulfillment, need-fulfillment and charity. Partridge contended that these moral duties are “supererogatory”. I do not think such a strong term applies to all duties that do not entail corresponding rights. Supererogation is behavior that can be equated with moral heroism, or saint-like. I don’t think that helping someone *in need* is a supererogatory act. Rather, we are obligated to help someone in need if we possess the capability and means of achieving this. This also means that we ought to help someone who we will not know in the future, because excluding someone on grounds that they will live in another generation will not do so in and of itself, as discussed in sections above. The bottom line is as follows: if we can be certain that people will live in the future, they will need to be included to our moral concern.

3.6.1 A transgenerational polity

According to Jenna Thompson, people are never part of a single generation. They live at a specific time, but they do not conceive of themselves as bounded by that time. Rather, they are born into a specific society, which has certain social institutions and habits, inherited from predeceasing generations, and in turn their own adopted policies will affect future generations. Moreover, people “regard themselves as inheritors of a history and a political tradition” (Gosseries and Meyer, 2009, p. 25). This historical outlook is crucial for the way people conceive themselves, because it connects past, present and future with each other in terms of deeds, achievement and aspirations. In carrying on a legacy, or improving on certain ideals, people express their respect for past generations and concern for the future. Their intergenerational relationships are bound by obligations. According to Thompson, individual interests are not limited to concerns that are bound by a specific lifetime, rather, the ideals

individuals have are informed by their hopes and dreams for their descendants, which in turn shape their conduct. Similarly, the projects and traditions they pursue are not meant to be abrogated when they deacease, but are to be passed on to their successors. In that sense, they care about their legacy and what will become of it after their lifetime. These concerns are grounded in a communitarian theory of justice, insofar as that ideals, institutions and habits are informed by shared values within a community. Communities share a conception of the good, and the actions of individuals are premised upon this communitarian perspective. In that sense, the obligations are shaped by past ideals that extend into the future. This could also be said for the medical “community”. The medical community shares the value of helping the ill and wounded, and provide the best possible care. While we are able to provide care to many illnesses, there are still numerous diseases left to await their ‘best possible treatment’. This ultimate aim to treat and prevent diseases is shared transgenerationally, and informs the duties or obligations that one specific generation of a community owes to his ancestors and successors. So, the duty to provide good medical care, necessarily entails that the medical community is required to continuously evaluate en improve on current medical practices. If they wouldn’t have such duty, than the current medical techniques would still be those of ancient times.

3.7 Conclusion

So far, we can conclude that there are grounds other than justice for engaging in biomedical research out of obligation. The advantage of the position as presented above is that a communitarian perspective is not limited to tend to the obligations of a specific group, such as doctors or researchers. Also the research participants can adopt such a communitarian perspective to support biomedical research.

What both views have in common is that they both require agents to imagine ‘to walk in another’s shoes’. Rawls original position does this by asking people to consider “What if you were to...?”, “How would you like it if...”, and use them to generate requirements for just social institutions (Barry, 1989, p. 369). This approach denies that agents act only out of self-interest, and that the theory of justice seeks to reach agreements on principles that cannot be easily rejected. The view put forward by Thompson similarly asks people to consider their obligations with respect to shared communitarian ideals. These obligations are embedded in relationships that fulfill the requirements of these shared ideals, and are held between generations, past as well as future. Moreover, Thompsons theory holds that moral demands can be made to

successors by carrying on a legacy, or take responsibility for the deeds of their predecessors.

Both approaches have important implications for the obligations to conduct research. Interestingly, it is not clear from the analysis whether we current generations are obligated to preserve and advance medical care by means of clinical research on behalf of future persons. It can also be argued that the research enterprise is directed at making improvements in the future, but more as an obligation to current living people, not those who are yet to come. Consider for example that a physician treats numerous patients, and for all these patients the current treatment is less than ideal, as is for example the case in chronic illnesses like rheumatism. Witnessing the struggles of these patients, a physician might become motivated to conduct research as an obligation to these current patients, to attempt to unravel what causes rheumatic disorders, so the patient that will come after them can hopefully be cured, or at least be treated better in keeping them pain-free. In that sense, it is not owed to the future to improve health care by conducting research, but an obligation to current living people. It will be more likely that future generations will benefit from research outcomes, but the incentive to invest in research are the current issues faced today. In that sense, we owe it to current patients that their future companions will be helped more adequately.

In this chapter I wanted to investigate whether future considerations can play a role in motivating current generations to undertake research and advance medical care, and if so, how. To answer this I have considered whether future generations have a right to a better health care than currently can be offered. Philosophical considerations make it difficult to assume that people that are not currently living have rights, in the sense that they place burdens upon the living in fulfilling their duties to meet that right. Simply because future generations do not yet exist, they cannot be ascribed rights as persons. Yet, this does not necessarily mean the current living do not have obligations to future generations. For example, because present living people can be fairly certain the human species will continue to exist in the future, their not yet existing does not provide enough objection to excluding them from our moral consciousness. We can be certain there will be people living fifty years from now, who will resemble us more or less in terms of their biological make-up. Therefore, we can also be certain they will have certain needs that are similar to ours, and that they will face similar issues in terms of health and disease. And exactly for this reason, I think it is important to improve on extending knowledge and make

attempts to improve current medical practices in order for future patients to be helped more adequately. The alternative not to invest in clinical research, and not to improve on current medical practices that are not without side effects and burdens, would deprive them. If it is not owed to them, then it is owed to current patients who still suffer on a daily basis. But it needs to be kept in mind that current suffering patients are treated with dignity and respect, and while their outlook might be hopeless and they can't be treated by current techniques, this is no reason to experiment on them without critically assessing the burdens that are involved in research.

This conclusion still leaves some questions regarding how interests of future generations are considered in the ethical decision-making regarding the permissibility of research, and which trade-offs are made. In the next chapter, these considerations are investigated more extensively. Especially the criteria that are evaluated and how (some of) these are related to the future will be focused upon, in order to answer the main question under which circumstances it is allowed to experiment on humans when the participants that undergo certain medical interventions do not have any prospect of direct benefit.

Chapter 4

The dynamics of ethical review

In the previous chapters I have discussed concepts of justice and intergenerational justice in particular and how these theories can serve as tools for thinking regarding ethical research, and about the issues of human experimentation. I have argued that biomedical research that does not have the aim to provide benefits for current participants, it is crucial that the results of the study should benefit future generations to be ethically permissible. Moreover, in order to experiment on humans research has to have a social value to be permissible at all.

In this chapter I will take a closer look at ethical review of biomedical research and experimentation on human beings. In the first part of this chapter I will discuss the role of Medical-Ethical Review Boards, who are delegated with the task to evaluate experiments to protect the interests and rights of research subjects. Alternatively, the moral assessment would be delegated to researchers themselves, or to participants. These options are inherently flawed, researchers can overestimate their research, while for participants the possible risks involved are not clear, impairing them from making an informed decision. In the second part of the chapter I will take a look at the criteria that are evaluated by ethical review boards. This second part will be to some extent informed by conducted empirical research, in which interviews were conducted with members of Dutch ethical review boards, to gain insight in the review procedure in practice.

The motivation for choosing the method of empirical research is as follows: while part of the research protocols are publicly accessible through online portals, it is not specified whether these submitted protocols were approved or disapproved to be undertaken. Annual reports by the Central Committee for Human Research (CCMO) in the Netherlands provide insight in how many protocols were assessed throughout the Netherlands, including percentages of approved and rejected protocols, but do not specify the specific protocols themselves, only the topic of the field the protocol covers. Similarly, ethical review boards publish in their own annual reports how many studies they reviewed and approved or rejected, but the neither the topic of the research protocols nor the reasons for approving or disapproving a protocol are specified. So, the option to analyze in retrospect was not possible for the reasons specified above. Descriptions of procedures and assessment criteria do not suffice in

order to gain insight into how these review boards actually operate. Instead, during these interviews the candidates were asked which criteria are involved in assessing research protocols. The questions ranged from general ones as to how the review procedure takes place, to more specific questions regarding which ethical criteria are evaluated during the review process, and which possible reasons there are for rejecting a research protocol.

Before I proceed it is important to point out that the empirical research carried out for the purposes of this thesis should not be viewed as a fully-fledged substantive account of what happens during ethical review. This cannot be the case because for such an account it would be required to conduct extensive interviews with *all* members of *all* ethical review boards in the Netherlands, including attending numerous meetings of these boards to observe what happens during ethical review, and what happens afterwards. While such an approach would be interesting and provide invaluable deep insights into the dynamics of ethical review, it would be too time consuming to be carried out for the scope of a master's thesis. Instead, the statements and analysis provided in this chapter should be perceived as *explorative*, to get a glimpse of the reviewing process in practice, the criteria that are assessed, which values are involved and how these values inform ethical decision making.

4.1 Independent Ethical Review

4.1.1 Ethical Review Boards

In the Netherlands, Europe, and the United States, as well as many other countries, researchers who desire to conduct experiments on human beings have to appeal to institutionally recognized Medical-Ethical Review Boards. Most of these review boards are part of (academic) hospitals or other medical institutions, and are established to protect the interests of research subjects by means of independent review.

While human experimentation has been conducted for centuries, ethical review boards have not been around for that long. This does not mean that before the second half of the twentieth century people were not concerned about human experimentation, but following certain explicit misconduct of using human beings as research subjects, the research enterprise has been under scrutiny. As stated by some authors, research ethics was “born in scandal” (Emanuel, Wendler and Grady, 2008), meaning that ethical guidelines were developed in response to these controversies. Public concerns have generated the development of specific standards in order to

govern human experimentation. The first step towards institutional review boards was made during the Nuremberg Trials in 1947, following the second world war, where it was decided that research on human subject could not be performed without the explicit voluntary consent of the research subject, research subjects could withdraw from a research study at any given moment they felt the need to abrogate their participation, that research on human subjects can only be allowed if the sought after knowledge cannot be obtained in other ways, risks to research subjects should be minimized, and the expected benefits should outweigh the risks. These principles are part of The Nuremberg Code, the first international document providing guidelines to the ethical conduct of research. Subsequently, over the course of the past decades, other guidelines have been developed, such as The Declaration of Helsinki (1964) and The Belmont Report (1979). Under influence of the changing methods of doing research, the Helsinki declaration has been revised several times, most notably in 1975, when the guideline was added that research protocols should be reviewed by an independent group who would judge whether the research was permissible. Nowadays, these groups are known as Institutional Review Boards or Ethical Review Boards. In the Netherlands, these review boards have been formally active since the early 1980's.

Ethical review boards are composed of a heterogeneous group of individuals, who possess certain expertise required for adequate assessment and evaluation of research protocols. In the Netherlands, the five required disciplines are: one or more clinicians/physicians, lawyers, methodologists and ethicists and a representative research participant. This last member is required to evaluate medical scientific research exclusively from the point of view of the participant. An additional required discipline to evaluate research regarding medical drugs is a clinical pharmacologist and/or a (hospital) pharmacist.

4.2 Principles of Research Ethics

As mentioned throughout this thesis, particularly in chapter 1, the biggest challenge of all clinical research that involves experimenting on human beings is to avoid participants from being exploited. Especially in the case of non-therapeutic research, the aim is to gain generalizable knowledge that can be used in improving medical practices, including treatments and diagnostics, but also in terms of prevention. As was argued, in order to obtain this knowledge, it cannot be avoided to conduct experiments on human beings, because no artificial developed system can include every biological aspect of the human body. And in order to fully investigate the

mechanisms underlying certain pathologies, a holistic approach needs to be taken, instead of trying to isolate or reduce the complexity of the entire system into a laboratory setting of *in vitro* studies. Because human beings are needed within the research process they are at risk of being exploited, because they carry burdens for the benefit of others. And exactly this risk of exploitation is what is at stake. As was argued in the second chapter of this thesis, exploitation occurs when the interests of participating research subjects are neglected, purposefully harming them. The very purpose of research guidelines is to protect research participant of exploitation, or at minimize the possibility. Recall from chapter 2 that in general, a participant is exploited when he only serves as a means to an end, in the Kantian sense, or, when a participant is unfairly exposed to exceedingly high research burdens, such as excessive risks or exceptionally invasive research methods. This last conception of exploitation is connected to the concept of distributive justice as discussed in chapter 2, which concerns the fair distribution of burdens and benefits. To minimize the possibility of exploitation, certain principles have been established that have to be fulfilled.

Three principles of research ethics can be identified that inform our understanding of ethical research (Smith Iltis, 2006, 4):

1. Respect for persons: meaning that the judgments of competent persons should be respected. If one is not capable of judging he is to be protected to a greater extent.
2. Beneficence: ethical treatment of persons requires that they are protected from harm and their wellbeing has to be secured.
3. Justice: the distribution of benefits and burdens needs to be conducted fairly. This means that a person should not be placed under excessive burdens and whenever one is entitled to a benefit one is to receive it.

In addition to international guidelines, the Netherlands has developed a law in order to formalize the ethical conduct of research (wet Medisch-wetenschappelijk onderzoek met mensen, 1998). This law includes many of the aspects specified by international guidelines, and is too lengthy to include in this thesis. The important point about this law is that researchers that do not act in accordance with the law are punishable, and to provide a legal ground for the protection of research subjects who participate in medical-scientific research. Essentially, the law applies when the integrity of research participants is infringed, for example the withdrawal of body tissue or the administration of substances that are not a part of a standard therapeutic intervention. Before research may begin, a positive judgment has to be given by a

recognized ethical review board, if a researcher starts with experiments before approval he is punishable by law.

Ethical review consists of several criteria. The most difficult criterion to evaluate is the possible *value* of the research. If succeeded, the results of the research can mean a tremendous step in improvement for patients suffering from a specific disease. These benefits can be both be short or long term, benefiting both current- as future generations of patients, depending on the nature of the disease. On the other hand, sometimes a study is only scientifically interesting to investigate, with the aim to publish something. At other instances commercial interests are at stake, for example when patents of medical drugs are close to expiration.

The overall goal of an ethical review is to ensure that the research protocol meets the standards set by the law and additional guidelines that govern research on human beings. Yet, it is not easy to find a balance between criticism and meddling. Committees might try to appeal to paternalism in the sense that they try to take the position of the researcher. Or, in some cases a committee member thinks he knows the research content better than the researcher. Still, many research protocols are approved, sometimes after changes in the research design. Why this could be the case? According to de Beaufort (1986), one possibility is that review boards ignore details due to the limited time they can spend on examining a research protocol. Another reason could be that review boards only deny research of which it is very apparent that the research is impermissible. Other reasons could be that committee members are too generous with respect to the activities of their colleagues, especially in local affairs. Or, researchers conduct research with very high standards, in the sense that they would not design unethical research protocols. Possibly, legal aspects are working preventively. In practice, committees usually do not vote whenever opinions are divided, but continue discussing until consensus is reached. Perhaps this is a better method than appealing to voting, for it could easily occur that outnumbered parties still have legitimate concerns. In case review boards disapprove a research protocol, the researchers involved can appeal to higher chamber or umbrella organization, if they disagree with the committee's negative judgment. In the Netherlands this umbrella organization that supervises local review boards is called the Central Committee for Human Research (CCMO), which operates directly under the Secretary of State. This committee also has a coordinating and consulting task, and evaluates research protocols that require vulnerable groups such as children or the mentally impaired.

4.3 Criteria of ethical review

The literature on research ethics specifies principles which have to be fulfilled in order for research to be ethical at all. These principles however, are only of limited help in practice. Sure, benefits and burdens have to be distributed equally, but who shall decide what is fair? Different theories provide different answers to that question. Trying to meet one goal might likely undercut another. In order to gain insight in the reviewing processes in practice, an empirical study was conducted by means of interviews with a number of committee members of different local committees. In general, ethical review criteria to be assessed are the following (ibid., p. 167):

- (i) Research design with respect to scientific validity;
- (ii) Scientific value of the research study;
- (iii) Clinical value of the research study;
- (iv) Risk-benefit ratio of possible benefits and burdens for the research participant; and
- (v) The manner in which the interests and rights of research subjects are secured, primarily by means of the information provided to the participant and the consent-procedure

I will consider each point in turn in order to sketch how the review process is conducted in practice.

4.3.1 Research design in terms of scientific validity

In order for a research to be permissible, all of the criteria should be considered equally and be balanced. In the reviewing process, the first criterion that is evaluated is the scientific design of a study, in terms of methodology. A valid research design is necessary for a research study to be ethical. This is the case because biomedical research is in essence of instrumental value to the medical practice. Its goals are to expand medical knowledge by means of the scientific method, in order to improve that medical practice. The ultimate aim is to collect generalizable knowledge, which can be used to gain more insight to certain mechanisms in relation to a disease, with the aim to benefit patients in the near and distant future. In order to produce and obtain reliable generalizable knowledge, a valid scientifically correct design is fundamentally required. If such design lacks such validity, it has no scientific value and even no social value, because no one will benefit from it. And if no one will benefit,

it is unjustified to put burdens on -sometimes vulnerable- groups of participants. For a study to be scientifically valid, its design needs to yield statistical valid data, as well as the research methods. This means that the size of the population and the inclusion criteria produce unbiased and reliable outcomes in answering the research question(s), and that adequate statistical analyses can be carried out. The results have to be useful to answer the research question, and to address the health problem in general. Another point is that the study must be designed in such a way that the objectives can be practically feasible regarding the environment of conduct. The methodologist member of the committee has the task to determine whether a study has a valid design, and if not, he or she is charged with making adequate recommendations that ultimately improve the research design in order to achieve scientific validity. In some cases these are minor points, for example adjusting the number of research participants, or using another statistical test. Yet, sometimes, large adjustments have to be made, which also include adjusting the methods of research or the research question in general.

In practice, if a study does not have any scientific validity, ethical review boards tend to not even look further. In the words of one candidate: *"If a research design and research question are not good, then you don't even need to take the protocol into consideration, by manner of speaking"* (candidate no. 1). As such, the first screening focuses on scientific validity and value. If a protocol is very unlikely to produce generalizable knowledge or is badly designed, the review board will either give a negative judgment, provide feedback in order for the researcher to improve, or advises the researcher to withdraw his protocol.

4.3.2 Scientific value

The scientific value of the research study is often reviewed by asking whether a research study will provide a step forward in medical knowledge, if it will bring something new, or whether the results are only marginal improvements in current knowledge. It is a very important step in the review to determine acceptable burdens and risks can be carried by the research participant. For example, if a research study is very fundamental, the range possible risks for the individual participant are less acceptable than in when a therapeutic benefit is ensured for the participant. Of course, in non-therapeutic, these benefits cannot be ensured, and therefore in order for the research to be justified the range of the step forward in producing medical knowledge regarding a specific mechanism involved in a disease is an important measurement.

Scientific value needs to be contrasted from social value, while both are loosely correlated. I will say more about this relation in the next sections.

Important to note is that for some candidates, the scientific value of a research protocol is subordinate to the clinical relevance of a study: “*The scientific knowledge in the medical field is instrumental in relation to the clinical relevance or the therapeutic goal. It is not a goal in itself, physiological knowledge of medical science is not a goal for its own sake*” (candidate no. 10). Others hold that the clinical value is not easily determined, especially when research is more fundamental and aims at answering a scientific question: “*There are a number of aspects of doing research. The first objective is to advance science [...] A lot of research is conducted with healthy volunteers in which immediate clinical benefits are not so important*” (candidate no. 9). However, research has to be innovative, the mere repeating of already conducted research studies is impermissible: “*Scientific value is always taken into account and is very important for the assessment, it has to be very plausible. If the committee thinks that the research protocol is only a repetition of previous gained knowledge in the past (which we already know!) or intended for the sole purpose of making money, then anything is too much. The research has to serve an important use*”. (candidate no. 7)

From the statement made during the interviews, scientific value is essential in determining whether a research protocol is given a positive assessment. Researchers have to specify the relevance of what they try to investigate, and why it is important. Gaps in current medical knowledge are an essential component in the justification of burdens.

4.3.3. Clinical value

In non-therapeutic research, especially more fundamental studies, clinical relevance is sometimes difficult to determine, and therefore to assess during a review. The clinical relevance is often voiced in statements of what a research will yield. Not only in terms of scientific medical knowledge, but more concretely of what the results might actually contribute with respect to treatments for future patients. In more advanced studies, that for example try to compare two different methodologies regarding treatment, the expected improvement is essential in determining clinical value, compared to what can be offered by regular practice. For example the simplification of diagnostic methods that are invasive and bothersome, such as endoscopy in colonoscopy, are methods that are very disturbing for patients.

Attempts to gain insight in whether such methods can be replaced by less invasive techniques such as MRI, are encouraged. Clinical relevance is an important component, for many candidates the most important criterion in justifying burdens for research participants. This is because the improving medical practice is the ultimate aim of biomedical research. In determining clinical value, the population size that will benefit from the research result is also important, as well the degree of what can be offered by current practice. Again, the translation process of research results into medical improvement is complex. Especially for early stage, fundamental studies, the clinical relevance might not be apparent. Yet, it is still valuable because the knowledge that results can yield can inform additional research goals that aim to improve medical practice. But still, the process is laborious and often takes a lot of time, not to mention that it is often uncertain whether translation will happen at all.

In general, studies that are of little clinical relevance are studies that investigate a marginally interesting mechanism, which only brings benefits to very few people, or in case of medical drugs result in a marginally improvement for the market, or sometimes even a suboptimal product that is less valuable than the ones already on the market. But there is a danger here. Especially regarding diseases that affect small populations, the so called “Orphan Diseases”. The population size suffering from a specific illness can be very little, but this does not mean that they should be excluded from research efforts altogether. That would be unfair, considering their disadvantaged position in society, and had bad luck in the natural lottery instead of their issues resulting from choice. I contend that population size can be important in determining clinical relevance, but that in case of orphan disease, special considerations have to be made. In these cases, utilitarian trade-offs, which are informing a huge part of ethical deliberations regarding the justification of research burdens, cannot apply. That would mean they such minorities would always be skipped in setting of research priorities, leaving these populations worse off while the majority might enjoy benefits. A better factor to consider is the impact of the disease on patients suffering from certain illnesses, and the likeliness of improvements aimed at by the research.

4.3.4 Risk-benefit ratio

The most important component of ethical review is risk-benefit assessment. In the risk-benefit analysis, the benefits of the research in terms of scientific value and clinical value come together, and are weighed against the risks and burdens for research participants. Burdens and benefits are inherently correlated to each other.

Before I go into detail, it is important to note that biomedical research is never without risk. But the risks and burdens of research are proportional to benefits in terms of ethical review. Especially in fundamental research, if potential risks are high and the clinical relevance cannot be directly identified, the scientific and social value are important factors regarding the justification of research risks (Emanuel, Wendler and Grady, 2008, 129). In order to be permissible, the benefits of research always need to outweigh the risks. If the balance is askew, protocols are either formally rejected or need to be rewritten entirely, to either reduce the risks, or increase the benefits.

Important in assessing the risks of research are the types of risk (physical, psychological, social), probability and magnitude (ibid, 129). During the review process, either pharmacologists or physicians are charged with the task to assess the potential risks involved in a research study, by reviewing the mechanisms and subsequent nature of the substance that the research tries to investigate, either by looking at empirical data obtained in animal models, in vitro research or related human trials. In general, research risks have to be limited to a minimum, reflected in the research design. To reduce risks, researchers often have to be very careful in their choice of participants and research methods.

From the conducted interviews, it appears that risks involved in research are evaluated differently in light of the kind of research participant and their living context. For healthy volunteers, the general assumption is that for the very fact that they are healthy, some research risks are more justified when compared to vulnerable patients. In some cases the decision to participate in a study relies primarily on the good judgment of the healthy participant. *"You always look at the vulnerability of the research subject. A healthy volunteer who is willing to participate in human biological research- that does not have any current therapeutic effect or possible distant future- someone who wants to participate on a voluntary basis, then we [as a committee] are prepared to approve of a muscle biopsy or reside in a cold or hot room for longer periods of time, or whatever. They should decide for themselves [...] One needs to be well informed and obviously the research should not be torture, but it is mainly their choice"* (candidate no. 7). However, consent does not fundamentally justify research risks. It can be doubted that risks are permissible because a researcher has obtained the consent of the research participants. This also holds for research risks that are very high, and the value of the research is also high. This suggests that consent is not sufficient for acceptable risk in research. This position is also put forward by Rid

(2012): social value determines whether it is justified to expose subject to risks; “[...] risk-benefit evaluations should fundamentally revolve around the relationship between the risks that individuals incur for purely research purposes and the potential social benefits of the research, with consent becoming a necessary, but not a sufficient condition for exposing participants to *substantial* risks of harm” (p. 204). Rid argues that the social value of research means that it has potential to improve health and wellbeing. Yet, this is difficult to determine. Early phase research does not have immediate improvements, rather, these improvements are distant in time.

Risks and benefits are assessed both individually and in relation with each other. The general opinion is that they are correlated with each other. The more “important” the research (population size, severity of the disease, how much/little is known about it), the more justified higher risks are. Currently, there is no literature that looks into social value of research in this manner, but it appears that ethical review boards reason this way. The higher the benefits for (future) patients, the more risks are allowed. Conversely, if risks are less likely to occur or are not that severe in nature, potential benefits may be less uncertain (ibid, 129). Yet, the risks must not become unacceptable. But it appears that at the same time, there is no normative threshold level of what level is acceptable, each case is considered individually by weighing the scientific value, social value and possible risks and harm to the participant. The circumstances and quality of life of the participant form an important component in this too. The question is whether a normative notion is necessary for adequate ethical evaluation of research proposals. I contend that such a notion is desirable. This does not mean that a quantitative calculus has to be endorsed to determine the balance of risks and benefits, but a shared understanding of what counts as permissible and what not is necessary to overcome the risk of appealing to purely subjective judgments. This can be achieved by adopting certain standards that are informed by empirical information regarding the clinical aspects of each type of disease. But a settled framework can be difficult to achieve. Utilitarian considerations of maximizing overall benefits and a cost benefit analysis are morally controversial, primarily because benefits and risks cannot be quantified that easily.

4.3.5 Informed consent

Another important component of the review process is the informed consent procedure. *“The committee pays attention mainly to two aspects: the balance between burdens and benefits to patients or to science, which refers to whether it can be justified at all to ask the patient [to participate], and second the extent to which*

patients are given the chance to say that they do not want to participate... that they really have a choice given the information they receive and that they have no impediment to make a choice" (candidate no. 11).

What the candidate refers to the latter mentioned aspect is the consent procedure. In order to make the recruitment ethical, the participant has to be informed about what awaits him when he joins a research study. Each participant receives a PIF document (proefpersoon-informatieformulier) which specifies the research aim, methodology and the risks and burdens. This procedure is meant to give the participant some authority to decide whether he or she wants to participate based on an informed decision, rather than faithfully and unconditionally trusting the investigator or physician. Recruiting participants without their consent is morally deplorable, and to ensure that the patient can give permission in full authority, informed consent is a very important aspect for ethical research procedures. It shows respect for the participant as a person, capable of making informed decisions and pursuing his own goals and values.

Informed consent has been a topic of debate over the past decades, critics arguing that the information to the participant is often too difficult to understand, or that the circumstances of the patients are constrained by suffering from a disease. Their disadvantaged position will impede them from making a rational decision. Moreover, these patients they are less free to make a decision compared to healthy volunteers. Therefore, ethical review boards pay a lot of attention to scrutinizing the information supplied to the participant. Pressure and misconceptions are absolutely necessary to avoid in obtaining valid consent. Although I have to note that in practice, informed consent might be more difficult to obtain than can be imagined: *"As a committee, we can only judge the written patient information document, we are not aware of what happens in practice. What the patient is told, if something is explained and what is told in addition to the supplied information, we have no idea what the context of the situation is"* (candidate no. 11).

The danger of disclosing too many technical details, resulting in overwhelming the research participant or conversely, to provide less information than necessary, resulting into deception of the participant, are given special attention to ensure that participants are very aware of their rights, and can either refuse or decide to withdraw themselves during the research process. Especially in non-therapeutic research that does not provide direct benefit for the participant, the disclosure of

risks and burdens, and what these could mean for the situation of the participant are even more important to explicitly mention before the research commences.

To summarize, in general, scientific value and clinical value determine which risks are acceptable for the research participant. If the risks are high, then the research has to be very promising in either establishing knowledge regarding a specific disease, or an improvement in terms of diagnostics or treatment. Moreover, the clinical value is bound by what is currently known about a certain disease or condition. If there is very little known, review boards are likely to allow higher risks for participants.

4.4 Time-related aspects

In addition to the standard criteria of review, this empirical study also focused whether there are time-related aspects evaluated in determining the permissibility of research. Especially in non-therapeutic research, one can imagine that a study that strives to achieve results applicable for clinical purposes within a relative short timeframe might receive preference over research that is more fundamental, and the clinical application is in the distant future. In a nutshell, the aim of addressing this issue was to gain insight in whether ethical review includes timeframes in their judgment. For example, it can be imagined that research studies pursuing fundamental, more scientifically oriented questions will gain knowledge that will take a longer amount of time to translate into clinical application, therefore putting burdens on current research participants who will not be able to witness this translation. The question is whether this is fair to them at all, and if so, when and why this can be justified. I hypothesized that in these cases, the interests for future patients and future medical must be at heart of making the decision to permit or deny a research study. Yet, it turned out to be that time related aspects are not considered in this sense at all. Indeed, the most important reason for conducting medical research is to improve medical practice in the future, but a specific timeline when this improvement ought to happen is not considered at all.

“These aspects are very difficult to predict. The possibility of misjudging this is huge pitfall... How wide is the horizon? That does not really matter... it is very difficult to predict when something becomes regular medical practice,... if you are staring to philosophy when large groups of citizens will benefit from certain results, that does not play a role. What happens is that an insecurity is brought into discussion where you cannot get away from anymore.” (candidate no. 8)

"It does not often occur that the committee remarks 'this will take too long'"(candidate no. 9)

"Time does not influence the decision making in that manner. If a research study wants to monitor on the long run, it is often a question whether it is logistically feasible" (candidate no. 7)

"Most of these things are not quantifiable. It would mean that you take an advance on something you don't know yet. Often you just don't know, first it has to be determined how something works [before anything can said about clinical application]"(candidate no. 10)

It appears that time related aspects correlate with phases in research. Time-related estimations are uncertain and often impossible to determine at all. One candidate mentioned the case of gene therapy:

"For example gene therapy, when this field rose in the late 1990's, everyone thought we had found a true breakthrough... We will just insert a few genes and it is done. But that has been a huge disappointment. Everyone thought, this will accumulate very soon"(candidate no. 8)

Still, I think the relation between fundamental research and a possible clinical application has to be likely. It does not have to be a direct relation, but there has to be a certain correspondence. Research studies involving human experimentation that only serve a purely scientific purpose are not desirable and easily justified. For many committee members, purely scientific research studies that serve no clinical purpose in any sense, not even in the far future, should be discouraged. Again, this relates to the fundamental ethical justification biomedical research, it is aimed at improving medical practice, by sometimes taking a detour by generating knowledge relevant in order to treat a specific disease, but essentially this knowledge is purely instrumental, it is not a goal in itself.

An indirect time-related consideration is increasing attention of translational research. Translational research aims at translating basic scientific knowledge into clinical applications. To me, this seems an effort to decrease the time span of translating knowledge into practice, to enhance human health and medical practices in a shorter amount of time than would be needed if these efforts weren't made. For this reason, the time questions considered during this empirical research can be placed within this context of translational research. However, translational efforts are

not a criteria for ethical review boards to consider, and therefore it might be possible that time horizons are not considered in determining whether a research proposal can be approved or not. Ethical review restricts itself to determining whether the given research proposal is sound and is needed to be investigated. Placing the research protocol in wider ethical considerations regarding research priorities is not part of their responsibilities.

4.5 The interests of future patients in ethical review

So far, I have focused on which criteria are evaluated in assessing a research protocol, and what important arguments are for either approving or disapproving a research protocol. I have not explicitly or extensively focused on the question of how concerns for future generations are involved within this process. However, the very nature of non-therapeutic research focuses on benefiting future patients, not the individual research participant.

The concerns for future generations I think, are primarily reflected in the clinical value of a research study, and to a lower extent in the scientific value.

“By conducting research with a few people [researchers] try to extend [the established knowledge] to hold for people in the future, whether or not with the same disease, [in order to] benefit them” (candidate no. 7).

Nearly all respondents of ethical review boards responded that the interests of future generations are always considered, in both therapeutic and non-therapeutic research. These interests are just not formulated explicitly within time horizons. The combined factors of scientific validity (generalizable knowledge), clinical value and scientific value in turn determine whether a research study is first even beneficial for future practices at all. If no generalizable knowledge can be obtained, then no one is able to benefit from it in the near or distant future. Secondly, the scientific value understood as the range of the step forward in establishing knowledge regarding a disease also has the interests of possible future benefits for current and future patients at heart. The bigger the step forward, the higher the scientific value, and the more likely future patients will benefit from the results of the research. As mentioned earlier, also fundamental knowledge can provide huge benefits for the future, by informing additional research goals aimed at clinical practice. Yet, the interests of future patients are not the only ones that inform current research. That would presume that future generations might experience other issues and diseases than current living people. This is not the case. While research is aimed at reaping benefits in the future,

there is an urgency to solve current issues and diseases as soon as possible. Yet, it is often the case in practice that research takes time, and that for some diseases the benefits of a research study will not benefit the current population, even if they are not part of a research study. There is still no cure for rheumatism, and the medicine available is only marginally improving the current condition of patients. Yet, in cases of chronic illnesses it is possible that current patients will reap the benefits in the future of current conducted research. Whether a current ill patient will be able to be cured in the future is largely dependent on how severe the disease is, and what the chances of survival are. In certain types of cancer this is very evidently not the case, people who participate in research studies for new cytostatics are often patients that have no chance of cure or survival. In these cases, the benefits will not be for them, or the immediate succeeding generation that will come after them. Diseases that are difficult to treat and often result in death on a short time span, research benefits are solely for future patients.

The analysis of criteria in ethical review reveals that interests of future patients are definitely involved in determining the ethical permissibility of a research study. Sometimes statements regarding future patients are explicitly made during the review process, for example “what will the benefit be for future patients”, but, essentially, if the research is scientifically valid, the relevance more than marginal, and a possible clinical innovation is likely, then it is believed that future patients will benefit from research results. Ethical review boards admit that often they assume that if the criteria can all be met, and if the risk-benefit ratio is favorable, research will always result in useful application for future business.

And yet I think this is not evident. Yes, I believe that improving medical care follows a specific sequence and requires fundamental research in order to establish knowledge, but many of the basic knowledge that is established through these studies never gets to the phase of useful clinical application (Crowley, 2003). There is a huge gap between the knowledge established by basic science, and clinical application. This, I think, holds also normative implications for setting research priorities. First and foremost, medicine should be concerned with the fate of people whose needs they tend to. Insofar as treatments are imperfect and bothersome, improving medical treatments and techniques is very important. But no one's interests are served with studies that eventually end up in archives never to be looked at again. Of course, failure is a huge part of science and research, because if the answers could be known in advance, it would not be called research. However, ‘negative’ results in which the

initial mechanisms could not be detected, or that a specific medical drug turns out not to be promising, are often not published. Partly this can be ascribed to the fact that journals – and especially top journals – have a bias in favor of publishing successful research results. The studies that didn't work out in the end fade into oblivion. This favoring of successful research results is of course reasonable on the grounds that it would sell more copies of the journal or article, and positive news is favored over negative ones. No one would buy a journal called 'Failures in Medical Research Quarterly'. But, keeping something like an online archive in which negative research results can be uploaded by researchers could be important in overcoming the lack of communication of the outcomes of research within the (medical) community, so everyone can keep up with the latest movements. In fact, this could improve the care for patients, because it allows for researchers to adjust their research methods and goals.

Another question concerns whether it is fair to put burdens on research participants in non-therapeutic settings when the research often does not accumulate into anything? I think it is too harsh to judge that considering the amount of research conducted and the small proportion of eventual successes there should be a reason to abandon all effort. But I do think that the link between successful research and clinical application should be made stronger. If we really take the interests of patients seriously, of those currently suffering from illnesses and the ones who will become ill in the future, then more effort should be put in translation to clinical practice. Fortunately, efforts of translational research are being made (Drolet and Lorenzi, 2011), be it that they face difficulties.

Thinking about the needs of patients helps to determine research priorities, and thinking about the fate of future patients stimulates action to bridge the gap between what we know (basic science) and what we should do (clinical application). Considerations of justice require that we need to help the disadvantaged members of society, and that these duties are even stronger for medical professionals. Imagining that if no efforts are taken to help specific groups of patients, many people will suffer just as much in the future, can make the mandate stronger to improve the situation of these patients as soon as possible, meaning that we have to make an effort *now*. The lack of knowledge or the lack of a treatment regarding a specific disease that causes suffering implies at least moral duty for medical professionals to do something about this, in order to attend to the medical needs of patients in the future. But this does not mean that research subjects should be exposed to unnecessary research risks,

because their interests prevail over the ones of science and society now, and in the future.

4.6 Conclusion

Within this chapter I have looked at the ethical reviewing process of clinical biomedical research. Ethical review boards are first and foremost instated to protect the research participant from exploitation. Their task is to review research proposals to determine whether it is allowed at all to ask a potential participant to join a study at all. Considering that a lot of research is conducted on people suffering from diseases, this implies that ethical review boards have the interests and the fate of patients at heart. A legitimate question to ask is whether independent ethical review is a foolproof way of securing the protection of research subjects. Given the fact that ethical review is primarily a bureaucratic enterprise and committees are not included in surveying 'the field', it is likely to say that research subjects can still be harmed. To minimize this, researchers are required to inform institutions in case unexpected (severe) harms occur, or expected (severe) harms. The review board retains the right to put the research on hold, and decide whether the research needs to be abrogated. Still, examples show that unexpected and undesired fatalities still occur every now and then. I think that this is no reason to doubt the relevance of independent ethical review, and the tasks of review boards. Yet, it does not exclude researchers from critically thinking about their research and the measures that have to be undertaken to make research ethically permissible. An ethical review board cannot think *for* them.

The empirical research showed that review boards are concerned with the fate of future patients. While it might be stereotypical to think that they are primarily judging from the sideline and are holding research and therefore clinical improvements back by focusing on protection, this is actually not the case. But the way in which future generations are considered are very implicit. This is reflected in the assumption that properly designed research will contribute to the wellbeing of patients in the future, while in practice this is far less apparent. Reviewers are right when they say that badly designed research cannot amount to anything, but there is absolutely no guarantee that properly designed protocols do the opposite. Failure is also part of doing science and research, and this is no different for research on human beings. But the stakes are high. Conventionally understood, the only benefit from performing non-therapeutic interventions is the generalizable knowledge intended to improve the care for future generations (Rid, 2012, 180). Upholding high threshold levels to what can be seen as

acceptable research risks would have the inherent danger to expose participant to exceedingly high risks, while low threshold face the risk of impeding important research from being conducted. Assigning a lot of weight to the latter potentially restricts progress in clinical care, defeating the purpose of clinical research in the first place.

For ethical research boards, the way to deal with this is to strike a balance between protecting the potential participants and allowing the continuation of clinical research. The criteria mentioned in this chapter are the current ethical requirements that provide a framework to which a research protocol is assessed. Favoring one criteria over another is undesirable, but not every research protocol can satisfy each criterion equally. It is therefore that ethical review boards need to balance each criterion against each other. A research study can be very important, but the risks involved might also be very high, making it harder to morally justify the burdens to the participants than research which involves less risks.

It was argued in chapter 2 that a normative notion of regarding the distribution of benefits of research risks would be helpful in determining what can be allowed, and what not. In practice this seems a difficult matter to establish, because determining acceptable research burdens is a matter of context and balancing. What can be acceptable in pediatric research is very different from what could be allowed in the case of competent adults, and research that requires a target disease excludes healthy volunteers from participating, inevitably placing higher burdens on the people who are already sick. Including normative notions might be confusing for ethical review in practice. However, not including a normative standard regarding acceptable risks is not without its own hurdles. It allows for variation in the analysis of research, facing the danger that sometimes research risks might be overestimated, while in other cases they might be undervalued. Not only do these inconsistencies result in either too little or too much protection of research subjects, but the entire relevance of independent ethical review itself.

Chapter 5

Conclusion

In this thesis I have looked at ethical issues regarding the experimentation on human beings in biomedical research. Because a lot of research is carried out that does not benefit the actual participant, the motivation for inquiring into ethical considerations was to investigate how biomedical research can be justified, especially regarding the burdens the participant carries when there is no personal gain to be identified. Therefore, the main question of this thesis was:

In light of non-therapeutic biomedical research: under what conditions is it fair to experiment on human research subjects for the benefit of future generations?

To answer this question I have first looked at the core value and purpose of biomedical research. I have found research is instrumentally valuable in the sense that it aims at improving medical knowledge and medical practice. This means that the knowledge established in the field of medical research has no value in and of itself. Research is being conducted in order to improve health and medical care, by establishing knowledge that can be generalized to hold for large groups of people, with the ultimate aim to benefit them. Biomedical research is important in the social battle of fighting disease, suffering and attaining to basic human needs. A lot of this has to do with the common understanding that a good health is of major importance for human happiness. Diseases can detrimentally affect health, resulting in premature death and suffering. In order to decrease suffering and pain, medicine tries to understand and positively affect pathological processes that threaten human health by attempting to find cures and treatments. Biomedical research is indispensable to this process. First, carefully organized research yields more valid and uniform insights regarding the usefulness of a treatment and the monitoring of a disease. If research would not be organized, than the possibility of providing solutions at random might be very likely to occur on a large scale. Also, innovating medical treatments by reinvestigating them is helpful in improving current medical practices that are far from ideal. By conducting research, physicians are also increasingly

capable in to make adequate choices regarding which treatments to provide, but even more so for the benefit of the patient, both current and future ones.

However, research comes at a cost. Because of its experimental nature, the exact effects cannot be fully predicted, consequently involving risks to the participants. How can these burdens be justified?

The above question is an issue of distributive justice, the distribution of benefits and burdens should be equally carried by a society. In the context of biomedical research, the distribution of benefits and burdens is at heart of every research study and its subsequent priority and justification. Several patterns of distribution are imaginable: (i) the benefits and burdens fall to the same party; (ii) the burden is carried by one party while another party enjoys the benefits; (iii) two parties share a burden, while only one party enjoys the benefits; and (iv) two parties enjoy the benefits, while only one of the parties carries the risks. In the case of non-therapeutic biomedical research, often the second scenario is likely to occur. Placing burdens on one party without providing them benefits is always at risks of exploiting this party for the sake of the gain of others. Theories of distributive justice try to deal with this problem by providing principles and values which can be appealed to in dealing with conflicts of distribution. In biomedical research a consequentialist approach is endorsed, by placing burdens on a small population of research subjects so hopefully a large group can enjoy the benefits. This is also an intergenerational conflict.

The literature on intergenerational justice suggests that current generations enjoy benefits at the costs of future generations. This is very evident in the case of environmental issues, such as the exploitation of natural resources, or the accumulation of waste, and climate change. As far as these issues are under human control, one is obligated to do something about it, to prevent future generations from harm. In the case of biomedical research, the issues are inverse: current generations carry the burdens, so that future generations can enjoy the benefits of research.

The consequentialist approach focuses on the outcomes of the research, that serve social utility in the form of (widespread) available treatments. The good that is produced by outcomes justifies the costs of carrying the burdens of research. Yet, these utilitarian considerations are informed by deontological considerations. This is framed in the language of duties and rights. In most western societies, people agree that there are certain basic human rights, and these include a right to a decent minimum of care, and have a right to be helped in need. These rights often entail a

duty on behalf of another party, that needs to respect and fulfill this right. In the context of medical care, in general, a person in need has a right to be helped in the form of treatment. Especially when the need is caused by something that lies outside of a person's control. But even if one is (partially) personally responsible for having caused an illness or disease, one has a right to be helped.

It is recognized that many diseases and illnesses can be treated nowadays, but there are still many left that await a cure. The people that currently cannot be helped adequately have a right that efforts are made that their interests are looked after. This is one of the reasons why biomedical research is carried out. To unravel the mechanisms involved in a disease, in order to find something to either prevent a disease from happening altogether, or find a possible cure. In my opinion, medical professionals have an obligation to serve the best interests of their patients, and this includes a moral duty to try and improve their practice, especially when that practice is lacking adequate knowledge. Their duties are not limited to the patients that are currently in their waiting room, but also the ones that will be there in the future. This does not only mean that the patients in the future deserve care and attention *then*, but also to try and alleviate their suffering by conducting research in the present. This should be important in informing research goals. Some argue even that doctors are required to improve their practice, if only it were because of their ability to practice in the way they do due to efforts of the past. In that sense, it is also a communitarian value. Sacrifices have been made in the past in order to benefit current living, it is only fair to carry on with their projects. In addition, justice requires that we take into consideration the interests of people that will live in the future and will probably face the same issues as patients today. All these reasons together form the need to keep on improving medical practices, with the ultimate aim to alleviate human suffering.

But there is an inherent conflict of interest in research between the interests of the research participant and the benefits to society at large, including future society. It is easy to exploit individual for the sake of others, which has happened in the past. In order to avoid exploitation, guidelines regarding research are developed. An important aspect of ethical research is independent ethical review, conducted by an institutional ethical review board, consisting out of a myriad of disciplines that represent a heterogeneous view that is publically accountable. In chapter 4 an analysis is made of conducted interviews with members of ethical review boards in the Netherlands, regarding the criteria that are being assessed in order to determine whether an experiment can be morally be allowed or not. From the analysis it appears

that while the main task of review boards is to protect potential research subjects from harm and exploitation, they also take the interests of the larger patient population to heart. But these considerations are very implicit, because it is presumed that properly designed research will result into benefits for the future. In practice this is actually not evident, because many non-therapeutic research that is fundamental in nature never makes it into clinical practice, or publication.

In order to take the needs of patients more seriously, this intergenerational perspective presented in chapter 3 could be helpful to determine which moral acts are required and by whom, and this in turn holds implications of what can be perceived as fair burdens of research. But an approach of intergenerational justice has its limits. It is difficult to say that considerations of justice are the only relevant considerations in discussion the practice of human experimentation, clinical research and medicine. Especially acting on the behalf of future generations can be a difficult topic, especially conceptual issues like assigning rights to them. As a minimum, future patients should not be worse off compared to present patients. Therefore, the least we can do is preserve medical knowledge in order for them to have equal chances. This, in fact, is a moral duty of present generations. But justifying to take burden for their sake are less evident, and originate primarily out of doing good (acting beneficent) than justice. I would like to conclude by saying that the duties to future generations are *prima facie*, and that the interests of current patients prevail if a conflict emerges. Furthermore, the duties of present generations become less stringent as future generations will be increasingly distant from us in time.

5.1 Reflection and recommendations

As all research probably concludes, there are still some loose ends. In this thesis I have primarily focused on what is required to do in terms of medical advancements from the perspective of distributive justice and intergenerational considerations. The decision for approaching ethical review boards was motivated by an assumption that they were an important party in the ethical decision making process, because they are charged with the task to evaluate whether a research protocol can be allowed or not. During the process of the investigation, it became more and more clear to me that there were in fact other equally relevant actors to talk to in order to give a more comprehensive answer to the question of needs to be done. These actors are clinical investigators, physicians and funding agencies. When I asked during my interviews whether priorities in research were included in the decision making process, the reply I got from almost all respondents was that they did not consider this to be relevant,

because they operated the other way around. Research protocols are submitted to them, and they evaluated whether these proposals were sound enough in a scientific way in order to pursue. But making decisions regarding which research is relevant and important to undertake in the first place is something to decide by funding agencies, research departments or institutions, and individual investigators. However, it was also expressed that the efforts made in ethical review – which are time consuming to say the least – sometimes fall short of doing what is actually important, and that is reviewing clinically important research. There is a huge machinery that spends a lot of time evaluating protocols that can primarily establish marginal improvements. Further research to inquire into the gap between the research that is designed and carried out and what is actually desired in the face of societal interests would be a tremendous enrichment to the discourse of human experimentation.

Another interesting question to pursue in future research is how time-related aspects can be helpful in determining research priorities. In this thesis time-horizons were an important obstacle in ethical review, because it brought a factor of uncertainty into the game. Non-therapeutic clinical research has its legitimacy in the fact that the research aims at *eventually* providing benefits to a group of patients who are currently suffering. But the group of patients that will actually benefit from these efforts is not the population that serves as research subjects. There is a gap between the present and future. The longer something will take to become clinical practice, and if the demand is high, the need to invest increases. It would be interesting to investigate how different actors deals with this tension, including a macro level perspective from politics.

Bibliography

- Arneson, Richard, 1990, "Liberalism, Distributive Subjectivism, and Equal Opportunity for Welfare," *Philosophy and Public Affairs*, 19: 158–194
- Ballantyne, A (2008) "'Fair Benefits' accounts of exploitation require a normative principle of fairness: response to Gbadegesin and Wendler, and Emanuel et al" *Bioethics*, Volume 22, No. 4, pp 239-244
- Barry, B. (1989) *Theories of Justice* (Vol. I) University of California Press
- Barry, B (1989) *Theories of Justice. A Treatise on Social Justice, Vol 1*. Harvester-Wheatsheaf, London, UK
- Beecher, H (1959) "Experimentation in Man", *Journal AMA*, 169, pp 461-478
- Beecher, H (1966) "Ethics and clinical research" *New England Journal of Medicine*, 274 (24), pp 1354-1360
- Beauchamp, T and Childress, J (2001) *Principles of Biomedical Ethics*. Oxford University Press, USA
- Beauchamp, T (2013) "The Principle of Beneficence in Applied Ethics", *The Stanford Encyclopedia of Philosophy* (Winter 2013 Edition), Edward N. Zalta (ed.), URL = <<http://plato.stanford.edu/archives/win2013/entries/principle-beneficence/>>.
- Beaufort, I de (1985) *Ethiek en medische experimenten met mensen*. Van Gorcum & Comp. B.V., Assen, Netherlands
- Bos, W; Tromp, K; Tibboel, D and Pinxten, W (2013) "Educational Paper: Ethical aspects of clinical research with minors", *European Journal of Pediatrics*, 172, pp 859-866
- Brandt, R (1964) "The Concepts of Obligation and Duty" *Mind* 73: 374-393.
- Buchanan, D and Miller, F (2007) "Justice in Research on Human Subjects" in Rhodes, Frances and Silvers (eds.) *The Blackwell Guide to Medical Ethics*, Blackwell Publishing Ltd

- Centrale Commissie Mensgebonden Onderzoek (2013) "Therapeutisch versus niet-therapeutisch onderzoek: bij minderjarige en wilsonbekwame personen" as retrieved on January 17, 2014 from <http://www.ccmo.nl/attachments/files/ccmo-notitie-therapeutisch-vs-niet-therapeutisch-versie-okt2013.pdf>
- Crowley, W (2003) "Translation of Basic Research into Useful Treatments: How Often Does It Occur?" *American Journal of Medicine*, Vol 114, pp 503-505
- Drolet, B and Lorenzi, N (2011) "Translational research: understanding the continuum from bench to bedside" *Translational Research*, 157, pp 1-5
- Estlund, D (2012) *The Oxford handbook of political philosophy*. Oxford University Press, USA
- Emanuel, Wendler and Grady (2008) "An Ethical Framework for Biomedical Research" in Emanuel, E; Grady, C; Crouch, R; Lie, R; Miller, F and Wendler, D (eds.) *The Oxford Textbook of Clinical Research Ethics*, New York: Oxford University Press, Inc.
- Feinberg, J (1966) "Duties, Rights and Claims" *American Philosophical Quarterly*, Vol. 3, No. 2, pp 137-144
- Feinberg, J (1973) "Duty and Obligation in the Non-ideal World." *The Journal of Philosophy* 70: pp 263-75.
- Foster, C (2001) *The ethics of medical research on humans*. Cambridge University Press, UK
- Gosseries, A and Meyer, L (2009) "Introduction" in Gosseries, A and Meyer, L (eds.), *Intergenerational Justice*. New York: Oxford University Press
- Kymlicka (2001) *Contemporary Political Philosophy: An Introduction*. Oxford University Press, USA
- Lamont, J and Favor, C (2013) "Distributive Justice", *The Stanford Encyclopedia of Philosophy* (Spring 2013 Edition), Edward N. Zalta (ed.), URL = <<http://plato.stanford.edu/archives/spr2013/entries/justice-distributive/>>.
- Meyer, L (2010) "Intergenerational Justice", *The Stanford Encyclopedia of Philosophy* (Spring 2010 Edition), Edward N. Zalta (ed.), URL: <http://plato.stanford.edu/archives/spr2010/entries/justice-intergenerational/>

- Nozick, Robert, 1974, *Anarchy, State and Utopia*, New York: Basic Books
- Partridge, E (1976) *Rawls and the duty to posterity*. Doctoral dissertation, University of Utah, USA
- Rawls, J (1958) "Justice as Fairness" *The Philosophical Review*, Vol. 67, No. 2, pp 164-194
- Rawls, J (1971) *A Theory of Justice*. Clarendon Press, Oxford, UK
- Rid, A (2012) "Risk and Risk-benefit Evaluations in Biomedical Research" in S. Roeser, R. Hillebrand, P. Sandin and m. Peterson (eds.) *Handbook of Risk Theory*, Springer Science+Business Media B.V.
- Rothman, D (1987) "Ethics and Human Experimentation" *New England Journal of Medicine*, 317: 1195-1199
- Ryan, A (1993) *Justice*. Oxford University Press, USA
- Schaefer et al (2009) "The obligation to participate in biomedical research" *Journal of the American Medical Association* 302: pp 67-72
- Smith Iltis, A (2006) *Research Ethics*. New York: Routledge
- Smith Iltis, A (2011) "Justice, Fairness, and Membership in a Class: Conceptual Confusions and Moral Puzzles in the Regulation of Human Subjects Research" *Journal of Law, Medicine and Ethics*, pp 488-501
- Swift, A (2006) *Political Philosophy: A Beginners' Guide for Students and Politicians*. Polity Press, Cambridge, UK
- The World Medical Association (1996) "The Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects" as retrieved on January 21, 2014 from:
<http://www.wma.net/en/30publications/10policies/b3/>
- Wet medisch-wetenschappelijk onderzoek met mensen (1998), as retrieved on January 18, 2014 from:
http://wetten.overheid.nl/BWBR0009408/geldigheidsdatum_18-01-2014

Appendix

I Interview questions

Appendix I - Interview questions

- What is your role within the committee?
- What is the review procedure?
- Which criteria are necessary in evaluating a research proposal?
- What is, in your opinion, the most essential motivation to conduct research on human beings?
- The law WMO specifies that: "It should be reasonably likely that the research will lead to the adoption of new insights in the field of medical science". In your opinion, how important is scientific progress/medical progress in the context of research involving human beings? (Probes: why? Improved medical care for the future?)
- Are there differences in review criteria between a research design that requests healthy volunteers and "ill" patients? (If yes, what are these differences, if not, why not?)
- Are there differences in the review procedure in terms of research topics (in the sense of priority)? (Probes: for example cancer research, heart disease, prosthetics, new medical devices) If yes, what are these differences and what are they based on (risks?)
- What could be a reason to reject a research proposal? Can you give an example? (Probes: research design/high risk/low priority of the topic?)
- Has there ever been a rejection of a research protocol because it promised too little in terms of scientific/medical advancement?
- Do time aspects affect the decision making? (Probes: promises of the researcher and the estimated period of expecting useful results)
- [The law WMO states that it should be: "...reasonably likely that the interest served by the research of the research subject and present and future patients should be in proportion to the objections and the risk to the research subject".]Which considerations regarding future generations play a role in the (ethical) review procedure? Can you give an example? (Probes: considerations, interests)
- Do you think there is anything like a duty to future patients in terms of health care? If so, what is this duty? If not, why not? (Probes: research fulfills a role in "health duties"/ moral obligation of science and scientists?)
- What do you think about the rights of future patients? Do they have a right to better health care? Why/why not?
- What is the trade-off between the interests of society (future generations, scientific knowledge, medical advancement) and protection of the research subject? What are these interests?
- Should more attention be paid to the interests of future generations in medical ethical review? Why/ why not? If so, how?